THE RELATIONSHIP BETWEEN UPPER ESOPHAGEAL SPHINCTER OPENING DURATION AS A FUNCTION OF LARYNGEAL ELEVATION

by

Elizabeth M. Bryson

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This thesis was presented

by

Elizabeth M. Bryson

It was defended on

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and approved by

Mark DeRuiter, MBA, Ph.D., CCC-A/SLP, F-ASHA, Vice Chair for Academic Affairs and Professor, Department of Communication Science and Disorders, University of Pittsburgh

Kendrea L. (Focht) Garand, Ph.D., CScD, CCC-SLP, BCS-S, CBIS, CCRE, Associate Professor, Director of CSD Student Awards, Department of Communication Science and Disorders, University of Pittsburgh

Thesis Advisor: James L. Coyle, Ph.D., CCC-SLP, BCS-S, F-ASHA, Professor, Departments of Communication Science and Disorders, Otolaryngology Head and Neck Surgery, Electrical and Computer Engineering, University of Pittsburgh

The Relationship Between Upper Esophageal Sphincter Opening Duration as a Function of Laryngeal Elevation

Elizabeth M. Bryson, BA

University of Pittsburgh, 2024

Swallowing is a complex, low-level autonomic function requiring the coordination of numerous muscles and nerves. Disordered swallowing, dysphagia, can result in an interruption of this coordination, manifesting as dysfunction within one or more phases of swallowing: oral, pharyngeal, esophageal. The aims of this study included: 1) compare upper esophageal sphincter opening duration (UESOd) and laryngeal elevation between patients with suspected dysphagia (n=50) and age-matched healthy persons (n=50); and 2) establish the relationship or correlation of UESOd to laryngeal elevation across the two investigated data sets. Videofluoroscopic images were retrospectively analyzed to measure UESOd, the interval between the first frame of upper esophageal sphincter (UES) opening and the first frame of UES closure, and laryngeal elevation, the total displacement of the larynx to the hyoid bone, in individuals swallowing approximately 3 mL thin liquid boluses. A comparison of group medians and analyses of group differences were performed to address the presenting aims. Results revealed a significant difference in UESOd between patient participants (*Mdn*=1200.00 milliseconds) and healthy participants (*Mdn*=633.33 milliseconds); $p < .001$. This difference carried a large effect size (d=2.15). Similarly, there was a significant difference in laryngeal elevation distance between patient participants (*Mdn*=0.26 pixels) and healthy participants (*Mdn*=0.31 pixels); p=.014. This difference carried a medium effect size (d=-0.49). For healthy participants, there was only a weakly positive and significant correlation found between measures of UESOd and laryngeal elevation; r=.29, p=.040. There was

no significant correlation found between UESOd and laryngeal elevation in patient participants; $r=-.03$, $p=.825$. Clinically, these results provide objective data on UESOd and laryngeal elevation that can aid in clinical decision making.

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Preface

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1.0 Introduction

Dysphagia is a swallowing disorder that arises from impairment within the swallowing mechanism, and causes dysfunction within one or more of the swallowing "phases" (i.e., oral, pharyngeal, and esophageal) (McCarty & Chao, 2021). Dysphagia is clinically relevant across the lifespan and can have serious implications on an individual's well-being and health, including dehydration, malnutrition, aspiration pneumonia, choking, and sometimes death (McCarty & Chao, 2021). Common patient populations contributing to dysphagia include, but are not limited to, neurodegenerative diseases, head and neck cancers, and strokes.

1.1 Swallowing

Swallowing is a life-sustaining, complex neurological function that requires coordination of more than 30 muscle pairs innervated by several nerves. The muscles involved in swallowing are located within the oral cavity, pharynx, larynx, and esophagus and are controlled by several cranial nerves (CNs) and spinal nerves. As outlined in Shaw and Martino (2013), the upper and lower facial musculature are innervated by CN VII and are primarily responsible for closing/protruding the lips and compressing the cheeks. Facial musculature generates the bilabial seal during swallowing that prevents anterior spillage and helps maintain intrabolus pressure. The masseter, temporalis, medial pterygoid, and lateral pterygoid muscles are responsible for mastication, which are innervated by CN V. Tongue musculature includes the extrinsic lingual muscles, involved in tongue location, and intrinsic lingual muscles, involved in tongue shaping (CN XII). Extrinsic lingual muscles include the genioglossus (CN XII), palatoglossus (CN X), styloglossus (CN XII), and hyoglossus (CN XII). Tongue musculature primarily assists in bolus manipulation during swallowing. Pharyngeal muscles responsible for elevating and tensing the velum (soft palate) include the levator veli palatini (CN X) and tensor veli palatini (CN V). Palatal elevation seals off the velopharyngeal port to prevent nasal regurgitation. Additional pharyngeal muscles responsible for pharyngeal contraction and elevation include the pharyngeal constrictors (CN X) and long pharyngeal muscles: stylopharyngeus (CN IX), salpingopharyngeus (CN X), and palatopharyngeus (CN X). Muscles responsible for hyolaryngeal movement include the mylohyoid (CN V), geniohyoid (C1), anterior belly digastric (CN V), posterior belly digastric (CN VII), and stylohyoid (CN VII). Of important note, the geniohyoid, anterior belly digastric, and mylohyoid have reversible origins and insertions. Therefore, their secondary actions include mandibular depression. The infrahyoid muscle group includes the sternothyroid, sternohyoid, omohyoid and thyrohyoid muscles (C1-C3). During swallowing, contraction of the thyrohyoid muscle assists in superiorly approximating the larynx to the hyoid. The thyrolaryngeal adductor muscles, including the cricoarytenoid, transverse arytenoid, and thyroarytenoid, close the vocal folds to protect the airway (CN X via recurrent laryngeal nerve branch) during swallowing to prevent ingested material from entering the lower airways. The muscle responsible for UES closure predominantly includes the cricopharyngeal muscle (CN X), although also includes musculature from the inferior pharyngeal constrictor and cervical esophagus (Shaw & Martino, 2013).

