

Acoustic Changes in Spasmodic Dysphonia After Botulinum Toxin Injection

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Summary: Botulinum toxin A injections in the left thyroarytenoid muscle were performed in 19 patients with adductor spasmodic dysphonia. Acoustic recordings were taken prior to and 1 week after injection and in a 2-week interval for a normal control group of 11 subjects. Fundamental frequency, standard deviation of fundamental frequency, jitter, shimmer, signal-to-noise ratio, and the voice break factor were studied. Each of the variables were measured from each subject's longest sustained phonation sample of the vowel quality /a/. Findings of the present study indicated: (a) Spasmodic dysphonia patients had significantly higher mean values of standard deviation of fundamental frequency, jitter, shimmer, and voice break factor and significantly lower mean values of signal-to-noise ratio when compared with normal controls; (b) a significant reduction post botulinum toxin injection was found for standard deviation of fundamental frequency and the voice break factor only. **Key Words:** Spasmodic dysphonia—Botulinum toxin—Acoustics.

Spasmodic dysphonia (SD) may be defined as an idiopathic focal dystonic disorder of the larynx. Two major types of spasmodic dysphonia have been described in the literature—the adductor type first observed by Traube in 1871 (1) and the rare abductor type described by Aronson (2) in 1973. The adductor type is characterized by a strained, effortful phonation punctuated by voicing arrest due to hyperadduction of the vocal folds at onset and during phonation. The abductor type, on the other hand, is characterized by a breathy, weak phonation, particularly at voicing onset, generally due to abrupt widening of the glottis. This study focuses on adductor SD. SD may be considered unique among voice disorders in that the etiology and the physical descriptions of the vocal

folds of SD patients are highly varied and may in fact masquerade as signs and symptoms of other disorders.

Treatment of this class of voice disorders has also ranged extensively, from psychotherapy to hypnosis, all with some reported success and undoubtedly with a great deal of failure. At this time, none of the therapeutic approaches, medical or surgical, can be considered curative. In fact, recurrent laryngeal nerve (RLN) resection can produce adverse effects. Aronson and De Santo (3) reported that after 3 years, 48% of 33 patients were considered worse than before RLN surgery.

Recently, three independent investigations (4, 5, 6) described a procedure in which botulinum toxin (Botox) is injected into the thyroarytenoid muscle to reduce the symptoms of SD. Botox acts presynaptically and prevents calcium-dependent release of acetylcholine, thus producing a chemical-type of denervation. Intramuscular injection of Botox

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has been used for several years to treat blepharospasm (7,8,9). Reports of SD patients treated with Botox indicated dramatic voice improvement lasting 3-9 months.

As yet the acoustic features following Botox injection have not been comprehensively described. Despite the general agreement that there is voice improvement after Botox injection, questions regarding post-injection vocal function remain. Specifically, the amount and direction of changes in the fundamental frequency of phonation, the degree of phonatory variability, and the number of phonatory breaks in subjects who undergo Botox injection are not yet known. The primary purpose of this study was to examine the acoustic characteristics associated with phonatory changes after Botox injection. Two key questions were addressed: What acoustic features of voice production distinguish SD patients from normal controls? What changes occur in the acoustic parameters of SD after injection of Botox?

METHODS

Subjects

Nineteen subjects (15 women, four men) with a diagnosis of SD were studied before and after Botox injection. The ages of the female SD subjects ranged from 34 to 78 years (mean 56.4) and of the male SD subjects from 37 to 40 years (mean 38). Diagnosis of adductor SD was made independently by an otolaryngologist and a speech pathologist after clinical examination. All subjects considered their symptoms of SD and their speech characteristics to be stable. All had SD for at least 1 year. The time of SD onset ranged from 1 to 12 years, with a mean of 5.95 years. None of the subjects had had either previous Botox injections or RLN surgery. All subjects indicated that they had had speech therapy at some time in the past. All subjects volunteered for the procedure and afterward indicated that their speech and voice improved by the time of their postinjection recording.

Two voice recordings from 11 normal controls (NCs) were made in a 2-week interval to evaluate the short-term normal variability. This group included seven women and four men with an age range of 39-63 (mean 51.7) for the women and 32-48 (mean 42.5) for the men. All NCs were healthy, nonsmoking subjects without any past or present history of laryngeal pathology or voice disorder. The NCs comprised staff members and other volunteers. Age and gender distribution for each sub-

ject of the NC and SD groups as well as the duration of disease for the SD subjects are listed in Table 1.

