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Relationship of Vocal Fold Atrophy to Swallowing Safety and Cough Function in Parkinson's Disease

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Objectives: When swallowing function is compromised in patients with Parkinson's disease (PD), cough plays a crucial role in clearing the airway and preventing pulmonary complications. The aim of this study was to determine the influence of vocal fold atrophy severity as measured by the bowing index (BI) on airway protection in PD.

Methods: Thirty participants with PD completed measures of voluntary and reflex cough. Flexible laryngoscopy with endoscopic evaluation of swallowing allowed for measurement of BI using ImageJ software. Swallowing safety was scored on the Penetration-Aspiration Scale (PAS). Regression and receiver operating characteristic (ROC) analyses were performed to test our study aim.

Results: Twenty-four of 30 participants had some degree of vocal fold atrophy (BI >0). When controlling for age, disease duration did not significantly influence BI. BI was not predictive of any sensorimotor parameters of cough including measures of cough airflow, reflex cough threshold, or urge to cough. BI discriminated participants with near-normal (PAS 1–3) swallowing safety from participants with impaired (PAS 4–8) swallowing safety (P = .01, sensitivity: 87.0%, specificity: 71.4%, cutoff value BI >4.6).

Conclusion: Vocal fold atrophy is a potential factor contributing to poor swallowing safety in PD. BI was not associated with cough function in this PD cohort, contrary to prior studies that have shown improved cough measures after vocal fold augmentation. Vocal fold atrophy in PD remains an important area of study as a targetable intervention for patients with airway protective dysfunction. Future studies should include measures of glottic closure during vocal fold adduction.

Key Words: Vocal fold atrophy, vocal fold bowing, bowing index, Parkinson's disease, dysphagia, dystussia, airway protective mechanisms.

Level of Evidence: 3

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INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the cardinal symptoms of bradykinesia, rigidity, resting tremor, and postural instability,[1] though deficits in respiratory muscle coordination and laryngeal muscle function are also described.[2,3] Aspiration pneumonia is often cited as the leading cause of mortality in PD, thus clinicians and researchers in the field have focused their efforts on active prevention of this complication.[4] Years of research have led to a broader understanding of airway protection as a continuum of behaviors starting with safe swallowing to avoid aspiration and extending to effective cough to eject aspirated material.[5] In PD, studies have demonstrated that a relationship exists between swallowing safety and sensorimotor cough parameters such as cough airflow measurements and cough threshold sensitivity.[6–9] Interventions to enhance airway protection and prevent aspiration pneumonia have been developed to target multiple behaviors along the continuum of airway protection. Novel interventions include rehabilitation of cough strength through expiratory muscle strength training (EMST),[10–13] upregulation of cough effectiveness via biofeedback strategies,[14] and even optimization of deep brain stimulation (DBS) to specifically improve laryngeal function.[15]

Patients with PD are typically referred to otolaryngologists and speech-language pathologists for evaluation and management of voice and swallowing deficits secondary to their disease. Laryngeal abnormalities such as vocal fold atrophy or tremor are commonly diagnosed in people with PD and have been suggested to contribute to poor vocal quality and voice difficulties.[16–19] However, the relationship between laryngeal abnormalities and dysfunction of swallowing and cough in PD is less clear. Physiologically, the vocal folds play a crucial role in swallowing safety by adducting to prevent aspiration and in cough function by adducting to allow the buildup of subglottic pressure during the compressive phase of cough generation. Glottic insufficiency from etiologies such as vocal fold paralysis and

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atrophy disrupts the mechanism of airway closure and can thus contribute to dysphagia and dystussia.[20,21]

Although we know that airway invasion and cough ineffectiveness in PD is multi-factorial,[5,22] the question remains as to whether the severity of vocal fold bowing in PD specifically has a significant effect on airway protective abilities. This information would allow for the identification of risk factors and potential treatment targets for deficits of swallowing and/or cough in PD. Therefore, the aim of this study was to determine whether abnormal laryngeal structure and function, as identified on laryngoscopy, were predictive of deficits in swallowing safety or cough function. It was hypothesized that structural anomalies of the larynx, such as vocal fold atrophy represented by bowing index (BI), would correlate with measures of airway invasion and voluntary and/or reflex cough deficits in people with PD.

