Characterization of swallow modulation in response to bolus volume in healthy subjects accounting for catheter diameter

Authors:

Lara Ferris MSpPath[1,2], Mistyka Schar BSpPath[2], Lisa McCall DipN[1], Sebastian Doeltgen PhD[3], Ingrid Scholten PhD[3], Nathalie Rommel PhD[4] , Charles Cock MD[2], Taher Omari PhD[2]

Affiliations:

1 Gastroenterology Dept., Women's and Children's Hospital, Adelaide, Australia

2 Gastroenterology Dept. & Human Physiology Dept., Flinders University, Adelaide, Australia

3 School of Health Sciences, Discipline of Speech Pathology, Flinders University, Adelaide, Australia

4 Neurosciences, EXPORL, KU Leuven, Leuven, Belgium

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[1] **Correspondence:** Lara Ferris, Human Physiology Dept., Flinders University, P. O. Box 2100, Adelaide, SA, Australia, 5001. T: +61 8 – 8204 7482; E: ferr0103@uni.flinders.edu.au

Abstract

OBJECTIVE: Characterization of the pharyngeal swallow response to volume challenges is important for swallowing function assessment. The diameter of the pressure-impedance recording catheter may influence these results. In this study we captured key physiological swallow measures in response to bolus volume utilizing recordings acquired by two catheters of different diameter.

STUDY DESIGN: 10 healthy adults underwent repeat investigations with 8 and 10 French catheters. Liquid bolus swallows of volumes 2.5, 5, 10, 20 and 30ml were recorded. Measures indicative of distension, contractility and flow timing were assessed.

METHODS: Pressure-impedance recordings with pressure-flow analysis were used to capture key distension, contractility and pressure-flow timing parameters.

RESULTS: Larger bolus volumes increased upper esophageal sphincter distension diameter ($p<0.001$) and distension pressures within the hypopharynx and upper esophageal sphincter ($p<0.05$). Bolus flow timing measures were longer, particularly latency of bolus propulsion ahead of the pharyngeal stripping wave ($p<0.001$). Use of a larger diameter catheter produced higher occlusive pressures, namely upper esophageal sphincter basal pressure ($p<0.005$) and upper esophageal sphincter post deglutitive pressure peak ($p<0.001$).

CONCLUSION: The bolus volume swallowed changed measurements indicative of distension pressure, luminal diameter and pressure-flow timing; this is physiologically consistent with swallow modulation to accommodate larger, faster flowing, boluses. Additionally, catheter diameter predominantly affects lumen occlusive pressures. Appropriate physiological interpretation of the pressure-impedance recordings of pharyngeal swallowing requires consideration of the effects of volume and catheter diameter.

Key words: dysphagia, deglutition, bolus volume, catheter diameter, pressure, impedance

Level of Evidence: NA

Introduction

Oropharyngeal swallowing is controlled and modulated via afferent inputs to primary motor cortex and brain stem.[1] Bolus properties and general somatic sensory input from the oropharynx and larynx are detected via cranial nerve pathways, with feedback to the central pattern generator networks within the medulla oblongata.[1,2] These modulating inputs are integrated with information from the primary motor cortex, which is especially involved for volitional or cued swallowing.[3] The modulation of the swallow motor mechanism results in coordinated timing of the swallow response with appropriate distension and contraction of the pharynx and UES.[1,3,4,5,6] This allows boluses of differing volume and consistency to transfer safely from the oral cavity into the esophagus with little or no increase in resistance to bolus flow.[5-8]

Traditionally, manometry assessment has been used to profile the pharyngeal and UES pressures generated during swallowing. Pharyngeal physiology involves coordinated movements of the velopharyngeal, hypopharyngeal and UES regions to ensure airway protection and full bolus clearance.[2] More recently manometry has been combined with impedance technology to measure and integrate bolus flow. Pressure-flow analysis (PFA) software has been developed to objectively and reliably analyse complex pressure-impedance data.[10, 11] The inverse of impedance, intraluminal admittance values, provide a reliable correlation of luminal diameter as indicated by a barium contrast column seen on videofluoroscopy, therefore providing a non-radiological alternative to track bolus presence.[12] Current evidence supports the notion that metrics which specifically quantify hypopharyngeal and UES distension pressures and bolus flow timing are often altered in patients with oropharyngeal dysphagia.[5, 10, 11, 14] Whilst the diameter of the recording catheter is known to alter the length tension and force generation of the esophagus[15-17], the effect of catheter diameter on contractility, distension pressure and flow timing in the pharynx is less clear. The aim of this study was to determine, in healthy young participants, which pressure-flow measures indicate physiological neuromodulation of pharyngeal swallowing in relation to increased liquid bolus volumes. We also aimed to observe the effect of catheter size using within subject repeat measurements with different diameter catheters.

Materials and Methods

All investigations were performed in the Gastroenterology Department at the Women's and Children's Hospital in Adelaide, Australia. The Human Research Ethics Committee approved the study protocol (HREC 2423). Informed consent was obtained from all participants prior to commencing measurements. Inclusion criteria - no gastrointestinal medical history i.e. no dysphagia, or gastroesophageal disease. Participants underwent investigations with two catheters of differing diameters (8 and 10 French) studied consecutively on the same day in randomised catheter order. A computer generated randomisation schedule determined which catheter was used first.

Measurement Protocol

The High Resolution Impedance Manometry (HRIM) catheters have pressure sensors and impedance electrodes spaced evenly across their length. The sensors detect pressures generated by swallow musculature contractions and the impedance electrodes record flow of ingested food/fluid. An electrical current is generated between two evenly spaced adjacent electrodes, referred to as one segment. The impedance within each segment differs depending on the conductivity of the surrounding environment and travelling bolus material.~~-~~. This study used 0.9% sodium chloride (NaCl) solution which is optimally conductive, and widely used as the standard for liquid swallows when performed in conjunction with impedance recordings (reference 10-14). ~~This study used 0.9% saline,sodium chloride (NaCl) solution highly optimally conductive, for liquid swallows. At this concentration, NaCl solution forms strong ionic bonds which best conduct the electrical current between the impedance electrodes (Fortunato, 2005).~~

The 10 French catheter incorporated 36 1cm-spaced unidirectional pressure sensors and 16 adjoining impedance segments (36P16Z), each of 2 cm (Unisensor AG catheter, Attikon Switzerland). The 8 French HRIM catheter incorporated 32 pressure sensors and 16 adjoining impedance segments (32P12Z) (Unisensor AG catheter, Attikon Switzerland). Each catheter was positioned trans-nasally straddling the entire pharyngo-esophageal segment. Lignocaine spray (5%) was used within the nose. A water based lubricant was used to assist with passage of the catheter. The pressure-impedance data were acquired at 20 samples/sec (Solar GI acquisition unit Medical Measurement Systems, Enschede,

The Netherlands). Participants were seated upright in the head neutral position. After a 5 minute accommodation period subjects were cued to swallow liquid saline boluses administered via syringe. Bolus volumes comprised three each of 2.5ml, 5ml, 10ml, 20ml and 30ml. On completion of the swallow protocol the catheter was removed and the subject was re-intubated with the alternative diameter catheter and the swallow protocol was repeated.

Analysis of Pressure-Impedance Recordings

Pressure- impedance data for each swallow were exported in .csv file format. The extracted data file was then analysed using AIMplot, purpose designed MATLAB based software (copyright T Omari; created in MATLAB version 7.9.0.529; MathWorks Inc., Natick, MA, USA). Impedance values were converted to their inverse product, *admittance* (admittance = 1/ohms; units in millisiemens, mS). Using AIMPlot, the analyst selected spatiotemporal landmarks after which the software automatically determined three separate regions of interest encompassing 1) the velopharynx and tongue base, 2) hypopharynx and 3) UES. Swallow function metrics were calculated within each region (see below) and were averaged per volume for each catheter configuration. The reliability of this method and the specific details of the analysis algorithms have been previously described.[10-13, 18, 20-23]

Individual Swallow Function Variables

All individual swallow function variables are indicated in Fig. 1. The *velopharyngeal tongue base contractile integral* (VCI) was based on the integral of pressures >20 mmHg within the region of the velopharynx and tongue base during the swallow. Contractility of the pharyngeal stripping wave proximal to the UES was calculated as the *pharyngeal peak pressure* (Peak P), defined as the maximum contraction of the pharynx. Additionally the *UES post relaxation peak pressure* (UES Peak P) was determined by the maximal peak pressure up to 1 second after relaxation offset. *The distension-contraction latency of the whole pharynx* (Ph DCL) was determined for the pharyngeal region proximal to the UES apogee position. This metric is a temporal relationship of average time from pharyngeal peak admittance to pharyngeal peak pressure. It defines the latency from maximum bolus distension to maximal pharyngeal contraction and is a marker of how well the bolus is propelled ahead of the pharyngeal stripping wave.

During bolus swallowing the maximum admittance estimates the area at the axial centre, or most distended part, of the lumen during bolus transport.[12, 14, 18] Hence, pressure measured at, or the relative timing of, maximum admittance is an accurate measure of pharyngeal intrabolus distension pressure and timing of maximum distension respectively. For this study, the intrabolus pressure at maximum admittance, 1 cm above the UES, was used to define *hypopharyngeal intrabolus pressure* (hIBP). This variable represents the videomanometry derived parameter *mid bolus pressure.*[24, 25] *The pharyngeal bolus presence time* (Ph BPT), indicating the bolus dwell time in the hypopharynx during the swallow, was shown by the upstroke and downstroke inflexions of the admittance curve. The maximum luminal cross sectional area within the UES, during bolus flow, was inferred based on the *UES maximum admittance* (UES Max Ad). [12, 14, 18]

The *UES basal pressure* (UES basal P) and UES relaxation pressure were determined using the *e-sleeve* method[26] based on the value and location of maximum axial UES pressure over time. The *UES integrated relaxation pressure* (UES IRP) was defined as the median of all lowest pressures (contiguous or non-contiguous) recorded over a 0.25 sec period. *UES Open Time* (UES OT) was defined by the period between the upstroke and downstroke inflexions of the UES admittance curve.

Global Swallow Function Variables

The *Swallow Risk Index* (SRI) combines four hypopharyngeal measures to derive a single value representative of global swallowing dysfunction and aspiration risk.[27] Previous studies with simultaneous videofluoroscopy (VFSS) in adults suggest the cut off for normality is < 15.[11, 13] The SRI is derived by the following formula:

$$SRI = \frac{Ph\ BPT \times IBP}{PP \times (DCL + 1)} \times 100$$

The *post swallow impedance ratio* (PSIR) is an integrated ratio which relates post swallow impedance to the impedance during pharyngeal bolus passage. The PSIR has previously been shown to rise with post swallow pharyngeal residue seen on VFSS.[11]

Statistical Analysis

A statistics package (IBM Corp. released 2013, IBM Statistical Package for the Social Sciences [SPSS] Statistics for Windows, v. 22.0 Armonk, NY: IBM Corp) was used to investigate the data. Measurements were predominantly parametric therefore for all comparisons repeated measures ANOVA were performed using a General Linear Model with repeated volume and diameter measures. Bonferroni adjustments were incorporated for all comparisons. A p value <0.05 was considered to indicate statistical significance. Partial Eta Squared (ηp^2) was used as a measure of effect size (ηp^2 of 0.1 = small effect, 0.3 = medium effect, 0.5 = large effect).

Results

All 10 participants (6 male: 4 female; mean age: 28yrs, range 24 – 33 years) were non-smokers with no gastrointestinal medical history reported. No participants took regular medications at the time of their participation. Following randomisation, 6 of the participants commenced investigations with the larger catheter. A total of 300 swallows were analysed amongst participants, across the two catheter configurations. The effects of bolus volume and catheter diameter are described below and presented in Table 1 and Fig. 2. Whilst main effects of bolus volume and/or catheter diameter were seen, no volume*diameter interactions were observed for any variable (Table 1).

Effects of bolus volume

Contractility measures Peak P, UES basal P, and UES Peak P were not affected by bolus volume (Table 1, Peak P, and UES Peak P data shown in Fig. 2b). However VCI, the pressure generated in the region from velopharynx to tongue base, significantly increased with volume (Table 1 and Fig. 2a). The UES distension area (UES Max Ad) was significantly elevated (Table 1 and Fig. 2c); pharyngeal and UES distension pressures (hIBP and UES IRP) were significantly higher ($p<0.05$ for both); the latency of bolus propulsion ahead of the pharyngeal stripping wave (Ph DCL) was significantly longer ($p<0.001$); and the UES open time (UES OT) was significantly longer for larger volumes ($p<0.05$). Of the global swallow function variables, the SRI was not affected by volume whilst PSIR was lower with larger volumes ($p< 0.001$).

Effects of catheter diameter on PFA metrics

The contractility metrics of the UES (UES basal P, UES Peak P) which were previously unchanged by volume were significantly greater when recorded with the larger diameter catheter (Table 1). The VCI, which increased with volume, was not significantly affected by catheter diameter (Fig. 2a). The UES relaxation during bolus flow was significantly reduced (higher IRP, Table 1) with the larger catheter. However, UES distension area (UES Max Ad) was unaffected by catheter size (Table 1). Bolus flow timing measures were less affected by catheter size, however UES OT was significantly shorter when assessed with the larger catheter (Table 1).

Discussion

Overall this study highlights that swallow metrics reflecting distension pressure, distension diameter, and pressure-flow timing were affected by bolus volume, while swallow metrics reflecting lumen occlusive pressures were affected by catheter diameter. Some metrics, for example UES IRP and UES OT, were affected by both volume and diameter, most likely because they are metrics influenced by both distension and occlusion and/or are subject to catheter mucosal contact during swallowing. The VCI was the only purely occlusive pressure measure that was influenced by bolus volume.

In healthy participants, larger bolus volumes are known to lead to an earlier onset and extent of hyolaryngeal excursion, earlier UES opening, greater distension diameter and longer opening duration.[5-7, 18, 27, 31-33] These modulated events with altered pharyngeal dilatation or distension, ensure minimal flow resistance and optimal airway protection during bolus passage.[5-7, 29, 32] Larger volumes elicit stronger lingual propulsive forces which initiate a swallow adapted to accommodate that bolus size.[8, 29] The effect of bolus volume on the occlusive pressure between velopharynx and tongue base previously reported by others[30] were clearly observed in this study (Fig. 2a). Nonetheless, pressures in the hypopharynx and UES remained unchanged in relation to volume challenge, confirming that motor function of these regions during regular swallows is largely stereotypical.[5-8, 31, 32]The oral cavity is specialised for distinguishing bolus characteristics whereas the pharyngeal contractility does not make these same distinctions. [33] However, in context of the earlier arrival of larger boluses into the pharynx

(i.e. earlier pharyngeal receptive dilatation)[5, 6] ahead of the pharyngeal stripping wave, a longer pharyngeal distension-contractile latency was observed.

As anticipated, UES distension area (inferred by admittance) was also markedly elevated when larger bolus volumes were swallowed (Fig. 2c). This was associated with an increase in hypopharyngeal distension pressure, particularly as the ability of the pharynx to accommodate a larger, faster moving bolus was challenged by the largest 20-30ml boluses. This suggests that the bolus area/diameter and distension pressure, when measured together, may provide a dependable physiological assessment in response to bolus volume. In patients this will likely be observed at a lower threshold and should be tested in future studies.

During swallowing UES opening is physiologically complex and relies on cricopharyngeal (CP) muscle relaxation, along with hyolaryngeal excursion, and modified sphincter dimensions based on bolus size and compressibility.[5-7] The CP muscle must deactivate for relaxation to occur, and this deactivation 'pause' is thought to be affected by bolus size.[18] There was a lengthened UES OT for larger boluses in this study, especially evident for 20 and 30mls. It has recently been shown that amongst healthy subjects larger liquid boli of 20ml were able to drive the UES open, which in itself leads to CP deactivation.[18] Mechanoreceptors deep within the CP muscle fibres are thought to send afferent feedback via vagal pathways which activate submental muscles for longer, in turn keeping the UES open at greater distension until the larger bolus has cleared.[18] In oropharyngeal dysphagia, with insufficient extent and/or duration of UES opening, elevated hypopharyngeal distension pressures are expected. Therefore when there is a mismatch between the volume swallowed and the UES opening time, the rate of trans-sphincteric flow increases and this leads to disproportionately elevated upstream pressures.[5, 20] A punctuated increase in hypopharyngeal distension pressure, at a particular volume, may mark the point of failure of bolus accommodation within the swallowing mechanism.[20]

