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ORIGINAL ARTICLE

Handheld Cough Testing: A Novel Tool for Cough Assessment and Dysphagia Screening

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Abstract

Aspiration pneumonia is a leading cause of death in Parkinson's disease (PD), occurring as a result of impaired cough and swallowing function. However, portable diagnostic tools for cough assessment and dysphagia screening are limited. Therefore, the aims of this study were to determine if: (1) 'Handheld Cough Testing' (HCT), a novel tool developed for cough assessments, could detect differences in cough airflow and sensation during reflex and voluntary cough tasks; and (2) HCT could screen for dysphagia in PD with high sensitivity. Twenty-two people with PD underwent HCT and swallowing assessments. Cough airflow ('PEFR') and sensation ('UTC') was recorded during reflex and voluntary cough tasks. Flexible endoscopy was used to identify people with and without dysphagia. Within-subject statistical analyses were used to detect differences in PEFR and UTC across cough tasks and between-subject statistical analyses were used to detect differences in cough function between people with and without dysphagia. Results revealed significant differences in PEFR ($p < 0.0005$) and UTC ($p < 0.0005$) across cough tasks using HCT. Additionally, reflex cough PEFR was significantly different between people with and without dysphagia ($p < 0.05$). A cut-off of 42.5 L/min exhibited an excellent ability to predict dysphagia in people with PD (90.9% sensitivity; 80.0% specificity). This study revealed that HCT was a valid tool for cough assessment and dysphagia screening. It identified differences in cough airflow and sensation during reflex and voluntary cough tasks and screened for people with dysphagia in PD with high sensitivity.

Keywords Parkinson's disease (PD) · Dysphagia · Aspiration · Cough · Handheld cough testing (HCT) · Deglutition · Deglutition disorders

Introduction

Aspiration pneumonia is a leading cause of death in Parkinson's disease (PD), developing as a result of impaired cough and swallowing [1–4]. Specifically, safe swallowing prevents the aspiration of foods and liquids into the lungs, while effective coughing senses and ejects aspirate material out of the airway when present. Reductions in airway sensitivity contribute to the high prevalence of silent aspiration in PD, making traditional clinical evaluations of swallowing ineffective at identifying dysphagic patients [5–9]. People with PD underreport and underperceive swallowing difficulties. Only 20–40% of patients with PD and dysphagia perceive swallowing problems, and less than 10% spontaneously report swallowing problems to their treating clinicians [10]. Together, these issues make early identification of dysphagia challenging and of critical clinical importance.

Cough has been found to be a powerful predictor of airway invasion (i.e., penetration and aspiration), making it an important tool for dysphagia screening. Deficits in reflex and voluntary cough airflow have been found to predict the presence of airway invasion in a variety of patient populations, with one of the most robust predictors being reduced cough peak expiratory flow rate (PEFR) [11–17]. Blunted measures of cough sensation, such as reflex cough thresholds and urge-to-cough (UTC) ratings, have also been found to be significantly different between healthy adults and people with dysphagia, silent aspiration, and aspiration pneumonia [5, 15, 18–25]. Integrating measures of cough airflow and sensation into standardized dysphagia screenings has the potential to improve long-term health outcomes in people at risk of aspiration pneumonia. Recent longitudinal

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work by Perry and colleagues revealed that implementing cough testing into standardized dysphagia screens significantly reduced rates of aspiration pneumonia in hospitalized patients with acute stroke, from 28 to 10% [26].

The gold standard equipment that is typically used to assess cough is expensive (≥ $10,000 USD) and cumbersome, limiting the feasibility of cough testing in clinical practice. However, because of the growing interest in using cough outcome measures as a screener for dysphagia, emerging research has begun to evaluate alternative approaches to reflex and voluntary cough testing. These methods include using handheld peak flow meters to measure voluntary cough airflow or using handheld nebulizers to assess reflex cough sensitivity [16, 20–22, 27, 28]. However, no commercially available handheld method for cough testing currently exists which also measures reflex cough airflow. Therefore, a novel method for cough testing was developed that uses affordable (≤ $200 USD), portable, and commercially available equipment to simultaneously measure voluntary cough airflow, reflex cough sensitivity, *and* reflex cough airflow—"Handheld Cough Testing" (HCT). The aims of this study were to: (1) validate HCT's use for cough assessment by determining if HCT could detect differences in cough airflow and cough sensation during reflex and voluntary cough; and (2) validate HCT's use for dysphagia screening by determining if HCT could screen for dysphagia in PD with high sensitivity.