MATERIALS AND METHODS

This study was a retrospective analysis of 30 consecutive adults with idiopathic PD who had previously undergone laryngoscopy, flexible endoscopic evaluation of swallowing (FEES), and spirometric cough testing as part of a prospective study analyzing swallowing and cough function. The study was approved by the institutional ethics board (Columbia University Teachers College, 15-430) and all participants provided informed consent prior to participating.

Data Extraction and Analysis

Laryngoscopy. Laryngoscopic examinations had been completed by a speech-language pathologist (SLP) with expertise in the performance of laryngoscopy and FEES. A 3.0 mm diameter flexible distal chip laryngoscope (ENT-5000; Cogentix Medical, New York, NY, USA) and video system with integrated light-emitting diode (LED) light source and liquid crystal display (LCD) (Cogentix Medical, DPU-7000A) were used to collect the data. The laryngoscope was passed transnasally, without use of topical anesthetic or vasoconstrictors, and positioned with the tip of the endoscope in the oropharynx in order to visualize the pharynx, larynx, and subglottic airway.

Laryngoscopic evaluations were analyzed on a desktop computer (Dell OptiPlex 7050, Dell Inc., Round Rock, TX, USA) with a 19" 1920 × 1080 resolution monitor (Dell). Laryngoscopic findings such as presence of laryngeal tremor, supraglottic hyperfunction (anterior/posterior and lateral ventricular fold squeeze),[23] arytenoid asymmetry, and other relevant pathologic findings were documented. Screenshots of the fully abducted vocal folds at rest with the anterior commissure and vocal processes visualized were extracted. The still image was then uploaded into ImageJ software (National Institutes of Health, Bethesda, MD, USA) for calculation of normalized bowing index (BI). BI was defined as the furthest distance (d) of the superomedial edge of the vocal fold from the line connecting the anterior commissure to the vocal process divided by length (L) of the membranous vocal fold × 100 (Fig. 1). Total BI was calculated by summing together the right and left BI measurements.[24,25] Analysis of laryngoscopic findings and BI measurements were performed by a laryngology fellow physician, blinded to participant identity. A second SLP examiner also independently performed BI measurements. Intra- and inter-rater reliability was completed on 20% of the data files to confirm accuracy and precision of BI measurements.

Data Extraction and Analysis

Swallowing assessment and safety evaluation. Review of FEES was undertaken by a consensus panel of three expert SLP raters who were blinded to participant identity. FEES had been completed using the equipment described above following a standardized protocol of bolus trials of different volumes and consistencies. Data were extracted from one 90-cc water swallow challenge as large-volume thin liquids have been shown to have the highest probability for identifying extreme impairment.[26] For this challenge, participants had been instructed to drink 90 cc of barium water (consisting of three tablespoons (~24 g) of barium powder (E-Z-Paque Barium Sulfate for Suspension [96% w/w; E-Z-EM Canada, Inc.]) mixed with filtered tap water) from a self-administered cup "as quickly as comfortably possible." The tip of the endoscope was then advanced into the laryngeal vestibule to visualize residue patterns within the larynx and subglottic space. Swallowing safety was judged using the validated eight-point Penetration-Aspiration Scale (PAS) (Fig. 2).[27]