Procedures

Botox injection

Botulinum toxin type A (Oculinum) doses ranged from 15 to 30 units depending on severity of symptoms in each patient. Botox was injected percutaneously into the left thyroarytenoid muscle. A monopolar Teflon-coated hollow electromyography (EMG) recording needle was used for the injection. Needle location in the thyroarytenoid muscle was verified by the presence of a voluntary interference pattern with no activation with inspiration or neck flexion.

Recordings

Voice recordings were taken 1 week before and 1 week after injection. Voice samples were recorded on a high-quality recorder (Nakamichi CR5A). Recording levels were consistent throughout data collection. Patients were seated comfortably on a chair in a sound-treated room. The microphone (Sony ICM50) was mounted on an adjustable headpiece, which kept it at a constant distance to the lips. Subjects were asked to take a deep breath and to sustain the vowel /a/ steadily at a comfortable intensity and pitch level for as long as possible. The second /a/ sample from a repeated vowel sequence was used for subsequent analyses. Digital processing of the acoustic signals was accomplished by using an

TABLE 1. Description of participating subjects, including gender distribution, age, and number of years since onset of spasmodic dysphonia

Spasmodic dysphonia			Normal controls	
Sex	Age	Yrs of SD	Sex	Age
M	38	5	M	46
M	40	2	M	48
M	37	12	M	32
M	37	3	M	44
F	78	3	F	50
F	44	12	F	44
F	52	10	F	62
F	54	9	F	45
F	50	2	F	63
F	54	12	F	59
F	69	8	F	39
F	53	1		—
F	74	2		—
F	60	2		—
F	71	2		—
F	34	9		—
F	42	8		—
F	38	1		—
F	75	10		—

IBM AT computer. Signals were low-pass filtered at 2,000 Hz and digitized with a sampling rate of 8,000 per second. Signal measurements were obtained using the software program C-speech version 2.1 (10). From the sample, the initial second and 1 s from the midpoint of the sustained vowel were analyzed. This provided a sample related to the onset characteristics of SD and a more stable sample associated with the relatively steady-state portion of sustained phonation. Thus a total of 2 s were analyzed.

Acoustic measurements

Five different acoustic parameters of each subject's digitized samples were analyzed: fundamental frequency (F_0), standard deviation of fundamental frequency (SDF_0), jitter, shimmer, and signal-to-noise ratio (SNR). SDF_0 is the square root of the variance around the mean fundamental frequency. We chose SDF_0 as an acoustic parameter in addition to F_0 , because SDF_0 represents the variability of F_0 for each single subject and reflects, in contrast to F_0 , phonatory instability. SDF_0 has also been referred to as voice "flutter" (11). Jitter is the cycle-to-cycle variation in frequency. Shimmer is the cycle-to-cycle variation in amplitude. SNR is the ratio of energy in the signal versus the noise components also contained in the acoustic spectrum.

Two additional measurements were obtained: the maximum phonation time (MPT)—defined as the time from the onset of voice to the end of the sustained vowel—and the number of phonatory breaks in the entire sustained vowel. We defined one voice break as a signal stop with a length longer than two cycles divided by the fundamental frequency. The number of voice breaks divided by the MPT was defined as the voice break factor (VBF).

Statistics

Since data indicated unequal variance across subject groups, we applied nonparametric statistics. The Wilcoxon Signed-Rank test for paired samples was used to compare the before and after injection data, and the Mann-Whitney test for independent variables was used to compare the pre between (pre Botox SD group vs. first measurement NC group) and post between (post Botox SD group vs. second measurement NC group) groups.

RESULTS

Fundamental frequency

The mean values (in Hz) (\pm SD) were similar for the two subject groups: 168 (\pm 43) pre Botox and

172 (\pm 55) post Botox injection for the SD patients and 164 (\pm 43) and 161 (\pm 45) for the two trials of the NC subjects. There were no significant differences between the before and after data of F_0 , nor for the pre between groups and post between groups ($p > 0.5$). Figure 1 shows the confidence intervals and the mean values of F_0 for the SD subjects pre and post Botox injection and the two measurements of the NC subjects.