Methods

Participants

This study was conducted in accordance with the amended Declaration of Helsinki and was approved by the institutional review board (Protocol ID # 17-293). Written informed consent was obtained from all patients prior to study enrollment. Consecutive people with PD were prospectively recruited at a clinical research laboratory for assessment of cough and swallowing function. Inclusion criteria were a diagnosis of PD by a movement disorders neurologist and assessment of cough and swallowing during the "on" stage of their PD medications. Exclusion criteria included a history of smoking within the last 5 years, stroke, head and neck cancer, or respiratory diseases/disorders. Demographic information was recorded for each participant, and included age, sex, and disease duration. All participants were blinded to the purpose of the study.

Cough Testing

The HCT setup comprised of a facemask (VacuMed KM202 Air Cushion Mask) coupled to a handheld nebulizer (Omron Micro-Air NE U22 V) and an analog peak flow meter (Mini-Wright Peak Flow Meter; Fig. 1). HCT was used to measure cough airflow and sensation during reflex and voluntary cough tasks. A total of seven cough tasks were completed by each participant and included one voluntary cough task and six reflex cough tasks. All cough tasks were presented in a randomized order. HCT was performed with participants seated comfortably in an upright position and with the facemask held securely around the nose and mouth by an assisting clinician.

For the voluntary cough task, participants were cued to perform one trial of a sequential voluntary cough into the HCT facemask. During this task, participants were instructed to "cough as if something went down the wrong pipe". A clinician model of three sequential coughs, also called a 3-cough epoch, was provided prior to the trial.

For the reflex cough tasks, participants were presented with nebulized capsaicin during continuous breathing. Six intensities of capsaicin were presented in a randomized order and included: 0, 10, 25, 50, 100, and 500 µM of capsaicin. The capsaicin was dissolved in a vehicle solution of 80% physiologic saline and 20% ethanol and aerosolized through the handheld HCT nebulizer. Participants were blinded to the capsaicin intensities and were provided with the instruction to "breathe in and out through your mouth, and cough if you need to." The nebulizer was turned on during tidal exhalation and remained on until a reflex cough was elicited or until five tidal breaths were completed (whichever occurred first). A minimum of 30 s rest and a single sip of water was provided between each reflex cough trial until residual sensation of the prior cough stimulus was resolved.

Outcome measures included cough PEFR, urge-to-cough (UTC), and reflex cough threshold. PEFR was measured in

Fig. 1 Picture of the Handheld Cough Testing (HCT) setup, which includes a facemask (VacuMed KM202 Air Cushion Mask), handheld nebulizer (Omron Micro-Air NE U22 V), and an analog peak flow meter (Low Range Mini-Wright Peak Flow Meter), coupled together by a tee connector (Teleflex Medical; 18 I.D. and 22 O.D.)

liters of air per minute from the analog peak flow meter and was recorded for all reflex and voluntary coughs. UTC was recorded after each reflex cough trial using a self-reported modified Borg scale (Fig. 2). Reflex cough threshold was defined as the lowest capsaicin intensity to elicit a reflex cough response.

Swallowing Evaluation

Swallowing was assessed by performing a flexible endoscopic evaluation of swallowing (FEES). A distal-chip endoscope was passed transnasal to visualize the pharynx, larynx, and subglottis while swallowing 90 mL of barium water [29]. This thin liquid serial swallowing task was selected due to its sensitivity in identifying swallowing impairments [30]. FEES recordings were rated by a speech-language pathologist blinded to participant identity and cough data. Judgements of airway invasion were made using the 8-point Penetration-Aspiration Scale (PAS; Table 1) [31]. PAS scores were used to categorize participants into one of two groups: no airway invasion (PAS ≤ 2) and airway invasion (PAS ≥ 3).