Finally, in regards to catheter diameter, as expected this within subject comparison study showed effects on a number of contractility, and some distension, metrics (see Table 1, Fig. 2). We consistently recorded pressures of higher amplitude in the UES with the larger catheter. Length

tension properties of luminal muscles maintain a longer muscle length during contraction in the presence of a larger diameter catheter, therefore increasing the tension (pressure) measured.[15-17] We expected the pharyngeal contractile pressure to be higher with a larger catheter. The fact that only a statistical trend for increased pressure ($p<0.077$) was observed highlights the potential variability in this parameter.

Possible confounding factors, such as the irregular shape of the pharynx in combination with our use of unidirectional pressure sensors, could have markedly impaired pressure measurements. Thus our potential to measure volume-related contractile pressure differences in this region may be compromised. Indeed, studies investigating the symmetry of deglutitive pharyngeal and UES pressures using state-of-the-art 3D HRM catheters have recently been published.[19-34] Whilst it could be argued that circumferential sensors are optimal for pharyngeal manometry the provision of circumferentially *averaged* results for each sensor is not necessarily akin to obtaining multiple separate, radially orientated readings.[24] Furthermore, parameters of pharyngeal peristalsis, even when based on circumferentially averaged pressure measurements, have shown significant intra- and inter- subject variability[35] and poor test-retest reproducibility of pharyngeal contractility measurements in particular.[23] As the factors driving the measured pharyngeal occlusion pressure are clearly complex, we believe a re-direction of attention to other, more reliable parameters, such as bolus distension area and pressure-flow timing is needed. Hypopharyngeal IBP and flow timing measures elucidated physiological modulation to volume challenges in this study, and as previously reported hypopharyngeal IBP is a symmetrical measure, likely due to the equalised pressures within the bolus space at this time point.[24]

In the UES zone specifically, the larger catheter detected a shorter UES OT and a higher UES IRP. We believe that this is most likely a result of the greater opportunity for contact between the UES wall and the impedance electrodes/pressure sensors, due to the larger catheter circumference. As previously discussed, asymmetry may have also influenced the UES IRP. Indeed it has been recently shown that, unlike pharyngeal intrabolus pressure,[24] UES relaxation pressures are asymmetrical.[34]

Conclusion

This study highlights the importance of including distension, flow and timing measures for meaningful assessment of swallow physiology and pathophysiology. Therefore, capturing key swallow modulation features using HRIM assessment requires the use of optimally conductive boluses of a range of volumes, ideally up to 20ml in patients, when considered clinically safe to do so. Furthermore, inaccurate interpretation of findings may occur if pressure results are not considered in context of the catheter characteristics used for acquisition of swallow assessment. Diagnostic reference ranges specific to catheter type and diameter are needed for reliable interpretation of oropharyngeal dysphagia assessment.

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Figures

Figure 1. Individual Swallow Function Variables derived using Pressure-Flow Analysis with AIM*plot* software.

The first step in the analysis routine was to view a complete pressure topography plot of all pressure (and embedded impedance) data for each swallow. Followed by identification of the following landmarks: the time of Upper Esophageal Sphincter (UES) relaxation onset and offset and the axial positions of the velopharynx, hypopharynx, UES apogee and UES distal margin.

