

Three-Dimensional Manometry of the Upper Esophageal Sphincter in Swallowing and Nonswallowing Tasks

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Objectives/Hypothesis: High-resolution manometry (HRM) is useful in identifying disordered swallowing patterns and quantifying pharyngeal and upper esophageal sphincter (UES) physiology. HRM is limited by unidirectional sensors and circumferential averaging of pressures, resulting in an imperfect understanding of pressure from asymmetrical pharyngeal anatomy. This study aims to evaluate UES pressures simultaneously from different axial directions.

Study Design: Case series.

Methods: Three-dimensional HRM was performed on eight healthy subjects to evaluate circumferential UES pressure patterns at rest, during the Valsalva maneuver, and during water swallowing.

Results: Multivariate analysis of the variance revealed a significant main effect of circumferential direction on pressure while at rest ($P < .001$); pressure was greater in the anterior and posterior portions of the UES versus lateral portions. A significant main effect of direction on pressure was not found during the Valsalva maneuver. During swallowing of a 5-mL water bolus, circumferential direction had a significant main effect on pressure immediately before UES pressure dropped ($P = .001$), while the UES was open ($P = .01$) and at UES closure ($P < .001$). There was also a significant main effect of sensor level along the vertical axis on pressure immediately before UES pressure dropped ($P = .032$) and at UES closure ($P < .001$). Anterior and posterior pressures were again greater than lateral pressures at all swallowing events.

Conclusions: These results confirm that UES pressures vary significantly based on their circumferential origin, with the majority of the total pressure generated in anterior and posterior regions. Improved understanding of UES pressure in a three-dimensional space can lead to more sophisticated treatments for pharyngeal and UES dysfunction.

Key Words: Deglutition, Valsalva maneuver, upper esophageal sphincter, high-resolution manometry.

Level of Evidence: 4.

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INTRODUCTION

Although the overall function of the upper esophageal sphincter (UES) is well understood, the specific physiology of relaxation and pressure generation has only recently begun to be investigated. The UES must maintain tonicity at rest to prevent exchanges between

contents of the esophagus and pharynx, but it must also relax in precise intervals, such as during swallowing, belching, and vomiting. Swallow-related UES activity is governed by complex biomechanics in which the hyoid and larynx move superiorly and anteriorly,¹ changing the anatomical configuration of the laryngopharynx and UES. This structural displacement, combined with cricopharyngeus muscle relaxation, results in a pressure drop within the UES, opening of the sphincter, and bolus passage; after bolus passage, the UES constricts to a pressure greater than baseline.¹ UES dysfunction can result in bolus residuals in the pharynx, bolus redirection into the airway, and swallowing inefficiency.^{2–4}

Manometry has been applied at the pharyngoesophageal segment to examine pressure profiles of the UES at rest, during swallowing, and during other nonswallowing tasks. High-resolution manometry (HRM) takes advantage of closely spaced pressure sensors arranged along the length of a catheter, allowing for the continuous collection of pressure measurements with greater spatial resolution than conventional manometry.^{5,6} HRM has revealed detailed temporal pressure profiles reflective of UES physiology as well as functional contributions of anatomic structures during swallowing and nonswallowing tasks. The usefulness of HRM has been shown in assessing functional differences in UES and pharyngeal pressure patterns unique to various situations, including head turn,⁷ chin tuck,⁷ effortful swallow,^{8,9} Mendelsohn maneuver,⁸ differing bolus size,^{10,11}