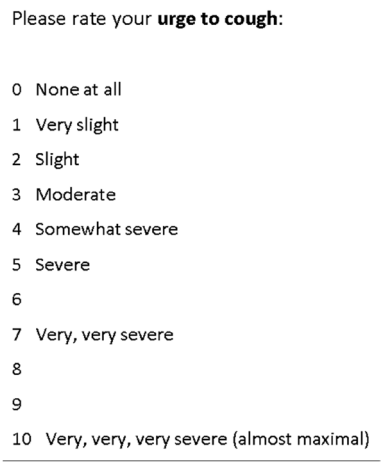

Fig. 2 Modified borg scale

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Macintosh, Version 25.0 (ICM Corp, Armonk, NY, USA). A $p < 0.05$ level was used to determine level of statistical significance. Descriptive statistics were calculated for age, sex, disease duration, reflex and voluntary cough PEFR, reflex cough threshold, UTC, and PAS. An analysis of variance was used to determine if age, sex, and disease duration were significantly different between the groups with and without airway invasion. For Aims 1 and 2, only capsaicin intensities that elicited a reflex cough response in > 50% of the participants were included in analyses of PEFR.

Aim 1: Determine if HCT Could Detect Differences in Cough Airflow and Cough Sensation During Reflex and Voluntary Cough Tasks

A Friedman test was used to determine if significant differences in median UTC scores were present across each of the six different capsaicin intensities. A repeated measures analysis of variance was used to determine if significant differences in PEFR were present across the reflex and voluntary cough tasks followed by post-hoc pairwise comparisons with Holm-Bonferroni corrections.

Aim 2: Determine if HCT Could Screen for Dysphagia in PD with High Sensitivity

A multivariate analysis of variance with post-hoc analyses were used to determine if differences in cough sensation were present between the airway invasion and no airway invasion groups. Dependent variables for cough sensation included: (1) UTC at each of the six capsaicin intensities; and (2) capsaicin intensity of reflex cough threshold. A

Table 1 Penetration Aspiration Scale (PAS)

Airway invasion grouping	PAS Score	PAS description
No airway invasion	1	Material does not enter the airway
	2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
Airway invasion	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
	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

Table 2 Distribution of PAS Scores

	PAS 1	PAS 2	PAS 3	PAS 4	PAS 5	PAS 6	PAS 7	PAS 8
Count ($N=20$)	6	1	2	0	6	0	1	4
%	30	5	10	0	30	0	5	20

Table 3 Descriptive statistics for PEFR and UTC across voluntary and reflex cough tasks

	Voluntary cough	Reflex cough						
		0 µM	10 µM	25 µM	50 µM	100 µM	500 µM	RCT
Total	$N=22$	$N=1$	$N=2$	$N=11$	$N=18$	$N=21$	$N=22$	$N=22$
PEFR Mean ± SD	137.0 ± 76.7	60.0	45.0 ± 7.0	74.0 ± 76.3	71.1 ± 38.9	59.0 ± 41.8	60.6 ± 44.2	65.0 ± 62.4
UTC (median, range)	N/A	0.0 (0.0–2.0)	0.0 (0.0–4.0)	1.5 (0.0–5.0)	4.0 (0.0–10.0)	4.0 (1.0–10.0)	6.0 (2.0–10.0)	3.5 (1.0–10.0)

PEFR peak expiratory flow rate, *UTC* urge-to-cough, *RCT* reflex cough threshold

second multivariate analysis of variance was used to determine if significant differences in cough airflow were present between the airway invasion and no airway invasion groups. Dependent variables for cough airflow included: (1) PEFR for voluntary coughs; (2) PEFR for reflex cough thresholds; and (3) PEFR for reflex coughs produced across the six different capsaicin intensities (as appropriate). Lastly, a receiver operating characteristic and area under the curve analysis was used to examine the discriminatory power and optimal sensitivity–specificity cut-off for all statistically significant dependent variables.

Results

Twenty-two people with PD were recruited for study participation, completed cough testing, and were included in the analysis for Aim 1. However, two participants did not tolerate the FEES exam, and therefore, only 20 participants were included in Aim 2. Recruited participants included 16 males and 6 females with an average age of 71.5 years (± 7.9) and an average disease duration of 6.6 years (± 4.5). Thirteen of the 20 participants exhibited airway invasion as seen during FEES (Table 2). There were no significant differences in age ($p=0.903$), sex ($p=0.63$), or disease duration ($p=0.11$) between the groups with and without airway invasion. Less than 50% of the participants produced a reflex cough at 0, 10, and 25 µM of capsaicin. Therefore, these capsaicin intensities were excluded from Aims 1 and 2.