The swallow response results from processing information received from afferent (sensory) neurons in the upper aerodigestive tract sent to the nucleus tractus solitarius (NTS) within the brainstem. The NTS is a sensory relay area and designated “swallowing center” within the medulla

(Kessler & Jean, 1985). Specifically, CN V provides sensory information from the mouth, while CN IX and CN X provide sensory information from the pharynx. The primary receptors for sensation of taste include CN VII (anterior 2/3 tongue), CN IX (posterior 1/3 tongue), and CN X (epiglottis). The NTS incorporates the input from these afferent neurons and communicates with the nucleus ambiguous (NA); the connecting network of neurons between the NTS and NA within the medulla is considered a central pattern generator for swallowing (Jean, 2001). The NA then relays efferent information through motor neurons resulting in muscle contractions responsible for the pharyngeal swallow via multiple CNs, including V, VII, X, and XII (Sasaegbon & Hamdy, 2017).

1.1.1 Biomechanics

The process of swallowing occurs over a series of interdependent stages. Two commonly deployed models used to describe the stages and biomechanics of swallowing include the Four Stage Model for swallowing liquids (Matsuo & Palmer, 2008) and the Process Model of Feeding for swallowing solids (Hiiemae & Palmer, 1999).

1.1.1.1 Oral Phase

As outlined by Matsuo and Palmer (2008), the oral phase begins with the oral preparatory stage for liquid boluses. During the oral prepatory stage, liquid enters the mouth and is held either on the anterior floor of mouth (“dipper”) or on the tongue surface against the palate (“tipper”) while the lips are closed preventing anterior spillage (Dodds et al., 1989). Meanwhile, the oral cavity is sealed posteriorly via closure of the linguavelar valve to prevent passive posterior leakage into the oropharynx resulting from the soft palate laying at rest against the posterior tongue. Then, the oral propulsive stage begins when the bolus is propelled towards the pharynx via tongue tip elevation towards the alveolar ridge that sequentially pushes the liquid bolus along the palate and into the pharynx with assistance from gravity (Matsuo & Palmer, 2008). For solids, as Hiiemae and Palmer (1999) define, the oral phase begins with stage 1 transport. During transport, food enters the mouth and is manipulated by the tongue. After stage 1 transport, food processing immediately begins. During food processing, the food bolus is reduced by mastication and softened by saliva. In contrast to thin liquids, the linguavelar valve is open during food processing because of the solid bolus' adhesion to the mucosa and slow flow (Saitoh et al., 2007). Once the solid bolus is safe for swallowing, stage II transport is initiated and the tongue propels the food towards the oropharynx. Furthermore, stage II transport for solids can occur in cycles; mastication and transport may continue if food remains in the oral cavity, also referred to as "piecemeal" deglutition (Ertekin et al., 1996).

1.1.1.2 Pharyngeal Phase

The pharyngeal phase is an involuntary stage that occurs within a second and has two important components: 1) propulsion of the bolus through the pharynx and UES; and 2) airway protection to prevent bolus entry (Matsuo & Palmer, 2008). During stage transition, the UES relaxes via vagal inhibition. As outlined by Matsuo and Palmer (2009), at the initiation of the pharyngeal phase, the velum elevates to seal off the nasopharynx. Elevation of the hyolaryngeal complex, also referred to as hyolaryngeal elevation (HLE), then occurs via contraction of the suprahyoid muscles (pull complex anteriorly), long pharyngeal muscles (pull complex superiorly), and thyrohyoid muscle (approximates larynx to hyoid). As the hyolaryngeal complex is displaced and tongue base retracts toward the posterior pharyngeal wall, the epiglottis inverts to close off the laryngeal vestibule in conjunction with vocal fold adduction to protect the airway. The upper esophageal sphincter's resting tone is inhibited and the pressure of the descending bolus assists in UES opening (Matsuo & Palmer, 2008). The superior, middle, and inferior pharyngeal constrictors sequentially contract, known as the pharyngeal stripping wave, to push the bolus downward for pharyngeal clearance (Schwertner et al., 2016).

1.1.1.3 Esophageal Phase

The esophageal phase begins once the bolus enters the lower part of the UES and descends into and through the lower esophageal sphincter (LES). The bolus is transported through the esophagus via peristaltic waves. Primary peristalsis is initiated by the swallow itself, while secondary peristalsis is initiated by distension of the esophagus (Hendrix, 1993). The LES is constricted at rest to prevent the regurgitation of stomach contents, but relaxes during swallowing to allow bolus entry into the stomach (Matsuo & Palmer, 2008).

1.2 Upper Esophageal Sphincter

Located at the inferior portion of the inferior pharyngeal constrictor muscle, the UES separates the pharynx and esophagus. The UES maintains tonic closure at rest while relaxing to allow ingested material to pass through during swallowing. This high-pressure zone is crucial for preventing swallowed material from entering the airway, including reflux (Singh & Hamdy, 2005).