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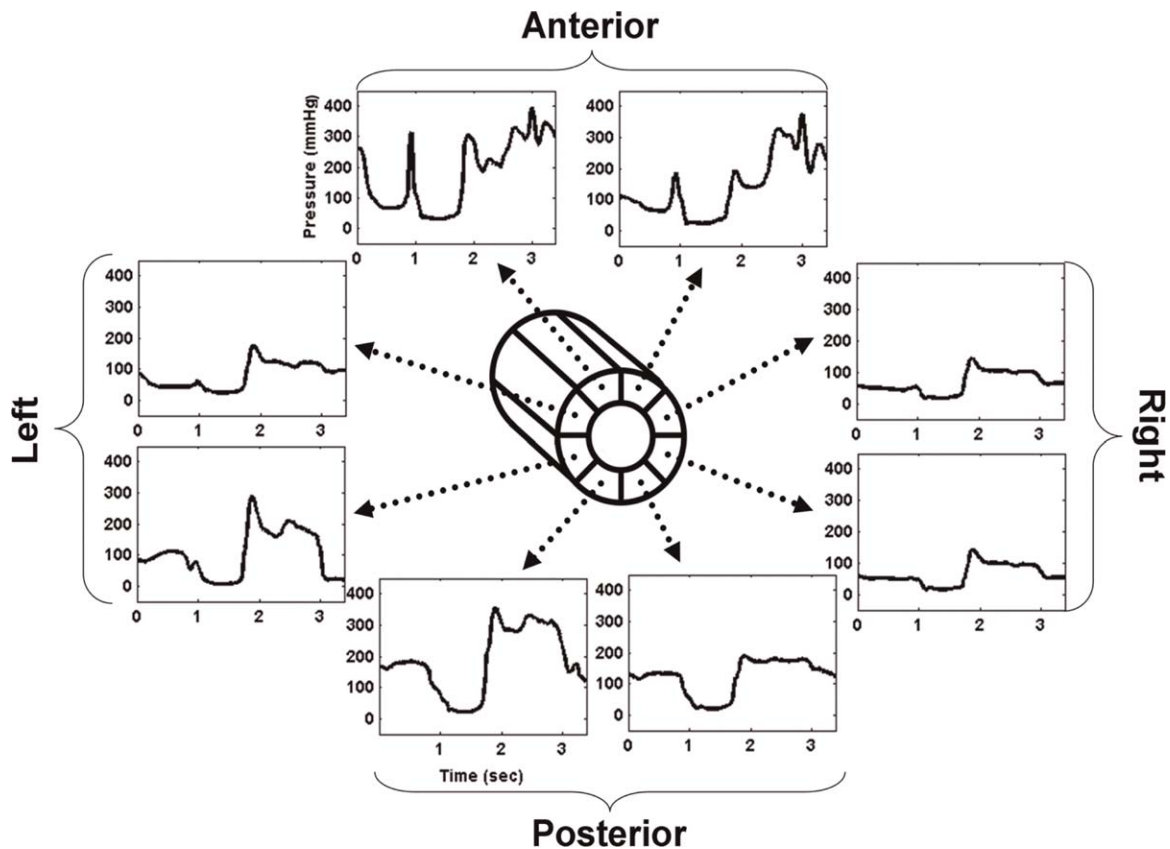


Fig. 1. Diagram of a single pressure sensor from a three-dimensional (3D) high-resolution manometry catheter. Eight individual sensors are located around the perimeter of the catheter, and each one outputs a unique pressure trace. To simplify results, sensors were grouped by averaging pairs of pressure traces into four regions: anterior, posterior, left, and right. Twelve of these 3D sensor levels are included along the length of the catheter.

and during electrical stimulation.¹² Furthermore, such pressure patterns at the UES and pharynx were shown to be capable of identifying features of disordered swallowing,^{13–15} making HRM a useful tool for quantifying swallowing behaviors.

Prior studies have demonstrated that the UES^{16,17} and pharynx¹⁸ generate asymmetrical longitudinal and circumferential pressures during swallowing, though such studies were limited to low-resolution techniques. These asymmetries are not surprising given the anatomical asymmetry in the pharynx and UES, generated in part by proximity to the larynx and thoracic outlet, configuration of the cricopharyngeal muscle, and distortion from laryngeal traction and displacement during swallowing. Standard HRM is unable to account for asymmetries because pressure sensors are either unidirectional or averaged around the circumference to produce a single recording through the axial plane at a given point in time. These clinically available catheters were designed to evaluate esophageal function where asymmetric pressures would be rare. To reveal the contributing sources of pressure with the UES region and determine which subset of pressures contribute to the values recorded by standard HRM, we evaluated UES function with a three-dimensional (3D) HRM catheter (3D-HRM) containing a series of circumferentially arranged independent pressure transducers. 3D-HRM has been used in

studying the esophagogastric junction, where it proved beneficial in eliciting asymmetrical sources of pressure contributions that reflected known anatomy, as well as corrected estimations made by previous manometric studies.^{19–21} Based on this prior work and the anatomic asymmetry of the UES, we predicted that 3D-HRM would reveal significant pressure differences between anterior, posterior, and lateral locations in the UES with baseline pressures and during swallowing and nonswallowing tasks invoking the UES. These differences would elucidate anatomical contributions responsible for the complex UES pressure physiology at both rest and during deglutition. Additionally, we predicted that 3D-HRM would identify pressure loci that contribute most to traditional HRM values, allowing for the interpretation of those values within the context of a 3D space.