The software then created a pressure topography sub-plot of the pharyngo-UES region (see contour plot in Top Panel) which was automatically populated with the relevant analysis features allowing rapid automated calculation of 10 separate swallow function variables as follows: ***velopharyngeal tongue base contractile integral*** (VCI) was calculated based on pressures >20 mmHg in the region of the velopharynx and tongue base; the time of pharyngeal maximum admittance (Time Ph Max Ad) guided the calculation of pressure at maximum admittance (P Max Ad) and therefore the ***hypopharyngeal intrabolus pressure*** (hIBP, at 1cm proximal of the UES apogee position i.e. position Y); the time of pharyngeal maximum contractile pressure (Time Ph Max P) guided the calculation of ***mean pharyngeal peak pressure*** (Peak P) and the ***pharyngeal distension-contraction latency*** (Ph DCL); the axial trajectory of the UES high pressure zone during the swallow (UES position) determined the UES admittance and pressure profiles (see graph in Bottom Panel) from which the ***UES maximum admittance*** value (UES Max Ad), the ***mean UES basal pressure*** (UES Basal P), the ***0.25s UES integrated relaxation pressure*** (UES IRP) and the ***UES post relaxation peak pressure*** (UES Peak P) were calculated; the ***UES open time*** (UES OT) was also estimated based on the time from rapid admittance upstroke (X1, Bottom Panel), signifying opening, to the inflexion of the admittance downstroke, signifying closure (X2, Bottom Panel); finally, the level of admittance recorded at UES closure (i.e. the downstroke inflexion; 25mS in this example) provided an admittance threshold for estimation of the ***pharyngeal bolus presence time*** (Ph BPT) (see X1 and X2, Top Panel).

Figure 2. Effects of Bolus Volume and Catheter Diameter on Velopharyngeal contractile integral, Pharyngeal Peak Pressure, UES Opening, and UES Post Swallow Peak Pressure

Data are estimated marginal means (95% CI) compared with general linear model repeated measure analysis, with catheter diameter and bolus volume as covariates (Bonferroni pairwise adjustments for multiple comparisons). Swallow function variables were derived by Pressure Flow Analysis, AIMplot software. * Pairwise significance ($p<0.05$) vs 30mls. # Pairwise significance ($p<0.05$) vs 20mls. ¤ Pairwise significance ($p<0.05$) vs 10mls.

Tables

Variable Subtype	Variable	ANOVA parameters	Volume Effect	Diameter Effect	Vol*Di Interaction
Contractility Variables	Velopharyngeal/Tongue base Contractile Integral	*F* *P* np^2	*10.930*↑ **0.011** 0.897	2.049 ns	0.832 ns
	Pharyngeal Peak Pressure	*F* *P* np^2	0.603 ns	4.014 0.077 0.399	0.366 ns
	Upper Esophageal Sphincter (UES) Basal Pressure	*F* *P* np^2	1.338 ns	*18.426*↑ **0.003** 0.697	0.416 ns
	UES Post Relaxation Peak Pressure	*F* *P* np^2	1.031 ns	*9.769*↑ **0.014** 0.550	0.284 ns
Distension Pressure Variables	Hypopharyngeal Intrabolus Pressure 1 cm above UES	*F* *P* np^2	*10.998*↑ **0.039** 0.936	3.950 0.094 0.397	1.196 ns
	UES Integrated Relaxation Pressure (0.25s)	*F* *P* np^2	*10.913*↑ **0.011** 0.897	*9.433*↑ **0.015** 0.541	0.085 ns
Distension Diameter Variable	UES Maximum Admittance	*F* *P* np^2	*56.539*↑ **<0.001** 0.978	1.959 ns	0.774 ns
Flow Timing Variables	Pharyngeal Distension-Contraction Latency	*F* *P* np^2	*36.401*↑ **0.001** 0.967	0.085 ns	0.265 ns
	Pharyngeal Bolus Presence Time	*F* *P* np^2	1.808 ns	4.246 0.073 0.347	1.573 ns
	UES Opening Time	*F* *P* np^2	*11.572*↑ **0.010** 0.903	*8.203*↓ **0.021** 0.506	0.857 ns
Global Swallow Function Variables	Swallow Risk Index	*F* *P* np^2	1.269 ns	0.170 ns	4.202 ns
	Post Swallow Impedance ratio	*F* *P* np^2	*10.834*↓ **0.011** 0.897	1.121 ns	0.586 ns

Table 1. Effects of Bolus Volume and Catheter Diameter on All Swallow Function Variables

Data are main effects and interaction effects of bolus volume and catheter diameter on swallow function variables, calculated with two-way, within group analysis of variance. F = F statistic for effect; P = statistical significance; np^2 = effect size; ↑↓ indicates the direction of the effect for larger volumes/larger catheter; ns = not significant.