1.2.1 Function/Anatomy and Physiology

The tonically closed UES attaches to the cricoid cartilage to form a c-shaped band via its primary muscle, the cricopharyngeus (CP) (Lang & Shaker, 1997). While the CP is the primary muscle of the UES, the UES also involves the inferior portion of the inferior pharyngeal constrictor and the superior portion of the upper cervical esophagus (Sivarao & Goyal, 2000). The cricopharyngeus (CP) muscle, also known as cricopharyngeal, is comprised of type 1 and type 2 muscle fibers, enabling its constriction at rest and fast relaxation during swallowing (Sivarao & Goyal, 2000). UES opening is a result of three events: increased pressure from a descending bolus, HLE, and inhibition of CP (Lang & Shaker, 2000). The CP is innervated by CN X and relaxation is a result of the inhibition of its vagal motor input via the NA. Once the CP is inhibited, its inertia against distension is reduced, and the suprahyoid muscles contract to displace the hyolaryngeal complex. During maximum displacement, the mylohyoid, thyrohyoid, and geniohyoid pull the anterior wall of the UES away from the posterior wall by way of their attachments to the hyoid (Sing & Hamdy, 2005). At rest, the UES has a pressure range 35-200 mm Hg that decreases at the onset of a swallow, facilitating HLE and UES opening (Sivarao & Goyal, 2000). When UES opening precedes arrival of the bolus head, proximal intraluminal esophageal pressure becomes momentarily subatmospheric, facilitating bolus flow. Once the bolus passes, the UES continues peristaltic activity and then resumes its resting tonic closure.

Within the literature, there is evidence that age and bolus size are contextual factors that influence UESOd (Humbert et al., 2018; Kahrilas, 1997). Ambrocio and colleagues (2023) analyzed the effects of age, sex, and bolus conditions (viscosity and volume) on UESOd in a sample of 195 healthy adults (21–89 years old) across seven swallow tasks (thin liquid to viscous liquids, puree, and solid). In analyzing the factor of age, older adults revealed to have significantly longer UESOd than younger adults. Conversely, sex did not reveal influence on UESOd. When isolating viscosity, mildly and moderately thick liquids significantly increased UESOd compared to thin liquids. When isolating volume, thin liquid cup sips increased UESOd compared to 5 mL thin liquid boluses. Ultimately, this investigation provides evidence that age and bolus conditions contribute to normal variations in UESOd. Specifically, UESOd increases with increases in age and bolus size.

1.2.2 Effects of Impairment

Impairment to the anatomy and physiology of the UES can have significant impact. Dysfunction of the cricopharyngeal muscle, either structurally (e.g., fibrosis) or functionally (e.g., denervation), can separate the bolus tail from the bolus, leaving bolus material within the pyriform sinus, unilaterally or bilaterally, that may be aspirated upon inhalation (Logemann, 1988). Eisenhuber and colleagues (2002) conducted a study to evaluate pharyngeal residue as a predictor for aspiration in 108 patients with dysphagia undergoing videofluoroscopic swallow studies (VFSSs). Results revealed 65% of patients with pharyngeal residue demonstrated post-swallow aspiration, indicating impaired UES opening and secondary residue to be a significant predictor for aspiration.

An organic cause of incomplete UES relaxation may include a cricopharyngeal bar, an impression along the posterior wall of the esophagus at the level of pharyngoesophageal junction that is observed during radiographic imaging (Cook, 2011). In a study conducted by Leonard and colleagues (2004), maximum UESOd in older adults with cricopharyngeal bars was found to be significantly reduced compared to older adults without cricopharyngeal bars. If a cricopharyngeal bar is significant enough in size it can cause partial obstruction and increased pressure. Often associated with a cricopharyngeal bar and its increased pressure is a Zenker's diverticulum, a posterior pouching through a weak area proximal to the cricopharyngeal muscle (Cook, 2011). Studies have established decreased compliance of the UES and failure of the UES to fully distend to be responsible for the increased forces generating the high-pressure zone resulting in Zenker's diverticulum formation (Law et al., 2014; Prisman & Genden, 2013). A commonly reported symptom of patients with Zenker's diverticulum includes dysphagia and regurgitation of undigested foods.

1.3 Hyolaryngeal Complex Movement

As aforementioned, hyolaryngeal movement contributes to swallow safety, helping to prevent bolus entry into the airway during swallowing. The larynx, which is suspended via ligaments and muscles attached to the hyoid bone, includes the cricoid cartilage, thyroid cartilage, epiglottis, arytenoids, corniculates, and cuneiforms (Sasaki & Isaacson, 1988). Therefore, anterior movement of the hyoid bone facilitates anterior-superior movement of the laryngeal structure. Given this anatomy and physiology, researchers and clinicians reference this as the hyolaryngeal complex; the hyolaryngeal complex includes the hyoid bone, thyrohyoid membrane, and laryngeal cartilages (Pearson et al., 2012).

1.3.1 Function/Anatomy and Physiology

The muscles responsible for displacement of the hyolaryngeal complex include the suprahyoid muscles and thyrohyoid muscle (Matsuo & Palmer, 2008). Suprahyoid muscles include digastrics (anterior and posterior belly), geniohyoid, stylohyoid, and mylohyoid. Additional muscles attached to the hyolaryngeal complex include the long pharyngeal muscles: stylopharyngeus, salpingopharyngeus, and palatopharyngeal (Pearson et al., 2012). The long pharyngeal muscles, innervated by CN X and CN IX, assist in raising the larynx and widening the pharynx. The anterior-superior displacement of the hyolaryngeal complex assists in inverting the epiglottis to close off the laryngeal vestibule and promote airway protection. The epiglottis moves in conjunction with the movements of the hyoid and thyroid cartilages due to its attachments to the internal surface of the thyroid cartilage and the hyoid bone (Vandaele et al., 1995).

The arytenoid cartilages lie within the larynx posteriorly and attach to the vocal folds. During laryngeal elevation, the arytenoids adduct and tilt toward the epiglottis to prevent laryngeal penetration (Abe & Tsubahara, 2011). Attached to the hyolaryngeal complex at the cricoid cartilage is the cricopharyngeus muscle. The cricopharyngeus is the internal portion of the inferior pharyngeal constrictor muscle and forms the UES. As the hyolaryngeal complex displaces, the anterior wall of the relaxed UES is mechanically stretched open via its insertion to the cricoid cartilage (Pearson et al., 2013).

