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Using high resolution manometry impedance to diagnose upper esophageal sphincter and pharyngeal motor disorders

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Abstract

Background: Oro-pharyngeal pathophysiology, including upper esophageal sphincter (UES) and pharyngeal disorders, can be assessed by pharyngeal high-resolution manometry impedance (P-HRM-I). We aimed to establish methodology to diagnose disorders utilizing P-HRM-I, hypothesizing that the objective measures could be used to diagnose disordered deglutition evidenced by greater aspiration scores.

Methods: Patients (n = 509, 18–91 years) were compared to controls (n = 120, 20–94 years). Variables measuring UES relaxation, UES opening extent, intrabolus pressure, and pharyngeal contractile strength were derived for 10 ml liquid swallows. Three associated pharyngeal pressurization patterns, which may be indicative of obstructed flow, were characterized: pan-pressurization (Type 1), distal compartmentalized pressurization (Type 2), and transient pressurization (Type 3). Deglutitive aspiration was determined from video fluoroscopy.

Results: UES relaxation pressure was best able to differentiate patients from controls (T 6.528, $p < 0.0001$). Patients with abnormal relaxation pressure (>8 mmHg) more frequently exhibited pharyngeal pressurization patterns and had adjunct evidence of reduced luminal distensibility (high intrabolus pressure and/or reduced UES opening). Utilizing this information, a diagnostic scheme was devised identifying 138 patients with UES disorder. A further 96 patients without evidence of UES disorder had abnormally weak pharyngeal pressures, confirming propulsive disorder. Amongst a sub-sample of 320 patients undergoing video fluoroscopy, those with pharyngeal pressurizations and adjunct evidence of reduced UES relaxation and/or distensibility had higher aspiration scores (Chi-square 60.169, $p < 0.0001$).

Conclusion: P-HRM-I can provide evidence for UES disorder based on pharyngeal pressurization patterns and abnormal findings for UES relaxation pressure, UES opening, and intrabolus pressure. Measuring pharyngeal contractility requires further optimization.

KEYWORDS
diagnosis, dysphagia, high-resolution manometry, impedance, swallowing, upper esophageal sphincter

Charles Cock is consided to be joint first author.

1 | INTRODUCTION

Deglutitive disorders lead to dysphagia symptoms in a wide range of pathologies[1] that impair relaxation and opening of the upper esophageal sphincter at the pharyngo-esophageal junction (UES disorder) or weaken the contractility of all or part of the pharyngo-esophageal segment musculature (propulsive disorder). The diagnosis of deglutitive disorders requires clinical swallow assessment for which high-resolution manometry impedance (P-HRM-I), a catheter-based diagnostic, is emerging in clinical gastroenterology, otolaryngology, and speech pathology practice.[2–7]

Current recommendations on P-HRM-I assessments of oropharyngeal swallowing include guidance on deriving eight physiological measures that define pharyngeal contractile vigor as well as UES pressure relaxation and opening.[8] These parameters have already been helpful for characterizing the physiological and potential rehabilitative effects of swallowing exercise,[9,10] sensory stimulation,[11] and novel surgical interventions.[12,13] These measurements can complement routine clinical and instrumental swallowing assessments by adding understanding of the pathophysiology of dysphagia that may help guide patient management. However, further evidence is required to objectively confirm that P-HRM-I assessments can differentiate disordered swallowing in patients from normal swallowing in asymptomatic controls and/or differentiate patients who are at aspiration risk from those who swallow safely. To provide this information, we performed a multi-center audit of a large sample of control and patient P-HRM-I assessments. With a focus on UES disorder, our primary aims were to (i) determine which P-HRM-I derived variables could distinguish pathological swallowing from healthy swallowing patterns as well as age-related effects and (ii) to use any identified measures to devise a framework to objectively diagnose a UES disorder. Evidence for pharyngeal propulsive disorder was also examined as a secondary aim. We hypothesized that the objective measures best able to distinguish pathological swallowing could be used to diagnose disordered deglutition evidenced by greater aspiration scores.

Key points

- Oro-pharyngeal pathophysiology, including upper esophageal sphincter (UES) and pharyngeal disorders, can be assessed by pharyngeal high-resolution manometry impedance (P-HRM-I).
- This study aimed to establish methodology to diagnose disorders utilizing P-HRM-I.
- P-HRM-I based assessments can provide evidence for UES disorder, however P-HRM-I assessment of pharyngeal contractility requires further optimization.

2 | METHODS

2.1 | Database

P-HRM-I studies from three centers were included: Flinders Medical Centre (Adelaide Australia), St George Hospital (Sydney, Australia) and University Hospitals of Leuven (Leuven, Belgium). Controls were healthy volunteers, asymptomatic of dysphagia. Patients had differing etiological/clinical backgrounds typical for an oropharyngeal swallowing disorders clinic. Informed consent was provided by all participants (approvals: Southern Adelaide Human Research Ethics 403/10, 283/11, 552/13, 76/17, 189/17; St Vincent's Hospital Human Research Ethics Committee; Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee, NTEC 2019.183; Medical Ethics Committee Leuven approve number S58093 (17.7.2015)).