MATERIALS AND METHODS

Data Collection

Four males and four females, ages 21 to 25 years, participated in this study with the approval of the institutional review board of the University of Wisconsin–Madison. All subjects were without known swallowing, neurological, or gastrointestinal disorders. Subjects were instructed to refrain from eating for 4 hours and drinking for 2 hours before the study to reduce the effects of satiety.

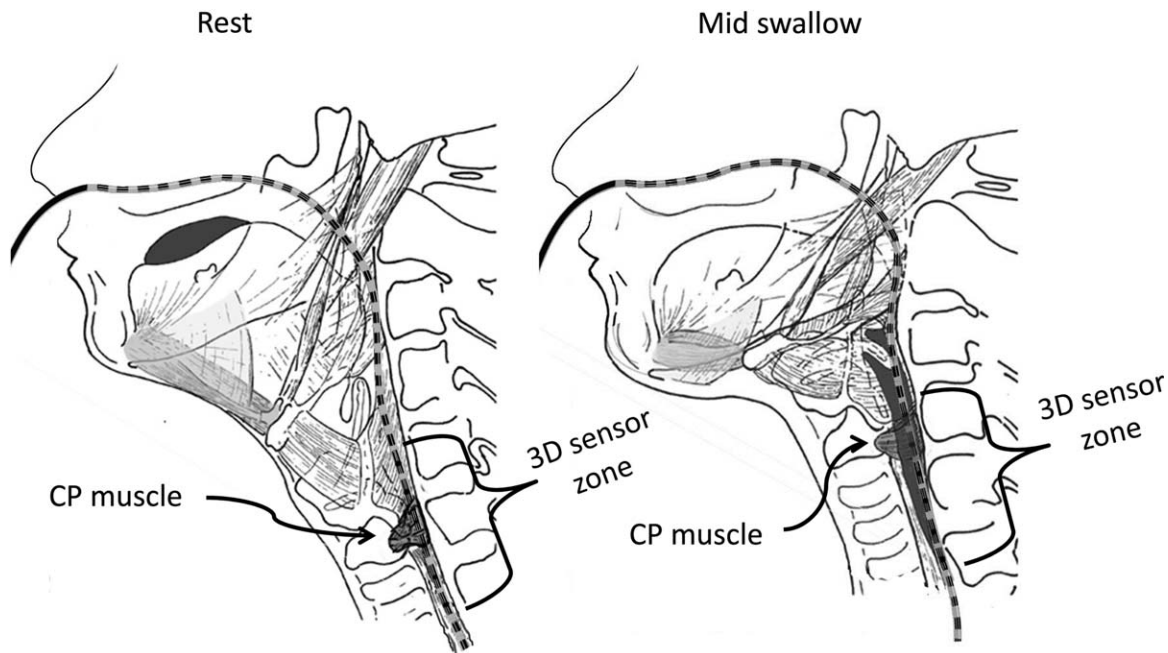


Fig. 2. Position of the three-dimensional (3D) catheter within the pharynx and superior esophagus at rest and midswallow. 3D sensors were positioned within the upper esophageal sphincter region, involving the cricopharyngeus (CP) muscle. During swallowing, the CP muscle elevates relative to the catheter due to laryngeal movement.

The ManoScan 3D HRM (Given Imaging, Atlanta, GA) was used for this study. This catheter is calibrated to record pressure between -20 and 600 mm Hg, with a fidelity of 2 mm Hg and a resolution of 50 Hz. This particular manometer has an outer diameter of 4.2 mm and contains 44 pressure transducer groups along the length of the catheter. A 93 -mm portion of the manometer supports 12 transducer groups that each contains eight transducers arranged circumferentially to acquire pressure data in 45° increments around the circumference of the catheter (Fig. 1). Each group of sensors is 5 -mm long, with 3 -mm spacing between.