1.3.2 Effects of Impairment

Reduced hyolaryngeal movement can result in increased risks of aspiration and reduced UES opening. Specifically, limited anterior-superior displacement of the hyolaryngeal complex may result in incomplete epiglottic inversion, leaving the laryngeal vestibule open, permitting bolus entry. Additionally, impaired displacement of the hyolaryngeal complex can impact UES opening, reducing its opening duration and distension. Restricted UES opening can result in impaired bolus clearance, leaving residue within the pharynx that is vulnerable to being aspirated.

Mendelsohn & McConnel (1987) analyzed 11 patients referred for pharyngeal dysfunction and nine healthy controls; data was simultaneously collected using both manometry and videofluoroscopy. As hyolaryngeal elevation occurred in healthy controls, the larynx moved anterior-superiorly away from the posterior pharyngeal wall. For patients with impaired laryngeal elevation, four patients had poor bolus clearance, with residue of over 30% of bolus volume. Furthermore, patients with impaired laryngeal elevation had altered intraluminal esophageal pressure. Results of this study reveal the important role laryngeal elevation plays in controlling passage of the bolus through the UES and mitigating aspiration risks. Additionally, Zhang and colleagues (2016) conducted a prospective cohort study of 89 patients with acute ischemic strokes who underwent VFSSs while swallowing 5 mL thin liquid boluses. Results revealed significant associations between aspiration (PAS $\geq$ 5) and age, velocity and duration of laryngeal elevation, delayed pharyngeal initiation, pharyngeal transit time, abnormal epiglottic inversion, and UES opening duration (Zhang et al., 2016). Lastly, Perlman and colleagues (1994) investigated the relationship between aspiration and seven variables indicative of pharyngeal dysphagia: vallecular stasis, pyriform sinus stasis, diffuse hypopharyngeal stasis, reduced hyoid elevation, reduced laryngeal elevation, deviant epiglottic function, and delayed initiation of pharyngeal stage. Data analysis revealed reduced hyoid elevation and abnormal epiglottic function to be significant predictors of aspiration (p = .05).

1.4 Current Diagnostic Practices

To properly assess dysphagia, implementation of both clinical judgment and instrumental assessments are crucial.

1.4.1 Clinical Swallow Examination

Speech-language pathology (SLP) clinicians are important healthcare team members who perform bedside clinical swallow examinations to assess swallowing safety and efficiency. A comprehensive clinical swallow examination consists of a patient interview, cranial nerve examination, swallow trials, motor speech examination, cognitive-communication/language screen, and quality of life inquiry (Garand et al., 2020). While a clinical swallow evaluation allows clinicians to make informed decisions and judgments, it cannot alone identify impaired UES physiology nor guide treatment because pharyngeal and UES function can only be inferred upon at the bedside (Garand et al., 2020).

1.4.2 Instrumental

Currently, gold standard assessments for diagnosing dysphagia include VFSSs and flexible endoscopic evaluation of swallowing (FEES). While FEES has benefits, such as portability and limited radiation exposure, its view becomes obstructed during the pharyngeal phase of swallowing due to pharyngeal constriction causing light to be reflected off of the tissue and into the endoscope (Langmore et al., 1988). Therefore, VFSSs allow clinicians to observe all events of the pharyngeal stage, including safety and pharyngeal efficiency. In order to standardize how SLP clinicians and researchers comment on airway protection during VFSSs, Rosenbek and colleagues (1996) developed an eight-point Penetration-Aspiration Scale. This multidimensional scale analyzes both the presence and depth of bolus traveled into the airway, as well as the examinee's response to bolus airway invasion.

As stated above, impaired HLE and or impaired UES opening duration can result in residue within the hypopharynx. This residue can be observed and quantified during VFSSs, such as using the residue scale developed by Eisenhuber and colleagues (2002). After a swallow has been initiated and completed, clinicians can grade the estimated amount of pharyngeal residue, also referred to as stasis, that remains in the vallecula and pyriform sinuses by comparing the height of the vallecula and or pyriform sinus to the bolus volume: 1 indicates mild residue equal to or less than 25% of the height of the structure, 2 indicates moderate residue equal to 25-50%, and 3 indicates severe residue greater than 50% and is significantly associated with aspiration (Eisenhuber et al., 2002).

While VFSSs are utilized to assess anatomy and physiology and bolus flow, they are unable to assess pressure changes. The current gold standard assessment for measuring pharyngeal and esophageal pressure changes is high resolution manometry. High resolution manometry records pressure changes from an intraluminal catheter with embedded pressure sensors that is placed through the nose and into the esophagus (Carlson & Pandolfino, 2015). Manometry has the advantage of sensitivity to UES relaxation and pressure changes that may not be detected during VFSSs. Therefore, manometry may be deployed simultaneous with VFSSs to capture biomechanical, pressure, bolus flow, residue, and timing measures (Coyle, 2022, personal communication).

1.4.3 Developing Techniques

One developing technique for non-invasive assessment of swallowing physiology currently being explored is high-resolution cervical auscultation (HRCA). HRCA uses acoustic and vibratory signals from noninvasive sensors attached to the anterior laryngeal framework (Coyle &

Sejdic, 2020). HRCA, thus far, has shown promise as a screening method and potential diagnostic adjunct to videofluoroscopy by accurately quantifying airway protection, detecting specific temporal and spatial swallow kinematic events, differentiating patient and healthy swallows, and classifying swallows based on the Modified Barium Swallow Impairment Profile (Donohue et al., 2020; Donohue et al., 2021; Martin-Harris et al., 2008).