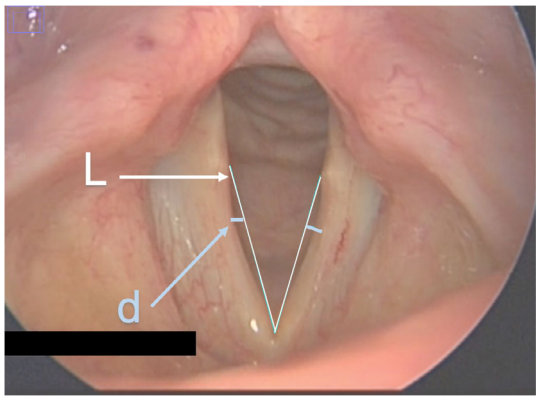

Fig. 1. Measurement of bowing index (BI) during laryngoscopy. BI = (d / L) x 100
d: furthest distance of superomedial edge of the vocal fold from the line L
L: length of membranous vocal fold from anterior commissure to the vocal process [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Cough assessment. Cough airflow data were analyzed by an SLP trained in spirometric methods. Cough data were acquired by fitting participants with a facemask covering the nose and mouth. The facemask was coupled to a pneumotachograph (MLT 1000, ADInstruments, Dunedin, New Zealand), differential pressure transducer (Validyne MP45), and side delivery port with a valve for nebulizer connection. Three trials of voluntary cough were elicited from participants by verbal instruction to breathe deeply and cough strongly into the face mask "like something went down the wrong pipe." Reflex cough was induced during three single-breath inhalations of capsaicin dissolved in a vehicle solution consisting of 80% saline and 20% ethanol and prepared at various concentrations (0, 50, 100, 200 μM). Capsaicin was delivered in a randomized block design as an aerosolized solution via nebulizer attached to a dosimeter. Participants were instructed to "breathe through your mouth and cough if you need to." There was a one-minute interval between presentations of capsaicin, during which participants took a sip of water to clear any residual sensation. Following each presentation, participants rated their urge to cough (UTC) using a modified Borg scale of 0–10, with 0 representing no UTC and 10 representing maximal UTC.[28] Cough airflow signals were digitized and recorded using LabChart 8 (ADInstruments) software to a desktop computer via PowerLab Data Acquisition System (ADInstruments). Airflow measurements were completed by a blinded, expert rater and included compression phase duration (CPD; seconds), peak expiratory flow rate (PEFR; Liters/second), and peak expiratory flow rise time (PEFRT; seconds) derived from waveforms of voluntary cough and reflex cough (Fig. 3). Cough volume acceleration (CVA; L/s/s) was computed as PEFR/PEFRT.

Swallowing Safety	PAS Score	PAS Score Description
No Penetration	1	Material does not enter the airway
Penetration	2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
	3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway
	4	Material enters the airway, contacts the vocal folds, and is ejected from the airway
	5	Material enters the airway, contacts the vocal folds, and is not ejected from the airway
Aspiration	6	Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
	7	Material enters the airway, passes below the vocal folds, and is not ejected out of the trachea despite effort
	8	Material enters the airway, passes below the vocal folds, and no effort is made to eject

Fig. 2. Swallowing safety categorized by the Penetration-Aspiration Scale (PAS)

Cough threshold was identified as the lowest concentration of capsaicin that elicited a reliable two-cough response (Cr2).

Statistical analysis

Correlational analyses were used to assess the association between age and disease duration with BI and PAS. Receiver operating characteristic (ROC) and Fisher's exact test analyses were performed to determine if laryngoscopy findings significantly predicted deficits in swallowing safety as measured by PAS. Linear regression analyses were performed using BI as the independent variable and the cough airflow and sensitivity measures as the dependent variables. Two-way random effects, absolute agreement, and intraclass correlation coefficients (ICC) were used to calculate intra- and inter-rater reliability for BI. Interpretation of ICC was judged to be "excellent" if >.90, "good" if between .75 and .90, "moderate" if between .50 and .75, and "poor" if <.50.

Statistical analysis was performed using Prism 8 (GraphPad Software, San Diego, CA, USA) and SPSS IBM Statistics 25.0 (IBM Corp., Armonk, NY). Statistical significance was set at $P \leq .05$.

RESULTS

The cohort was comprised of 30 participants (23 male, 7 female) with a mean age of 71.5 years. Mean disease

Fig. 3. Example of airflow waveforms produced during a reflex cough task. Vertical lines depict phases of the cough waveform. B-C: inspiratory phase; C-D: compression phase duration (CPD); D-E: peak expiratory flow rise time (PEFRT); E: peak expiratory flow rate (PEFR); Cr1-3: reflex cough waveforms [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE I.
Participant Demographic Information and Laryngoscopy Findings.