SDF_0

Highest values (in Hz) (\pm SD) were found in the SD subject group, with a mean of 12.1 (\pm 5.9) pre Botox and 5.7 (\pm 4.1) post Botox injection. The NC group showed a mean of 2.0 (\pm 1.2) and 2.1 (\pm 1.2), respectively. Statistical analysis demonstrated that SD patients had significantly lower SDF_0 post Botox injection compared with pre injection ($p < 0.001$). There was no difference between the two trials of the NC group ($p > 0.5$). Comparison of the pre between groups and post between groups revealed that the NC subjects had lower mean SDF_0 values compared with the pre mean value of the SD subjects ($p < 0.0001$) and also when compared with the post mean value of the SD subjects ($p < 0.001$). Figure 2 shows the confidence intervals and the mean values of SDF_0 for the SD group pre and post Botox injection and the two measurements of the NC group.

Jitter

Highest values (in ms) were in the SD group, with a mean (\pm SD) of 0.28 (\pm 0.21) pre Botox and 0.22 (\pm 0.38) post Botox injection. The NC group means

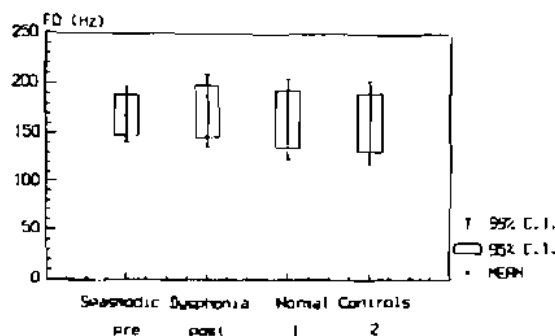


FIG. 1. Fundamental frequency pre-post Botox. Confidence intervals (CI) of 99% and 95% and mean values of the fundamental frequency (F_0) (in Hz) for the spasmodic dysphonia group pre and post Botox injection and the two trials within a 2-week interval of the normal control group.

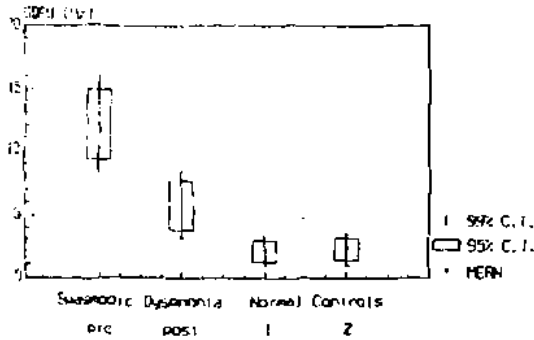


FIG. 2. Standard deviation of fundamental frequency, pre-post Botox. Confidence intervals (CI) of 99% and 95% and mean values of the mean standard deviation of fundamental frequency (SDF) (in Hz) for the spasmodic dysphonia group pre and post Botox injection and the two trials of the normal control group.

were $0.028 (\pm 0.01)$ for the first trial and $0.035 (\pm 0.02)$ for the second trial 2 weeks later. Statistical evaluation revealed that although the mean value after Botox injection was lower, the difference for the SD subjects pre and post Botox injection was not significant ($p > 0.05$). An increase in the variability of the jitter measures for the SD group after injection could be noticed, but this was mainly due to an outlier. However, removal of this outlier did not change statistical results. There was no significant difference between the two trials of the NC group ($p > 0.05$). When the jitter values of the SD group were compared with the NC group, they were significantly higher. For SD subjects pre Botox injection versus NCs (first trial) statistical results were $p < 0.0001$, and for SD subjects post Botox injection versus NCs (second trial), $p < 0.01$. Figure 3 displays the confidence intervals and the mean

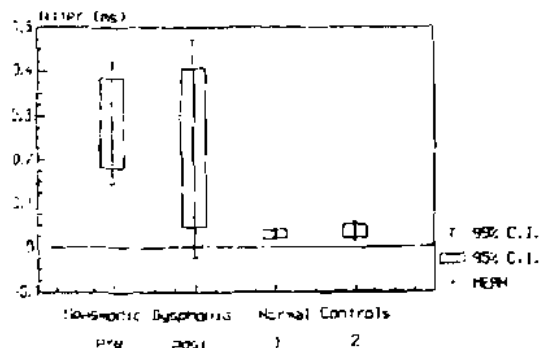


FIG. 3. Jitter pre-post Botox. Confidence intervals (CI) of 99% and 95% and mean values of jitter (in ms) for the spasmodic dysphonia group pre and post Botox injection and the two trials of the normal control group.

values of jitter for the two measurements of both groups.