1.5 Measurement of UES Opening and Laryngeal Elevation

Traditionally, HLE has not been separated into its individual hyoid and laryngeal components. Thus, laryngeal elevation has largely been judged upon hyoid movement. Historically, researchers and clinicians during frame-by-frame analysis have taken videofluoroscopic images in the lateral plane and measured hyoid displacement and UES opening in millimeters without consideration for individual variations across participants. To address the need for facilitating on-line judgments of hyolaryngeal movement that account for individual differences, researchers have been investigating anatomical benchmarking using the cervical spinal length. Brates and colleagues (2020) investigated the use of an anatomical scalar in a mixed-age sample of healthy adults. Data collected included videofluoroscopic images capturing three swallow trials of 5 mL and 20 mL liquid barium conditions. Hyoid excursion was measured in millimeters using rest-to-peak displacement and peak only methods in all planes, as well as individually scaled to and normalized using C2-C4 distance. Results revealed significant differences observed in hyoid movements across sex, bolus volume, and age groups. When normalized and measured using C2-C4 units, all differences between younger and older individuals were neutralized. Ultimately, these results validate the expression of hyoid excursion as a percentage of the distance of C2-C4.

2.0 Project Goals and Design

The presenting descriptive, retrospective case-control study involved the analysis of laryngeal elevation and UESOd in patients with suspected dysphagia and age-matched, healthy community-dwelling adults. The results of this study may inform future research, as well as establish objective data that may assist in the analysis of swallowing physiology across the adult lifespan.

2.1 Research Questions and Specific Aims

The aim of this study was to assess the correlation of UESOd to laryngeal elevation, as well as compare maximum UESOd and laryngeal elevation between patients with suspected dysphagia undergoing VFSSs and age-matched healthy persons without dysphagia. Temporal measurements of UESOd and spatial measurements of laryngeal elevation were used to address these aims.

The proposed research questions included: 1) what is the correlation between UESOd and laryngeal elevation?; and 2) is there a difference in the correlation between UESOd and laryngeal elevation between dysphagic patients and healthy controls?

2.2 Hypotheses

Based upon the above literature review, three hypotheses were developed. H1: Healthy persons without dysphagia will exhibit longer UESOd than age-matched patients with suspected dysphagia when swallowing the same bolus type and volume. H2: There will be a positive correlation between UESOd and the distance of laryngeal elevation in both groups. Thus, as distance of laryngeal elevation increases, UESOd will also increase. H3: Healthy participants will exhibit a greater correlation between UESOd and laryngeal elevation than dysphagic patients.

2.3 Significance

Vose and colleagues (2018) conducted a survey of 162 SLPs investigating clinical decision making for swallowing impairments observed in videofluoroscopic imaging. The authors aimed to examine whether SLPs make judgments on impairments that align with evidence-based practice and whether they make treatment recommendations that are physiologically based. Results revealed wide variability in diagnosis and treatment recommendations. Specifically, clinicians overidentified impairments that were not present and infrequently identified the specific impairment(s) responsible for swallowing dysfunction, which increased as the complexity of the dysphagia increased. Additionally, clinicians demonstrated overemphasis on bolus flow impairments (i.e., airway invasion and residue) in treatment recommendations instead of the underlying pathophysiology causing these outcomes. Alarmingly, 32% of surveyed SLP's in the USA *admitted to* **never** performing frame-by-frame analysis of videofluoroscopic images after examinations. Therefore, available evidence suggests that at least a portion of practicing SLPs demonstrate a gap in knowledge of typical (normal) swallowing physiology, resulting in overdiagnosis and ineffective treatment. By establishing the correlation of UESOd to laryngeal elevation across the adult lifespan, clinicians can be provided novel, objective data that may improve clinical decision making.

Lastly, the presenting study will contribute to a larger research project aimed at establishing 1) a portable technology that utilizes acoustic and vibratory signals from noninvasive sensors and advanced signal processing, machine learning techniques to assess swallowing (Coyle & Sejdic, 2020; Donohue et al., 2020; Donohue et al., 2021); and 2) an AI-based videofluoroscopic swallow study auto-measurement image processing system that delivers preliminary kinematic and airway protections results immediately after the examination ends (Caliskan et al., 2020; Zhang et al., 2021).

2.4 Methods

The studies collecting data from both and patient and healthy participants were approved by the Institutional Review Board of the University of Pittsburgh [IRB# 19040040] [IRB# 22040175]. Inclusion criteria for patient participants included referral to VFSSs by clinicians at the University of Pittsburgh Medical Center (UPMC) Presbyterian hospital due to suspected or confirmed dysphagia. Inclusion criteria for healthy individuals included no history of dysphagia, surgery to the head or neck, neurological disorders, or chance of being pregnant. All participants gave written consent prior to enrollment. Data collection for both data sets followed different protocols at two different timepoints. Patient participant bolus administration was not measured precisely, as data was collected concurrently with VFSSs conducted by clinicians following clinical procedures. However, healthy participants were given exact measurements of 3 mL thin liquid boluses via teaspoon and self-administered thin liquid sips from a cup (mean = 15 mL) by researchers. To collect VFSSs, a standard fluoroscopy system (Precision 500D system, GE Healthcare, LLC, Waukesha, WI) was used with a pulse rate of 30 pulses per second (PPS) and recorded through a 30 Hz sampling rate frame grabber module (AccuStream Express, HD, Foresight Imaging, Chelmsford, MA). Collected videofluoroscopic videos were then segmented into individual swallow events, defined as the frame in which the bolus crosses the ramus of the mandible until the frame in which the bolus tail passed through the UES *or* the hyoid returned to rest.