To provide data uniformity, only data acquired with the MMS platform and *Unisensor* solid-state HRM-Impedance catheters were included (supplied by Medical Measurement Systems, The Netherlands). A range of catheter designs were utilized across the three Centers (K102559-E-1245-D; K103659-E-12100-D; K103659-E-1180-D; K103659-E-1236-D; K83259-E-1263-D), these incorporated 25–36 1 cm spaced pressure sensors (unidirectional) and an impedance electrode array comprising 12–18 segments of 2-cm width. The P-HRM-I studies were prospectively uploaded (Sept 2016–Oct 2021) and analyzed using Swallow Gateway™ software (Finders University, Adelaide Australia).[14,15] 10 ml thin liquid bolus swallows were used as this test bolus had been acquired in triplicate by all Centers. Bolus media included electrolytes for conductivity, either normal saline or the Standardized Bolus Medium (SBMkit, Trisco Foods, Brisbane, Australia).[16] For video fluoroscopy, radio-opaque contrast was added (liquid barium or an iodinated contrast medium).

2.2 | Analysis P-HRM-I recordings: pharyngeal pressurization patterns

Pharyngeal pressurization waves are recognizable on P-HRM-I recording and considered suggestive of obstructed pharyngeal outflow resulting from impaired luminal distensibility or miss-timed luminal opening,[17] analogous to esophageal pressurizations reported in relation to 'type 2' esophageal achalasia and esophago-gastric junction outflow obstruction.[18,19] Swallows were viewed with the pressure heat-map color scale set to range −10 mmHg (blue) to 100 mmHg (red). The hypopharyngeal pressure profile over time for each swallow was visually assessed for presence of pressurization patterns during UES relaxation exceeding 20 mmHg. Three different pressurization patterns were characterized.[17] Sustained pressurizations occurring for the majority of the UES relaxation period were subtyped into those with no visible stripping contraction and a simultaneous pan-pressurization (Type 1) and those terminated by arrival of an intact stripping contraction (Type 2). Transient pressurization patterns (Type 3) occurred for brief periods during the early-mid phase of UES relaxation and terminated before arrival of the stripping contraction (Figure 1).

2.3 | Analysis P-HRM-I recordings: swallow variables

Swallow variables prescribed by a pharyngeal high-resolution manometry working group[8] were derived. Together, these variables can determine the neurophysiological and biomechanical properties of the pharyngo-esophageal segment region during deglutition.[16,20]

2.3.1 | Upper sphincter relaxation and distensibility

Four of the variables are considered most relevant to the UES region.

(i) Upper sphincter integrated relaxation pressure (UES IRP, mmHg) indicating the extent of pressure drop during UES relaxation.
(ii) Upper sphincter relaxation time (UES RT, s) indicating duration of pressure drop during UES relaxation.
(iii) Upper sphincter maximum admittance (UES MaxAd, mS) corresponding to maximum luminal opening cross-sectional area (CSA).
(iv) Intrabolus distension pressure (IBP, mmHg) corresponding to the pressure 1 cm superior of the UES apogee position at the time of maximum hypopharyngeal distension deduced from impedance.

As described below, these variables define whether neural UES relaxation is incomplete and allow associated inferences regarding whether the distensibility of the UES lumen is impaired.

The cricopharyngeus muscle (CPM) is the major muscle component of the UES high-pressure zone. The UES pressure profile (contraction—relaxation—contraction) is known to correlate with the state of CPM activity (activation–deactivation–activation).[21] Thus, a high UES IRP (>95th percentile) and/or short UES RT (<5th percentile) may indicate failure of CNS circuits that mediate the extent and/or timing of CPM deactivation, leading to *incomplete* UES relaxation.[17]

However, appropriate neural deactivation of CPM is not the only aspect influencing the ability of the UES to open sufficiently to enable effective bolus flow. Bolus forces acting from within, hyolaryngeal traction forces acting extrinsically, and the intrinsic compliance of the relevant tissue layers are the main determinants of UES opening. The distensibility of the gastrointestinal lumen and sphincters can be inferred using modalities that simultaneously determine luminal CSA (or its equivalent i.e., Ω impedance or mS admittance) and the corresponding intraluminal distension pressure.[22,23] Thus, a low UES MaxAd (<5th percentile ~ reduced CSA at the peak distension) and/or high IBP (>95th percentile indicating elevated luminal pressure at peak distension) were considered congruent with *impaired* UES distensibility.

2.3.2 | Pharyngeal contractility

Pharyngeal contractile integrals quantified contractile strength of the total pharynx (PhCI, mmHg.cm.s) and its sub-component regions; the

