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Three-dimensional Analysis of the Human Pharyngoesophageal Sphincter

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Objectives: Dysfunction of the pharyngoesophageal segment (PES) is a common cause of oropharyngeal dysphagia. Surgical dilation of the PES uses cylindrical dilators that expand radially in a circular shape. Animal studies, however, suggest that the PES is kidney-shaped. The purpose of this investigation was to evaluate the 3D shape of the human PES with a novel casting method.

Methods: A platinum-cured liquid silicone polymer was infused under pressure into the upper aerodigestive tract of nine human cadavers to construct 3D casts of the maximally distended PES. Cross-sectional and volumetric analysis were performed using computed tomography and serial sectioning of the models. Canonical variate analysis was used to identify the shape features that best distinguishes the PES from the cervical esophagus.

Results: The mean age of the cadavers was 77.9 (SD ± 10.6) years, with 67% women. Analysis of the casts confirms that the human PES possesses a kidney-shaped structure at maximal distention, which is discretely different from the adjacent esophagus ($P < 0.001$). The posterior body of the cricoid cartilage formed the anterior wall of the PES, which provided a rigid structure responsible for preservation of the kidney shape during distention. The diameter of the maximally distended PES at the cricopharyngeus was highly variable (range = 0.86–4.68 cm²; SD = 1.33 cm²).

Conclusion: The data suggest that the human PES is not round and that targeted expansion at the level of the cricopharyngeus with an eccentrically shaped dilator may provide improved distention.

Key Words: Dysphagia, laryngology, pharynx.

Level of Evidence: 4

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INTRODUCTION

Oropharyngeal swallowing dysfunction (OPSD) denotes impairment of the swallowing process through the pharyngoesophageal segment (PES). Complications of OPSD include malnutrition, dehydration, social isolation, pneumonia, pulmonary abscess, hospital admission with increased length of stay, and death.¹ This is associated with an estimated $500 billion annual healthcare cost.² Common causes of OPSD include physical obstruction due to cricopharyngeus muscle dysfunction or cricopharyngeal webs, head and neck cancer with associated treatments, neurogenic and neuromuscular disorders, traumatic brain injury, and functional origin. Early recognition of swallowing impairment allows implementation of swallowing rehabilitation, surgical management if indicated, medication formulation adjustments, and diet allocation to reduce complications associated with aspiration.³,⁴

Previous work by our group using an ovine model determined that the PES has a complex, kidney shape, which is in contrast to the simplistic cylindrical shape of the esophagus.⁵ This shape reflects the rigid anterior boundary, composed of the posterior border of the cricoid cartilage and the dynamic and mobile muscles of the PES. These muscular components comprise the inferior pharyngeal constrictors, which taper downward along the pyriform fossae in the hypopharynx and narrow the esophageal inlet at the level of the cricopharyngeal muscle. Therefore, we have hypothesized that disorders affecting PES opening are best treated with a device that models the natural PES shape. A bougie or radial expansion balloon creates a circular dilation that may not provide optimal treatment because it has the tendency to deviate to one side of the PES, typically the side that is most patent. The purpose of this investigation was to evaluate the shape of the maximally distended human PES in a 3D cadaveric model.

MATERIALS AND METHODS

Specimen Preparation

Nine human cadaver heads were prepared by isolating the cervical esophagus and trachea from surrounding soft tissue. The
distal trachea was clamped with a curved Kelly forceps (Medline Industries, Inc., Northfield, IL), and the distal esophagus was sutured securely around flexible Argyle suction tubing (Medline Industries, Inc.) using 2-0 silk suture (Ethicon, Cincinnati, OH) in order to allow high-pressure injection of casting agent (Fig. 1A). The oropharynx and nasopharynx were closed by oversewing the circumvallate papillae to the posterior pharyngeal wall and posterior pharyngeal pillars with 0 silk suture (Ethicon). Each specimen was suspended in a prone position to distract the esophagus from the spine (Fig. 1B). We then performed a single, rapid injection cast of the enclosed pharynx, PES, cervical esophagus, larynx, and proximal trachea using a platinum-cured silicone rubber-casting agent (Mold Star 16 FAST; Smooth-On, Inc.; Easton, PA). Once maximal pressure was obtained, the injection port was clamped with a Kelly forceps, and all sites were checked to ensure no casting material extruded.