Aim 1: Determine if HCT Could Detect Differences in Cough Airflow and Cough Sensation During Reflex and Voluntary Cough Tasks

Descriptive statistics for PEFR and UTC are outlined in Table 3. Results revealed significant differences in UTC across the six capsaicin intensities, $\chi^2(5)=83.463$, $p<0.0005$. As capsaicin intensity increased, UTC also increased (Table 4). Results also revealed a significant difference in PEFR across the cough tasks, $F(4, 68)=10.084$, $p<0.0005$, partial $\eta^2=0.372$. Post-hoc analyses revealed that PEFR for voluntary coughs were significantly greater than the PEFR for reflex coughs at 50 µM ($p=0.002$), 100 µM ($p=0.002$), 500 µM ($p=0.001$), and reflex cough threshold ($p=0.004$). There were no significant differences in PEFR within any of the reflex cough tasks ($p>0.05$).

Table 4 Pairwise comparisons of UTC scores across stimulus intensities

Stimulus intensity (µM)	Comparison (µM)	Mean difference	Std. Error	Sig
0	10	−0.045	0.564	$p=0.936$
	25	−1.159	0.564	$p=0.040$
	50	−2.250	0.564	$p<0.0005$*
	100	−3.023	0.564	$p<0.0005$*
	500	−3.750	0.564	$p<0.0005$*
10	25	−1.114	0.564	$p=0.725$
	50	−2.205	0.564	$p<0.0005$*
	100	−2.977	0.564	$p<0.0005$*
	500	−3.705	0.564	$p<0.0005$*
25	50	−1.091	0.564	$p=0.797$
	100	−1.864	0.564	$p=0.001$*
	500	−2.591	0.564	$p<0.0005$*
50	100	−0.773	0.564	$p=0.171$
	500	−1.500	0.564	$p=0.008$*
100	500	−0.727	0.564	$p=0.197$

p-values shown indicate the raw *p*-values. A "*" indicates a statistically significant difference after applying a Holm-Bonferroni correction

Aim 2: Determine if HCT Could Screen for Dysphagia in PD with High Sensitivity

Differences in PEFR and UTC between the airway invasion and no airway invasion groups are outlined in Table 5. Results did not reveal any significant differences in cough sensation between the groups with and without airway invasion, $F(7, 12) = 0.471$, $p = 0.838$, partial $\eta^2 = 0.215$. Specifically, there were no differences in reflex cough thresholds ($p = 0.086$) or UTC at any of the capsaicin intensities ($p > 0.05$). However, cough airflow did reveal significant differences in PEFR between the two groups, $F(5, 10) = 6.326$, $p = 0.007$, partial $\eta^2 = 0.760$. Post-hoc analyses revealed that the no airway invasion group had significantly lower reflex cough PEFR at 50 µM of capsaicin when compared to the airway invasion group, $F(1, 14) = 7.825$, $p = 0.014$, partial $\eta^2 = 0.359$. No significant differences in PEFR were present between the two groups for voluntary coughs ($p = 0.301$), reflex cough thresholds ($p = 0.269$), or reflex coughs produced at 100 µM ($p = 0.334$) or 500 µM ($p = 0.508$) of capsaicin. Therefore, a receiver operating characteristic analysis was completed only for reflex cough PEFR at 50 µM of capsaicin. The area under the curve for reflex cough PEFR at 50 µM was 0.864 (95% CI 0.614 to 1.000), indicating that reflex cough airflow testing at 50 µM of capsaicin demonstrated an 'excellent' ability to predict the presence/absence of airway invasion in people with PD (Fig. 3) [32]. A cut-off value of 42.5 L/min was found to be the most optimal cut-off for predicting people with and without airway invasion, with an observed sensitivity of 90.9% and specificity of 80.0%.

