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Investigating Parkinson's disease with dual high resolution pharyngeal manometry with impedance and videofluoroscopy

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Abstract

Purpose: To characterize pharyngeal function in people with Parkinson's Disease using both high resolution impedance manometry (HRIM) and videofluoroscopy (VFSS) and to explore correlations between VFSS and HRIM metrics.

Methods: All participants received both VFSS and HRIM within 24 h-time window. A standard VFSS protocol (IDDSI 0: 1 mL, 3 mL, 20 mL, and 100 mL) was performed. A solid-state unidirectional catheter (36 pressure sensors) was used to acquire manometric data for triplicate swallows (IDDSI 0: 5 mL, 10 mL, 20 mL), quantitative swallow analysis was completed through Swallowtail™ and SwallowGateway™. Parameters were compared to published norms and statistical tests explored correlational associations ($p < 0.05$).

Results: Twenty-one participants (76% male; mean age 70 years, SD7.16) with mild–moderate severity PD were recruited with 73% reporting Eating Assessment Tool (EAT-10) scores ≥3 indicating swallow impairment. Compared to normal metrics, one third of participants had abnormally elevated hypopharyngeal contractile integral (HPCI), hypopharyngeal peak pressure, upper esophageal sphincter (UES) integrated relaxation pressure (UES IRP), and reduced UES maximum admittance. Five participants showed compromised swallow safety (Penetration-Aspiration Scale score ≥6). One third of participants had abnormal VFSS values for pharyngoesophageal segment (PES) opening duration, maximum PES opening distance, and maximum hyoid displacement measures. Some HRIM metrics had a strong correlation with pharyngeal VFSS measures ($r > 0.60$, $p < 0.05$).

Conclusion: This study identifies early manometric signs of pharyngeal dysfunction in people with PD. The congruence of the VFSS and HRIM measures confirms the hypothesis of insidious early decline in swallow function in PD despite maintenance of airway safety (i.e., low aspiration rates).

KEYWORDS
dysphagia, high resolution, manometry, Parkinson's disease, videofluoroscopy

1 | INTRODUCTION

Swallowing difficulties are common in people with Parkinson's Disease (PD),[1] especially as the disease progresses, with aspiration pneumonia the leading cause of death.[2–5] Early identification of swallowing changes is important so that clinicians may provide early intervention, reduce dysphagia-related health complications and improve overall quality of life.[6] Videofluoroscopic swallow study (VFSS) and flexible endoscopic evaluation of swallowing (FEES) are common instrumental swallowing assessments in clinical practice. Timing, movement and coordination of oropharyngeal structures during swallowing, aspiration and post-swallow residue are often reported. In recent years, high-resolution manometry (HRM), using a solid catheter with multiple pressure sensors at 1-2 cm intervals, has been proposed as a safe and objective tool for evaluating pharyngeal timing and pressures.[7] High resolution impedance manometry with impedance (HRIM) offers additional perspectives on swallow biomechanics by providing quantitative changes of pressure in relation to bolus flow and the ability to identify where bolus sits. Jones and Ciucci suggested that the precise and objective nature of HRIM swallow pressure measures may identify subtle changes in swallowing dysfunction before gross signs of swallow deficits are seen through FEES or VFSS.[8]

As HRIM is relatively new, a limited number of studies have reported pharyngeal manometric swallow measures in PD. Clinical characteristics of velopharyngeal, meso-pharyngeal, and upper esophageal sphincter (UES) pressure-integral[8–11] and esophageal measures[12,13] in different stages of PD have begun to be explored. A recent collaborative paper proposed important HRIM core metrics that relate to swallowing safety and efficiency based on an international expert group Delphi-consensus recommendations.[14] No previously published studies investigating PD cover the full set of recommended metrics. Other adjunct measures including UES contractile measures, flow timing measures, and composite global efficiency measures have also recently been introduced to quantify overall swallow dysfunction and bolus modulation effects.[7,15,16] Moreover, researchers have suggested that instrumental swallowing assessment using multimodal evaluation of swallowing difficulties combining VFSS, HRM, and patient-reported outcome measures of swallowing concerns, may provide a more robust method for identifying swallowing dysfunction in PD.[8] This study aimed (a) to report quantitative VFSS and HRIM parameters in individuals with PD, and (b) to explore the correlations between HRIM and quantitative VFSS parameters. Our study aimed to add to our growing understanding of the pathophysiology of early swallow changes in PD and the clinical merits of both VFSS and HRIM in this population.