Shimmer

Again, highest values for shimmer (in %) were observed in the SD group for their pre-Botox measurements with a mean (\pm SD) of $16.6 (\pm 13.1)$, followed by the lower post-injection mean value of $12.2 (\pm 12.9)$. There was no overlap with the NC subjects, who exhibited definitely lower values of $2.4 (\pm 0.9)$ and $2.5 (\pm 0.8)$ for the two measurements, respectively. Statistical analysis demonstrated that there was no significant difference for the SD group pre and post Botox measurement ($p > 0.1$) and no difference for the NC group between the two trials ($p \geq 0.5$). Comparison of the pre- and post-Botox values with the first and second trial values of the NC group, respectively, were both significantly different ($p < 0.0001$), with the NC group having the lower values. Figure 4 shows the confidence intervals and the mean values of shimmer for SD and NC subjects.

SNR

Mean SNR values (in dB) (\pm SD) ranged for the SD subjects from $12.6 (\pm 4.9)$ pre Botox to $13.6 (\pm 4.9)$ post Botox injection. There was no overlap with the NC subjects, who displayed the higher values of $21.2 (\pm 2.9)$ and $20.9 (\pm 2.05)$ for the two trials, respectively. Regarding the SD group, no significant change in SNR pre and post Botox injection could be evaluated ($p \geq 0.4$). In the NC group the difference between the two trials was again negligible ($p > 0.5$). Comparison of the pre between groups and post between groups showed that the

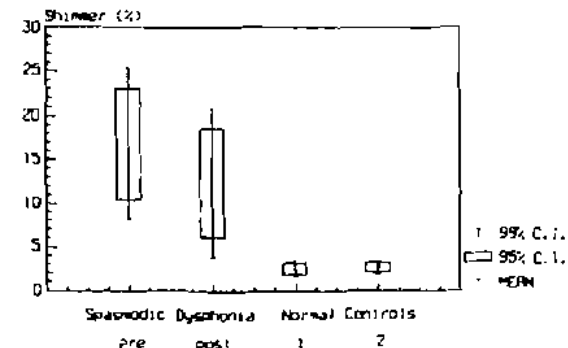


FIG. 4. Shimmer pre-post Botox. Confidence levels (CI) of 99% and 95% and mean values of shimmer (in %) for the spasmodic dysphonia group pre and post Botox injection and the two trials of the normal control group.

NC group exhibited the significantly higher mean values of SNR in both comparisons ($p < 0.001$). These data are shown in Fig. 5.

Descriptive statistics of F_0 , SDF_0 , jitter, shimmer, and SNR for the SD and NC groups are summarized in Table 2.

Maximum phonation time

Mean values (in s) (\pm SD) ranged, for the SD group, from 14.9 (\pm 7.8) for pre Botox and 11.6 (\pm 6.8) for post Botox injection to 17.7 (\pm 7.1), and 16.7 (\pm 8.3) for the first and second measurement of the NC group, respectively. While the post-Botox MPT values were shorter than pre Botox injection, the difference was not statistically significant ($p > 0.1$). The difference between the two trials of the NC group was not significant ($p > 0.1$). Statistical comparison of the pre between groups and post between groups also revealed no significant differences ($p > 0.1$; $p > 0.05$). Viewing the individual data showed that eight SD patients showed increased and 11 patients decreased MPT values after Botox injection.

Voice break factor

As anticipated, the NC subjects exhibited no voice breaks, thus resulting in a VBF equal to zero for all NC subjects. The mean value of VBF (\pm SD) for the SD subjects was 1.16 (\pm 0.24) pre injection and was reduced to 0.17 (\pm 0.09) post injection. This difference was statistically significant ($p < 0.01$). Confidence intervals of the VBF for the SD group pre and post Botox are shown in Fig. 6.