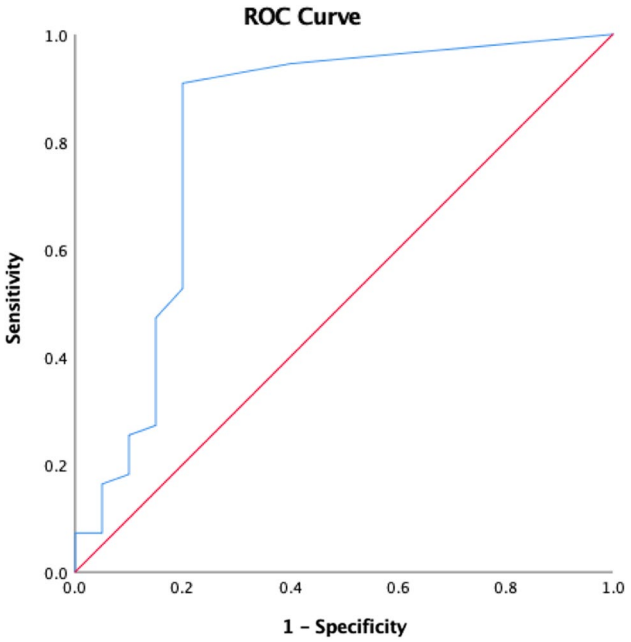

Fig. 3 Receiver operating curve for PEFR discriminating between airway invasion and no airway invasion during a 90 cc water swallowing task

Discussion

Aspiration pneumonia is a leading cause of death in PD, thought to develop as a result of concomitant dysfunction in cough and swallowing [2, 3]. Assessing cough is important when evaluating people at risk of aspiration pneumonia [33] because it provides a more comprehensive understanding of airway protective function (i.e., the ability to eject aspirate

Table 5 Differences in cough airflow and sensation between groups

	No airway invasion	Airway invasion	*p*-value
PEFR (mean ± SD)			
Voluntary cough	105.7 ± 86.4	163.4 ± 66.2	$p = 0.301$
Reflex cough threshold	34.2 ± 51.5	83.0 ± 67.0	$p = 0.269$
50 µM	35.0 ± 33.1	86.8 ± 34.8	$p = 0.014$*
100 µM	38.5 ± 51.4	68.7 ± 36.6	$p = 0.334$
500 µM	42.8 ± 50.3	68.0 ± 42.9	$p = 0.508$
UTC (median; min–max)			
Reflex cough threshold	3; 2–10	3; 1–7	$p = 0.248$
0 µM	0; 0–2	0; 0–2	$p = 0.950$
10 µM	0; 0–4	0; 0–3	$p = 0.465$
25 µM	2; 0–3	1; 0–5	$p = 0.319$
50 µM	5; 0–10	3; 0–6	$p = 0.525$
100 µM	7; 3–10	4; 1–10	$p = 0.128$
500 µM	7; 3–10	5; 2–10	$p = 0.579$

*Indicates a statistically significant *p*-value

material when present) and is a powerful screener for dysphagia and aspiration [6, 27, 34, 35]. However, clinically feasible methods to assess cough are limited, impacting the ability to identify at-risk patients. The present study evaluated the clinical utility of HCT, a novel cough setup developed for reflex and voluntary cough assessment and dysphagia screening. It was hypothesized that differences in cough airflow and sensation across reflex and voluntary cough tasks would be detected using HTC, and that measures of cough function would be significantly different between people with and without airway invasion in PD using the HTC setup. The findings from this study support these hypotheses.

Reflex cough is an important airway protective response intended to eject aspirate material out of the lungs in order to maintain a homeostatic pulmonary environment. One critical feature of reflex cough is the ability to generate expulsive expiratory airflow sufficient enough to clear the airway from penetrant and aspirate material. Results from the present study revealed that cough airflow (PEFR) was significantly lower for the reflex cough tasks when compared to the voluntary cough task. This finding is consistent with previous research in PD using gold standard cough instrumentation and contributes to accumulating evidence characterizing patterns of airway protective function in PD [18]. The lower PEFR observed in this study for reflex coughs may be indicative of an impaired ability for people with PD and airway invasion to eject aspirate material from the lungs, and thus, be at an increased risk for developing dysphagia-related pulmonary infections. While voluntary cough testing can be easily and expeditiously administered in the clinical setting (e.g., cueing someone to cough on command), this research supports the notion that reflex cough assessments should also be included in clinical evaluations when assessing airway protection and cough in PD. Evaluating only voluntary coughs without the inclusion of reflex coughs may overestimate cough effectiveness and airway protective function in this patient population.