Characteristic	Distribution
Age, mean in years (SD) [range]	71.5 (8.28) [55–87]
Sex, no. (%)	
Female	7 (23.3)
Male	23 (76.7)
Disease duration, mean in years (SD) [range]	6.46 (3.81) [1–16]
Penetration-Aspiration Scale (PAS) score, no. (%)	
1	1 (3.3)
2	0 (0)
3	6 (20.0)
4	0 (0)
5	9 (30.0)
6	2 (6.7)
7	3 (10.0)
8	9 (30.0)
Bowing index (BI), mean (SD) [range]	7.57 (5.06) [0–15.1]
Presence of laryngeal tremor, no. (%)	5 (16.7)
Presence of moderate/severe supraglottic hyperfunction, no. (%)	13 (43.3)

duration was 6.46 years, and mean length of symptom onset was 8.6 years (Table I).

Laryngoscopic findings

Twenty-four of 30 participants (80%) demonstrated some degree of vocal fold atrophy (BI >0) with mean BI of 7.57. Five participants (16.7%) showed evidence of laryngeal tremor and 13 participants (43.3%) had moderate or severe supraglottic hyperfunction on phonation. Participant age (R^2 = 0.015, P = .524) and disease duration (R^2 = 0.007, P = .663) did not significantly correlate with BI.

Reliability

ICC for BI measurements was excellent for intra-rater reliability (ICC = 0.977; CI, 0.821–0.997; P < .001) and excellent for inter-rater reliability (ICC = 0.913; CI, 0.302–0.988; P = .013).

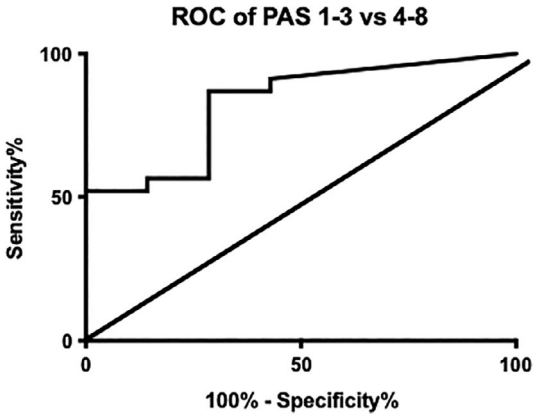

Fig. 4. Receiver operating characteristic (ROC) curve of swallowing safety predicted by bowing index (BI)

Swallowing safety

Seven participants demonstrated safe swallowing as defined by no airway invasion (PAS 1) or penetration above the level of the vocal folds (PAS 2–3), while the remaining 23 participants had impaired swallowing safety with penetration to the level of the vocal folds or aspiration (PAS 4–8). Regression analysis revealed that BI explained 13.4% of the variance in PA score (R^2 = 0.134, F = 4.345, P = .046). As BI increased (representing worsening vocal fold atrophy), PAS score also increased (representing worsening dysphagia severity). Based on ROC analysis, the optimal cutoff value for the BI to discriminate between participants with safe swallowing (PAS 1-3) and impaired swallowing safety (PAS 4–8) was >4.6 (P = .01, sensitivity: 87.0%, specificity: 71.4%; Fig. 4). The presence of laryngeal tremor or supraglottic hyperfunction were not significantly predictive of swallowing dysfunction based on Fisher's exact test analyses. Participant age (R^2 = 0.003, P = .765) and disease duration (R^2 = 0.001, P = .888) did not significantly correlate with PAS.

Cough function

Cough airflow and sensitivity measures were available for 28/30 participants (Table II). Age was negatively correlated with PEFR (R^2 = 0.230, F = 7.760, P = .010), however no other significant correlations were observed between age or disease duration with cough measures. Regression analyses did not demonstrate any significant relationships between BI and any of the cough airflow parameters for either voluntary cough or reflex cough. There was also no relationship between BI and reflex cough sensitivity based on UTC and cough threshold.

