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Upper esophageal sphincter impedance as a marker of sphincter opening diameter

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1Gastroenterology Unit, Child, Youth & Women’s Health Service, North Adelaide; 2School of Paediatrics and Reproductive Health, University of Adelaide, Adelaide, Australia; Departments of 3Geriatric Medicine and 5Radiology and 7Center for Swallowing Disorders, University Hospital Leuven; 4Translational Research Center for Gastrointestinal Diseases and 6Department of Neurosciences, ExpORL, University of Leuven, Leuven, Belgium

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Omari TI, Ferris L, Dejaeger E, Tack J, Vanbekevoort D, Rommel N. Upper esophageal sphincter impedance as a marker of sphincter opening diameter. Am J Physiol Gastrointest Liver Physiol 302: G909–G913, 2012. First published February 9, 2012; doi:10.1152/ajpgi.00473.2011.—The measurement of the physical extent of opening of the upper esophageal sphincter (UES) during bolus swallowing has to date relied on videofluoroscopy. Theoretically luminal impedance measured during bolus flow should be influenced by luminal diameter. In this study, we measured the UES nadir impedance (lowest value of impedance) during bolus swallowing and assessed it as a potential correlate of UES diameter that can be determined nonradiologically. In 40 patients with dysphagia, bolus swallowing of liquids, semisolids, and solids was recorded with manometry, impedance, and videofluoroscopy. During swallows, the UES opening diameter (in the latter fluoroscopic view) was measured and compared with automated impedance manometry (AIM)-derived swallow function variables and UES nadir impedance as well as high-resolution manometry-derived UES relaxation pressure variables. Of all measured variables, UES nadir impedance was the most strongly correlated with UES opening diameter. Narrower diameter correlated with higher impedance (r = −0.478, P < 0.001). Patients with <10 mm, 10–14 mm (normal), and ≥15 mm UES diameter had average UES nadir impedances of 498 ± 39 Ohms, 369 ± 31 Ohms, and 293 ± 17 Ohms, respectively (ANOVA P = 0.005). A higher swallowing risk index, indicative of poor pharyngeal swallow function, was associated with narrower UES diameter and higher UES nadir impedance during swallowing. In contrast, UES relaxation pressure variables were not significantly altered in relation to UES diameter.

We concluded that the UES nadir impedance correlates with opening diameter of the UES during bolus flow. This variable, when combined with other pharyngeal AIM analysis variables, may allow characterization of the pathophysiology of swallowing dysfunction.

deglutition disorders; manometry; electric impedance; radiology; diagnosis

PHARYNGEAL AUTOMATED IMPEDANCE MANOMETRY (AIM) analysis is a new methodology that can be used to analyze the patterns of flow and pressure generated during bolus swallowing. AIM analysis has high intrarater and interrater reproducibility (3) and derives pharyngeal pressure-flow variables, which are objective markers of deglutitive function altered in relation to ineffective swallowing and aspiration risk (3–5). Identification of the nadir impedance during bolus swallow is a critical measure used in AIM analysis that identifies the center of a swallowed bolus in both time and space. Hence the pressure at nadir impedance corresponds to the pressure during passage of the bolus center, and the time interval from nadir impedance to peak pressure measures the time lag from passage of bolus center to passage of contractile wave (3–5).

The ability to nonradiologically measure upper esophageal sphincter (UES) diameter during bolus swallowing may have clinical relevance, particularly for the identification of UES dysfunction. UES opening failures attributable to increased UES resistance to pharyngeal dysfunction are important determinants of efficacy of therapies targeting reduced UES resistance. It is well established that focal UES constriction can be identified manometrically as elevated intrabolus pressure (6, 8, 9). However, intrabolus pressure is a function of both UES diameter achieved during opening and the forces driving the bolus. Hence, in circumstances of weak bolus propulsion, intrabolus pressures can be difficult to measure accurately and may not be elevated. A similar conundrum exists for videofluoroscopy assessment, as it can be difficult to distinguish failure of UES opening attributable to obstruction rather than poor or weak bolus propulsion.

Theoretically the absolute value of the nadir impedance should be influenced by luminal diameter, but to date this has received little or no attention. In this study, pharyngeal and UES impedance manometric variables were examined in patients with dysphagia for potential correlates of UES opening diameter during bolus swallowing.

MATERIALS AND METHODS

Subjects. We analyzed videofluoroscopic investigations performed in 40 adult patients with dysphagia (24 men, mean age 46 yr, age range 23–95 yr) and 8 adult controls (3 men, mean age 38 yr, age range 24–47 yr). At the time of initial investigation, all subjects were enrolled in study protocols that were approved by the Research Ethics Committee, University Hospitals Leuven, Belgium. In dysphagic patients, underlying diseases/conditions were identified through a review of medical records. Eighteen patients had a neurological history (10 stroke and 2 Parkinson’s disease, 1 Huntington’s disease, 1 multiple sclerosis, 2 dementia, 1 spina bifida, and 1 postneurosurgery). Eight patients had underlying gastrointestinal disease (oesophageal motility disorders, gastroesophageal reflux disease). Four patients had an oropharyngeal tumor. Six patients had pulmonary disease...
(chronic obstructive pulmonary disease, lung abscess, pneumonia). The remaining four patients were respectively post cervical surgery, had Wegener disease, post septic shock, and diabetic.

Measurement protocol. Studies were performed in the Radiology Department, University Hospitals Leuven with a 3.2-mm diameter solid-state manometric and impedance catheter incorporating 25 1-cm-spaced pressure sensors and 12 adjoining impedance segments, each of 2 cm (Unisensor USA, Portsmouth, NH). Subjects were intubated after topical anesthesia (lignocaine spray), and the catheter was positioned with sensors straddling the entire pharyngo-esophageal segment (velo-pharynx to proximal esophagus). Pressure and impedance data were acquired at 20 Hz (Solar GI Acquisition System; MMS, Enschede, The Netherlands) with the subject sitting upright. Most subjects were tested with at least five boluses in the lateral view; liquid (×3), semisolid (×1), and solid boluses (×1). A standard liquid contrast material (Micropaque®) was given as liquid bolus and used with thickener (Thick & Easy) for semisolid boluses. A low osmotic hydrosoluble iodium compound (Ultravist®) was used when aspiration was suspected. The viscosity of the administered boluses was determined by a Rheomat 115 Viscometer. The Bingham viscosity of the liquid Barium (Micropaque®) was 0.22 Pa·s, 4.50 Pa·s for the semisolid bolus, and 15.7 Pa·s for solids. All controls were given boluses of 10-ml volume, whereas patients were given either 5-ml or 10-ml volumes as determined on clinical grounds by the attending specialist. Solid boluses consisted of a 4-cm² piece of bread soaked in the appropriate radiological marker. All bolus stock contained 1% NaCl to enhance conductivity.

Fluoroscopy analysis. Video loops of the fluoroscopic images of swallows acquired at 25 frames/s were reviewed by a speech pathologist, who did not partake in the initial studies and was blinded to the impedance manometry findings. Only swallows recorded in the lateral view were analyzed, and only the first swallow that followed any bolus administration to the mouth was analyzed. Rapid-repeat swallows and swallows with poor image quality were not included for analysis. Fluoroscopic images of swallows were blindly scored for the occurrence of aspiration using a validated eight-point penetration-aspiration scale (PAS) (7) and bolus residue using a six-point bolus residue scale, which defined the number of structures (valleculae, piriform sinus, and/or posterior pharyngeal wall) with residue (4, 5).

Fluoroscopy onscreen analysis software (MMS) was used to measure the maximum UES opening diameter (in the lateral view) during bolus swallowing. First, onscreen measurements were calibrated to the known distance between adjacent pressure sensors located along the catheter (10 mm, average of 3 readings taken). Commencing before swallow onset (defined by the timing of laryngeal elevation), the axial position of the UES proximal margin was identified (Fig. 1A).
fluoroscopic images of the swallow were then advanced frame by frame, and the maximum dimension of the UES was measured at 15–20 mm below the level of the upper limit of the tracheal air column (entrance laryngeal vestibule) at approximately the level of cervical vertebrae C5-C6. (Ø in Fig. 1A).

**Pharyngeal AIM analysis.** Pharyngeal AIM analysis of impedance manometry text data files was performed using AIMplot, a purpose-designed MATLAB-based analysis program developed to increase the applicability of the methodology for routine use (3). Pharyngeal AIM analysis derives four pharyngeal pressure-flow swallow variables and combines them into a swallow risk index (SRI). The technique has been described in detail previously (4, 5). In brief, the spatial limits of the pharyngeal stripping wave (from velo-pharynx to proximal margin of the UES high pressure zone) are identified by a region of interest (ROI) from the pressure isocontour plot (Clouse Plot). The value and timing of pharyngeal peak pressure (PeakP) are measured and then the pressure at nadir impedance (PNadImp) and the time from PNadImp to PeakP (tNadImp-PeakP) are determined. The average PNadImp, PeakP, and tNadImp-PeakP along the length of the pharyngeal segment are then calculated. The flow interval is an estimation of the duration of impedance drop within the distal pharynx within a second ROI (ROI 2) from −0.25 to 2.5 s of swallow onset (2, 3). The SRI was developed based on an iterative analysis evaluating the pattern of change in the four swallow variables in relation to the occurrence of aspiration. A higher SRI correlates with swallowing dysfunction and aspiration severity, and a mean SRI of 15 or more for liquid swallows has been shown in neurological patients to be optimally predictive of aspiration risk (3, 4).

**High-resolution manometry analysis of UES relaxation.** UES relaxation variables were measured within a third ROI (ROI 3) with spatial limits being defined to encompass the onset/setoff of UES relaxation and the orad movement of the UES high-pressure zone (Fig. 1B). With the use of the pressure values within ROI 3, UES relaxation variables were calculated by the established method of Ghosh et al. (2). These were UES relaxation interval, nadir relaxation pressure, intrabolus pressure, and the deglutitive UES resistance (calculated as intrabolus pressure/relaxation interval). With the use of impedance values within ROI 3, the value of nadir impedance at all positions along the ROI 3 was determined (Fig. 1, C and D) and averaged for the UES region (Fig. 1D).

**Statistical analysis.** The primary analysis compared fluoroscopically measured UES diameter with data determined for all measured swallow variables. Correlation between of average UES diameter and average swallow variable data was determined using Pearson Product Moment Correlation. Comparisons between patients and controls were performed using Student’s t-test. Comparisons in relation to bolus type characteristics and UES diameter level were performed using one- or two-way ANOVA with pairwise multiple comparison procedures (Holm-Sidak method), overall significance level at \( P = 0.05 \).

**RESULTS**

A total of 40 control swallows (24 liquid, 16 semisolid) and 186 patient swallows (112 liquid, 42 semisolid, and 32 solid) were analyzed. The mean \( \pm 95\% \) confidence interval reference range for UES opening diameter in controls was 10–14 mm. UES diameter of 19 patients was within this normal range with 16 patients narrower than normal (<10 mm) and 5 patients wider than normal (≥15 mm). Table 1 compares control and patient averages grouped for all boluses and according to the width of UES diameter measured. UES nadir impedance was the only impedance manometry variable showing pairwise statistical significance between patients with UES diameters <10 mm vs. both 10–14 mm and >15 mm (ANOVA \( P = 0.005 \), Table 1). UES nadir impedance was the most strongly correlated with UES opening diameter. Narrower average UES diameter correlated with higher average nadir impedance (\( r = -0.478, P < 0.001 \) for patients only) (Fig. 2). In patients, average bolus residue score (\( r = -0.450, P < 0.005 \)), flow interval (\( r = -0.350, P < 0.05 \)), and SRI (\( r = -0.284, P < 0.05 \)) were also significantly higher in relation to narrower average UES diameter. All UES relaxation variables correlated poorly with UES diameter and failed to reach statistical sig-

**Table 1. Swallow functional variables in relation to UES diameter**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n = 8)</th>
<th>Patients (n = 40)</th>
<th>UES Diameter &lt;10 mm (n = 16)</th>
<th>UES Diameter 10–14 mm (n = 19)</th>
<th>UES Diameter ≥15 mm (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>UES Diameter &lt;10 mm</td>
<td>UES Diameter 10–14 mm</td>
<td>UES Diameter ≥15 mm</td>
</tr>
<tr>
<td>PAS, mmHg</td>
<td>1 ± 0</td>
<td>3 ± 0*</td>
<td>3 ± 1</td>
<td>2 ± 2*</td>
<td>2 ± 1</td>
</tr>
<tr>
<td>BRS, mmHg</td>
<td>2 ± 0</td>
<td>3 ± 0</td>
<td>4 ± 1</td>
<td>2 ± 0*</td>
<td>2 ± 0*</td>
</tr>
<tr>
<td>PeakP, mmHg</td>
<td>152 ± 17</td>
<td>153 ± 15</td>
<td>183 ± 26</td>
<td>128 ± 19</td>
<td>153 ± 33</td>
</tr>
<tr>
<td>PNadImp, mmHg</td>
<td>22 ± 4</td>
<td>33 ± 4</td>
<td>42 ± 7</td>
<td>29 ± 6</td>
<td>22 ± 4</td>
</tr>
<tr>
<td>tNadImp-PeakP, ms</td>
<td>413 ± 30</td>
<td>270 ± 18†</td>
<td>249 ± 27</td>
<td>265 ± 28§</td>
<td>359 ± 22</td>
</tr>
<tr>
<td>Flow interval, ms</td>
<td>505 ± 59</td>
<td>1151 ± 104†</td>
<td>1440 ± 163</td>
<td>945 ± 134§</td>
<td>1012 ± 334</td>
</tr>
<tr>
<td>SRI</td>
<td>6 ± 2</td>
<td>24 ± 4†</td>
<td>34 ± 8</td>
<td>18 ± 3‡</td>
<td>16 ± 8</td>
</tr>
</tbody>
</table>

**UES HRM Analysis**

<table>
<thead>
<tr>
<th></th>
<th>UES relaxation interval, ms</th>
<th>UES nadir pressure, mmHg</th>
<th>UES intrabolus pressure, mmHg</th>
<th>UES resistance, mmHg/ ms</th>
<th>UES nadir impedance, Ohms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 8)</td>
<td>429 ± 45</td>
<td>19 ± 5</td>
<td>33 ± 5</td>
<td>93 ± 20</td>
<td>280 ± 11</td>
</tr>
<tr>
<td>Patients (n = 40)</td>
<td>653 ± 45*</td>
<td>13 ± 2</td>
<td>24 ± 2</td>
<td>51 ± 6*</td>
<td>411 ± 24*</td>
</tr>
<tr>
<td>UES Diameter &lt;10 mm</td>
<td>608 ± 75</td>
<td>13 ± 2</td>
<td>24 ± 2</td>
<td>54 ± 7</td>
<td>498 ± 39*</td>
</tr>
<tr>
<td></td>
<td>706 ± 69§</td>
<td>12 ± 3</td>
<td>24 ± 3</td>
<td>50 ± 12‡</td>
<td>369 ± 31a</td>
</tr>
<tr>
<td>UES Diameter 10–14 mm</td>
<td>509 ± 75</td>
<td>12 ± 2</td>
<td>25 ± 2</td>
<td>49 ± 10</td>
<td>293 ± 17a</td>
</tr>
<tr>
<td>UES Diameter ≥15 mm</td>
<td>509 ± 75</td>
<td>12 ± 2</td>
<td>25 ± 2</td>
<td>49 ± 10</td>
<td>293 ± 17a</td>
</tr>
</tbody>
</table>

Data are control/patient means ± SE for all boluses. Patients with a mean upper esophageal sphincter (UES) diameter of 10-14 mm are considered within normal range. *Patients significantly different to controls using Student’s t-test (\( P < 0.05 \), \( P < 0.005 \)). †Patients with normal UES diameter are significantly different to controls using Student’s t-test (\( P < 0.05 \), \( P < 0.005 \)). ‡ Patients significantly different in relation to diameter using one-way ANOVA and pairwise multiple comparison procedures (Holm-Sidak method); ‡ considerably different to <10 mm, ‡ significantly different to 10-14 mm, ‡ significantly different to ≥15 mm. PAS, penetration-aspiration scale; BRS, bolus residue scale; AIM, automated impedance manometry; PeakP, peak pressure; PNadImp, pressure at nadir impedance; tNadImp-PeakP, time from nadir impedance to peak pressure; SRI, swallow risk index; HRM, high-resolution manometry.
nificance (UES relaxation interval, $r = 0.022$; nadir pressure, $r = -0.034$; intrabolus pressure, $r = 0.014$; UES resistance, $r = -0.086$).

There were no statistically significant differences between semisolid and solid boluses for any measured variable. Data for these bolus types were therefore combined and compared with liquid boluses. Allowing for effects of differences in UES diameter, increased liquid bolus volume (5 ml vs. 10 ml) did not alter any variable significantly (data not shown); however, increased bolus viscosity reduced PAS scores ($1.5 \pm 0.3$ vs. $2.5 \pm 0.2$, $P < 0.05$), reduced flow interval ($800 \pm 86$ ms vs. $1,055 \pm 75$ ms, $P < 0.05$), reduced SRI ($13 \pm 3$ vs. $21 \pm 3$, $P < 0.05$), increased UES intrabolus pressure ($29 \pm 2$ vs. $23 \pm 2$ mmHg, $P < 0.05$), and reduced UES nadir impedance ($336 \pm 20$ vs. $403 \pm 17$ Ohms, $P < 0.05$).

### DISCUSSION

In patients with pharyngeal dysphagia, we examined the relationship between UES maximum opening diameter and a wide range of impedance manometry- and fluoroscopy-derived variables. Our findings show that, during bolus swallowing, UES nadir impedance is the best correlate of UES opening diameter and therefore may be a useful variable for assessing swallowing physiology.

We have previously recognized that the nadir impedance corresponds to the time when the lumen is maximally distended by a swallowed bolus, and therefore it has been used as a time reference point for the measurement of pressures using AIM methods. In this study, we have uniquely combined impedance measurement with high-resolution manometry to measure impedance during bolus flow within the high-resolution manometry-defined UES high-pressure zone. By pinpointing the measurement of impedance in time and space, such that it corresponds precisely to the location of the UES during swallow, we have been able to demonstrate that higher nadir impedance correlates with narrower diameter during UES maximum opening. This confirms what should indeed be expected based on theoretical first principles, whereby impedance of a filled chamber is inversely proportional to its cross-sectional area. This is the governing principle behind the function of the endoscopic functional luminal imaging probe (EndoFLIP), which has been used to measure dimensions and function of luminal and sphincteric regions of the gastrointestinal tract (2).

Several pharyngeal AIM variables and the SRI were correlated with patient average UES diameter. We have previously demonstrated that pharyngeal AIM variables are altered in

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**Fig. 2.** Scatter plot of UES diameter and UES nadir impedance.

**Fig. 3.** UES nadir impedance in a patient with UES obstruction. Data from a 10-ml liquid swallow recorded in a 58-yr-old man who developed dysphagia symptoms after anterior cervical fusion (C5-C6) surgery in whom fluoroscopy demonstrated high obstruction and no evidence of aspiration. A: videofluoroscopy image midswallow showing the manometric catheter (sensor number) in situ, and the arrow identifies the site of maximal pathological constriction during flow (at sensor position 13). B: Clouse color topography plot of the entire pharyngo-esophageal segment, showing the time of nadir impedance (Nadir Z, purple line) during bolus passage. C: plot of the nadir impedance during bolus passage showing that the highest value of impedance occurs at the same axial location of the site of maximal pathological constriction. D: plot of the pressures recorded axially along the pharyngo-esophageal segment at the time of maximal bolus flow (as shown in B). As has been demonstrated previously by Pal et al. (6), a marked step down of intrabolus pressure occurs at approximately the same axial location of the site of maximal pathological constriction.
relation to ineffective swallow (3, 4). Within the study cohort, narrower UES opening diameter was related to poor swallowing function (higher SRI) rather than UES obstruction (higher UES resistance). This is evidenced by the fact that no UES relaxation variable correlated with UES diameter. Deglutitive UES resistance (intrabolus pressure/relaxation interval) should be indicative of resistance to flow across the sphincter (1). In our study, this index and/or its component parts were not significantly altered in relation to UES diameter. Elevated pharyngeal intrabolus pressures have been described in patients with UES obstruction (6, 8, 9); values for PNadImp were higher with reduced UES diameter (Table 1), but this did not reach statistical significance. Hence, on balance, our findings suggest that the patient cohort studied predominantly suffered problems related to pharyngeal dysfunction rather than poor UES compliance. Indeed among the patients studied, only one, a patient studied after cervical fusion surgery, had clear evidence of UES obstruction. In this patient, elevated nadir impedance at the axial position of obstruction was clearly apparent (Fig. 3). Although encouraging, further studies in patients with fluoroscopically self-evident physical UES obstruction (e.g., cricopharyngeal bar) are clearly needed to establish a benchmark for the methodology in this group. Nevertheless, it should be recognized that reliably attributing poor UES opening to the cause of ineffective swallowing and aspiration can be very difficult to achieve with currently available methods. In a typical clinical setting, patients present with a wide range of pathologies and severities of dysphagia, and the lack of objective methods to better discriminate degrees of UES dysfunction means that interventions designed to weaken the UES (UES myotomy and Botulinum toxin injection) are being poorly targeted.

The development of AIM analysis has shown that it is possible to combine several different impedance pressure variables to derive an index of risk linked to swallowing dysfunction. The SRI, for example, appears to be a robust predictor of ineffective swallow and aspiration risk (3, 4). The fact that swallows with a higher SRI opened the UES less lends further support to the potential utility of the SRI. Extending our study further, impedance and pressure may be combined to describe UES function in more mechanical terms such as wall tension and compliance during bolus passage.

Our study has some limitations that were difficult to overcome given the need to capture all swallows fluoroscopically and the clinical nature of the patients enrolled who were mostly experiencing severe dysphagia with significant aspiration risk. For this proof-of-principle study, we combined data for semisolid and solid boluses administered to each subject. We hypothesized that, as semisolid and solid boluses have similar bolus conductivities (due to the addition of NaCl), the dominant factor influencing UES nadir impedance value would be UES diameter. Our findings are consistent with this hypothesis. We also had little control of bolus volumes administered to each patient, as this was based on clinical grounds. Although volume may influence the variables measured, we were unable to demonstrate any volume effects within the available dataset. Our measurements of diameter are based on two-dimensional fluoroscopic images recorded in the lateral view only. The UES is clearly a three-dimensional structure, which often distends asymmetrically in patients with dysphagia. Finally, air is swallowed concurrently with a bolus, and this may cause impedance to rise. By using the nadir impedance value, we reduce the potential impact of air; however, to date we have not critically examined air as a confounding factor. It is likely that the above-described limitations could have influenced the results, contributing to the variability in the data and the intermediate correlations seen. Despite this, the fact remains that UES nadir impedance was the best correlate of UES diameter in this study.

In conclusion, we provide evidence that the UES nadir impedance during bolus flow may reflect the diameter of the UES opening during bolus flow. This variable is easy to measure and, when combined with other pharyngeal AIM swallow variables, may be useful for characterizing swallow physiology and the causes of swallowing dysfunction. However, the variability seen in the measurement is high, and it remains to be determined whether this technique will be able to provide data that can influence clinical practice. Further studies are needed to validate this observation in patients with pharyngeal dysphagia attributable to obstructive pathology and other luminal settings, such as the esophagus and esophageal-gastric junction.

**REFERENCES**