Topical 2% viscous lidocaine hydrochloride was applied to the nasal passages and manometric catheter as a lubricant and topical anesthetic. Once the catheter was positioned with the 3D portion in the UES region, subjects were allowed to rest for several minutes before testing began.

Baseline recordings of UES pressure were acquired by having subjects sit quietly without movement, swallows, speech, coughs, or other behaviors that may have altered UES pressure. Three sensor levels were found to incorporate the UES region in each subject at rest and were selected by identifying the region of constantly elevated pressure indicative of the UES.⁷ Subjects also performed a series of five Valsalva maneuvers, involving compression of the abdomen and chest cavity against a closed glottis. The UES high-pressure zone was found to span three sensor levels during this task as well. Finally, each subject swallowed five boluses of 5 mL of water via syringe. Jones et al.²² found that the UES region involved approximately five sensor levels along the manometer during a swallow due to elevation of the larynx and soft palate relative to the catheter (Fig. 2). Although the exact location of the UES in relation to the sensors during swallowing was unknown in this study, we selected five sensor groups on the manometer to accommodate for UES movement relative to the catheter.

Data Analysis

Baseline pressures from each of the 24 sensors within the UES zone (3 sensor levels \times 8 directions) were averaged over the

length of each task. The mean pressures per sensor position per task were then combined from all subjects, resulting in a single mean pressure value for each sensor position at rest (24 positions). This process was repeated for the Valsalva maneuver tasks. For the swallowing tasks, recordings from the circumferential pressure transducers at each sensor level were averaged together into a single mean swallowing pressure trace. A custom MATLAB program (MathWorks, Natick, MA) was then used to find the time point immediately before mean pressure drop to near 0 mm Hg, halfway through the nadir period, and time of peak pressure upon UES closure for each sensor level (Fig. 3). These events were selected based on key landmarks of the swallowing pressure profile as determined by the average pressure of all eight sensors per level.⁷ To simplify analysis for this study, the eight circumferential sensors were statistically collapsed via averaging into pairs to form four zones of pressure measurement: anterior, posterior, left, and right. Although this approach decreased circumferential resolution, it increased statistical degrees of freedom on which to calculate differences in normal subjects.

A 3×4 repeated measures multivariate analysis of variance (MANOVA) was performed on UES baseline and Valsalva pressures (three sensor levels, four directions). A 5×4 repeated measures MANOVA was performed on swallowing pressures (five sensor levels, four directions). An α criterion of $.05$ was chosen to represent significance. The Greenhouse-Geisser corrections were used when the assumption of sphericity was not met. Pairwise comparisons were corrected using the Bonferroni method. Effect sizes are reported as a partial η^2 .

RESULTS

Pressure in the UES region at rest was found to be asymmetrical and dominated by the anterior and posterior directions. Analysis of the baseline pressures revealed a significant main effect of direction on pressure ($P < .001$) (Fig. 4), with anterior and posterior pressures significantly greater than both left and right

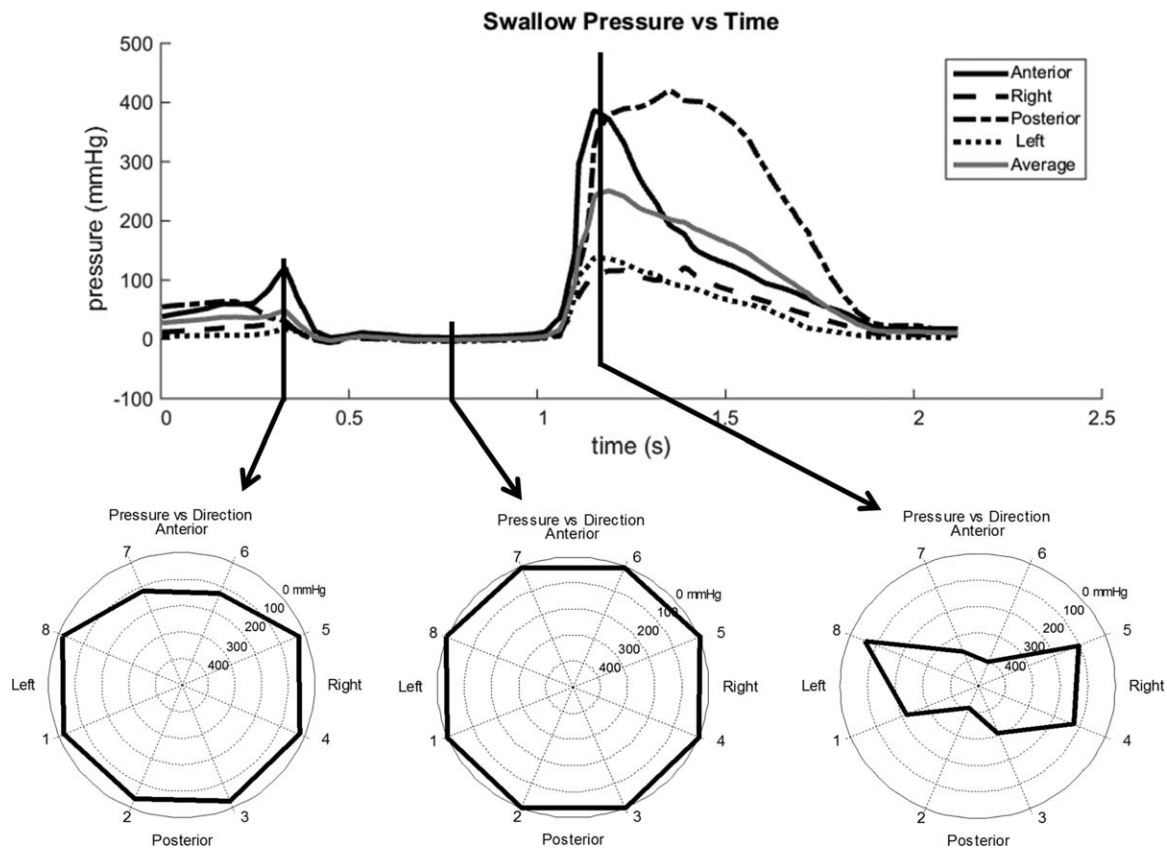


Fig. 3. Pressure trace from a typical swallow of 5 mL of water at a single sensor level. Directional sensors around the perimeter of the catheter were averaged into a single pressure trace (solid grey line) to identify landmarks typical of a traditional high-resolution manometry (HRM) pressure recording. These landmarks were then analyzed with the three-dimensional HRM system to identify inherent asymmetries within the upper esophageal sphincter during a swallow, demonstrated by the inset polar graphs showing pressure values from the original eight circumferential sensors before averaging into pairs.

pressures. There were no significant interactions between pressure and sensor level.

There was no main effect of direction on pressure during the Valsalva maneuver ($P = .18$) (Fig. 5). As expected, pressures at all positions were greater than their counterparts at baseline, but lateral pressures increased to a greater extent than anteroposterior pressures, and therefore eliminated any statistical differences between the directions. Similar to baseline pressure distribution, there was no significant interaction between sensor position and level.

Analysis of pressures during 5-mL bolus swallows revealed a significant main effect of direction on pressure during the course of a swallow immediately before pressure dropped from UES opening ($P < .001$) (Fig. 6A) while the UES was open ($P < .01$) (Fig. 6B) and at UES closure ($P < .001$) (Fig. 6C). During these events, pressure within the UES followed a similar pattern to baseline pressures, where anteroposterior pressures were often greater than lateral pressures. Postswallow peak pressures were also elevated up to 100% of baseline. Furthermore, with the inclusion of five sensors to span the assumed UES superior movement during swallowing tasks, there was a significant effect of sensor level on pressure at the preswallow peak ($P = .004$) and at UES closure ($P < .001$). There were no

significant interactions between pressure and sensor level.

DISCUSSION

The asymmetrical pressure generated at the UES demonstrated in this study confirms results from past studies of the pharynx and UES that used low-resolution manometry.^{16,17} Even at rest, UES pressure was primarily generated from anterior and posterior locations. The significant circumferential pressure differences inform on traditional HRM measurements such that a single averaged pressure is comprised of widely varying pressures. Because pressure is unequally distributed within the UES, values obtained with traditional HRM do not represent true pressure maxima or minima within this region. This problem is magnified with any manometer using unidirectional sensors, as sampling of pressure data will represent only a single direction within the UES zone, whereas these current data reveal anterior and posterior pressures can be three to four times higher than lateral pressures at baseline and during swallowing (Figs. 4 and 6).

We know from anatomic studies and videofluoroscopy that the UES rests between the spine and larynx at the level of the cricoid region. The pressure pattern

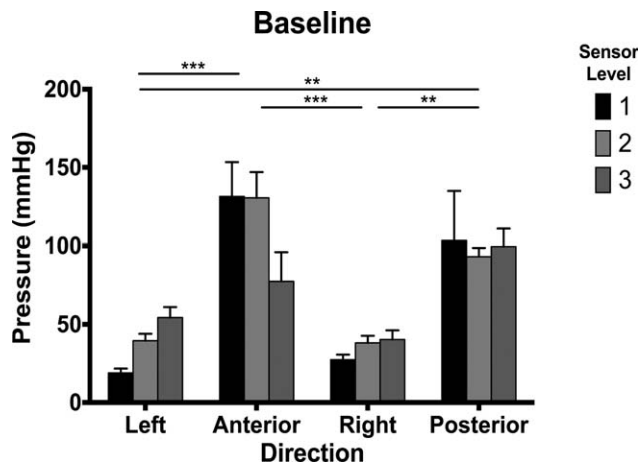


Fig. 4. Average upper esophageal sphincter (UES) pressures at baseline for anterior, posterior, left, and right directions. Sensor levels 1, 2, and 3 represent the superior, middle, and inferior portions of the UES, respectively. Multivariate analysis of the variance indicated a significant main effect for sensor direction on pressure, where anterior and posterior positions were found to have significantly higher pressures compared to left and right positions. Error bars indicate standard error of the mean. ** $P < .01$. *** $P < .001$.

revealed in this study therefore suggests that anteroposterior pressures recorded at rest in this region are, in part, passive pressures of spine and cricoid cartilage resting against the manometric sensors. Anterior pressure generated by the cricoid is also supported by slight vertical asymmetry with the average pressure lower at the inferior sensor where the cricoid cartilage would transition to the posterior membranous portion of the trachea. In addition, electromyography studies indicate there is some nearly continuous, low-level muscle activity in the cricopharyngeus muscle at rest. The cricopharyngeus muscle extends from lateral cricoid attachments to wrap the superior esophagus with its dominant muscular component situated within the posterior portion of the pharynx. Lateral pressures would therefore represent the cricopharyngeus muscle activity supporting a closed UES.

This conceptualization of pressure source is also supported by the changes that occur with a Valsalva maneuver. In this study we find circumferential pressure equalization (Fig. 5), with the majority of change occurring in the lateral sensory groups. UES contraction increases lateral pressures, and the breath-hold posture draws the cricoid away from the spine to reduce the effect of anteroposterior forces. This result indicates that performing certain voluntary maneuvers can alter pressure distribution, and that the Valsalva maneuver might engage the cricopharyngeus muscle to achieve this change.

These results also improve our understanding of how the UES generates and modulates sustained pressures. Although the cricopharyngeus muscle is thought to be the main source of active forces within the UES region at rest,^{23,24} baseline activity may be superseded by the contact pressures from rigid anatomic structures. As pressure will only occur on a suspended catheter when it is compressed, it would be expected that

pressures on opposite sides of the manometer appear to reflect each other with minor differences due to irregularity in sensor contacts.

The UES during swallowing of 5-mL water boluses produced directionally dependent pressure patterns similar to those experienced at baseline at the selected landmarks. Despite the displacement of the larynx during a swallow^{1,25} and the changing absolute pressure values, significant differences in pressure were found between circumferential sensor positions immediately prior to UES opening, at peak UES pressure upon closing, and even when the UES was considered open during the nadir period. UES pressures at the evaluated swallowing events can be broken down into pressures from different origins within the UES. Anteroposterior pressures were generally greater than their lateral counterparts during each of these events. The unequal pressure distribution during the nadir period was a surprise, as we had hypothesized all pressures to be near zero within the UES space during the time of bolus flow through the UES zone. More inferior and laterally directed sensors reflected pressures close to or below zero, whereas more superior- and anteroposterior-directed sensors retained positive pressures during maximum opening. The unequal distribution is likely the result of an asymmetric opening dominated by lateral expansion and thus lower pressures. Additionally, sensor level was found to have a significant effect on pressure immediately prior to UES opening and at peak UES pressure upon closing. This result was expected and was likely an artifact of the methodology, because five levels were selected to account for total UES movement despite the UES only known to span three levels at a given time. Thus, superior sensors represent the location of the UES during the opening phase, but this also results in the measured and expected pressure difference from inferior sensors.

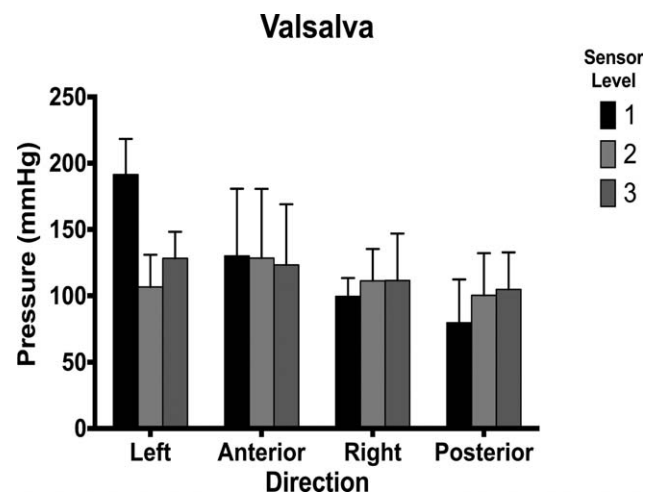


Fig. 5. Average upper esophageal sphincter (UES) pressures during the Valsalva maneuver for anterior, posterior, left, and right directions. Sensor levels 1, 2, and 3 represent the superior, middle, and inferior portions of the UES, respectively. No significant main effects were found for direction or sensor level on pressure. Error bars indicate standard error of the mean.

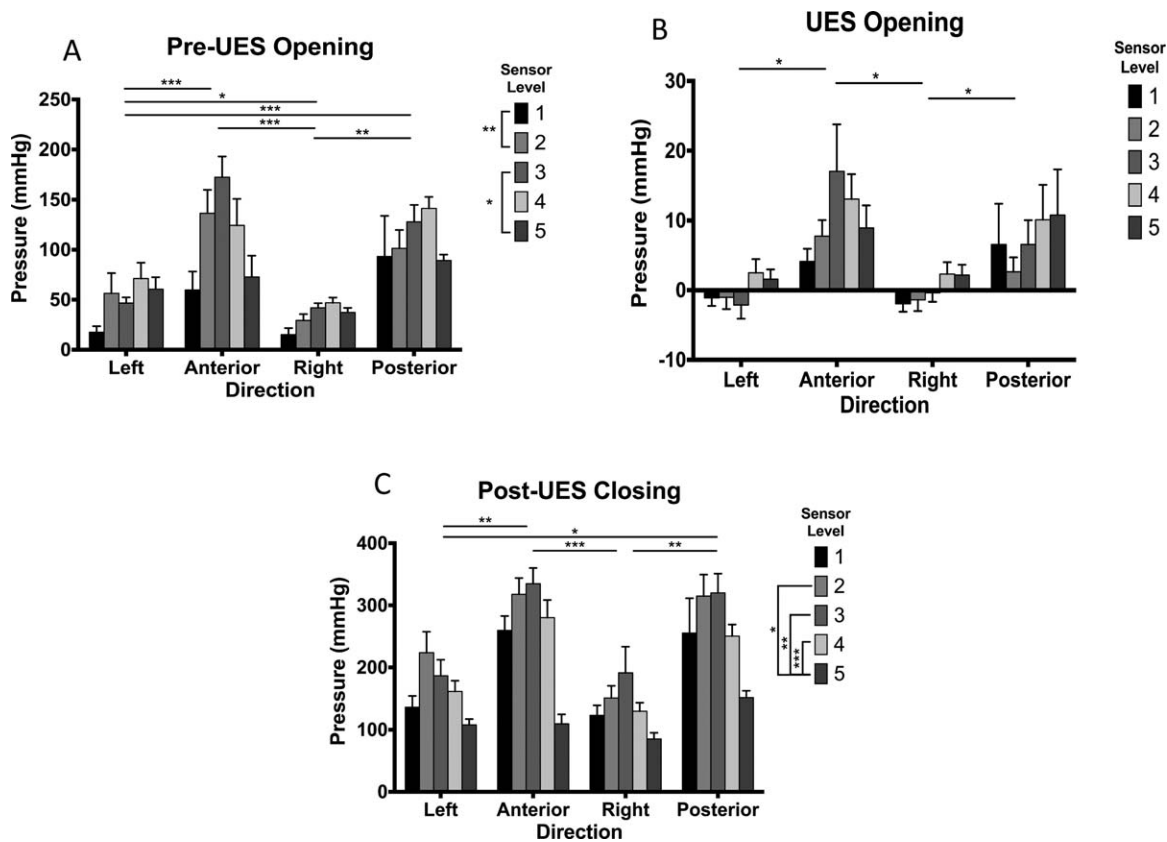


Fig. 6. Average upper esophageal sphincter (UES) pressures during a swallow of 5 mL of water for anterior, posterior, left, and right directions. Sensor levels 1 to 5 correspond to the superior-most to inferior-most portions of the UES, respectively. (A) Pre-UES opening pressures. Significant differences between sensor levels were found. A main effect of direction on pressure was also found, with significant differences occurring between anterior and posterior versus left and right directions. (B) UES pressures during the nadir period. A main effect for direction on pressure was still found, with significant differences occurring between anterior and posterior versus left and right directions. (C) UES pressures upon UES closure after bolus passage. Significant differences between sensor levels and between directions were found, with significant differences occurring between anterior and posterior versus left and right directions. Error bars indicate standard error of the mean. * $P < .05$. ** $P < .01$. *** $P < .001$.

The results of this study provide additional rationale behind the surgical procedure in the management of cricopharyngeal dysfunction. For cricopharyngeal myotomy, it is recommended that the cricopharyngeus be cut at a midline posterior location for both open²⁶ and endoscopic laser approaches.²⁷ This may be the ideal location given the increased pressure from the posterior aspect across multiple tasks, especially swallowing. Similarly, reports of botulinum toxin A (Botox) injection to the cricopharyngeus muscle generally follow Schneider et al.'s²⁸ methods of injecting into the posterior and ventrolateral sides of the muscular segment. Based on our study, this treatment choice is supported for optimizing results as well as limiting the risk for Botox spread to laryngeal muscles.

When studying cricopharyngeal dysfunctions, a 3D catheter may be more sensitive to failed muscular relaxation. The lateral pressure decline during swallowing identified in this study may not occur with UES disease, and the equalization of UES pressures that were seen with the Valsalva maneuver may fail to occur with poor laryngeal elevation. This information also reveals the vulnerability of unidirectional sensors when evaluating UES function in a patient population. When trying to characterize pressure dysfunctions, errors would likely

be made simply due to the rotation of the sensor to a low- or high-pressure space. These new data provide a basis to re-explore what should be considered normal for pressure and pressure changes during UES-related events, most importantly swallowing.

We experienced some possible limitations in the study. Although we studied a limited number of subjects, we believe the pressure patterns found are applicable to the wider population of normal swallowers because of the consistency within and between subjects. Next, we were unable to precisely discern the location of the UES at all times during swallows. To compensate for this, we selected five levels of sensors based on a previous study of radiographically confirmed UES location.²² Future studies will precisely associate pressure with UES structure through radiography. Finally, by selecting specific events during swallows at each sensor group level, we eliminated the factor of time during swallows. Future studies should examine how pressure changes over time within the UES.

CONCLUSION

This study revealed asymmetric pressures in the UES at rest and during a 5-mL bolus swallow. The

anterior and posterior locations in the UES often generated greater pressures than the lateral locations throughout these tasks, reflecting known anatomy and indicating a need to consider such subpressures when interpreting traditional HRM measurements. During the Valsalva maneuver, subjects increased lateral UES pressures near levels generated in anterior and posterior directions. In light of this information we will need to acknowledge the limitations of a single pressure recording or an averaged pressure at the level of the UES when evaluating pressure events associated with swallowing. These results should help us to optimize interventions within the UES aimed at correcting pressure abnormalities in our patient population.

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