DISCUSSION

This study is the first to examine whether a relationship exists between airway protective outcomes and laryngeal abnormalities such as vocal fold atrophy in patients with PD. In our analysis, we found that vocal fold atrophy was predictive of swallowing safety. Specifically, more severe vocal fold atrophy, as indicated by a BI of at least 4.6, was predictive of PAS scores ≥4 with 87.0% sensitivity and 71.4% specificity. No direct relationship was established between BI and sensorimotor cough parameters.

Early investigations into laryngeal abnormalities in PD demonstrated findings of vocal fold bowing at rates ranging from 70% to 94%.[16,29,30] Other noted laryngeal abnormalities included abnormal phonatory posturing, tremor, and glottic incompetence. In our cohort, 80% of participants were found to have vocal fold bowing (BI >0), which affirms the relatively high rates of atrophy previously quoted. Since functional vocal folds are essential for achieving glottic closure, a necessary component of both swallowing and cough generation, it was hypothesized that vocal fold atrophy may have significant negative implications for both of these behaviors in PD. Deficits of swallowing and cough are known to be progressive and

TABLE II.
Cough Airflow Measures for Voluntary and Reflex Cough.

	CPD (s)	PEFR (L/s)	PEFRT (s)	CVA (L/s/s)	UTC	Cr2 (μM)
Voluntary cough	0.339 (0.223)	2.955 (0.796)	0.0790 (0.0154)	41.430 (15.830)	n/a	n/a
Reflex cough*	0.310 (0.147)	2.454 (0.473)	0.0745 (0.0250)	38.130 (14.100)	5	100

Values for airflow measures (CPD, PEFR, PEFRT, CVA) are mean (standard deviation).
Values for sensory measures (UTC, Cr2) are median.
CPD = compression phase duration; Cr2 = cough threshold; CVA = cough volume acceleration; PEFR = peak expiratory flow rate; PEFRT = peak expiratory flow rise time; UTC = urge-to-cough.
*Reflex cough parameters except Cr2 were measured in response to 200 μM capsaicin

pervasive in PD, and likely result in the high rates of aspiration pneumonia, the leading cause of mortality in this population.[31] Therefore, it would be useful to understand if and how vocal fold atrophy impacts swallowing and cough function in PD leading to research and interventions that improve airway protection.

Ideally, safe swallowing is achieved primarily with adequately timed laryngeal vestibular closure via arytenoid approximation and epiglottic inversion that prevents any penetration of material into the airway.[32–34] However, patients with PD and complex dysphagia may only attain safe swallowing by relying on secondary prevention of aspiration after penetration or even ejection of material after aspiration. Glottic competence achieved from true vocal fold closure is thought to provide secondary prevention against aspiration in case of penetration into the laryngeal vestibule.[20,21] Thus it is logical that a higher BI indicating more atrophied vocal folds and incomplete glottic closure would be predictive of a higher propensity for aspiration (PAS 6-8). It is less clear why higher BI would also predict higher likelihood of penetration to the vocal folds (PAS 4–5), though this could be related to the negative pressure generated by the incomplete glottic closure moving the bolus towards the laryngeal vestibule.

Further along the spectrum of airway protection, effective cough production is also reliant on glottic competence for generation of adequate subglottic pressure to eject aspirated material from the distal airways. We did not anticipate that vocal fold atrophy would affect sensory cough parameters such as UTC or cough threshold, and this was confirmed in our analysis. However, we were surprised to find cough airflow measures were also not correlated with severity of BI. Several possible explanations exist for these unexpected results. First, cough is a higher-pressure task than swallowing and therefore a greater physiologic compensation may occur to achieve glottic closure despite vocal fold atrophy. Additionally, the complex motor coordination required to generate a strong cough may be impacted so significantly by PD that a small change in glottic closure will not be reflected in airflow measures in the way they might be in non-PD participants. Finally, the lack of a relationship between BI and cough airflow parameters could simply be due to a limitation in using BI as a measurement of vocal fold atrophy.