Casts were allowed to cure for 24 hours before harvest and then dissected free and cleaned. After removal, the cast was imaged with a helical CT scanner (Xoran Technologies, Ann Arbor, MI) using 0.4 mm slice thickness with coronal and sagittal reformatting to provide 3D representation of the PES. Representative axial slices were examined from the hypopharynx at the level of the vocal folds, subglottis at the level of the upper border of the anterior cricoid cartilage, cricopharyngeus muscle, and cervical esophagus. A 2 cm outer-diameter CT-compatible polyvinyl chloride Charlotte pipe (Ace Hardware, Chicago, IL) reference was used for calibration, and cross-sectional areas were determined at each slice with ImageJ (version 1.52g, U.S. National Institutes of Health, Bethesda, MD).6

**Data Acquisition and Statistical Analysis**

Geometric morphometric analysis was performed to compare the morphology of the narrowest region of the maximally distended PES at the level of the cricopharyngeus with the morphology of the cervical esophagus at a level 1.5 to 2 cm below the cricopharyngeus muscle. Representative axial slices were obtained from CT data, and digital semilandmarks were generated using tpsDig2 (Morphometrics at SUNY Stony Brook, http://life.bio.sunysb.edu/morph/) to model the circumferential shape at each level. Generalized Procrustes superimposition was performed using MorphoJ.

Procrustes superimposition is a geometric manipulation that assigns landmarks to defined points of a shape and measures the similarity between them by assessing how far they must be manipulated to reach the same position. The term derives from the mythologic Greek character Procrustes, a son of Poseidon, who terrorized travellers by offering them a bed at his inn while they travelled between Eleusis and Athens. Procrustes required all travellers to fit within certain dimensions of his bed and would dismember or stretch them accordingly.²¹

Shape variances were assessed using principle component analysis in MorphoJ (version 1.04b), and canonical variate analysis was used to identify the shape features that best distinguishes the PES from the cervical esophagus.

Statistical analysis was conducted using Stata 12.0 (StataCorp, College Park, TX). Descriptive statistics were determined for each critical segment of the PES. Mean areas of each segment were compared using unpaired t tests. A Bonferroni correction was applied for multiple tests.

RESULTS

Casts of the nine human specimens produced high-fidelity, durable models of the anatomic structure and relationships of the various levels of the PES, with all landmarks readily identifiable in seven casts (Fig. 2A). Two specimens had inadequate esophageal length to create a cast providing an esophageal measure but had laryngeal and PES landmarks available for analysis. Adequate pressure injection was verified by ensuring complete filling of the laryngeal ventricles and outlined surfaces of the petiole and tongue base. Figure 2B demonstrates positions of axial cuts used for shape analysis. PES structure was

![Graphical display of cross-sectional areas through upper esophageal sphincter. The pharyngoesophageal segment tapers in size distally until reaching the cricopharyngeus, which is not significantly different area than the esophagus.](image1)

![Representative figure with 2 cm diameter object fitting within left half of upper esophageal sphincter at level of vocal folds.](image2)

![Dilation of upper esophageal sphincter with single 20 mm balloon dilator demonstrates limited or absent distention of right hemispincter.](image3)
distinctly kidney-shaped in cephalic regions, tapered to the smallest cross-sectional area at the level of the cricopharyngeus muscle, and then mildly morphed at the proximal esophagus into a circular shape.

The largest cross-sectional PES area of the specimen was at the level of the vocal folds and narrowest at the level of the cricopharyngeus. The human PES tapers from a kidney-shaped mean (± SD) cross-sectional area of 7.59 (± 1.52) cm² at the level of the vocal folds to a narrowest mean area of 2.80 (± 1.33) cm² at the cricopharyngeus muscle ($P < 0.0001$), then slightly enlarges to 3.01 (± 1.11) cm² at the level of the esophagus 1.5 to 2 cm below the cricopharyngeus ($P = 0.75$). Mean area calculations of the PES at the cephalic levels were significantly greater than at the cricopharyngeus and esophageal level, although the cricopharyngeus and esophageal segments did not have significantly different areas (Fig. 3). As shown in Figure 4A, a representative sample of the PES at the level of the vocal folds, a scaled circular object with 20 mm diameter can fit within half of the PES area with minimal effect on the surrounding walls. Figure 4B demonstrates this limited effect in a human PES with a 20 mm balloon dilator.