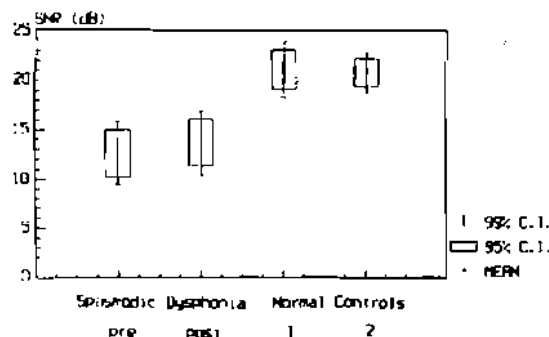


FIG. 5. Signal-to-noise-ratio, pre-post Botox. Confidence intervals (CI) of 99% and 95% and mean values of signal-to-noise ratio (SNR) (in dB) for the spasmodic dysphonia group pre and post Botox injection and the two trials of the normal control group.

CONCLUSIONS

Of the seven parameters studied, SD subjects were found to be significantly different compared with the NC subjects in five measures: (a) SD subjects had significantly higher mean values of SDF_0 , (b) SD subjects had significantly higher mean values of jitter, (c) SD subjects had significantly higher mean values of shimmer, (d) SD subjects had significantly lower mean values of SNR, and (e) SD subjects had significantly higher VBF. SD subjects had slightly shorter MPT mean values, without being significantly different from those of the NC subjects. There was no difference in F_0 between the SD and the NC group.

The NC group showed a negligible variability between their two trials within a 2-week interval for all acoustic parameters. The SD group exhibited significant differences pre Botox and post Botox injection in two of the seven acoustic parameters: (a) SDF_0 mean values were significantly reduced after Botox injection, and (b) a significant reduction of the VBF could be found.

DISCUSSION

This study of acoustic changes in 19 SD patients after Botox injection demonstrated that of the seven acoustic features of voice production studied, five significantly distinguished SD patients from normal controls: SDF_0 , jitter, shimmer, SNR, and VBF. There was no difference between the two groups for F_0 and the MPT.

The results suggest that patients with SD may exhibit some characteristics of voice similar to those of patients with neurological diseases (12). Ramig and associates (13) indicated that acoustic analysis (F_0 , jitter, shimmer, SNR) of voices of neurologically impaired patients may contribute to differential diagnosis and document disease progression. In contrast, Ludlow and co-workers (14) demonstrated that only the vocal pathology and not the neurologic subgroups differed significantly in frequency perturbation from normal controls. From the present results it may be hypothesized that SD patients represent a subset of neurological voice disorders. It remains to be determined if the acoustic features evaluated in our study for SD patients, which could distinguish the SD group from the NC

TABLE 2. Group means, standard deviations, and ranges for five acoustic parameters in spasmodic dysphonia patients and normal controls

	Spasmodic dysphonia		Normal controls	
	pre Botox	post Botox	1	2
F ₀ (Hz)	168 (43) 84-249	172 (55) 73-287	164 (43) 78-210	161 (45) 76-208
SDF ₀ (Hz)	12.1 (5.9) ^a 2.35-22.2	5.7 (4.1) ^{b,c} 1.55-18.6	2.0 (1.2) 0.35-4.8	2.1 (1.2) 0.5-4.4
Jitter (ms)	0.28 (0.21) ^a 0.03-0.68	0.22 (0.38) ^d 0.03-1.4	0.028 (0.01) 0.01-0.05	0.035 (0.02) 0.01-0.08
Shimmer (%)	16.6 (13.1) ^a 2.7-54.05	12.2 (12.9) ^e 2.4-43.0	2.4 (0.9) 1.35-3.97	2.5 (0.8) 1.2-4.05
SNR (dB)	12.6 (4.9) ^a 5.41-21.65	13.6 (4.9) ^a 4.01-21.6	21.2 (2.9) 17.45-26.2	20.9 (2.0) 16.3-23.8

^a Significantly higher than NC @ $p < 0.0001$.

^b Significantly higher than NC @ $p < 0.001$.

^c Significantly lower than pre Botox @ $p < 0.001$.

^d Significantly higher than NC @ $p < 0.01$.

^e Significantly lower than NC @ $p < 0.001$.

group, can separate the SD group from patients with other neurologic voice disorders.