Limitations

Given the retrospective nature of this study, vocal fold atrophy was evaluated using previously recorded still-light laryngoscopy for static measurement of BI on abduction. Though BI has been described in the literature and was reliably quantified in our study, there is no reference for how to precisely translate its numerical value into severity of atrophy.[25,35] Therefore, it is difficult to characterize the true severity of the vocal fold atrophy we observed. Also, since BI is measured on abduction it may not dependably correlate with glottic closure on adduction especially during complex events such as swallowing and cough generation, which are reliant upon glottic closure for effectiveness. Future studies should consider measuring glottal gap during tasks that elicit vocal fold adduction such as breath hold maneuvers or utilizing stroboscopic light to assess glottic closure during phonation. These modifications could potentially identify relationships that exist between vocal fold atrophy and cough airflow parameters that were anticipated but not found in this analysis. Regardless, BI remains a valuable screening measure and has been shown to correlate with glottal gap measurements in cases of bilateral vocal fold atrophy.[25] Although this analysis was retrospective, the data were collected prospectively for another study focused on cough and swallowing outcomes in PD. However, because of the retrospective nature it is possible that the limited sample size of 30 participants may have influenced the outcomes. Lastly, it is possible that there was insufficient severity and variability in BI, PAS, or cough measures to elucidate robust trends.

Clinical Implications

Based on our findings, if swallowing safety deficits are identified on FEES, vocal fold atrophy should be explored as a potential contributor. Even if vocal fold atrophy only plays a minor role in airway protection for patients with PD, it represents a potential therapeutic target with well-established interventions. Behavioral therapy such as Lee Silverman Voice Therapy (LSVT LOUD) and vocal fold injection augmentation have both been utilized as treatments for dysphonia in PD and are more recently being re-explored as potential interventions for dysphagia in PD.[36–41]

Furthermore, even though we did not find a relationship with BI and cough airflow measures in this analysis, other recent studies have demonstrated immediate improvement in cough airflow parameters such as peak expiratory flow and CVA after vocal fold injection augmentation in non-PD patients with glottic insufficiency.[42,43] These promising results suggest a potential role for prospective trials of injection augmentation in patients with PD and vocal fold

atrophy with outcomes measured by pre- and post-injection formal swallowing and cough function evaluations as collected in our study.

CONCLUSION

Dysphagia, dystussia, and aspiration pneumonia are highly prevalent and leading contributors to morbidity and mortality from PD. The causes of dysphagia and dystussia in PD are multi-factorial, with respiratory, laryngeal, and supralaryngeal deficits identified in the literature. The influence of vocal fold atrophy, which is commonly diagnosed in patients with PD, has not been extensively studied as it relates to swallowing safety or cough function. This study is the first to identify a relationship between vocal fold atrophy and swallowing safety in PD. In fact, our results demonstrate that vocal fold atrophy is predictive of reduced swallowing safety in PD independent of age and disease duration. Specifically, a BI >4.6 predicted airway invasion to at least the vocal folds (PAS ≥4). Our analysis did not identify a significant relationship between BI and cough airflow or sensitivity parameters, though a relationship may still exist that is simply not captured by BI as an indicator of vocal fold atrophy. A better understanding of the role of vocal fold atrophy in swallowing and cough function could ultimately endorse interventions that optimize airway protection and decrease the likelihood of aspiration pneumonia in patients with PD.