Research staff collected videofluoroscopic data along with electronic signals for 116 patients undergoing VFSSs conducted by speech-language pathologists on staff at UPMC Presbyterian hospital. Patients during their VFSSs were administered barium sulfate solutions in thin liquid (Varibar Thin liquid, barium sulfate for oral suspension, 81% w/w, manufactured by E-Z-EM Canada Inc.; Bracco Diagnostics, 2019), Varibar nectar (barium sulfate oral suspension, 40% w/v, manufactured by E-Z-EM Canada Inc.; Bracco Diagnostics, 2020), Varibar pudding (barium sulfate for oral paste, manufactured by E-Z-EM Canada Inc.; Bracco Diagnostics, 2016), and a short-bread cookie coated with Varibar pudding. For the purposes of the larger IRB approved research study, only thin liquid swallows were extracted for analysis. The subset of swallows from the patient cohort that were analyzed by the principal investigator (PI) for the presenting study included 20 females and 30 males with an age range of 29 to 84 years.

One hundred and seventy healthy volunteers were originally recruited via the Pitt+Me registry, the Claude E. Pepper Registry, and advertisements placed in UPMC facilities. For this data set, only thin liquids were administered to limit fluoroscopy exposure. Participants swallowed ten randomly ordered thin liquid boluses (five 3 mL sips by spoon and five self-selected volume cup sips). For boluses presented via spoon, researchers instructed participants to “Hold the liquid in your mouth and wait until I tell you to swallow”. For boluses presented via cup, participants were instructed to “Take a comfortable sip of liquid and swallow whenever you are ready”. The subset of swallows from the healthy cohort that the PI analyzed for this study included 30 females and 20 males, with an age range of 22 to 87 years.

2.4.1 UESOd Data Collection

Temporal kinematic measurements of UESOd were completed by trained raters who had completed a priori intra and inter-rater reliability test with ICCs of over 0.80 for previous lab purposes. Therefore, the PI of this study was blinded to the dependent variable of UESOd. A custom image processing application, similar to ImageJ software, was used to perform temporal kinematic measurements on segmented swallows. UES opening was defined as the first frame in which the anterior and posterior walls of the UES had begun to separate (Figure 1), while UES closure was defined as the first frame in which there was no visible column of air or barium contrast separating the anterior and posterior walls of the UES (Figure 2).

Figure 1- UES Opening

Figure 2- UES Closure

2.4.2 Laryngeal Elevation Data Collection

Before measuring laryngeal elevation within the investigated data sets, the PI of this study completed a priori intra and inter-rater reliability test with ICCs of over 0.80. A customized swallow image annotating application (Version 1.3.8) developed by one of the lab's engineers was used to retrospectively analyze laryngeal elevation across patient and healthy data sets. To analyze and measure laryngeal elevation, the PI individually uploaded segmented swallows into the annotating application and marked anatomic landmarks of interest: anterior-posterior points of the hyoid bone, anterior-inferior corners of C2 and C4, anterior-inferior and superior-inferior corners of C3, and the anterior and posterior base of the larynx (Figure 3).

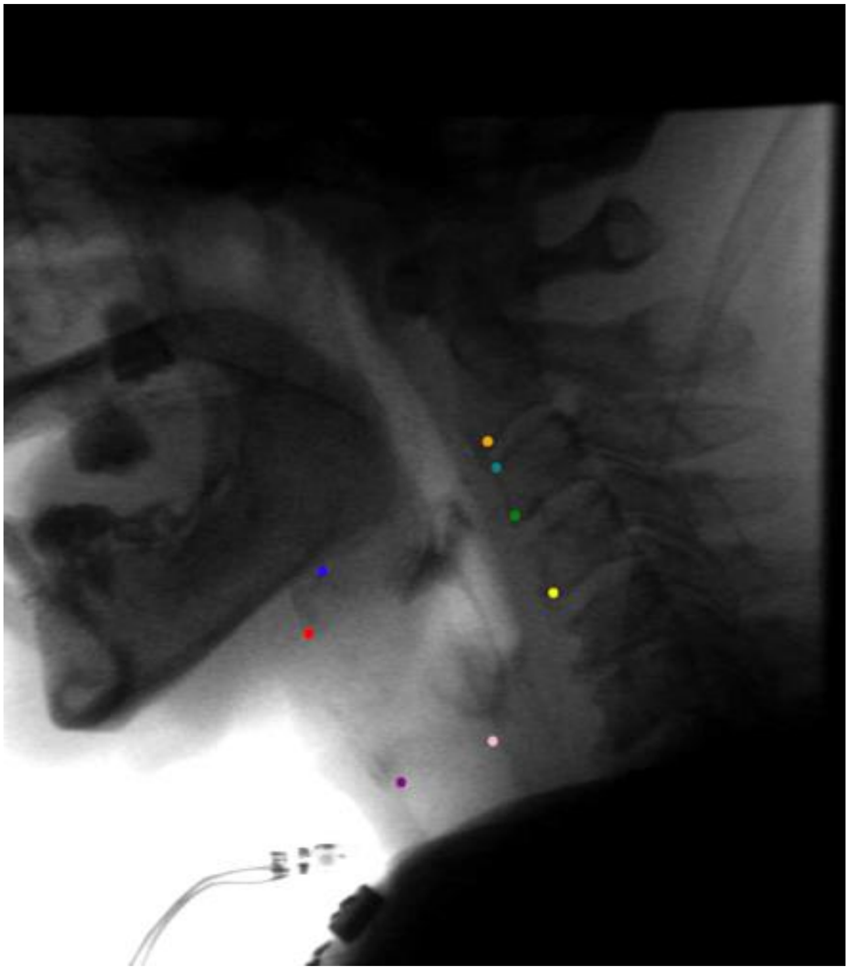

Figure 3- Laryngeal Elevation Landmarks

In order to calculate the maximum value of laryngeal elevation, the distance between the center point of the hyoid and the center point of the laryngeal base was determined for each frame. Then, laryngeal elevation was measured as the difference between the baseline distance between the hyoid and laryngeal base and the minimum distance between the hyoid and laryngeal base across the segmented swallow.