Key points

- High resolution impedance manometry metrics are highly correlated with VFSS metrics and describe early subtle changes in pharyngeal swallow function in patients with early-stage Parkinson's Disease.
- HRIM and VFSS findings are complementary and evaluate differing aspects of the swallow. Incorporation of both techniques into diagnostic and assessment frameworks will help inform treatment selection for each individual.
- Early functional changes in swallowing, are recognized by patients with PD as demonstrated by elevated Eating Assessment Tool-10 scores, and can also be detected by both videofluoroscopic evaluation and HRIM, suggesting that screening followed by targeted evaluation may enable optimized exercise or rehabilitation regimens to be developed based on quantitative findings.

2 | METHODS AND MATERIALS

This prospective observational analytical study was completed as part of a conjoint therapeutic clinical trial. All procedures performed involving human participants were in accordance with the ethical standards of the national research committee and ethical approval gained by Health and Disability Ethics Review Committee (HDEC:19/CEN/131). Written informed consent was obtained from all the participants included in this study prior to study commencement.

All participants were diagnosed with PD by their neurologists, treated with anti-parkinsonism medications, and consecutively referred to our university clinic from November 2019 to May 2022 for swallowing or voice treatment. Exclusion criteria were neurological diseases other than PD, diagnosed with atypical PD, head and neck cancer or had head and neck radiotherapy treatment, undergone any neurosurgical treatment or laryngeal surgery, or other comorbidities affecting swallowing. Participants who could not undergo either VFSS or HRIM were also excluded. Participants were all in an "on" state during assessments with stable symptoms. Participants independently completed self-rated questionnaires of their perceived level of Parkinson's severity using Parkinson's Disease Questionnaire-8 (PDQ-8, scores range from 0 to 40 but are standardized out of 100 with 100 representing the greatest severity)[17] and swallowing problems using Eating Assessment Tool-10 (EAT-10, scores ranges from 0 to 40, with any score above 3 considered abnormal).[18] Self-rated questionnaires, VFSS and HRIM were all completed within a 24-h period (but not conducted concurrently).

2.1 | HRIM

A 10-French solid-state unidirectional high-resolution manometry catheter (36 pressure sensors spaced at 1 cm intervals and 16 adjoining impedance sensors each 2 cm) (Model K103659-E-1180-D, Unisensor AG, Attikon, Switzerland) was used for all trials. Topical anesthesia (cophenylcaine 4%) was sprayed in the nasal passages.

The catheter was lubricated (using A-gel aqueous lubricant) to ease the passage and inserted transnasally to detect the pressures along the entire swallowing tract from velopharynx to stomach Once the catheter was positioned correctly (by viewing manometry readings) participants rested for 5-min and an initial accommodation period was observed. For pharyngeal data recording, participants were seated in a head-neutral, upright position. A Standardized Bolus Medium (SBM) kit (Trisco Foods Pty Ltd, Brisbane, Australia), which is made in accordance with the International Dysphagia Diet Standardization Initiative (IDDSI) framework (http://iddsi.org/framework/), was used to ensure standardized bolus viscosity and conductivity across different consistencies (SBMkit consists of apple flavored sodium-chloride concentrate solution). A standardized HRIM protocol[14] was followed and for the purposes of this paper, triplicate cued swallow trials of three bolus conditions (total nine swallows) (thin liquid IDDSI 0: 5 mL, 10 mL, 20 mL) were collected for pharyngeal analysis. Each bolus was measured and administered via a 20 mL syringe with a minimum 20 s break between swallows. Participants were encouraged to attempt single swallows per bolus where possible. All HRIM studies were performed by an experienced researcher who had completed training in HRIM. The researcher labeled swallows during the procedure for later analysis and an assistant recorded swallow variation with cough, adverse events, and protocol completion rate in a recording sheet. Once the protocol was completed, raw data was acquired at 20 Hz (Solar GI acquisition system, MMS, The Netherlands).

2.2 | Swallow gateway analysis

Pressure and impedance data were exported (ASCII format) and uploaded to Swallow Gateway™ (Flinders Partners Pty Ltd, Australia) for semiautomated analysis. Each pharyngeal swallow was analyzed by a researcher who had successfully completed the SwallowGateway analysis course and was blinded to participant characteristics. All metrics, and their definitions, are described in Table 1.[7,15,16] Analytic methods and reliability of SwallowGateway analysis have previously been described.[7] To allow comparison with international research, the cut-off values (5th and 95th percentile) for each parameter were derived from the SwallowGateway normative study data (www.swallowgateway.com).[19] Half of the data (11/21 participants) were randomly selected and analyzed by a second trained, blinded rater.