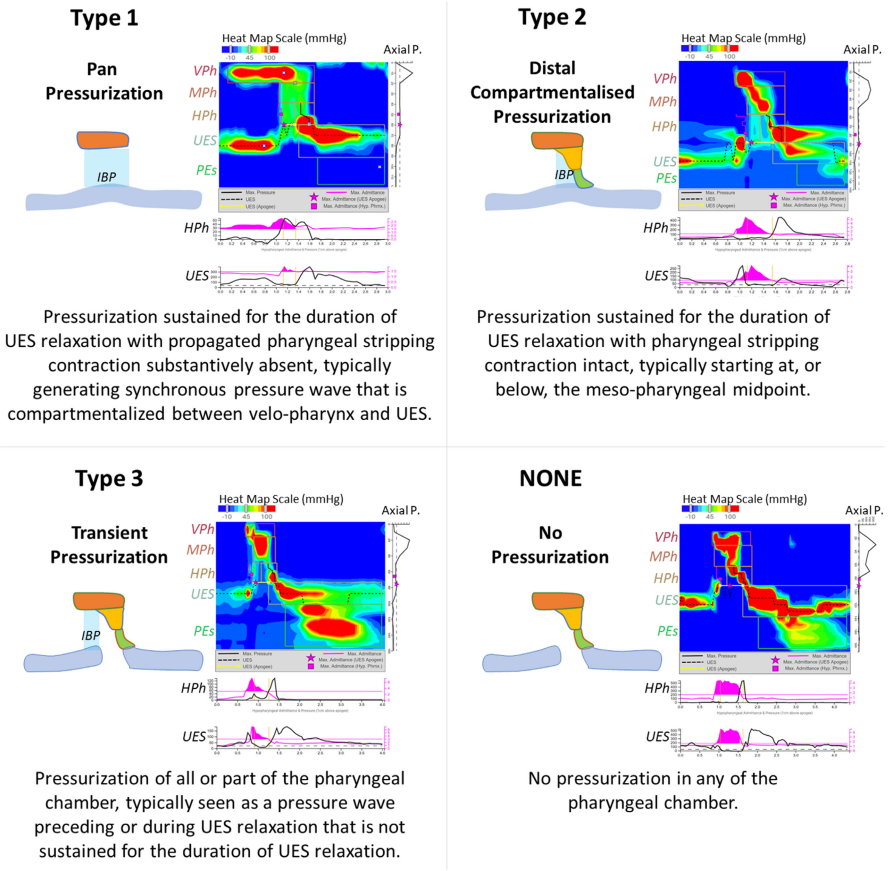

FIGURE 1 HRM Impedance recordings of swallows demonstrating different pharyngeal pressurization patterns during UES relaxation. Each panel shows a schematic drawing alongside a pressure heat map of a representative patient example swallow (low pressures blue to high pressures red). Line plots below show pressure (black line, mmHg) and bolus admittance (pink line, mS) in the hypopharynx and UES high-pressure zone. The line plot left shows axial pressure gradient at the time of maximum UES opening. HPh, hypopharynx; IBP, intrabolus pressure; MPh, mesopharynx; PEs, proximal esophagus; UES, upper esophageal sphincter; VPh, velopharynx.

velo-, meso-, and hypopharynx (VCI, MCI, HPCI, mmHg.cm.s). The mean peak pressure in the hypopharyngeal region (PeakP, mmHg) was also determined, this being the only P-HRM contractile metric to date validated for defining adequacy of pharyngeal propulsive forces in the context of UES dysfunction (post-CRT cricopharyngeal stricture[24]). Low PeakP readings have also been found to be the best predictor of post-swallow aspiration and piriform sinus residue.[25]

2.3.3 | Other Swallow variables

The *Swallow Risk Index* (SRI) assessed global swallow function.[16] SRI combines four variables; PeakP (as above), IBP (as above) and two flow timing measures, pharyngeal distension to contraction latency (DCL, s), measuring the time from peak of the bolus distension wave to the peak of the contraction wave, and bolus presence time (BPT, s), measuring the dwell time of the bolus in the hypopharynx. Abnormal DCL and/or BPT indicate altered timing and/or duration of the bolus distension wave, indicative of poor oro-lingual bolus coordination and/or inappropriate modulation to volume.[2,16,26]

2.4 | Dysphagia signs and patient-reported outcomes

For all patients who underwent concurrent video fluoroscopy, severity of airway aspiration could be determined using the penetration-aspiration scale (PAS) score.[27] The maximum PAS for 10 ml liquid swallows was used to determine aspiration risk (score 1 = none, 2–5 = penetration, 6–8 = aspiration below vocal folds). If available, data for the normalized residue ratio scale, defining post-swallow vallecular and piriform residue (NRRSp and NRRSv[28]) and Sydney swallow questionnaire (SSQ) defining patient-reported symptoms,[29] were included.

2.5 | Statistical analysis

Proportionate data were compared using Fisher's Exact test. Grouped data for continuous measures were compared using Mann–Whitney *U* Test and Independent Samples Kruskal–Wallis Test for multiple comparisons and adjusted by Bonferroni correction. A *p*-value <0.05 was considered to indicate statistical significance.

3 | RESULTS

One hundred and twenty asymptomatic controls, including 19 octa/nonagenarians (45% male, average (SD) age 56 (21) years; range 20–94 years), were included alongside 509 patients (58% male, average (SD) age 64 (14) years; range 18–91 years). The patient group was heterogeneous with a range of different etiological/clinical presentations, the largest subgroups ($n \geq 5$ cases) being Parkinson's disease (66, 13%), head and neck cancer (66, 13%), cerebrovascular accident—stroke (28, 5.5%), motor neuron disease (27, 5.3%), Zenker's diverticulum (26, 5.1%), obstructive sleep apnea syndrome (26, 5.1%), non-neurological post-extubation intensive care patients (24, 4.7%), myopathy (22, 4.3%), cricopharyngeal bar (15, 2.9%), anterior cervical discectomy and fusion surgery (13, 2.6%), osteophytes (13, 2.6%), globus (11, 2.2%), vocal fold palsy (10, 2%), and presbyphagia (5, 1%). The remaining patients included idiopathic causes (44, 8.6%), gastrointestinal disease (37, 7.3%), and other causes with <5 individual case examples of non-neurological origin (44, 8.6%) or neurological origin (32, 6.3%).

Compared to the control group, patients overall had weaker meso-pharyngeal and hypo-pharyngeal contractility, higher IBP, higher UES IRP, reduced UES MaxAd, shorter DCL, and higher global SRI (Table 1). Only three variables, all indicative of UES relaxation and distensibility; UES IRP, IBP, and UES MaxAd, also showed an overall age group related effect (Table 1). The individual data distributions for these key UES variables are shown in Figure 2A,B. UES IRP demonstrated the most robust differences for age (Figure 2B).