3.0 Results

All statistics were conducted using R, RStudio, and the ggpubr, dplyr, tidyverse, coin, and effsize packages. According to a Shapiro-Wilk test, data did not meet the normality assumption. Therefore, a nonparametric test of median differences was selected as an alternative. A Wilcoxon rank test was performed to determine differences between healthy and patient participants with respect to UESOd and laryngeal elevation, as previously described. There was a significant difference in UESOd between patient participants (*Mdn*=1200.00 milliseconds, *IQR*=266.67) and healthy participants (*Mdn*=633.33 milliseconds, *IQR*=166.67); W= 2178, $p < .001$. This difference carried a large effect size, according to Cohen's d estimate (d=2.15). Similarly, there was a significant difference in laryngeal elevation distance between patient participants (*Mdn*=0.26 pixels, *IQR*=0.172) and healthy participants (*Mdn*=0.31 pixels, *IQR*=0.154); W=817, p=.014. A medium effect size was noted for this difference (d=-0.49). To examine the relationship between these physiologic measures of swallowing, a Spearman's rank correlation was selected to assess the linear relationship between UESOd and laryngeal elevation for patients and healthy participants. For the healthy participants, there was a weakly positive and significant correlation found between measures of UESOd and laryngeal elevation; r=.29, p=.040. However, for the patient participants, there was no significant relationship or correlation found; r=-.03, p=.825. To further investigate the relationship between laryngeal elevation and UESOd, a linear regression was fit to the data. No significant result was found, R^2=.038, $F(1, 47)$=1.86, p=.179.

3.1 Reliability

To mitigate measurement error within the investigated data sets, the PI maintained intra-rater reliability by randomly selecting one out of every ten swallows to re-analyze and compute ICCs. Intra-rater reliability achieved was excellent (ICCs = 0.99 or above). Inter-rater reliability was performed with assistance from a trained lab member following a similar protocol: 10% of every 50 swallows were randomly selected to re-analyze. Inter-rater reliability achieved was also excellent (ICCs = 0.99 or above).

4.0 Discussion

The aims of this study were to compare maximum UESOd and laryngeal elevation, as well as establish the correlation of UESOd to laryngeal elevation in patients with suspected dysphagia and age-matched healthy persons. Overall, study findings revealed longer UESOd in the patient data set compared to age-matched healthy controls. However, the distance of laryngeal elevation was greater in the healthy data set. The large clinical effect size derived using Cohen's d indicated that the average patient's UESOd was more than two standard deviations longer than the average healthy participant's UESOd. Conversely, patients produced on average one half standard deviation less laryngeal elevation than the average healthy participant's laryngeal elevation, resulting in a medium clinical effect size. Lastly, a statistically significant correlation only existed between UESOd and laryngeal elevation in the healthy participants.

4.1 Group Differences

Group medians were calculated in order to compare UES opening maximum duration and laryngeal elevation between patients with suspected dysphagia undergoing VFSSs and age-matched healthy persons without dysphagia. The above results failed to support H1, partially failed to support H2, and supported H3. The first results showed longer UESOd in patient swallows compared to healthy swallows. One potential theory for longer UESOd in patient swallows is the component of UES opening diameter. It is possible healthy participants may have had larger UES opening diameter requiring a shorter duration compared to patient participants (i.e., healthy participants with larger UES opening diameter have more complete bolus passage in a shorter amount of time). Another potential explanation for longer UESOd in patients is the natural adaptive function to brainstem neural substrates in patients. There is evidence to support that patients with dysphagia capitalize on intact cortical neural substrates to behaviorally compensate for impairments within the swallowing mechanism (Robbins & Levine, 1993). Therefore, it is possible that the patients within the investigated study are prolonging UESOd as a compensation for limited UES opening diameter.

The second results revealed a greater distance of laryngeal elevation in the healthy participants compared to the age-matched patient participants. One theory for this observation is greater traction forces of the thyrohyoid muscle in healthy participants versus patients with suspected dysphagia. As mentioned in the above literature review, the thyrohyoid muscle is responsible for elevating the larynx by approximating it to hyoid bone (Pearson et al., 2012). It is likely that a greater distance in laryngeal elevation can be attributed to stronger muscle contractions of the thyrohyoid muscle. In addition, the larynx itself is suspended by ligaments and muscles attached to the hyoid bone. Therefore, movement of the hyoid pulls the entire laryngeal structure during HLE. Displacement of the hyoid in healthy participants could be playing a factor in greater laryngeal elevation. Another explanation for greater laryngeal elevation observed in healthy participants is the timing of UES inhibition. As highlighted in the above literature review, the UES is inhibited during the pharyngeal phrase prior to HLE resulting in subatmospheric proximal intraluminal esophageal pressure, facilitating bolus flow. It is possible that patient participants presented with mistiming (i.e., delayed onset) of UES inhibition resulting in an anchoring effect on the larynx and laryngeal elevation via its posterior attachment to the UES at the level of the cricoid cartilage.

The third set of results showed a significant correlation between UESOd and laryngeal elevation in only healthy participants. When compared to healthy adults, patients with dysphagia are less coordinated in the timing of swallow events (Matsuo & Palmer, 2009). It can be assumed that the investigated healthy swallows were more coordinated than the dysphagic swallows. Therefore, UESOd and laryngeal elevation may have occurred at the same time and lasted for the same amount of time in healthy swallows, resulting in a significant correlation. The miscoordination in the timing of UESOd and laryngeal elevation events in patients could be a potential reason as to why a significant correlation was not found for this population.