2.3 | Videofluoroscopic study of swallowing

A standard VFSS protocol[20] was performed using a videofluoroscope (DF-323H, Toshiba, Japan; recorded at 30 frames per second). A 20 mm diameter radio-opaque ring was taped under the participant's chin for calibration during analysis. Images were obtained on a Toshiba Ultimax Fluorography C-arm (Model BLF-600R, Toshiba, Japan) in the lateral plane and recorded onto a digital media stick. An experienced medical radiation technician and a speech pathologist conducted all procedures. Participants were recorded in a standing position wherever possible. In a lateral view, participants swallowed 1 mL, 3 mL, and 20 mL of IDDSI 0 thin liquid barium (EZ-PAQUE Barium Sulfate suspension, 60%w/v; 41%w/w, E-Z-EM, Inc, Westbury, NY) administered by syringe with the instruction to swallow "all in one go" when prompted. For sequential swallowing, 100 mL of IDDSI 0 thin barium liquid was provided in a cup with a straw with the instruction "swallow until it's all gone".

2.4 | VFSS data analysis

All VFSS studies were analyzed quantitatively by an experienced researcher who had completed VFSS analysis training. VFSS data were analyzed using "Swallowtail" [version 3.0.5 (2013–2019) Belldev Medical, Illinois, USA]. Each swallow was rated using the 8-point penetration-aspiration scale (PAS) (where 1 = no penetration/aspiration and 8 = aspiration below the vocal cords with no attempt to clear).[20] Swallow studies were analyzed frame by frame and measured quantitatively for timing, displacement, and residue measures (Table 1)[20] and compared to 65+ years norms from the composite accumulative normative data base.[20] Twenty percent of VFSS videos were randomly selected and analyzed by a second experienced, blinded researcher.

2.5 | Data analysis

Average results for the triplicate swallows for nine bolus conditions (three volumes) were tabulated in an excel spreadsheet for statistical analysis using SPSS [IBM Corp., IBM Statistical Package for the Social Sciences (SPSS), v 27.0 Armonk, NY, IBM Corp]. Descriptive data are reported as mean ± SD or median (interquartile range). Relationships between quantitative variables were assessed using Spearman rank order correlation. p-value of <0.05 was considered statistical significance. Group comparisons were performed using the Mann–Whitney U test or independent samples t-test after testing each variable for normal distribution (Shapiro–Wilk Test). Inter-rater reliability (two-way random method) yielded good intraclass coefficient for individual manometric and VFSS measures ranged from 0.77–0.99 ($p < 0.05$).

3 | RESULTS

Thirty-four participants were recruited but some data was excluded from analysis (due to technical failure/ new equipment error $n = 11$; swallow labelling errors $n = 2$). Twenty-one participants (76% male, mean age 69, SD 8) were included in the final dataset; with 73% ($n = 15/21$) self-reporting swallowing disturbances and scoring outside the normal range (>3 points) on the EAT-10. Participant characteristics are presented in Table 2. Participants all demonstrated mild PD severity by the Hoehn and Yahr rating and PDQ-8 scores.

TABLE 1 Data measures.

Measures (unit)	Abbreviation	Description
HRIM pressure flow parameters (Ferris et al., 2021; Omari et al., 2020)		
Pharyngeal lumen occlusive pressures		
Pharyngeal contractile integral (mmHg.cm.s)	PHCI	An integral pressure measure of pharyngeal contractile vigor spanning from the velopharynx to the upper margin of the UES
Velopharyngeal contractile integral (mmHg.cm.s)	VCI	An integral pressure measure of pharyngeal contractile vigor spanning the velopharyngeal region only
Mesopharyngeal contractile integral (mmHg.cm.s)	MCI	An integral pressure measure of pharyngeal contractile vigor spanning the mesopharyngeal region only
Hypopharyngeal contractile integral (mmHg.cm.s)	HPCI	An integral pressure measure of pharyngeal contractile vigor spanning the hypopharyngeal region only
Peak pressure (mmHg)	PeakP	Mean pharyngeal peak pressure
UES relaxation & opening		
UES integrated relaxation pressure (mmHg)	UES IRP	A pressure measure of the extent of UES relaxation pressure, generated as the median of the lowest pressure in a non-consecutive 0.20–0.25 s window
UES relaxation time (s)	UES RT	A measure of the duration of UES relaxation – a pressure interval below 50% of baseline or 35 mmHg, whichever is lower, in units of second.
UES maximum admittance (unit- millisiemens) (mS).	UES MaxAdm	A measure of extent of UES opening. The highest admittance value (inverse of impedance) recorded during trans-sphincteric bolus flow
Intra-bolus distension pressure (mmHg)	IBP	The pressure 1 cm superior to the UES apogee position at the time of maximum hypopharyngeal distension (indicated by impedance/admittance)
UES contractile measure		
UES contractile integral (mmHg.cm.s)	UES CI	An integral pressure measure of UES contractile vigor, post swallow
UES basal pressure (mmHg)	UES BP	The peak pressure at the level of the UES pre swallow
UES peak pressure (mmHg)	UES PeakP	The peak pressure at the level of the UES measured immediately post pharyngeal contraction
Flow timing variables		
Pharyngeal distension-contraction latency (mS)	DCL	A timing measure from maximum pharyngeal distension to the pharyngeal luminal occlusive contraction – a correlate of how well the bolus is propelled ahead of the pharyngeal stripping wave.
Bolus presence time (mS)	BPT	The dwell time of the bolus in the pharynx
Global swallow efficiency measures		
Swallow risk index	SRI	A composite formula score designed to capitalize on the directionality of aberrant swallow parameters. The original report described SRI in patients with neuro-muscular disease and aspiration on radiology
Quantitative videofluoroscopic swallowing measures (Leonard & Kendall, 2019)		
Timing (Seconds)		
Oro-pharyngeal transit time	OPT	Duration of bolus transit from the posterior nasal spine to the time of bolus exit from valleculae
Hypo-pharyngeal transit time	HPT	Duration of bolus transit from bolus head exit from valleculae to the time of bolus tail clearance of the PES
Total pharyngeal transit time (OPT+ HPT = TPT)	TPT	Total time is taken from the onset of the swallow (when first movement of the bolus passes through posterior nasal spine) to clearance of bolus tail through the UES
Airway closure	Airwaycl	Total time taken from the swallow onset and completion of supraglottic closure
Airway closure duration	Airwaydur	Total time airway is closed during the swallow (complete supraglottic airway closure to epiglottis return to upright position after bolus clearance)
Maximum hyoid displacement duration	Hdur	Total time hyoid is maximally displaced (retain at the anterior-superior position) during the swallow
PES opening duration	PESdur	Total time UES is open during the swallow
Displacement (cm)		
Maximum opening of the PES	PESmax	Maximum distension of the PES