The upper limit of normal (95th percentile) for UES IRP was >8 mmHg, and IBP was >25 mmHg and the 5th percentile for UES MaxAd was <3.7 mS. Overall, 28% of patients were considered to have an abnormally *high* UES IRP value. Patients with evidence for impaired UES distensibility due to an abnormally *high* IBP and/or a *low* UES MaxAd were more likely to also have a *high* UES IRP (Figure 3A). Thus, all three measures were considered interrelated and suggestive of UES disorder.

Type 1 pharyngeal pressurization was observed in 6.5% of patients and never observed in asymptomatic controls, thus always abnormal. Type 2 pressurization was observed in 10.6% of patients and two controls (both over 80 years). Type 3 pressurization was observed in 26.3% of patients and 17.5% of controls. Few (<10%) of the patients without any visible pressurization pattern had high UES IRP. The majority (>75%) of patients with Type 1 and 2 pressurization patterns had high UES IRP. Only 1/3 of patients with a Type 3 pressurization pattern had high UES IRP (Figure 3B). A scheme to diagnose a putative UES disorder and propulsive or other disorders was devised utilizing the patterns and metrics shown in the current study to best able to discriminate patients from controls (Figure 4). Prevalence of evidence for UES disorder according to this scheme ranged from 8% in obstructive sleep apnea to 54% in patients with known osteophytes. Pharyngeal propulsive disorder was most common in myopathy patients (Figure 5A).

Video fluoroscopy imaging data were available for 320 patients, aspiration risk was greatest in the group with evidence of UES disorder (Figure 5B); medians for max PAS scores were highest in both UES and propulsive disorder groups (Figure 5C). Patient-reported data (SSQ) were collected for 91 patients at the time of investigation. Patients with deglutitive disorders were more symptomatic, and the highest median SSQ was observed in the group with evidence of propulsive disorder (Figure 5D). Post-swallow bolus residue data were available for 90 patients. Vallecular residue was not significantly different;however, piriform sinus residue was significantly elevated in patients with propulsive disorder (Figure 5E).

TABLE 1 Swallow variable main effects in relation to patient and older age group

Phenomena	Variable	Controls vs. patients (MWU)	Age group effects (KWT)
Pharyngeal contractility	PhCI	*T* 0.565	*T* 3.466
	VCI	*T* 1.218	*T* 1.815
	MCI	↓*T* 3.443, $p = 0.001$	*T* 1.598
	HPCI	*T* 0.857	↑*T* 9.967, $p = 0.019$
	PeakP[a]	↓*T* 5.015, $p < 0.001$	*T* 0.823
UES relaxation and distensibility	**UES IRP**	**↑*T* 6.528, $p < 0.0001$**	**↑*T* 71.964, $p < 0.0001$**
	UES RT	*T* 1.377	*T* 0.481
	UES Max Ad.	**↓*T* 6.847, $p < 0.0001$**	**↓*T* 21.532, $p < 0.0001$**
	IBP[a]	**↑*T* 3.183, $p = 0.001$**	**↑*T* 19.594, $p < 0.0001$**
Bolus distension timing	DCL[a]	↓*T* 7.283, $p < 0.0001$	*T* 4.117
	BPT[a]	*T* 1.129	*T* 5.898
Global function	**SRI**	**↑*T* 6.005, $p < 0.0001$**	**↑*T* 18.522, $p < 0.0001$**

Note: Data are *T* and *p*-value (if significant) for Mann–Whitney *U* Test (MWU) and Independent Samples Kruskal–Wallis Test (KWT). "↓↑" indicates the directionality of change in the metric.
[a]Identifies the four variables that are included in Swallow Risk Index (SRI). Variables showing significant effects in relation to both patient and older age group are highlighted in bold.

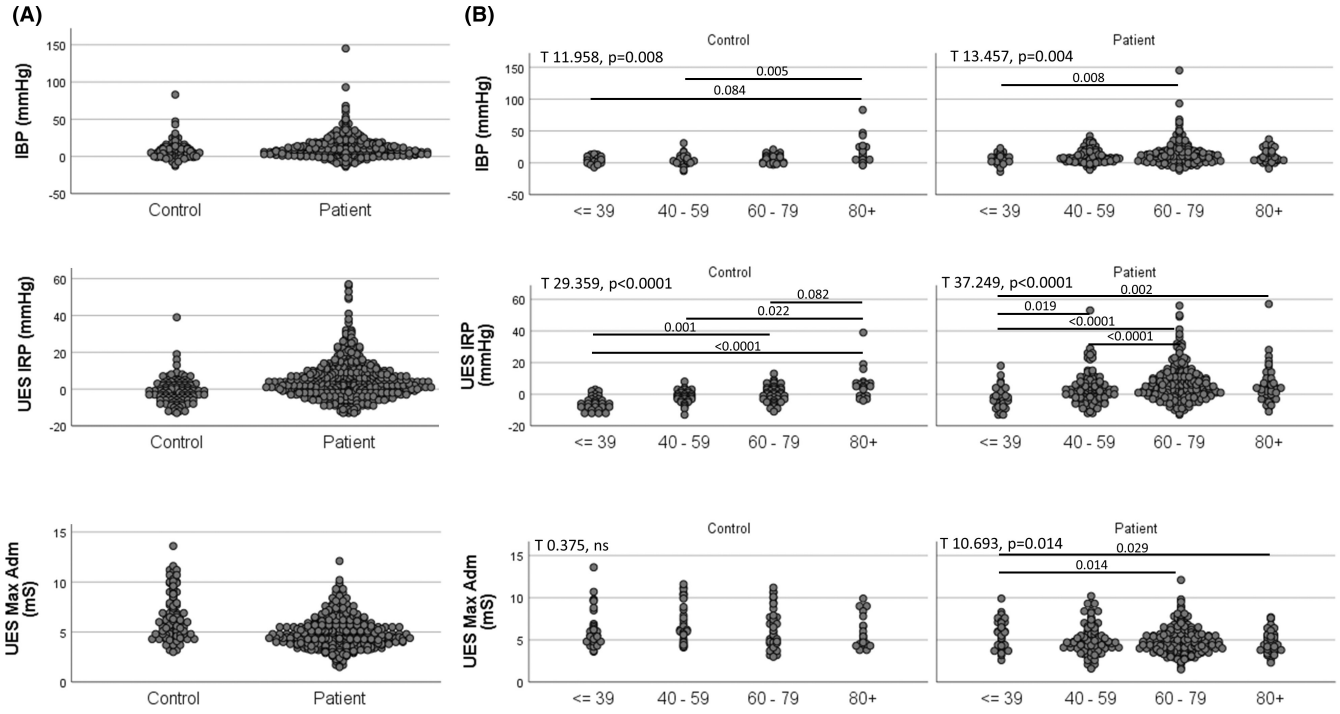

FIGURE 2 Data distribution for key upper esophageal sphincter variables. (A) Group (see Table 1 for significance). (B) Age sub-group differences within controls and patients. Compared by Independent Samples Kruskal–Wallis Test (*T*, *p*-value); pairwise comparisons are adjusted by Bonferroni correction for multiple tests

4 | DISCUSSION

Swallowing disorders occur when normal bolus transfer from the oropharynx to esophagus is impaired due to incomplete relaxation and/or impaired distensibility of the UES region and/or insufficient propulsive force being generated by the pharyngeal musculature contracting sequentially across three anatomically distinct regions. Thus, P-HRM-I-based assessments of UES relaxation and luminal distensibility, in combination with pharyngeal muscle contractility, provide a logical starting point for characterizing oropharyngeal motor disorders. In a range of clinical and experimental settings, P-HRM-I can be used to assess swallowing physiology, pathophysiology, and the impact of therapeutic interventions,[8] and it can be performed simultaneously, concurrently, or independently of radiographic or endoscopic imaging and is practical for bedside use in settings such as intensive care.[30] This study used

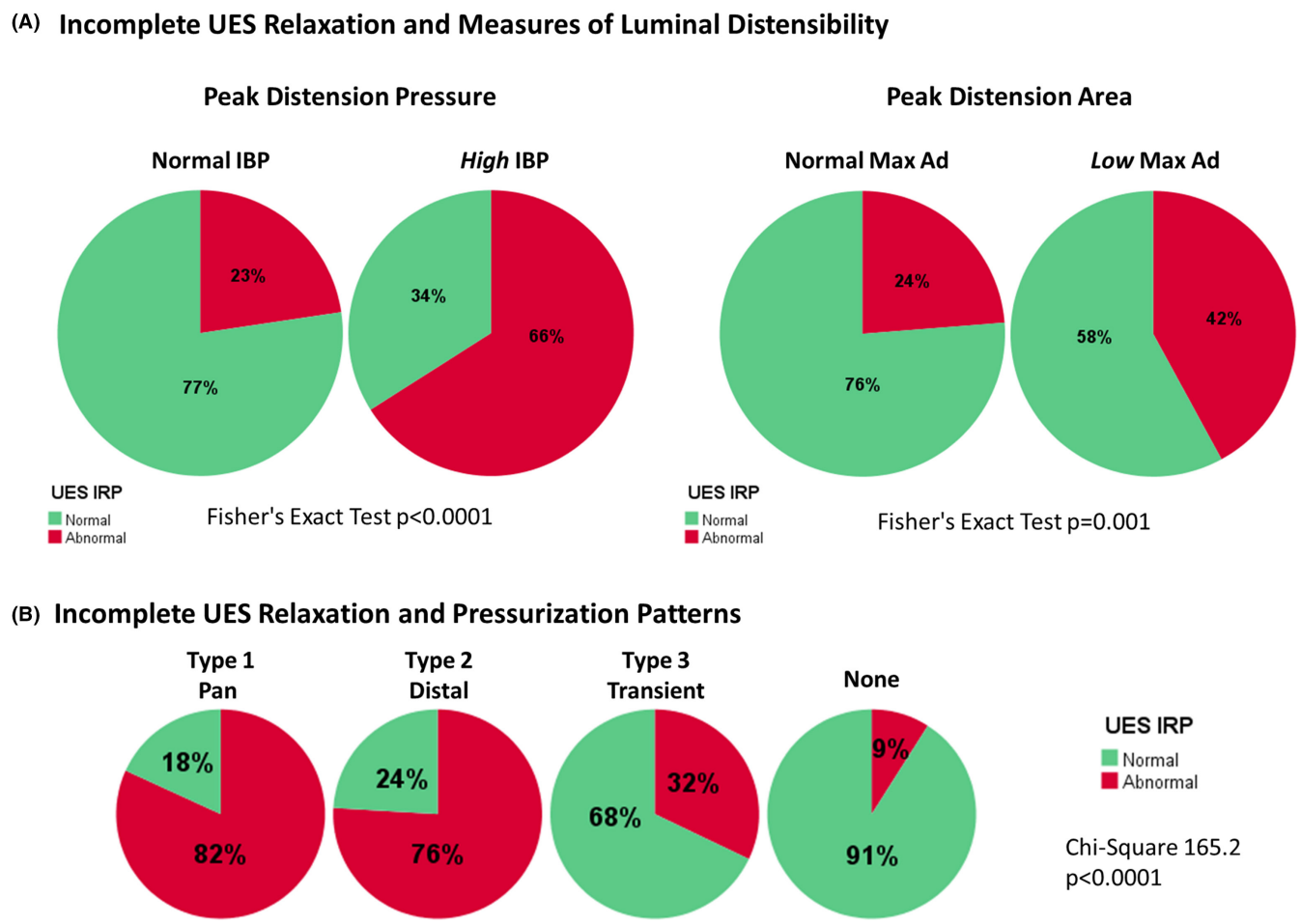

FIGURE 3 Association of abnormal UES IRP and other abnormalities suggestive of UES Disorder. (A) At peak distension, luminal distensibility is a function of cross-sectional area and distension pressure. Most patients with a high IBP and many patients with low UES MaxAd have associated incomplete UES relaxation. (B) Pharyngeal pressurization patterns are suggestive of obstructed pharyngeal outflow, and most patients with a Type 1 and 2 and many patients with Type 3 pressurization have associated incomplete UES relaxation.

an extensive control dataset to establish the objective normative thresholds defining evidence of disordered UES function within a broad patient cohort. Those patients who were objectively defined with disordered swallowing demonstrated higher aspiration scores.

4.1 | Evidence of UES disorder

Our use of parameters of UES relaxation and luminal distensibility is supported by past evidence from conventional manometry studies that have assessed exercise and cricopharyngeal muscle disruption.[31,32] The P-HRM-I literature also suggests that UES IRP and/or hypopharyngeal IBP are reliable predictors of post-chemoradiotherapy stricture[24] and are improved when the CP muscle is disrupted by dilatation[33] and cricopharyngeal peroral endoscopic myotomy (c-POEM).[12] Here, we confirmed previous reports of age-related impairment of UES function.[21,34–39] The patients exhibiting a range of evidence for a UES disorder were found to demonstrate the greatest aspiration scores. This is consistent with a report demonstrating association between aspiration and evidence for impaired UES relaxation.[40]

The UES IRP metric appeared to be the best able to differentiate patients from controls and detect age-related changes in UES function; thus, an abnormal UES IRP may provide the basis for diagnosing UES disorder. To reduce chances of false positive findings, it would be prudent to also identify adjunct features that could lend further support to diagnosis of UES disorder. These adjunct features could include abnormal findings for functionally associated metrics (IBP, UES admittance) and/or observation of pharyngeal pressurization patterns.

It is important to recognize that disordered UES outflow and pharyngeal contractile dysfunction are common co-presentations that exhibit complex biomechanical interactions. For example, the Type 1 pharyngeal pressurization pattern (Figure 1), which may be consistent with a downstream defect that impairs bolus flow through the UES, may also occur in conjunction with a pharyngeal propulsive disorder. For such cases, P-HRM-I may not be definitive and further investigation would be required to determine the optimal intervention. Conversely, an inadequate pharyngeal propulsive pump may fail

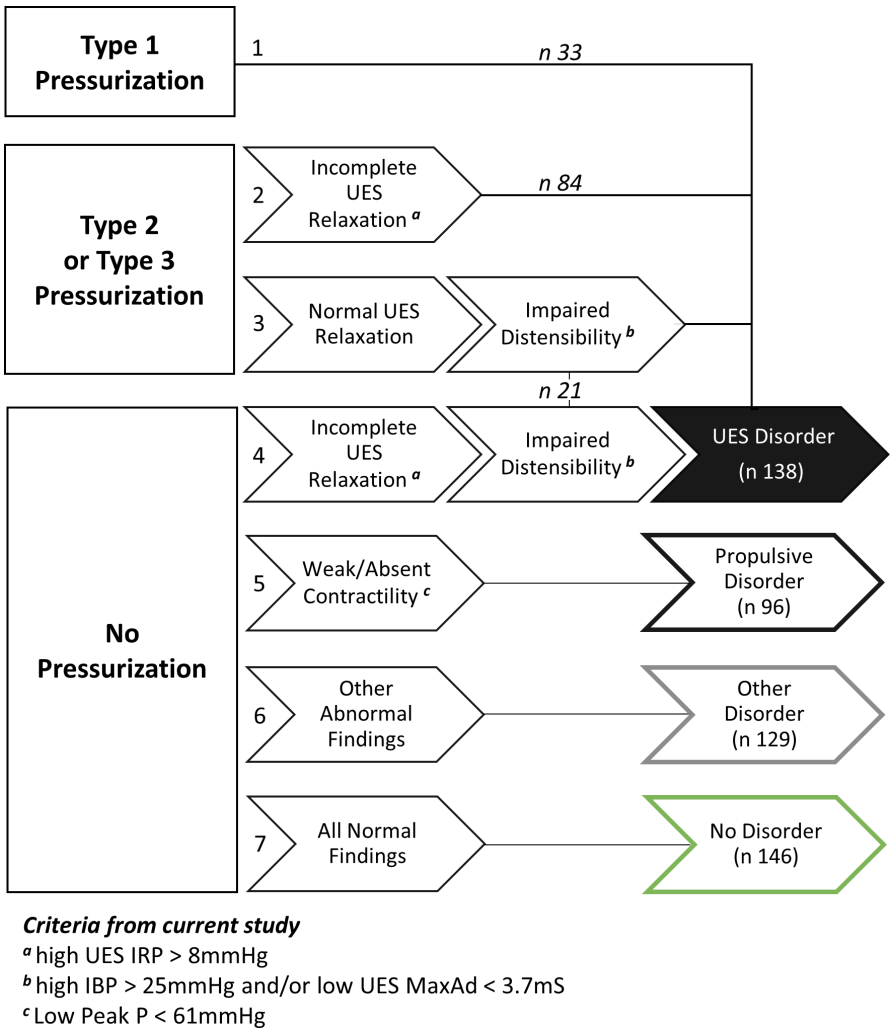

FIGURE 4 P-HRM-I Scheme for Putative UES disorders. *Rational*: This generic scheme uses selected patterns and variables best able to discriminate patients from healthy controls. Type 1 pan-pressurization pattern (Level 1) was given primacy as a clear biomechanical signature of outflow obstruction never seen in controls. Type 2 and 3 pressurization patterns were considered consistent with UES Disorder when seen in combination with evidence of incomplete UES relaxation (Level 2) and/or adjunct findings of impaired distensibility (Level 3). In patients without pressurization patterns, both incomplete UES relaxation *and* further adjunct findings of impaired distensibility were considered necessary to confirm UES Disorder (Level 4). For patients lacking any evidence for UES Disorder (Levels 5–7), pharyngeal propulsion was then considered, with weak or absent contractility defining a propulsive disorder (Level 5). The remaining cases were defined as having other disorders if they showed abnormal findings for one or more study variables and/or the SRI (Level 6), or otherwise no disorder if all variables were within normal ranges (Level 7). Disorder prevalence and associated dysphagia signs shown in Figure 5.

to generate the pressure required to reveal downstream defects that impair bolus flow. Thus, there is also the potential for a false negative finding. In post-chemoradiotherapy patients, weak propulsive forces negate the predictive value of IRP and IBP for detecting loss of UES distensibility due to cricopharyngeal stricture.[24] We would speculate that, in selected cases with a severely weakened pharynx, a low UES MaxAd alone may indicate a diminished UES opening resulting from impaired extrinsic hyolaryngeal traction forces and/or weak luminal distending forces due to poor propulsion, rather than UES disorder. A similar inter-relationship of propulsion and UES opening has been quantified radiologically.[41] Application via P-HRM-I would require further examination in a relevant patient population as well as clarity around metrics to characterize propulsive disorders, as discussed below.

4.2 | Evidence of pharyngeal propulsive disorder

The optimal way to objectively measure and quantify contractile forces for diagnostic purposes is presently a matter of debate. Contractile integrals are recommended.[8] However, within the current dataset, we observed very broad ranges for CI normal values (e.g. PhCI normal range 116–562 mmHg.cm.s), leading to a substantial overlap amongst controls and patients. Nevertheless, we utilized mean PeakP, a metric previously validated for determining hypopharyngeal contractile forces[24,42] as well as being predictive of aspiration and bolus residual.[25] In the current study, PeakP was best able to discriminate patients from controls on grounds of contractility. Amongst patients without UES disorder, those determined to have low PeakP were likely to aspirate and, in a subset analysis, had

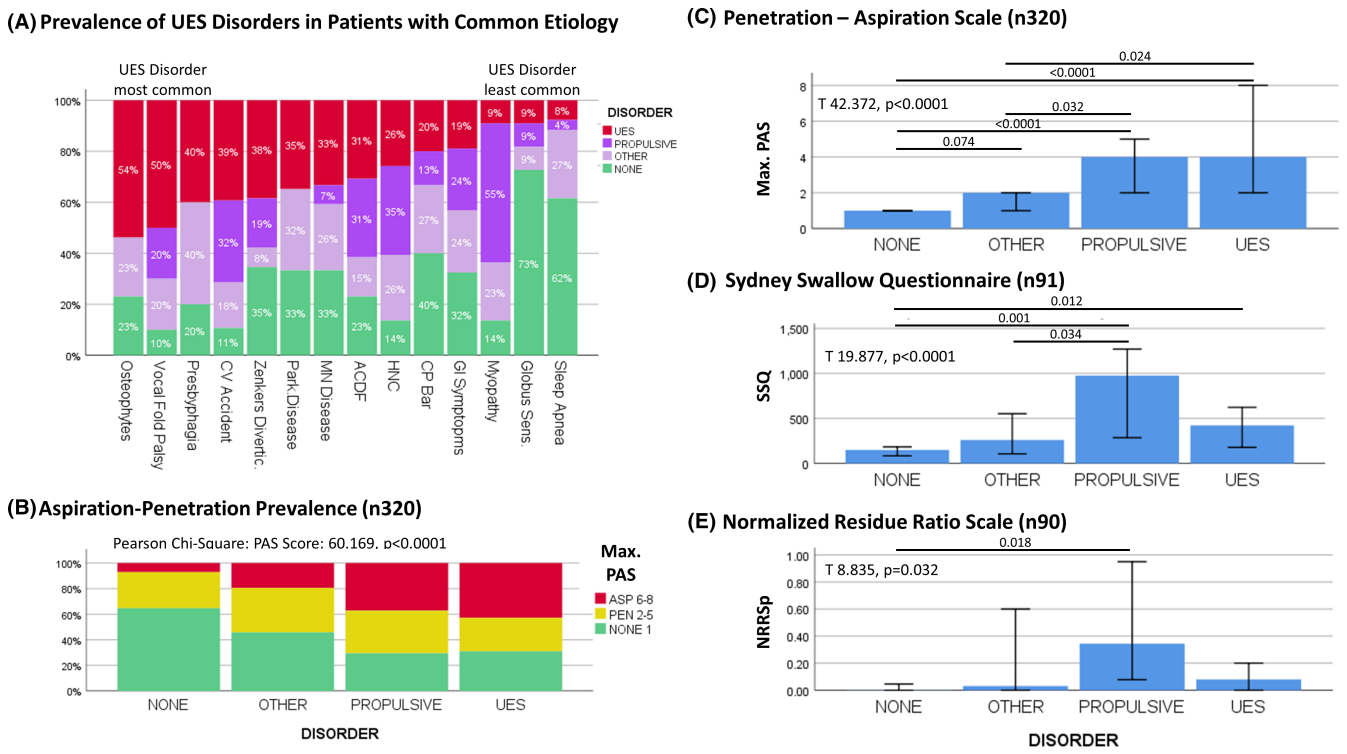

FIGURE 5 Disordered pharyngeal function in relation to etiology, instrumental assessment, and patient-reported outcome measures. (A) Prevalence of UES disorder (UES), propulsive disorder, other abnormalities (OTHER), and no abnormalities (NONE) within main etiological subgroups. (B) Prevalence of aspiration-penetration within different disorder groups. (C) Aspiration severity scores by disorder group. (D) Swallow questionnaire by group. (E) Piriform sinus residue by group. Data in C–E are medians with 95% confidence interval error bars with groups compared by Independent Samples Kruskal–Wallis Test (*T*, *p*-value); pairwise comparisons are adjusted by Bonferroni correction for multiple tests.

the greatest post-swallow residues and were the most symptomatic group overall based on available data from SSQ scores. Whilst very encouraging, diagnosis of pharyngeal propulsive disorders was not the primary aim of our study, and further investigations are required to determine the optimal classification method that considers all relevant anatomical regions.

4.3 | Strengths and limitations

The current study provided a rich dataset of swallowing assessments performed with reliable, state-of-the-art pressure-impedance technology, evaluating expert-recommended swallow function variables and showing swallowing safety, efficacy, and patient-reported symptoms. This allowed us to characterize the prevalence of upper sphincter abnormalities across the broad spectrum of dysphagia as well as within homogeneous patient subgroups. Importantly, we included patient subsets that demonstrate biomechanical features that may masquerade as a UES disorder, such as osteophytic cases with spinal protrusions unrelated to UES function per se. We also included several patient groups typically considered to have UES disorder; in these groups, the incidence of objective findings consistent with UES disorder was varied. This may suggest reduced sensitivity of our proposed approach or alternatively demonstrates that sometime features such as CP bar do not always produce a biomechanical signature of obstruction such as the reduced maximal dimension of UES and increased upstream IBP that has been described in relation to prominent CP bar.[43] Indeed, CP bar without associated abnormal features is unlikely to contribute to symptoms.[44]

There are several additional limitations that are important to acknowledge. Use of unidirectional pressure sensors may have introduced variability due to pharyngeal anteroposterior contractile asymmetry. Differences in system, catheter, and conductivity properties of the different test boluses used may have added variability to UES admittance readings. The outcomes of video fluoroscopy (aspiration and residue) and patient-reported outcomes were only available for a subset of the total cases described in this work. Other radiological parameters relevant to pharyngo-esophageal bolus flow were not examined. The analysis of data based on a single test bolus condition allowed us to report a large sample size; however, we recognize that effects of volume and viscosity of swallow challenges are also important to characterize; bolus flow rate and patterns of swallowing behavior are heavily influenced by test bolus conditions.[16,45] The normative thresholds for objective measures used to apply the proposed diagnostic scheme were based on the current dataset available. The scheme proposed is both preliminary and generic, and further research, including a more comprehensive suite of video

fluoroscopy measures, will be required to validate and optimize it. We acknowledge that the 20-mmHg pressure threshold used here to trigger characterization of pharyngeal pressurization patterns was intuitively based, optimal diagnostic variables may change as analytics evolve, and the abnormal diagnostic thresholds provided are protocol and system-specific. Our study considered UES opening and distension pressures independently in order to make inferences regarding luminal distensibility, whilst theoretically possible to integrate these measures to derive a single measure of UES distensibility (akin to the 'distensibility index' derivable using impedance planimetry[23]), we felt that taking this additional step was unnecessary to achieve our study aims and would introduce an unvalidated measure based on a potentially erroneous oversimplification of a relationship that requires more complex computational algorithms to determine accurately.

5 | CONCLUSION

Interventions to ameliorate dysphagia are planned based on suspected underlying pathophysiology in patients with radiological evidence of oropharyngeal swallowing disorders (aspiration or pharyngeal residue). Therefore, outcomes of swallowing assessments need to provide a differential diagnosis of a UES-based, pharyngeal-based, or combined disorder that can guide optimal treatment. In addition to dietary adjustments to ensure safe swallowing, targeted swallow exercises (e.g. Shaker exercise) or invasive intervention (dilatation or myotomy) may be considered for a suspected UES disorder; while a separate set of swallowing exercises or treatments (e.g. intravenous immunoglobulin in myopathies or neuro-muscular electrical stimulation paradigms) are considered for pharyngeal propulsive disorder. P-HRM-I based assessments can provide evidence for UES disorder that may explain dysphagia symptoms and guide therapy. The role of P-HRM-I-assessed pharyngeal contractility to define a propulsive disorder requires further optimization. This study represents a step toward achieving a broader classification system for oropharyngeal motor disorders based on this new diagnostic modality.

AUTHORS' CONTRIBUTIONS

TO, CC, NR: conceptualization, resources, data curation, formal analysis, methodology, software, writing – original draft, and writing– review & editing. PW, MSz, and MSc: data curation, formal analysis, and writing – review & editing. JT: conceptualization, resources, and writing – review & editing.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST

T Omari and N Rommel hold inventorship of the international patent family that covers the analytical methods described. The Swallow Gateway™ software service is owned and provided by Flinders University. All other authors report no conflict of interest.

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