Generalized Procrustes superimposition of the semilandmarks of all specimen are displayed in Figure 5A. Mean variance between the PES and esophagus at each semilandmark is visualized in the vector plot in Figure 5B. As the axial section moves from the cervical esophagus to the PES, there is posterior deflection in the midline and flaring anterolaterally creating the characteristic kidney shape. Principal component analysis (PCA) (Fig. 5C) indicates that the first two principal components (PC1 and PC2) account for the majority of shape variance, with PC1 alone accounting for 89% of total variance. The distribution of each specimen on the PCA plot demonstrates two distinct shape clusters. Canonical variance analysis with 10 thousand permutation tests confirms that the esophagus and PES are significantly different anatomic shapes ($P = 0.002$).
DISCUSSION

We present the first volumetric anatomic evaluation of the human PES in axial dimensions, which confirms our group’s previous work in the ovine model and demonstrates interspecies conservation of the PES structure. In this study, we produced a high-quality 3D dimensional model of the cadaveric human PES to demonstrate that the PES possesses a kidney-shaped rather than a circular configuration like the neighboring esophagus.

Videofluoroscopic swallowing studies represent the current gold standard for evaluation of the PES during swallowing, but this diagnostic test is not capable of evaluating the axial dimensions of the PES. Attempts to use real-time cross-sectional imaging with ultrasound and dynamic CT imaging have been demonstrated but not validated and are not standard practice. Understanding the axial dimensions of the PES is critical to evaluating the likelihood of physical obstruction and counseling patients regarding treatment options and efficacy. Similarly, our model investigated the PES with maximal distention, whereas most routine swallowing is done in a submaximal state. Akin to the Frank-Starling curve and cardiac function, there may be differences in bolus PES distention and dynamic activity through different swallowing tasks. Pharyngeal swallowing power, defined based on the force to drive a bolus through the PES by fluid dynamics, recognizes these adjustable properties with different bolus volumes and consistencies. Further work is needed to understand the volumetric PES character during swallowing various textures and volumes.

This study represents an important finding because it confirms anecdotal experience that treating the PES with a circular dilator in many instances can be insufficient to achieve maximal dilation effect. If there is webbing or scarring that ablates one side of the PES, then simple dilation may not be effective. Blind dilation without simultaneous laryngoscopy will not appreciate the location or extent of obstruction in many situations, and dilation with transnasal esophagoscopy further appreciates this phenomenon. Clinical significance of this work relates to the need for better, more durable therapy for oropharyngeal dysphagia in the context of physical obstruction such as cricopharyngeal bars and webs. Repeated studies and systematic reviews show significant heterogeneity between dilation technique, size, efficacy, and duration of effect. Dilution of the PES with a 20 mm diameter dilator addresses only 41% of the mean cross-sectional area of the PES according to our measures. Comparison of the Figure 4A schematic to a still frame image of an attempted dilation of a large mucosal web obstructing half the PES shows the limited efficacy of dilation with a bougie of standard size and shape (Fig. 4B). In our center, we use a double balloon dilation technique that effectively and safely dilates a greater portion of the PES in patients with mechanical obstruction. Our previous ovine study measured the narrowest area of the PES to be 437 mm², whereas the mean PES cross-sectional area in our human study was 280 mm². In both human and ovine studies, the cross-sectional area enlarged slightly and became circular upon entering the esophagus. Conservation of the relative shapes through the PES across species, although with larger dimensions in ovine models, supports the validity of the ovine model for investigation into human PES function and treatment.

Our models produced high-fidelity structures of the PES in adult male and female cadavers. In some cases, we could see the imprint of a cricopharyngeus muscle (Fig. 3) or a hypopharyngeal web. Recent work by Mehdizadeh et al. (2019) identified that a high proportion of cadavers had PES webs (68%), indicating this is a common occurrence that likely increases with age as a result of the microtrauma caused by the tens of millions of swallows over a lifetime. These webs are well-known entities, although the clinical significance of them is difficult to evaluate given an underappreciation in the general population and up to 15% among patients reporting dysphagia based on radiographic studies. Increased radiographic resolution is thought to identify a larger number of webs and physical obstructions, although we expect anatomic studies represent the gold standard given better tissue-level resolution and evaluation. We did not have enough available cadavers to provide a population-level analysis by PES casting; however, we expect we would find similarly higher numbers than the reported radiologic studies.

This study is not without limitations. The investigation was performed on a limited number of elderly cadavers who donated their bodies to science and may not be generalizable to the general population. We found it is essential to perform casting studies on unpreserved, fresh tissue specimens because tissue distensibility and pliability reduced with preservation techniques and repeated freezing cycles. Attempts to replicate these results may vary depending on cadaver preservation technique. Nonetheless, the data from this investigation confirm the results of previous study and suggest that the human PES is not round but shaped like a kidney.

CONCLUSION

The data suggest that the human PES is not round and that targeted expansion at the level of the cricopharyngeus with an eccentrically shaped dilator may provide improved distention. Targeted expansion with an eccentrically shaped dilator may provide improved distention among patients with physical PES obstruction.

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