4.2 Methodological Considerations

The methodological factor of bolus condition is significant in its effect on results. The target condition analyzed in this study included 3 mL thin liquid boluses. For healthy participants, bolus conditions were controlled and precisely measured by researchers. Conversely, patient participants were not given precisely measured boluses by researchers due to data being collected contemporaneously during clinical VFSSs conducted by clinicians. Therefore, it is possible patient participants had variations in bolus volumes (e.g., 2-5 mL bolus sizes) impacting UESOd. As explained by Jacob and colleagues (1989), there are confirmed differences in UESOd between different small thin liquid bolus volumes (i.e., 5 mL versus 1 mL). Additionally, as highlighted in the above literature review, there is reported evidence of larger boluses facilitating greater UESOd (Ambrocio et al., 2023; Kahrilas, 1997). Due to the nature of this study, UESOd results are limited to the condition of 3 mL thin liquid boluses. If this study were to be repeated using a larger bolus condition, we may hypothesize that there may be a difference in median UESOd results.

Another methodological factor that may impact results is the variation in age within the investigated data sets; patient participants included 20 females and 30 males, ages 29-84 years, and healthy participants included 30 females and 20 males, ages 22-87 years. As mentioned above, there is evidence that aging causes normal variations in UESOd. Specifically, older adults exhibit greater UESOd (Ambrocio et al., 2023; Humbert et al., 2018). Within the presenting study, the younger adults may have had shorter UESOd, while the older adults may have had longer UESOd. These age implications likely caused variations within the data, influencing results. Unlike age, the variations in sex are unlikely impacting results because there is evidence to support sex does not cause variations in UESOd (Ambrocio et al., 2023; Humbert et al., 2018; Molfenter & Steele, 2013).

4.3 Limitations

There are a few limitations to acknowledge. One limitation is the small sample size (N=100). The investigated patient swallows (n=50) and healthy swallows (n=50) are likely not large enough to be representative of patients and healthy adults in general, impacting the generalizability of results. Another potential limitation is the variability across clinicians who conducted VFSSs in the patient participant data sets. Because the procedures for patient VFSSs were not standardized, clinicians may have presented boluses at different time points throughout the study (e.g., delivering the small liquid bolus at the end of the study when a patient is fatigued) or may have delivered different verbal instructions impacting patient performance. Additionally, bolus sizes were not measured by clinicians, whereas healthy participants were administered exact measurements by researchers. Therefore, there may be uncontrolled variations in the target volume analyzed. A fourth limitation worth mentioning is the heterogeneity of the patient sample. Patient participants were not controlled for diagnosis, likely causing variability.

5.0 Directions for Future Research

This study provided comparison of UES opening maximum duration and laryngeal elevation between patients with suspected dysphagia and age-matched healthy persons, as well as analyzed the correlation between UESOd and laryngeal elevation. Results revealed greater UESOd in patients versus healthy participants, raising the question of the effect of UES opening diameter on duration. Further investigation of UES opening diameter is warranted for a more comprehensive analysis of UES opening efficiency. Another area of further investigation warranted is the combination of the presenting results with hyoid displacement to assess the effect of total hyolaryngeal complex elevation on UES opening.

Additionally, this study is part of a larger series of studies investigating a noninvasive technology, HRCA, to assess swallowing safety and deliver estimations of kinematic events: hyoid bone displacement, laryngeal vestibule closure duration, UESOd, and UES distension (Coyle & Sejdic, 2020; Donohue et al., 2020; Donohue et al., 2021; Donohue et al., 2021; Khalifa et al., 2023; Sabry et al., 2020). It is the hope that the laryngeal elevation data collected in this study by the PI will be used to train the machine learning algorithms used in HRCA signal processing to estimate laryngeal elevation on novel data.

In regard to clinical considerations, this study may provide clinicians with objective data on UESOd and laryngeal elevation across patient and healthy adult populations. These findings also suggest there is increased UES opening efficiency in healthy swallows compared to patient swallows, furthering available data on normal swallowing physiology. Lastly, by establishing the correlation of UESOd and laryngeal elevation in only healthy swallows, clinicians have evidence to support diagnostic statements regarding the manifestation of dysphagia in the mistiming of

UESOd and laryngeal elevation within patient swallows, and the possibility of considering laryngeal elevation as a treatment target for reduced UESOd.

6.0 Conclusion

This descriptive, retrospective case-control study provided analysis of UESOd and laryngeal elevation in patients with suspected dysphagia and age-matched, healthy-dwelling adults. The results of this study demonstrated UESOd to be longer in patients with suspected dysphagia compared to age-matched healthy community-dwelling adults. Conversely, the median distance of laryngeal elevation was greater in healthy adults without dysphagia. Statistically significant differences existed between patient and healthy groups for both UESOd and laryngeal elevation. However, a significant correlation only existed between UESOd and laryngeal elevation in healthy participants. While results revealed statistically significant findings across measures, this study requires further investigation, including continuation in a larger sample size.

Bibliography

Abe, H. & Tsubahara, A. (2011). Observation of arytenoid movement during laryngeal elevation using videoendoscopic evaluation of swallowing. *Dysphagia, 26*(2), 150-154. https://doi.org/10.1007/s00455-010-9285-1

Ambrocio, K. R., Ramsey, R., O'Rourke, A., Beall, J., & Garand, K. L. (2023). Normal variations in upper esophageal sphincter function during deglutition: A secondary analysis of videofluoroscopic data. *The Laryngoscope*, https://doi.org/10.1002/lary.31173

Bracco Diagnostics (2016). Full prescribing information: Varibar pudding. Retrieved from https://www.bracco.com/en-us/x-ray-ct

Bracco Diagnostics (2019). Full prescribing information: Varibar thin liquid. Retrieved from https://www.bracco.com/en-us/x-ray-ct

Bracco Diagnostics (2020). Full prescribing information: Varibar nectar. Retrieved from https://www.bracco.com/en-us/x-ray-ct

Brates, D., Steele, C. M., & Molfenter, S. M. (2020). