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ORIGINAL ARTICLE

High-Resolution Pharyngeal Manometry and Impedance: Protocols and Metrics—Recommendations of a High-Resolution Pharyngeal Manometry International Working Group

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Abstract

High-resolution manometry has traditionally been utilized in gastroenterology diagnostic clinical and research applications. Recently, it is also finding new and important applications in speech pathology and laryngology practices. A High-Resolution Pharyngeal Manometry International Working Group was formed as a grass roots effort to establish a consensus on methodology, protocol, and outcome metrics for high-resolution pharyngeal manometry (HRPM) with consideration of impedance as an adjunct modality. The Working Group undertook three tasks (1) survey what experts were currently doing in their clinical and/or research practice; (2) perform a review of the literature underpinning the value of particular HRPM metrics for understanding swallowing physiology and pathophysiology; and (3) establish a core outcomes set of HRPM metrics via a Delphi consensus process. Expert survey results were used to create a recommended HRPM protocol addressing system configuration, catheter insertion, and bolus administration. Ninety two articles were included in the final literature review resulting in categorization of 22 HRPM-impedance metrics into three classes: pharyngeal lumen occlusive pressures, hypopharyngeal intrabolus pressures, and upper esophageal sphincter (UES) function. A stable Delphi consensus was achieved for 8 HRPM-Impedance metrics: pharyngeal contractile integral (CI), velopharyngeal CI, hypopharyngeal CI, hypopharyngeal pressure at nadir impedance, UES integrated relaxation pressure, relaxation time, and maximum admittance. While some important unanswered questions remain, our work represents the first step in standardization of high-resolution pharyngeal manometry acquisition, measurement, and reporting. This could potentially inform future proposals for an HRPM-based classification system specifically for pharyngeal swallowing disorders.

Keywords Deglutition · Deglutition disorders · Dysphagia · High-resolution manometry · Intraluminal impedance · Pharynx

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Introduction

In 2017, an independent *High-Resolution Pharyngeal Manometry* (*HRPM*) *International Working Group* was formed as a grassroots cooperative effort between clinicians and research investigators. The primary goal of this group was to facilitate communication between researchers and clinicians with clinical experience utilizing pharyngeal manometry to aid in the translational adoption of this novel technology. The entire Working Group includes 35 members from 20 different institutions (full list of the working group members is included in "Acknowledgments"). Our Mission is to create a standardization of high-resolution pharyngeal manometry acquisition, measurement, reporting, education,

and training as well as advocate with payers and healthcare systems. Our Vision is to improve the quality of dysphagia care through the clinical implementation of high-resolution pharyngeal manometry. This Working Group is independent and not sanctioned by any one organization or industry party.

A framework for clinical high-resolution *esophageal* manometry, called the *Chicago Classification*, was established through an international consensus process and describes disorders of the esophagogastric junction and disorders of esophageal motility [1]. At the present time, there is no comparable framework for pharyngeal disorders.

The aim of this current initiative was to establish a consensus around protocols and metrics and a diagnostic framework for HRPM. To achieve this, the Working Group undertook three tasks:

(i) To recommend a HRPM protocol based on a survey of current expert practices.
(ii) To perform a review of the literature to identify evidence underpinning particular HRPM metrics including HRPM with impedance.
(iii) To establish a core outcomes set of HRPM metrics via a Delphi consensus process.

Methods

Working Group Survey

A questionnaire was devised to survey the current HRPM practice of experts working in major referral centers who had performed > 200 solid-state HPRM investigations. The respondents (4 United States, 2 Australia, 1 Europe, and 1 New Zealand) identified themselves as speech and language pathologists (71%), physicians/surgeons (29%), and/or scientists (43%). All were engaged in clinical research and most (86%) were in clinical practice where HRPM was being used to aid diagnosis and to guide treatments.

Literature Review

A literature review was undertaken to examine the evidence underpinning pharyngeal pressure topography with and without impedance for the assessment of pharyngeal swallowing physiology and pathophysiology. An initial PubMed search using the search terms 'manometry' and 'pharynx' identified 832 publications between 1958 and June 2018. The database was then filtered to only include peer-reviewed publications that described pharyngeal pressure recordings using 'high-resolution' methodologies. To accomplish this, all Methodology Subgroup members reviewed the list of publications and had the opportunity to add any literature not included in the initial search results that they considered relevant. Papers were considered relevant if they presented pharyngeal and/or UES pressure data based on HRPM, defined as utilizing an array of at least 10 pressure sensors of 1 cm spacing. All papers that did not meet these criteria were deleted from the database, resulting in a total of 92 potentially relevant publications. The relevant publications were then randomly allocated among the Subgroup members who determined whether studies assessed swallow metrics against twelve previously agreed outcome topic areas (Table 2). Each member was then assigned an outcome topic area and undertook a 'mini-review' of the relevant publications (HRPM references in Table 2).

Delphi Consensus and Core Outcomes Set

The Working Group's consensus recommendation was determined via a Delphi process which is an established method for determining core outcomes sets [2]. The Delphi Consensus Group, comprising 10 of the Working Group members currently from 9 different programs, was asked to consider a total of 22 metrics (with associated definitions) and to indicate their support for inclusion of each metric in the core outcomes set. A voting score within the range of 1–9 was used to determine consensus for inclusion; whereby 1–3 indicated decreasing levels of clear disagreement (1 = absolute disagreement), 4 indicated slight disagreement, 5 was neutral, 6 indicated slight agreement, and 7–9 indicated increasing levels of clear agreement (9 = absolute agreement).

In addition to scoring the level of agreement, the Delphi Group was also asked to provide commentary for/against each metric based on available evidence and their experience. When several different metrics described the same phenomena within the same metric class (e.g., contractile pressure integral vs. mean peak pressure vs. absolute peak pressure), the Group was instructed to apportion support to favor the metric they considered to be the 'best' over all others.

A priori it was determined that consensus required that at least 70% of the Working Group agreed with the metric (scoring 7–9) and no more than 20% disagreed with the metric (scoring 1–3). All other score distributions were taken to indicate no consensus.

After completion of each round of voting, the scores for all metrics and any for/against commentary was anonymously tabulated and circulated to the Group for consideration before re-scoring. Thus, members could change their score in light of the group's collective opinion. Voting rounds continued until a stable consensus was reached.

Results

Working Group Survey

The main survey findings are summarized below:

Most respondents (72%) were acquiring both pharyngeal and esophageal data. All had the equipment and catheters to record impedance data and all were equipped to simultaneously acquire radiographic imaging.

Catheter intubation was routinely performed by speech and language pathologists (57%); however, physicians, surgeons, scientists, and nurses were also placing catheters. Most respondents (86%) utilized topical anesthesia to the nasal passages. The Working Group noted a recent trial showing a small reduction in pharyngeal pressures after application of 0.4 ml of 2% viscous lidocaine on a cotton tip applicator [3]. Without further confirmatory evidence, the clinical relevance of the reported change in healthy subjects was considered to be unclear. Previous studies utilizing flexible endoscopic evaluation of swallowing (FEES) [4, 5] have reported increased risk of penetration or aspiration in normal adults with doses of 0.5–1 ml of atomized 4% lidocaine. However, no difference has been observed with smaller amounts (0.2 ml) of atomized lidocaine [6]. Johnson et al. [7] also found no difference in laryngeal sensory testing following nasal anesthesia with 4% cocaine. Multiple studies have shown that topical nasal anesthesia may improve patient comfort and tolerance [4–6]. There are no studies evaluating other methods for nasal anesthesia that may avoid pharyngeal spillage, such as nasal packing. Until further evidence is available, the Working Group felt that clinicians should use anesthesia judiciously; by recognizing that use of anesthesia is not always necessary, utilizing the smallest effective dosing and by taking reasonable steps to minimize the spread of anesthetic to the pharyngeal mucosa.

All respondents were applying lubricant gel to aid catheter passage. Having the patient sip water (or a safer consistency if needed) through a straw once the catheter tip enters the pharynx helps with ease of catheter placement. All respondents were performing investigations with the patient sitting or semi-reclined with head in neutral position. Most (57%) were allowing 5 min for accommodation to the catheter prior to administration of test boluses, others were allowing up to 10 min.

Most respondents (71%) used their own standardized test protocol. All reported tested using thin liquid bolus consistencies equivalent to *International Dysphagia Diet Standardization Initiative* (*IDDSI*) 'Level 0' or SI unit of millipascal second. Other consistencies were variably used; however, extremely thick liquid consistency boluses that may be equivalent to IDDSI 'Level 4' were the second most commonly used. It is important to note that respondents were not routinely using flow rate and/or viscosity testing to verify consistency.

All respondents were testing verbally cued bolus swallows. All were administering liquid boluses via syringe while some also reported using spoon, cup, and/or straw. Most (71%) reported that they sometimes incorporated swallow maneuvers and alternative head positions during the procedure (exact maneuvers and positions not specified). Merit of assessing volitional bolus swallowing was not directly surveyed. None of the respondents self-reported assessing natural swallows.

Self-described thin liquid boluses of 5 ml volume were the most commonly used (86%). A few respondents were using < 5 ml volumes (14%) and others were using 10 ml volumes (57%). Most would use larger 15–20 ml volumes. Obtaining three or more repeat swallows was considered sufficient to provide internal consistency of measurements. Overall, the Working Group felt that decisions related to maximum bolus volume and number of repeats tested need to be applied on a 'case-by-case' basis influenced by a number of factors including subject tolerance and clinical signs at time of procedure and previously known aspiration and residue risk. Simultaneous videofluoroscopy, while not always necessary, provides for the safest investigation of the highest risk patients.

Recommended HRPM Protocol

Survey responses served as the basis for protocol development (Table 1). This suggested protocol captures the commonalities among the different practices that are indicative of what most of the experts were doing in their clinical/research practice. Consistent themes were (i) the judicious use of topical anesthesia (86%), (ii) a minimum 5-min accommodation period (57%), (iii) bolus delivery via syringe (100%), and (iv) the need to modify consistency of test boluses (71%) that are based on a recipe that ensures the reproducibility of consistencies, either according to the IDDSI framework (http://iddsi.org/) or the use of SI Units of viscosity (mPa s) as has been recommended by The European Society for Swallowing Disorders [8].

Literature Review

A range of specific HRPM phenomena were found to be considered diagnostically important [9, 10] (Table 2). As a starting point, the Working Group focused its efforts on exploring swallow metric *classes* that describe four swallow phenomena. These features were (i) lumen occlusive pressures generated at the velum, mesopharynx, hypopharynx, and UES, (ii) hypopharyngeal intrabolus pressure, (iii) UES relaxation pressures, and (iv) UES opening duration

Table 1 Recommended HRPM protocol based on majority expert agreement

System to use	Any solid-state HRM system including a catheter configured with at least 10 pressure sensors at 1 cm spacing If adjacent impedance is included then electrode segments at 2 cm spacing
Catheter placement	Requires education and training Apply lubricant gel to catheter Apply topical anesthesia to nasal passage Liquid sips via straw during placement Wait 5 min for catheter accommodation
Test boluses	Position-seated with head neural Delivery-syringe preferred Volumes-5 ml, 10 ml & sometimes 20 ml (case by case) Minimum 3 repeats (case by case)

Table 2 Outcomes against which swallow metrics were assessed

Outcome	Topic area description	HRPM references
A	Reports normative values for metrics	[10, 11, 15, 44, 49, 52, 53, 55, 57–66]
B	Reports physiological effects on metrics in relation to bolus characteristics	[11, 12, 14, 19, 20, 34, 44, 49, 55, 58–60, 65–68]
C	Reports physiological effects on metrics in relation to provocative swallowing	[14, 18, 57, 63]
D	Reports effects of normal aging on metrics	[15, 22, 36, 55]
E	Reports metrics derived for a patient cohort vs. metrics derived for a control cohort	[12, 13, 20–24, 44, 53, 59, 69–71]
F	Reports metrics derived for patients in relation dysphagia severity by instrumental assessment	[13, 16, 17, 19, 21, 23, 25, 27, 34, 39, 41, 47, 48, 59, 71–75]
G	Reports metrics derived for patients in relation dysphagia severity by clinical assessment	[12, 26, 33, 54, 76]
H	Reports metrics derived for patients in relation to a surgical intervention	[37, 76]
I	Reports metrics derived for controls or patients in relation to a swallow exercise	[9, 15, 28, 62, 77, 78]
J	Reports metrics derived for controls or patients in relation to a pharmacological intervention	[3, 35, 36]
K	Reports metrics derived for controls or patients in relation to a neural or muscular stimulation intervention	[79–81]
L	Reports reliability of metrics	[13, 34, 39, 40, 82–85]
M	Reports not characterized above	[43, 45, 46, 81, 86–103]

and extent. The major findings are summarized below and in Table 3, which illustrates how these swallow phenomena have been shown to relate to outcomes, providing an indication as to their relative importance as diagnostic measures.

(i) Pharyngeal and UES Lumen Occlusive Pressures

Lumen occlusive pressures generated by muscle contraction within pharyngeal and UES regions are commonly measured to identify specific regional impairments that may guide therapeutic strategies to improve contractile function; although this remains to be formally tested. Metrics described defined pressures within four anatomical regions (velo-, meso-, hypopharynx, and UES; Fig. 1a–c) that were assessed independently or combined (e.g., velo + mesopharynx [11–13], meso + hypopharynx [14], or the whole pharynx [15, 16]). UES occlusive pressures were measured *pre-deglutitive* or *post-deglutitive* (Fig. 1b). Pressures generated by the velopharyngeal region are typically sustained and multimodal [17] (Fig. 1b) and mechanistically serve to seal the nasopharynx when the pharynx is being challenged with large boluses. Velopharyngeal pressure increases with bolus volume [11, 12, 14] and with inverted body positioning [18]. In contrast, the regions inferior to the velopharynx appear to be less consistently affected with some reports of higher pressure with increased bolus size [19, 20] and bolus consistency [12]. Pressures throughout the pharynx and UES have been measured to be weaker in patients with

Table 3 Summary of trends seen in HRPM metric classes in relation to a range of different effects documented in the literature

Main effect assessed (outcome topic)	Metric class (↑↓ indicate direction of effect)					
	Pharyngeal lumen occlusive pressure	Hypopharyngeal intrabolus pressure	Upper esophageal sphincter			
			Pre-deglutitive pressure	Relaxation pressure	Opening admittance	Post-deglutitive pressure
Bolus volume (B)	↑ with Vol.	↑ with Vol.		↑ with Vol.	↑ with Vol.	↑ with Vol.
Pen-aspiration on VF (F)	↓ with Asp.	↑ with Asp.		↑ with Asp.	↓ with Asp.	
Control vs. patients (E)	↓ in Pat.	↑ in Pat.	↓ in Pat.	↑ in Pat.	↓ in Pat.	↓ in Pat.
Bolus consistency (B)	↑ with Cons.	↑ with Cons.		↑ with Cons.		
Aging (D)	↑ with Age		↓ with Age	↑ with Age	↓ with Age	↑ with Age
Clinical symptom scores (G)	↓ with Sx.	↑ with Sx	↓ with Sx	↑ with Sx	↓ with Sx	
Effortful swallow (I)	↑ with ES					↑ with ES
Chin tuck (C)						↓ with Tuck
Ipsilateral head turn (C)	↑ with Turn		↓ with Turn			↑ with Turn
Mendelsohn swallow (I)	↑ with MS					↑ with MS
Opioid agonist (J)	↓ with Opi.	↑ with Opi.		↑ with Opi.		
Neuro or muscular stimulation (K)	↑ with Stim.				↑ with Stim.	
Artificial UES restriction (C)		↑ with Restrict		↑ with Restrict		

Abbreviations: penetration (pen), videofluoroscopy (VF), upper esophageal sphincter (UES), volume (vol), aspiration (asp), patient (pat), consistency (cons), symptoms (sx), effortful swallow (ES), Mendelsohn swallow (MS), stimulation (stim), opioid (opi)

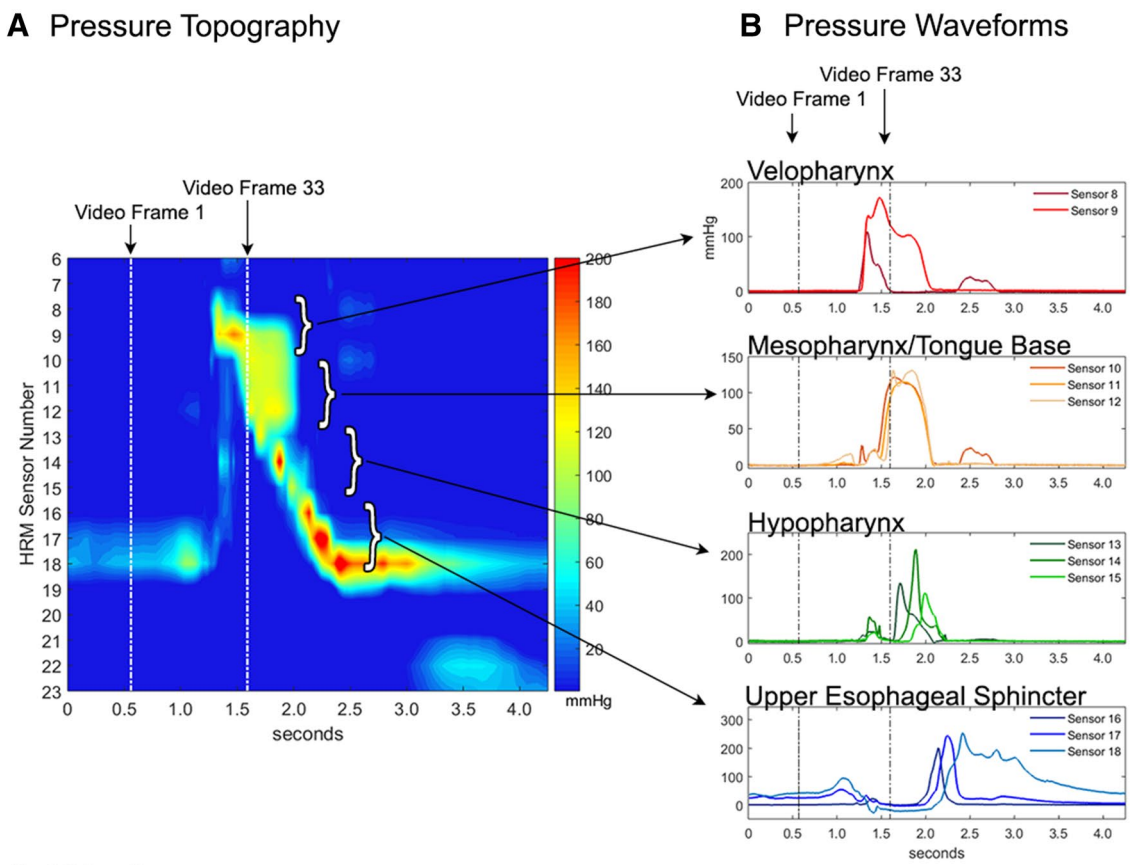
dysphagia symptoms or in relation the dysphagia sequelae such as aspiration [16, 20–25]. Global and regional weakness of the pharynx is undoubtedly a feature of some specific pathologies [12, 20, 23]. However, studies that include a large sample (75 + patients) only describe data averaged across broad etiologies [24, 26, 27].

Measurement of the contractile *peak pressure* has the practical advantage of being easy to determine without highly specialized software. The concept of a contractile *integral*, which defines pressure over space and time (*mean pressure* × *duration* × *length*), has gained in popularity as a measure of the 'vigor' of the pharyngeal swallowing response [15, 16]. Altered pharyngeal pressure in relation to aging, during swallow exercises, and with volume challenges have been detected by both peak pressures and pressure integrals [12, 14, 15, 28].

The added value of a pharyngeal contractile integral, over peak pressure is not proven at this time. However, it can be argued that a contractile integral may have greater value for recording pressures within the velopharyngeal and mesopharyngeal regions in particular, because pressure generation within these regions displays typically sustained and/or multimodal features, in contrast to the characteristically brief and single peaked pressures generated by the hypopharynx (Fig. 1b).

(ii) Hypopharyngeal Intrabolus Pressure

Hypopharyngeal intrabolus pressure (IBP) is a marker of UES restriction to bolus flow during swallowing. Abnormal IBP suggests an increased pressure gradient across the pharyngo-esophageal junction that may drive reciprocal compensatory changes in upstream functions, such as augmented meso- or velopharyngeal pressure generation. Bolus flow restriction can be rectified following cricopharyngeal myotomy or dilatation [29–31] but a recent systematic review revealed inadequate evidence to guide clinical decision making [32]. The HRPM literature shows that hypopharyngeal IBP physiologically increases with bolus size and consistency [11, 12, 14, 19, 33], is elevated in some patient cohorts [12, 13, 21, 22], elevated in relation to dysphagia sequelae [19, 21, 27, 34], and following exposure to opioids [35, 36]. There are methodological challenges associated with reliably defining IBP. Three approaches are below:



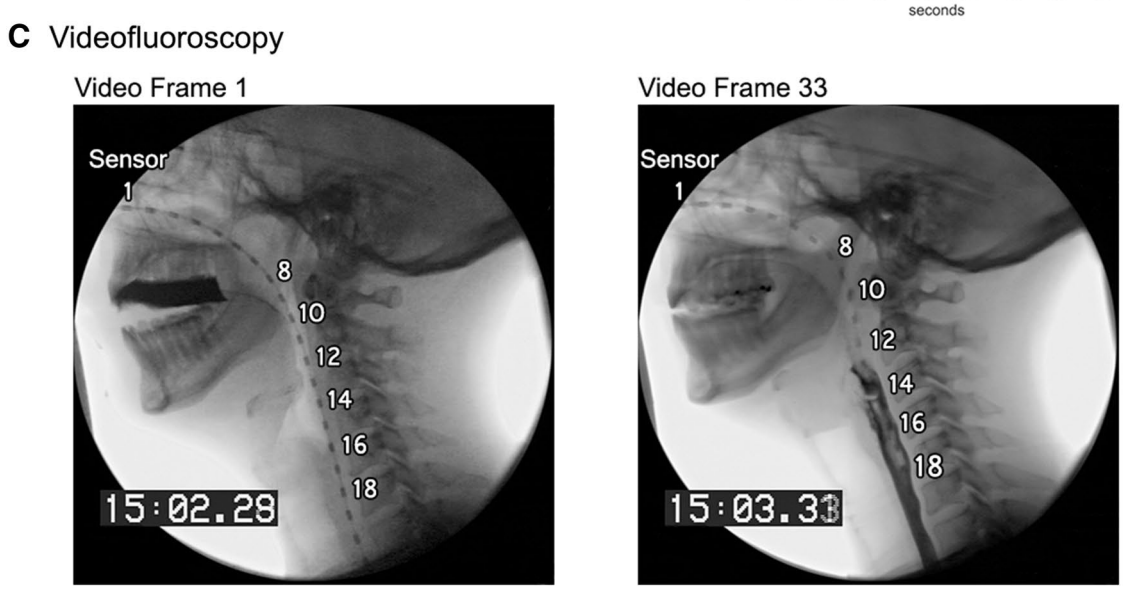


Fig. 1 HRPM with simultaneous videofluoroscopy. **a** An example pharyngeal pressure topography plot during cued volitional swallowing of a 10 ml thin liquid barium bolus (IDDSI 0). Vertical lines correspond to the time points of the two radiographic images in C. **b** Individual pressure signals recorded by sensors at the different axial locations along the pharynx. The four graphs show the individual pressure signals occurring within each anatomical region and illustrate the variable nature of pressures recorded throughout the pharynx. Vertical lines correspond to the time points of the two radiographic images in (**c**). **c** Radiographic images before and during the swallow. The catheter in situ is visible in the image and the relevant pressure sensor numbers are labeled. Technical Details: The measurements were performed in a 42-year-old male subject using a 2.75-mm-diameter solid-state high-resolution manometry catheter incorporating 36 1-cm-spaced pressure sensors (Given Imaging). Data were acquired at 50 samples/s (Manoscan, Given Imaging, USA) and analyzed using MATLAB (The MathWorks Inc., Natick, MA, USA)

(i) *Mid-hypopharyngeal IBP*, defined by the pressure within the advancing bolus measured at the midpoint of radiologically determined bolus flow [17, 33].
(ii) *Hypopharyngeal pressure increment* (*HPI*), defined by the average pressures preceding the onset of the upstroke of pharyngeal contraction to a 20 mmHg threshold [14] (Fig. 2b).
(iii) *Hypopharyngeal pressure at nadir impedance* (*PNadImp or PNI*), defined by the pressure at the time of maximum hypopharyngeal distension deduced by impedance topography [21, 37] (Fig. 2b). IBP defined in this way has been considered the impedance-based equivalent of mid-IBP [38].

All methods for calculating IBP have their limitations. Mid-IBP has a long history of use prior to the advent of HRPM [29]; however, measurement requires simultaneous videofluoroscopy and perfectly synchronized image analysis that can be time consuming. The average pressure increment has only been reported in one study of non-dysphagic patients [14] and has not been assessed in relation to pathologic swallowing. PNI requires impedance recording which does not always come as standard adding to the device cost.

Mid-IBP and PNI were found in our review to be the most utilized measures of IBP. PNI is the only IBP metric tested for intra- and inter-rater reliability [13, 34, 39, 40]. Original reports calculated the average PNI for the entire hypopharyngeal region proximal to the UES [21, 34, 41]; however, this has been recently refined to only utilize the discrete nadir impedance pressure measured 1 cm proximal to the UES apogee position [12, 13, 35, 37, 40]. This iteration of the metric (Fig. 2a, b) has been validated as a measure of augmented pharyngeal flow resistance [35] and, among a range of different measures, appears to be the most predictive of strictures following head and neck cancer treatments [37].

A final cautionary point for any hypopharyngeal HRPM measures is that they may be subject to hypopharyngeal pressure transients predominantly caused by contact of the tilting epiglottis with pressure sensors along the catheter [42]. Any analysis should ideally recognize such pressures because i) they are potentially erroneous and therefore can influence numerical values generated for IBP and ii) they may reliably predict epiglottic inversion that may have clinical relevance for some patients.

(iii) UES Relaxation Pressure

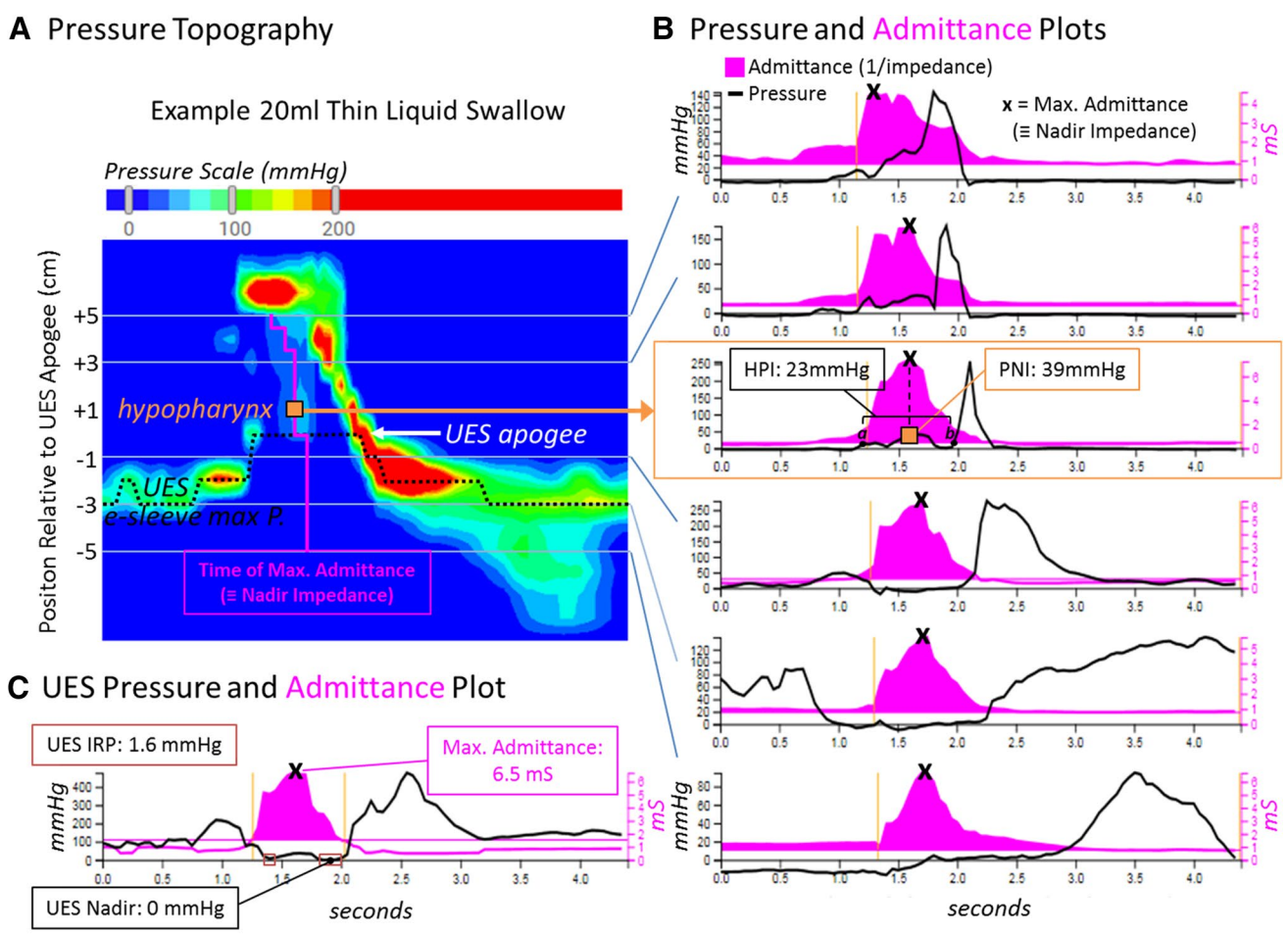
UES pressures have been shown to be a direct correlate of cricopharyngeal electromyography and therefore are indicative of brain stem mediated activation and deactivation of cricopharyngeus muscle [43–46]. UES pressures during bolus swallowing and for the period of greatest relaxation are also indirect measures of IBP, physiologically increasing with bolus size [11, 14, 46] and elevated in some patient cohorts compared to controls [12, 20, 22, 24, 44] as well as in relation to dysphagia sequelae [13, 47, 48]. UES relaxation pressures also increase with age [15, 22, 36], inverted body positioning [18], and following exposure to opioids [35, 36].

The advent of HRPM has greatly improved assessment of UES relaxation pressures by utilizing the *e-sleeve* method [49, 50] to accommodate the sometimes significant elevation of the UES during swallowing [51]. This method measures all axial pressures within the limits of UES high-pressure zone and 'maps' the dynamic movement of the UES high-pressure zone over time based on the location of maximum axial pressure (Fig. 2a, c). UES relaxation parameters can then be derived from the profile of maximal pressures over time [22, 49, 52]. Two dominant approaches to defining UES relaxation pressure are described in the HRPM literature, namely the minimum relaxation pressure (or *nadir pressure*) and the *integrated relaxation pressure* (Fig. 2c). UES integrated relaxation pressure (UES IRP) quantifies the lowest non-consecutive 0.20–0.25 s of UES pressure during relaxation (Fig. 2c). UES IRP emulates the esophagogastric junction 'IRP 4s' that is widely used for the diagnosis of achalasia and esophageal outflow obstruction [1]. In esophageal diagnosis, IRP has been shown to be superior to discrete nadir relaxation pressure for distinguishing abnormal EGJ relaxation [50]. There is a paucity of directly comparative data from HRPM studies evaluating both UES nadir pressure and UES IRP. However, as UES high-pressure zone and catheter can move independently over the active swallow period, it could be argued that UES IRP, being based on a series of measurements, may be more comprehensive than taking a single data point of lowest pressure.

(iv) UES Opening Impedance

The mechanisms that determine UES opening extent include strength and timing of supra- and infra-hyoid muscle activation and the distension pressure generated by the swallowed bolus driven by pharyngeal propulsion. Additionally, UES opening is dependent upon the appropriate reciprocal neural deactivation and compliance of the cricopharyngeus and associated muscles and structures [10, 42–46].

Bolus impedance is a direct correlate of luminal diameter/area and therefore intraluminal impedance (or the inverse product called '*admittance,*' Fig. 2c) has been used to measure the timing and extent of opening of the UES [44, 53]. UES impedance during bolus swallows, correlates with bolus size [11, 12, 46] (Fig. 2d) and is altered in patient cohorts compared to controls [12, 13, 22, 44, 53, 54] and with aging [44, 55].



Delphi Consensus and Core Outcomes Set

A total of four voting rounds were required to reach a stable level of agreement on all 22 evaluated metrics of which consensus to recommend was achieved for eight metrics. The recommended swallow metrics and key comments expressed during the Delphi rounds are detailed in Tables 4 and 5. The recommended metrics allow characterization of diagnostically important swallowing phenomena.

Discussion

The major outcomes of this work were the development of a recommendation for a standard HRPM protocol and an associated core outcomes set of recommended diagnostic measures. This work can potentially inform future proposals for a HRPM-based classification system specifically for characterization of pharyngeal swallowing disorders.

As part of the process the determining a consensus-based framework, the Working Group undertook an extensive literature review that provided the evidence underpinning what clinicians performing HRPM should seek to measure.

◂**Fig. 2** HRPM measures of intrabolus pressure, UES relaxation and UES opening. **a** An example pharyngeal pressure topography plot of the entire pharyngo-esophageal segment during cued volitional swallowing of a 20 ml thin liquid bolus (IDDSI 0). **b** Individual pressure (black lines) and admittance (pink) signals recorded at different axial locations along the pharyngo-esophageal segment. Note: *Admittance* is the inverse product of impedance (1/impedance; units in millisiemens, mS) and therefore *rises* in relation to bolus presence. The time of maximum admittance (≡nadir impedance) is identified by 'x'; this marks maximum bolus distension at each location along the pharynx allowing the trajectory of bolus movement to be mapped over time and space during the swallow (also illustrated by the pink line in Panel A). Knowing when maximum bolus distension occurs allows the corresponding intrabolus distension pressure to be determined; known as the *pressure at nadir impedance* (PNI). The discrete PNI that is measured at 1 cm proximal of the UES apogee position is a validated marker of pharyngeal flow resistance (orange squares in Panels **a** and **b**). Another marker is the *hypopharyngeal pressure increment* (HPI) which is determined by averaging all hypopharyngeal pressures preceding the onset of the upstroke of pharyngeal contraction to a 20 mmHg threshold; shown in this example as the average of pressures between points '*a*' and '*b*'. **c** The time-profile of upper esophageal sphincter (UES) pressure (black line) based on the 'e-sleeve' method (utilizing 'max P.' in Panel A) and the corresponding UES admittance (pink). The *UES nadir pressure* and *UES integrated relaxation pressure* (UES IRP) measure the extent of pressure relaxation. UES IRP is the median of the lowest 0.25 s of UES pressure (non-contiguous; see red squares during relaxation). *UES maximum admittance* ('x') measures the extent of UES opening. **d** Average data showing increasing intrabolus pressure (flow resistance) and UES admittance (UES opening) when the subject was challenged with larger bolus volumes. Technical Details: The measurements were performed in a 55-year-old female subject using a 2.7-mm-diameter solid-state high-resolution impedance-manometry catheter with 32 1-cm-spaced pressure sensors and 16 (2 cm) impedance segments (Unisensor AG, Attikon, Switzerland). Data were acquired at 20 samples/s (Solar GI HRM system, MMS Enschede, The Netherlands) and analyzed via the *Swallow Gateway* open access analysis portal (https://www.swallowgateway.com)

The knowledge bank of HRPM literature is growing but, for many reasons, the literature is incomplete and complex to decipher. Nevertheless, the review suggests that published individual swallow metrics can be meaningfully consolidated (Table 3).

Specification of a recommended core outcomes set of pressure and/or impedance-derived swallow metrics provides a starting point for the development of a framework for scientific and clinical communication. The Working Group's consensus recommendation was determined via the Delphi process, which is a widely used and accepted method for gathering data from a panel of experts involving a formal group communications and several rounds of discussion and voting.

The current work has multiple limitations that are important to discuss. The Working Group did not address technological questions regarding factors that can influence the quality and reliability of measurements such as data and image synchronization and sampling frequency, catheter diameter and pressure sensor type, spacing and orientation. These are important issues to be investigated in the future. The varied use of different manufactured catheters and software may preclude some clinicians from being able to utilize impedance metrics. They are included, however, in the recommended outcomes set as these impedance measures had significant evidence in the literature to suggest clinical utility and gained majority support in the Delphi consensus process. While methods for calculation of the different metrics were provided, we recognize that multiple approaches can be found in the literature and we do not suggest that one method of calculation is superior to another.

Despite growing enthusiasm for HRPM as a diagnostic modality, how HRPM can influence patient management remains unclear. The ability of HRPM to predict outcomes, determine therapeutic effects, monitor disease recovery or progression or enable biofeedback training is currently unknown. Of particular interest may be the effect of pharyngeal swallowing maneuvers on HRPM measurements and their role in evaluating efficacy or guiding clinical practice. There are also still unanswered questions regarding protocol standardization, particularly in relation to recommended bolus consistency administration. At this time, there is no current consensus or evidence to suggest the appropriate bolus consistencies in either diagnostic or therapeutic examinations.

Furthermore, the current work does not address critically important questions around where the *limits* of HRPM lie, as a standalone test. These include: When is an HRPM-only procedure appropriate? What are the circumstances under which adjunct radiology should be considered essential? Should HRPM be preserved as a comprehensive, stand alone, pharyngeal examination to diagnose a pharyngeal dysfunction only or should a standardized protocol allow for (limited) assessments below the esophageal transition zone? If esophageal dysfunction is present, which in some

Table 4 Summary of key comments from the Delphi consensus group

Comments regarding use of regional Contractile Integrals vs. Mean Peak Pressure/Maximum Pressure. Consensus recommended use of Contractile Integrals
"*Peak pressures are very variable and prone to catheter artefacts*"
"*Peak pressures only indexes one aspect. This however would be a very important measure if examining impact of a specific maneuver manuever or therapeutic intervention on a single max' pressure generation*"
"*Absolute pressure peak might be useful in specific maneuvers in therapy*"
[*In regard to the hypopharynx*] "*Prefer* [*Mean Peak Pressure*] *to HCI because the hypopharyngeal contraction is usually short and uni-modal and therefore the advantage if deriving an integral seems unclear*"
Comments regarding Velo-, Meso-, and Hypo-pharyngeal sub-components. Consensus recommended PhCI as a global measure and to separate sub-component Contractile Integrals
"*Patients with failed or weak pharyngeal propulsion often compensate with high mesopharyngeal pressures generated by tongue base, if we combine these regions the composite measure might appear 'normal' even when focal velo or hypopharyngeal weakness exists*"
"*Feel it is important to divide the regions for clinical and therapeutic target reasons*"
Comments regarding UES Relaxation Metrics. Consensus recommended *UES IRP*. "*UES IRP takes into account both duration and extent of relaxation, so I think it's a better measure, however UES nadir pressure and relaxation time may help to understand the reason for elevation of IRP*"
[*Regarding UES Relaxation Time*] "*Although may be problematic in low basal UES tone, in our experience this is not all that common and it is a clinically and surgically relevant measure*"
Comments regarding Intra-Bolus Pressure Metrics. Consensus recommended Pressure at Nadir Impedance.
[*Regard to Hypopharyngeal Pressure Increment*] "*would be difficult with circumferential sensors due to the influence of epiglottis and other non-propulsive pressures*"
[*Regarding Pressure at Nadir Impedance*] "*this metric now on fairly solid footing following acceptance of the St George Group paper on prediction of stricture in HNC*"
Comments regarding metrics that require impedance measurement. Consensus recommended inclusion of Impedance
[*Regarding Pressure at Nadir Impedance*] "*Neutral on because the system that I currently use does not have impedance in the smaller catheter*"
[*Regarding Pressure at Nadir Impedance*] "*also agree that not all centres have impedance, but impedance makes the data much more robust and since we are trying to advocate for a standard, I think we should include*"
[*Regarding UES Maximum Admittance*] "*I believe that this is important, but I am hesitant to recommend, as a core outcome set, measures that require impedance*"

populations may be frequently (as recently reported for laryngectomy patients [56]), then what esophageal findings should be considered relevant to symptoms? These and other issues are challenging to address and will raise many questions and concerns among experts in the field.

Conclusion

A recommended protocol and outcomes set of diagnostic measures was determined following an extensive evidence-based process. This work represents the first step in an evolving process to establish both clinical and research HRPM

Table 5 Descriptive terminology, acronyms, and technical definitions for HRPM core outcomes set

Metric class	Metric [Delphi group agreement level]	Acronym	Definition
Pharyngeal lumen occlusive pressure	*Pharyngeal contractile integral* [Agree 100%, Neutral 0%, Disagree 0%]	PhCI	PhCI is a global measure of pharyngeal contractile vigor within a space–time box on the pressure topography plot spanning from the velopharynx superiorly to the upper margin of the UES. The PhCI is the mean pressure within this domain multiplied by duration (s) and length (cm) in units of mmHg s cm [15, 16]
	Velopharyngeal contractile integral [Agree 100%, Neutral 0%, Disagree 0%]	VCI	VCI is a measure of contractile vigor within a space–time box on the pressure topography plot spanning the velopharyngeal region only. VCI is the mean pressure within this domain multiplied by duration (s) and length (cm) in units of mmHg s cm [15]
	Mesopharyngeal contractile integral [Agree 90%, Neutral 0%, Disagree 10%]	MCI	MCI is a measure of contractile vigor within a space–time box on the pressure topography plot spanning the mesopharyngeal region only. MCI is the mean pressure within this domain multiplied by duration (s) and length (cm) in units of mmHg s cm [15]
	Hypopharyngeal contractile integral [Agree 90%, Neutral 0%, Disagree 10%]	HCI	HCI is a measure of contractile vigor within a space-time box on the pressure topography plot spanning the hypopharyngeal region only. HCI is the mean pressure within this domain multiplied by duration (s) and length (cm) in units of mmHg s cm [15]
Hypopharyngeal intrabolus distension pressure	*Hypopharyngeal intrabolus pressure* [Agree 80%, Neutral 10%, Disagree 10%]	IBP	IBP is defined by the pressure 1 cm superior of UES apogee position at the time of maximum hypopharyngeal distension deduced from impedance topography in units of mmHg [11, 12, 35, 37]
UES relaxation & opening	*UES integrated relaxation pressure* [Agree 100%, Neutral 0%, Disagree 0%]	UES IRP	UES IRP is a measure of the extent of UES relaxation. UES IRP is the median of the lowest non-consecutive 0.20–0.25 s of e-sleeve pressure in units of mmHg [15, 37, 52]
	UES relaxation time [Agree 90%, Neutral 0%, Disagree 10%]	UES RT	UES RT is a measure of the duration of UES relaxation. UES RT is the e-sleeve pressure interval below 50% of baseline or 35 mmHg, whichever is lower, in units of sec [26, 75]
	UES maximum admittance [Agree 80%, Neutral 0%, Disagree 20%]	UES MaxAd	UES MaxAd is a measure of extent of UES opening. UES MaxAd is the highest admittance value recorded during trans-sphincteric bolus flow in units of millisiemens (mS) [11, 22, 44, 46]

guidelines and will require revision based on future objective evidence. It is envisaged that a classification framework for pharyngeal disorders, akin to *Chicago Classification*, could ultimately emerge from this and future efforts.

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Compliance with Ethical Standards

Conflict of interest Taher Omari declares that he is a co-inventor of a relevant patent (AU2011301768 Patentee: Women's and Children's Health Network Incorporated). Michelle Ciucci declares that she has no conflict of interest. Kristin Gozdzikowska declares that she has no conflict of interest. Esther Hernández declares that she has no conflict of interest. Katherine Hutcheson declares that she has a travel stipend from Medtronic Inc. Corinne Jones declares that she has no conflict of interest. Julia Maclean declares that she has no conflict of interest. Nogah Nativ-Zeltzer declares that she has no conflict of interest. Emily Plowman declares that she has relevant funding through National Institute of Neurological Disorders and Stroke (1R01 NS100859-01). Nicole Rogus-Pulia declares that she has no conflict of interest. Nathalie Rommel declares that she is a co-inventor of a relevant patent (AU2011301768 Patentee: Women's and Children's Health Network Incorporated). Ashli O'Rourke declares she is a Consultant for Medtronic Inc.

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