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BIBLIOGRAPHY

1. Kalia L V, Lang AE. Parkinson's disease. *Lancet* 2015;386:896–912.
2. Fontana GA, Pantaleo T, Lavorini F, Benvenuti F, Gangemi S. Defective motor control of coughing in Parkinson's disease. *Am J Respir Crit Care Med* 1998;158:458–464.
3. Leopold NA, Kagel MC. Laryngeal deglutition movement in Parkinson's disease. *Neurology* 1997;48:373–375.
4. Fall PA, Saleh A, Fredrickson M, Olsson JE, Granérus AK. Survival time, mortality, and cause of death in elderly patients with Parkinson's disease: a 9-year follow-up. *Mov Disord* 2003;18:1312–1316.
5. Troche MS, Brandimore AE, Godoy J, Hegland KW. A framework for understanding shared substrates of airway protection. *J Appl Oral Sci* 2014;22: 251–260.
6. Pitts T, Bolser D, Rosenbek J, Troche M, Sapienza C. Voluntary cough production and swallow dysfunction in Parkinson's disease. *Dysphagia* 2008; 23:297–301.
7. Troche MS, Schumann B, Brandimore AE, Okun MS, Hegland KW. Reflex cough and disease duration as predictors of swallowing dysfunction in Parkinson's disease. *Dysphagia* 2016;31:757–764.
8. Pitts T, Troche M, Mann G, Rosenbek J, Okun MS, Sapienza C. Using voluntary cough to detect penetration and aspiration during oropharyngeal swallowing in patients with Parkinson disease. *Chest* 2010;138:1426–1431.
9. Troche MS, Brandimore AE, Okun MS, Davenport PW, Hegland KW. Decreased cough sensitivity and aspiration in parkinson disease. *Chest* 2014;146:1294–1299.
10. Pitts T, Bolser D, Rosenbek J, Troche M, Okun MS, Sapienza C. Impact of expiratory muscle strength training on voluntary cough and swallow function in Parkinson disease. *Chest* 2009;135:1301–1308.
11. Troche MS, Rosenbek JC, Okun MS, Sapienza CM. Detraining outcomes with expiratory muscle strength training in Parkinson disease. *J Rehabil Res Dev* 2014;51:305–310.
12. Hegland KW, Davenport PW, Brandimore AE, Singletary FF, Troche MS. Rehabilitation of swallowing and cough functions following stroke: an expiratory muscle strength training trial. *Arch Phys Med Rehabil* 2016; 97:1345–1351.
13. Troche MS, Okun MS, Rosenbek JC, et al. Aspiration and swallowing in Parkinson disease and rehabilitation with EMST: a randomized trial. *Neurology* 2010;75:1912–1919.
14. Brandimore AE, Hegland KW, Okun MS, Davenport PW, Troche MS. Voluntary upregulation of reflex cough is possible in healthy older adults and Parkinson's disease. *J Appl Physiol* 2017;123:19–26.
15. Troche MS, Brandimore AE, Hegland KW, Zeilman PR, Foote KD, Okun MS. Tailored deep brain stimulation optimization for improved airway protective outcomes in Parkinson's disease. *Interdiscip Neurosurg Adv Tech Case Manag* 2016;5:3–5.
16. Blumin JH, Pcolinsky DE, Philadelphia M, Atkins JP. Laryngeal findings in advanced Parkinson's disease. *Ann Otol Rhinol Laryngol* 2004;113:253–258.
17. Yücetürk AV, Yilmaz H, Eğrilmez M, Karaca S. Voice analysis and videolaryngostroboscopy in patients with Parkinson's disease. *Eur Arch Otorhinolaryngol* 2002;259:290–293.
18. Gillivan-Murphy P, Carding P, Miller N. Vocal tract characteristics in Parkinson's disease. *Curr Opin Otolaryngol Head Neck Surg* 2016;24:175–182.
19. Perez KS, Ramig LO, Smith ME, Dromey C. The Parkinson larynx: tremor and videostroboscopic findings. *J Voice* 1996;10:354–361.
20. Giraldez-Rodriguez LA, Johns M. Glottal insufficiency with aspiration risk in dysphagia. *Otolaryngol Clin North Am* 2013;46:1113–1121.
21. Rajaei A, Barzegar Bafrooei E, Mojiri F, Nilforoush MH. The occurrence of laryngeal penetration and aspiration in patients with glottal closure insufficiency. *ISRN Otolaryngol* 2014;2014:1–5.