A second critical feature of reflex cough is the UTC. This sensory perception facilitates the conscious desire to eject aspirate material from the lower airway, especially in the presence of low intensity cough stimuli (e.g., micro-aspiration) when a robust reflexive response may be otherwise absent. Researchers using gold standard instrumentation have previously identified a direct relationship between reflex cough stimulus intensities and UTC in healthy and diseased populations [5, 19, 36, 37]. Specifically, as stimulus intensity increases, so too does UTC. The results from this study support this stimulus-to-UTC relationship. For both the airway invasion and no airway invasion groups, significant increases in UTC were observed with each increase in capsaicin intensity. Additionally, the airway invasion group consistently demonstrated lower median UTC ratings across the continuum of capsaicin intensities when compared to the no airway invasion group. This supports the notion that people with airway invasion have blunted cough sensation which may place them at risk of dysphagia. However, these differences in UTC between the airway invasion groups did not reach statistical significance which is in contrast to previous research. It is possible that this study was too underpowered to detect statistically significant differences or may reflect inherent differences in cough testing methodologies. For example, the only currently available research investigating the differences in urge-to-cough between normal and dysphagic people with PD has completed using a "single breath" method [5, 6], while the procedures used in this study used a "continuous breathing" method.

Significant differences in reflex cough PEFR were also present between the airway invasion and no airway invasion groups, indicating that reflex cough testing with HCT at 50 µM was an effective tool for dysphagia screening. When presented with 50 µM of capsaicin, a reflex cough PEFR greater than 42.5 L/min was found to be the most optimal cut-off for identifying people with airway invasion and dysphagia. The reflex cough threshold for the majority of the participants (> 80%) was 50 µM, which is likely why it was found to be the optimal PEFR cut-off as well. Subthreshold capsaicin intensities (< 50 µM) did not elicit reflex coughs in the majority of participants, and therefore were not effective at measuring reflex cough airflow. Additionally, using suprathreshold capsaicin intensities (> 50 µM) resulted in a ceiling effect with similarly strong coughs across intensities and among the participants.

A higher PEFR for the impaired airway invasion group was an unexpected finding. One plausible explanation relates to the interaction between cough reflex sensitivity and operating lung volume. In healthy adults, lung volume significantly affects PEFR, with a larger operating lung volume associated with higher PEFR [38]. Additionally, dysphagic adults have been found to have slower reflex cough reaction times and reduced cough reflex sensitivity when compared to non-dysphagic adults [21]. Therefore, it is possible that the dysphagic group may have had slower reflex cough reaction times which allowed for greater inspiratory volume, larger operating lung volumes, and ultimately a higher PEFR when compared to the non-dysphagic/no airway invasion group.

This study is not without limitations. First, FEES was used to determine the presence of airway invasion. Because visualization of airway invasion during the swallow is often obliterated on FEES due to "endoscopic white", it is possible that transient events of penetration and aspiration were missed. However, we believe this was mitigated by using barium water, which has been previously found to significantly increase the sensitivity of detecting airway invasion and abnormal PAS scores [29]. Second, while a significant difference in reflex PEFR was seen between the two groups, it is possible that this study was underpowered to

detect significant differences in voluntary PEFR and UTC between the dysphagic and non-dysphagic, both of which have been identified in previous research. Third, each trial during HCT was presented only once, and therefore the reliability of the outcome measures cannot be assessed. Lastly, future research including the use of simultaneous respiratory inductive plethysmography and HCT is recommended in order to explore the relationship between lung volume, cough reaction times, and cough outcome measures. This would help to confirm or refute our hypotheses regarding reasons for lower PEFR in the no airway invasion group as compared to the airway invasion group.

Conclusions

HCT is a novel, portable tool valid for cough assessment and dysphagia screening. An optimal capsaicin intensity and PEFR cut-off value for dysphagia screening was identified, which exhibited a sensitivity of 90.9% and specificity of 80.0% for predicting the presence of airway invasion. Identifying that 50 μM of capsaicin was the single-most effective concentration for dysphagia screening is an important observation because it improves the clinical ease and feasibility of HCT by reducing the need to prepare, transport, and administer multiple capsaicin intensities. Using portable, affordable, and commercially available equipment, the HCT is a clinically feasible tool valid for cough assessment, dysphagia screening, and potentially identifying people at risk of aspiration pneumonia.

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Author Contributions JC takes full responsibility for the content of the manuscript, including the accuracy of the data and analysis. JC proposed the study concept and design, collected all data, performed the statistical analyses, and prepared the manuscript for publication. MT contributed to study design, had access to all the data, and assisted in data analysis and manuscript preparation.

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Compliance with Ethical Standards

Conflict of interest J.C. has no disclosures to endorse; M.T. receives employee salary from Teachers College, Columbia employee, and Grant funding from the Michael J. Fox Foundation and the CurePSP Foundation.

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