Viewing the changes in the acoustic parameters of the SD group after injection of Botox compared with the pre-injection values, a significant reduction of two parameters, SDF₀ and VBF, was found. Since all SD patients indicated that their speech and voice had improved at the time of their post-injection recording, the improvement may be related to the acoustic parameters of the VBF and the SDF₀. SD patients still retain characteristics of dysphonia, and Botox cannot be considered to return the voice to normal. In effect, the "successful" Botox injection results in one paralytic vocal fold. Although this paralysis is in some cases minimal, it

must be deemed a pathologic rather than a "normal" voice condition. Voices of unilateral vocal fold paralysis sound more or less hoarse. Acoustic correlates of hoarse voice quality include jitter and shimmer values above normal (15,16) and lower values of SNR (17). Taking these facts into account, the results of the present study concerning jitter, shimmer, and SNR, which did not change significantly after Botox injection, are not surprising.

In contrast to SDF₀, F₀ was neither significantly affected by the Botox injection nor different from normal controls. This result of voice F₀ is somewhat similar to results of Davis and colleagues (18), who reported that the modal speaking fundamental frequency of adductor SD was not different from age- and sex-matched controls.

At the present time, Botox treatment for SD has been documented in the literature only by a few studies, mainly in the form of case reports. Blitzer and associates (4) gave a clinical description of impressive voice improvement after Botox injection for five patients (three women, two men). Miller and colleagues (5) presented a case report of two male patients with adductor SD; they found reduced intrathoracic pressures postinjection. Ludlow and co-workers (6) is to our knowledge the only study of a relatively large population (16 patients) with adductor SD. They focused on speech features after Botox injection and found a significant reduction in pitch, voice breaks, phonatory aperiodicity, and sentence time after Botox injection. These positive changes occurred only when the injection resulted in unilateral vocal fold paralysis.

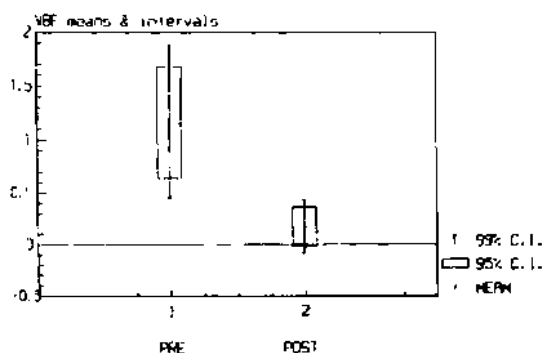


FIG. 6. Voice break factor, pre-post Botox. Confidence intervals (CI) of 99% and 95% and mean values of the voice break factor (VBF) for the spasmodic dysphonia group pre and post Botox injection.

Viewing the MPT measurements only, slightly more SD patients (57.9%) showed decreased MPT values. This may be explained by the paralytic state of the vocal folds after injection, which could cause a higher airflow rate during phonation. Thus, patients run out of air for phonation earlier. In contrast, the preinjection state shows adductor spasms of the true and false vocal folds obstructing the exhaled airstream, thus prolonging MPT. For those who had increased MPT values (42.1%), the increase may have been due primarily to the improved control of the intrinsic laryngeal musculature afforded by Botox. The recent EMG study of Ludlow and associates (19) demonstrated that muscle potentials after Botox were reduced not only in the paralyzed but also in the nonparalyzed thyroarytenoid as well as both cricothyroid muscles. They suggested that symptom relief following Botox injection may be the result of reduced muscle action feedback to the motoneuron pools. Still, there is a need for further research examining the paralytic versus the spastic condition by aerodynamic means (airflow rate, subglottic pressure) combined with simultaneous EMG recordings of the laryngeal muscles.

Voice and pitch breaks have been described as one characteristic of adductor SD (2,20,21). Ludlow and colleagues (6) reported a significant reduction of voice and pitch breaks in the speech of SD patients after Botox injection. They identified voice breaks as "gaps in the fundamental frequency which did not occur at word or syllable boundaries." Our study of sustained phonation in SD allows for a more specific definition of voice break. The VBF was one of the two parameters that was significantly reduced after Botox injection.

VBF may provide a useful acoustic index of improvement after Botox injection as well as an index of SD severity. SDF_0 , which also seems to be a sensitive parameter for measuring phonatory stability may further add to an acoustic categorization of the severity of SD. SDF_0 and VBF reflect the vocal fold status of SD change after Botox injection. Quantification of SD based on these factors may prove useful in the future in identifying changes as a result of therapeutic intervention.

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