22. Curtis JA, Molfenter S, Troche MS. Predictors of residue and airway invasion in Parkinson's disease. *Dysphagia.* 2019. https://doi.org/10.1007/s00455-019-10014-z.
23. Rubin AD, Praneetvatakul V, Gherson S, Moyer CA, Sataloff RT. Laryngeal hyperfunction during whispering: Reality or myth? *J Voice* 2006;20:121–127.
24. Bloch I, Behrman A. Quantitative analysis of videostroboscopic images in presbylarynges. *Laryngoscope* 2001;111:2022–2027.
25. Omori K, Kojima H, Slavit DH, Kacker A, Matos C, Blaugrund SM. Vocal fold atrophy: quantitative glottic measurement and vocal function. *Ann Otol Rhinol Laryngol* 1997;106:544–551.
26. Jordan Hazelwood R, Armeson KE, Hill EG, Bonilha HS, Martin-Harris B. Identification of swallowing tasks from a modified barium swallow study that optimize the detection of physiological impairment. *J Speech Lang Hear Res* 2017;60:1855–1863.
27. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. *Dysphagia* 1996;11:93–98.
28. Davenport PW, Vovk A, Duke RK, Bolser DC, Robertson E. The urge-to-cough and cough motor response modulation by the central effects of nicotine. *Pulm Pharmacol Ther* 2009;22:82–89.
29. Hanson DG, Gerratt BR, Ward PH. Cinegraphic observations of laryngeal function in Parkinson's disease. *Laryngoscope* 1984;97:348–353.
30. Merati AL, Heman-Ackah YD, Abaza M, Altman KW, Sulica L, Belamowicz S. Common movement disorders affecting the larynx: a report from the neurolaryngology committee of the AAO-HNS. *Otolaryngol Head Neck Surg* 2005; 133:654–665.
31. Hegland KW, Okun MS, Troche MS. Sequential voluntary cough and aspiration or aspiration risk in Parkinson's disease. *Lung* 2014;192:601–608.
32. Vose A, Humbert I. "Hidden in plain sight": a descriptive review of laryngeal vestibule closure. *Dysphagia.* 2018. https://doi.org/10.1007/s00455-018-9928-1.
33. Logemann JA, Kahrilas PJ, Cheng J, et al. Closure mechanisms of laryngeal vestibule during swallow. *Am J Physiol* 1992;262:G338–G344.
34. Kiyohara H, Adachi K, Kikuchi Y, Uchi R, Sawatsubashi M, Nakagawa T. Kinematic evaluation of penetration and aspiration in laryngeal elevating and descending periods. *Laryngoscope* 2018;128:806–811.
35. Kaneko M, Hirano S, Tateya I, et al. Multidimensional analysis on the effect of vocal function exercises on aged vocal fold atrophy. *J Voice* 2015; 29:638–644.
36. Berke GS, Gerratt B, Kreiman J, Jackson K. Treatment of Parkinson hypophonia with percutaneous collagen augmentation. *Laryngoscope* 1999; 109:1295–1299.
37. Hill AN, Jankovic J, Vuong KDAT, Donovan D. Treatment of hypophonia with collagen vocal cord augmentation in patients with parkinsonism. *Mov Disord* 2003;18:1190–1192.
38. Sewall GK, Jiang J, Ford CN. Clinical evaluation of Parkinson's-related dysphonia. *Laryngoscope* 2006;116:1740–1744.
39. Sharkawi A El, Ramig L, Logemann JA, et al. Swallowing and voice effects of Lee Silverman Voice Treatment (LSVT): a pilot study. *J Neurol Neurosurg Psychiatry* 2002;72:31–36.
40. Miles A, Jardine M, Johnston F, de Lisle M, Friary P, Allen J. Effect of Lee Silverman Voice Treatment (LSVT LOUD®) on swallowing and cough in Parkinson's disease: a pilot study. *J Neurol Sci* 2017;383:180–187.
41. Howell RJ, Webster H, Kissela E, et al. Dysphagia in Parkinson's disease improves with vocal augmentation. *Dysphagia.* 2019. https://doi.org/10.1007/s00455-019-09982-z.
42. Dion GR, Achlatis E, Teng S, et al. Changes in peak airflow measurement during maximal cough after vocal fold augmentation in patients with glottic insufficiency. *JAMA Otolaryngol Head Neck Surg* 2017;143: 1141–1145.
43. Ruddy BH, Pitts TE, Lehman J, Spector B, Lewis V, Sapienza CM. Improved voluntary cough immediately following office-based vocal fold medialization injections. *Laryngoscope* 2014;124:1645–1647.