TABLE 1 (Continued)

Measures (unit)	Abbreviation	Description
Maximum hyoid displacement	Hmax	Distance between hyoid at rest and maximally displaced (highest anterior-superior position)
Hyoid-larynx displacement	HLmax	The difference in distance between hyoid and larynx at rest and maximally approximated during swallow
Ratio (area/area)		
Pharyngeal constriction ratio	PCR	Maximum constriction of the pharynx / pharyngeal area at rest
Bolus clearance ratio	BCR	Bolus residual/ area of bolus in the pharynx prior to PES opening (Jardine et al., 2020)

TABLE 2 Participant demographics characteristics and self-reported disease severity scores.

Variables		*n* (%)	Mean ± SD (Range)
Age group	≤ 70 years	11 (52%)	69.67 ± 7.16 (59–86)
	> 70 years	10 (48%)	
Sex	Male	16 (76%)	
	Female	5 (24%)	
Years of diagnosis	≤ 5 years	12 (57%)	7.67 ± 6.39 (1–18)
	> 5 years	9 (43%)	
Parkinson's disease questionnaire-8 (Standardized score) (0 = no impact of symptom, 100 = maximum impact)	≤ 32 points	11 (52%)	29.18 ± 15.92 (0–50.00)
	≥ 33 points	10 (48%)	
Eating assessment tool-10 score (0–3 normal range, 40 = maximum)	< 3 points	6 (27%)	7.76 ± 6.75 (0–26)
	= 3–6 points	4 (21%)	
	≥ 7 points	11 (52%)	
Eating a normal diet with no modification to food or drink (IDDSI 7)		21 (100%)	

Note: PDQ-8 severity—0 = no impact of symptoms, 100 = maximum impact association; Hoehn and Yahr (1967) staging - H&Y I (17.74), H&Y II (33.14), H&Y III (37.05), H&Y IV (47.86).

3.1 | HRIM metrics

Participants had abnormally *high* (above 95th percentile) contractility in the mesopharyngeal (>200 mmHg.cm.s) (24%) and hypopharyngeal regions (>165 mmHg.cm.s) (33%), *high* hypopharyngeal peak pressure (> 353 cmHg) (38%) and impaired UES distensibility measures as seen by UES IRP (>2 mmHg) in 33% and UES MaxAdm (<4 milli siemens, below 5th percentile) in 24%. Abnormally high UES CI (> 1014 mmHg.cm.s) was found in 24% of participants. Few participants (< 20%) exhibited abnormalities in other HRIM measures. HRIM metrics compared to norms are given in Table 3.

3.2 | VFSS quantitative timing, displacement, and ratio metrics

Few participants showed PAS scores ≥6 across VFSS swallow trials (1 mL: $N = 0$; 3 mL: $N = 1$; 20 mL: $N = 1$; 100 mL: $N = 5$). Forty-three percent of participants demonstrated abnormally *short* (less than 1SD normative range) PES opening duration (<0.53 s) and 29% had impaired maximum opening of PES (<0.6 cm) (for 20 mL IDDSI 0 trials). One third (33%) recorded impaired maximum elevation of the hyoid (male <1.6 cm and female <1.1 cm). VFSS measures compared to norms are given in Table 4.

3.3 | HRIM variables in relation to quantitative VFSS measures

Contractile integral measures (PhCI, HPCI), UES measures (UES IRP, UES RT, UES MaxAdm), and distension to contraction latency all showed strong correlation with VFSS measures ($p < 0.05$, $r > 0.60$). Correlations between both HRIM and VFSS measures are given in Table 5.

4 | DISCUSSION

This study reports HRIM and VFSS metrics in 21 individuals with mild PD and explored the association between these two instrumental evaluation types. More than one-third of participants presented with abnormal hypercontractility (above 95th percentile) in the hypopharyngeal region, impaired UES relaxation and abnormal luminal distensibility. This suggests that the pharynx is compensating for poor trans-sphincteric flow by increasing hypopharyngeal

TABLE 3 HRIM variables compared to normative range.

HRIM measures 5 mL- IDDSI 0 (Thin liquid)			HRIM measures 10 mL-IDDSI 0			HRIM measures 20 mL-IDDSI 0		
Measure/ normative data 5th to 95th percentile	Mean (SD)	Number of pathological subjects	Measure/normative data 5th to 95th percentile	Mean (SD)	Number of pathological subjects	Measure/normative data 5th to 95th percentile	Mean (SD)	Number of pathological subjects
Pharyngeal contractility								
PhCI (mmHg.cm.s) 109 to 504	337.47[a] (290–429)	↑ 2/21	PhCI 110 to 504	332.41[a] (269–430)	↑ 2/21	PhCI 124 to 515	368.05[a] (315–440)	↑ 3/21
VCI (mmHg.cm.s) 17 to 179	83.28 (46.30)	↑ 1/21	VCI 18 to 211	65.84[a] (48–132)	↑ 1/21	VCI 22 to 243	95.70 (70.58)	↓ 1/21
MCI (mmHg.cm.s) 40 to 233	144.10[a] (115–216)	↑ 4/21	MCI 41 to 224	149.81[a] (128–187)	↑ 2/21	MCI 44 to 200	165.11[a] (127–202)	↑ 5/21
HPCI (mmHg.cm.s) 19 to 159	141.43 (79.79)	↑ 7/21	HPCI 22 to 154	99.43[a] (74–161)	↑ 6/21	HPCI 23 to 165	138.73 (66.52)	↑ 6/21
PeakP (mmHg) 58 to 360	285.42 (125.61)	↑ 5/21	PeakP 62 to 327	282.29 (117.62)	↑ 8/21	PeakP 65 to 353	316.87 (121.94)	↑ 8/21
UES relaxation & opening								
UES IRP (mmHg) −16 to 2	0.52 (13.44)	↑ 7/21	UES IRP −15 to 3	−4.23[a] (−6.6 to 0.6)	↑ 4/21	UES IRP −14 to 5	−2.58[a] (−5 to 3)	↑ 4/21
UES RT (s) 0.4 to 0.7	0.56 (0.10)	↑ 1/21	UES RT 0.4 to 0.7	0.60 (0.11)	↑ 2/21	UES RT 0.4 to 0.8	0.64 (0.09)	↑ 1/21
UES Max Adm (millisiemens-mS) 3 to 5	3.41 (0.55)	↓ 4/21	UES Max Adm 3.6 to 6.6	4.05 (0.52)	↓ 3/21	UES Max Adm 4 to 8	4.57 (0.77)	↓ 5/21
IBP (mmHg) −12 to 17	3.59[a] (5–12)	↑ 3/21	IBP −10 to 17	4.63[a] (−0.2 to15)	↑ 4/21	IBP −8 to 22	7.35 (14.18)	↑ 3/21
UES contractile measure								
UES CI (mmHg.cm.s) 193 to 1014	803.20 (382)	↑ 5/21	UESCI 204 to 1078	741.28[a] (423–918)	↑ 3/21	UESCI 172 to 1122	878.86[a] (487–1087)	↑ 4/21
UES BP (mmHg) 30–154	103.91[a] (72–139)	↑ 3/21	UES BP 28–166	95.72[a] (68–119)	↑ 2/21	UES BP 29–188	95.93[a] (734–123)	↑ 2/21
UES PeakP (mmHg) 112 to 567	405.01 (142.25)	↑ 3/21	UES PeakP 120 to 593	394.44 (161.80)	↑ 3/21	UES PeakP 119 to 597	424.01 (150.75)	↑ 3/21
Flow timing variables								
DCL (mS) 0.3 to 0.6	0.49 (0.87)	None	DCL 0.36 to 0.7	0.533 (0.10)	None	DCL 0.4 to 0.7	0.59 (0.10)	↑ 2/20
BPT (mS) 0.4 to 0.8	0.60[a] (0.5–0.7)	↑ 1/21	BPT 0.4 to 0.9	0.60[a] (0.5–0.9)	↑ 4/21	BPT 0.5 to 1.3	0.68[a] (0.6–1)	None
Global swallow efficiency measures								
SRI 0 to 4	0.55[a] (0–3)	↑ 3/21	SRI 0 to 5	1.06[a] (0.3–2.6)	↑ 2/21	SRI 0 to 10	1.09[a] (0.3–2.8)	None

Abbreviations: BPT, bolus presence time; DCL, pharyngeal distension-contraction latency; IBP, Intra-bolus distension pressure; MCI, mesopharyngeal contractile integral; PCI, Pharyngeal contractile integral; PeakP, peak pressure; SRI, Swallow risk index; UES, Upper-esophageal sphincter; UES IRP, UES integrated relaxation pressure, UES RT-UES relaxation time; UESMaxAdm, UES maximum admittance; UES CI, UES contractile integral; UES BP, UES basal pressure; UES PeakP, UES peak pressure; VCI, Velopharyngeal contractile integral.

[a]Median (IQR) (for non-normally distributed variables), NA- not applicable, ↑ above the 95th percentile of the normative range, ↓below the 5th percentile of the normative range.

TABLE 4 VFSS measures compared to the normative range.

VFSS measures		
Measure/normative data 20 mL IDDSI 0 (-1SD to +1SD range)	**Mean ± SD**	**% Pathological subjects**
Timing measures		
OPT(s) 0.11 to 0.35	0.20 (0.11)	None
HPT(s) 0.42 to 0.78	0.55 (0.11)	None
TPT (s) 0.89 to 1.83	0.71[a] (0.7–0.8)	None
Airwaydur (s) 0.39 to 1.31	0.76[a] (0.6–1)	None
Hdur (s) 0.02 to 0.22	0.32 (0.11)	None
PESdur (s) 0.53 to 0.75	0.51 (0.12)	↓ 9/ 21
Displacement measures		
PESmax (cm) 0.6 to 1.08	0.69 (0.18)	↓ 6/21
Hmax (cm) Male 1.64 to 3.0 Female 1.16 to 2.62	1.58[a] (1.4–1.8)	↓ 7/21
HLmax (cm) Male 0.84 to 2.28 Female 0.69 to 1.69	1.10 (0.46)	↓ 2/21
Ratio (area/area)		
PCR 0 to 0.168	0.04[a] (0.02–0.09)	↑ 1/21
BCR 0 to 0 0.11	0.02[a] (0–0.06)	None
Penetration-aspiration rating		
PAS 1 to 2	1[a] (1–1)	↑ 2/21

Abbreviations: Airwaycl, airway closure; Airwaydur, airway closure duration; BCR, Bolus clearance ratio; Hmax, maximum hyoid displacement; Hdur, maximum hyoid displacement duration; HLmax, hyoid-larynx displacement; HPT, hypo-pharyngeal transit time; OPT, oro-pharyngeal transit time; PES, pharyngoesophageal sphincter; PESdur, PES opening duration, PESmax, maximum opening of the PES, PCR, pharyngeal constriction ratio; TPT, Total pharyngeal transit time.
[a]Median (IQR), ↑ above the +1SD of the normative range, ↓below the -1SD of the normative range.

pressure generation. Poor trans-UES flow may be due to loss of UES distensibility (and hence elevated UES pressures) or uncoordinated UES relaxation (mis-timing between bolus flow and UES relaxation/ opening). Congruent with HRIM findings, more than one-third of participants presented with abnormally narrow PES opening distance (PESmax), short PES opening duration (PESdur) and decreased maximum hyoid displacement (Hmax) during thin liquid swallow trials on VFSS. The reduction in UES diameter and opening time would require increase bolus velocity to allow complete transfer of bolus and therefore hypopharyngeal pressure would need to increase to achieve this (hence the elevated HPCI). Decreased hyoid displacement also relates to inability to distract the UES and to hold it open for adequate bolus transfer, seen on metrics as a reduction in opening duration. Confirmation of strong correlation of HRIM variables [HPCI, UES relaxation time (UES RT), and UES MaxAdm] with VFSS parameters supports the fact that these differing evaluation methods identify similar pharyngeal functional changes—if just from a differing perspective. It is pleasing and reassuring to see the direct correlation of these metrics and this gives confidence to clinicians interpreting study metrics from either technique that they are seeing physiologic change accurately.

4.1 | Pharyngeal weakness and UES motility in individuals with PD

Elevated contractility (HPCI, MCI) was identified in the current cohort and indicates greater force generation by pharyngeal muscle fibers. This may be a compensatory response to increased resistance at the pharyngoesophageal segment, with elevated HPCI utilized to overcome this differential or due to poor hyolaryngeal elevation failing to distract the UES in a timely manner (as suggested by decreased Hmax values in VFSS). Other authors have suggested hypercontractility may reflect muscle fiber transformation to slow-twitch fibers which demonstrate sustained tetanic contraction.[21] Our study did not examine histologic specimens or electrophysiological metrics to allow us to confirm or refute this suggestion. We also identified abnormally high PeakP suggesting increased muscle tension during swallowing, again a possible compensatory strategy to negotiate greater outlet obstruction in people with PD. Similar findings were reported by Szczesniak and colleagues in a study of 64 people with PD compared to age-matched healthy controls.[10] They identified significantly elevated PhCI, velopharyngeal contractile integral (VCI), and HPCI, although no significant difference was evident for MCI.[10]

In the current cohort we found abnormally high UES IRP and decreased UES MaxAdm indicating possible increased flow resistance and impaired UES distensibility. UES IRP is a measure sensitive to changes in both pressure difference and duration of relaxation. Our findings are consistent with previous work.[11]

4.2 | Comparative findings of VFSS and HRIM metrics

Longer bolus transit time (OPT, HPT, and TPT measured on VFSS) was significantly correlated with elevated contractility (VCI, HPCI, PhCI), elevated hypopharyngeal peak pressure, and increased UES maximum admittance on HRIM. This suggests attempts by the pharynx to compensate weakness—the pharyngeal muscles are producing more effort (hence elevated pressures) to try to increase bolus velocity and pass the bolus distally, in order to maintain normal bolus transit time. Extended bolus transit times

TABLE 5 Correlations between average for pressure-impedance metrics and videofluoroscopic measures.

	VFSS Quantitative measures												
	Duration measures (s)							Displacement measures (cm)			Ratio		
HRIM measures	OPT	HPT	TPT	Airwaycl	Airwaydur	PESdur	Hdur	PESmax	Hmax	HLmax	PCR	BCR	PAS
PhCI	0.599*	WC	WC	WC	WC	WC	WC	−0.438	WC	WC	WC	WC	WC
VCI	0.547*	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC
MCI	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	0.431	WC	WC
HPCI	WC	WC	0.472*	0.614**	−0.719**	WC	WC	−0.429	WC	WC	WC	WC	WC
PeakP	WC	0.476*	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC
UES IRP	0.407	WC	WC	WC	WC	WC	WC	0.484*	WC	WC	WC	WC	0.407
UES RT	WC	WC	WC	−0.611**	0.617**	WC	WC	WC	WC	WC	WC	WC	WC
UES MaxAdm	WC	WC	0.606**	WC	WC	0.453*	WC	WC	WC	WC	WC	WC	WC
IBP	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC
UES CI	WC	WC	WC	WC	WC	0.515*	WC	WC	WC	WC	WC	WC	WC
UES BP	WC	WC	WC	WC	WC	WC	0.571*	WC	WC	WC	WC	WC	0.424
UES PeakP	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC
DCL	WC	WC	WC	WC	WC	0.596**	WC	WC	WC	WC	WC	WC	0.582**
BPT	WC	WC	0.407	WC	WC	WC	0.400	WC	WC	WC	WC	WC	WC
PCI	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC	WC
SRI	WC	WC	WC	WC	WC	WC	WC	−0.414	WC	WC	WC	WC	WC

Note: Data from spearman rank order correlation coefficients (r), WC: non-significant weak correlation (0 to 0.39), Moderate correlation (0.4 to 0.59), Strong correlation (0.6 to 0.79), Statistical significance (in bold) *$p < 0.05$, **$p < 0.01$.

Abbreviations: airwaycl, airway closure; airwaydur, airway closure duration; BCR, Bolus clearance ratio; BPT, Bolus Presence Time; DCL, pharyngeal distension-contraction latency; Hmax, Maximum hyoid displacement; HLmax, Hyoid-larynx displacement; HPCI, hypopharyngeal contractile integral; HPT, Hypo-pharyngeal transit time; IBP, Intra-bolus distension pressure; IR, post-swallow impedance ratio; MCI, mesopharyngeal contractile integral; OPT, Oro-pharyngeal transit time; PCI, pharyngeal contractile integral; PeakP, peak pressure; PES, pharyngoesophageal sphincter; SRI, swallow risk index; TPT, total pharyngeal transit time, Hdur, MAximum hyoid displacement duration; PESdur, PES opening duration; PESmax, maximum opening of the PES; PCR, pharyngeal constriction ratio; UES CI, UES contractile integral, UES BP, UES basal pressure; UES IRP, UES integrated relaxation pressure; UES, Upper-esophageal sphincter; UES RT, UES relaxation time; UES PeakP, UES peak pressure UESMaxAdm, UES maximum admittance; VCI, velopharyngeal contractile integral.

suggest that the compensation is incomplete. Despite increasing UES MaxAdm (reducing resistance) bolus transit durations are still prolonged because there is also decreased opening duration of the UES. Airway duration measures acquired on VFSS (Airwaycl, Airwaydur) were strongly correlated with HPCI and UES RT in the current study also suggesting that the airway is attempting to stay closed for the full duration of bolus passage. No previous studies evaluated pharyngeal pressure metrics with bolus transit scores from VFSS[22,23].

As we expected, PES opening duration (PESdur) was positively correlated with UES MaxAdm, UES contractile integral (UES CI), and distension to contraction latency (DCL). In effect, this is normal biomechanics in action and preserved in this cohort of participants with mild PD. A longer UES opening time increases UESmaxAdm. The extent of PES opening is positively correlated with UES IRP, as we would expect because UES opening requires cessation of UES tonic contraction reducing UES resistance and thereby helping normalize the IRP.

Szczesniak et al. suggested that reduced hyoid elevation affects the extent of UES opening and that this can lead to increased resistance to bolus flow.[10] This association matches our clinical finding where impaired hyolaryngeal function on VFSS was seen alongside abnormally high pressure in the hypopharynx and UES regions. Lack of superior motion of the hyoid complex diminished distraction at the UES and so an increase in hypopharyngeal drive is needed to achieve bolus transit.

Finally, the PAS score was negatively (significantly) correlated with DCL which has been established in previous work.[22] A shorter time between distension and contraction during bolus flow will effectively segment the bolus and result in need for repeat swallows, or leave residue in the pharynx after the swallow has completed. This poses a possible risk for swallow safety as inability to fully clear bolus from the pharynx can predispose to post-deglutitive aspiration. Further research is needed to validate the relationship between these variables.

4.3 | Clinical implications

Gradual and subtle changes occur in the pharynx that may initially go unnoticed by the patient. The individual may slowly adapt to the changes by instituting changes in diet choices, lengthening of mealtimes, and adding compensations such as fluid with meals. In this cohort of participants with mild PD, the congruence of HRIM measures with VFSS metrics is heartening and provides support for the use of these tools individually and in concert to describe swallowing function. The complementary nature of the parameters helps elucidate pathophysiologic swallow changes and therefore, may provide an indication of which intervention may be most useful for any individual. Reassuringly, both assessment platforms identified early swallow changes, when penetration-aspiration scores alone did not, indicating that they are sensitive to swallow decline. We can also, therefore, expect that they would identify improvements in swallow metrics that may occur following intervention, confirming that reassessment with HRIM and VFSS to monitor therapy benefit, may be valid.

4.4 | Limitations and future directions

HRIM and VFSS were performed sequentially (not simultaneously), and results may vary due to different swallows being analyzed. However, we performed both assessments during the "on" state and within a 24-h window, to minimize any possible changes in participant status. Secondly, we reported pharyngoesophageal swallow biomechanics of 21 early/mid-stage PD participants. Although we analyzed a reasonable number of swallows in each participant, these are preliminary findings derived from a small cohort. Recruitment efforts were unable to include many participants in the moderate to advanced stage of PD. Future studies should include a larger sample size with a wider range of disease severity. We have compared our findings with normative data and did not evaluate a stand-alone age-matched control group. Normative data ranges are provided by the open-source SwallowGateway web-based application and are homogenized data from adults across wider age range (20-78 years), and therefore may not be generalizable to older people (> 65 years). Some changes highlighted in the study may be due to aging rather than specific to PD.

5 | CONCLUSION

This study is the first to identify early manometric signs and congruent VFSS metrics of pharyngeal dysfunction in the PD population using validated HRIM metrics across increasing thin bolus volumes. It helps us define the place of HRIM evaluation in the PD population. The congruence of VFSS and HRIM measures confirms our biological hypothesis of slow early decline in PD that is subtle and as yet has not resulted in airway violation or severe swallowing consequences. Multi-modal evaluation of deglutition, combining objective HRIM with VFSS and patient-reported outcome measures provides a comprehensive clinical characterization of swallow biomechanics, assisting in the diagnosis of pharyngoesophageal disorders in people with PD. Understanding subtle and early physiological changes in PD has the potential to optimize dysphagia diagnostic frameworks for PD and support targeted early maintenance exercises or rehabilitation regimens to preserve safe swallowing.

AUTHOR CONTRIBUTIONS

Conceptualization and designing the research study: SS, AM, JA. *Data curation*: SS, AM, JA. *Formal analysis*: SS, AM. *Performed the research*: SS, AM, JA. *Writing–original draft*: SS. *Writing–review & editing*: SS, AM, JA.

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CONFLICT OF INTEREST STATEMENT

The authors have no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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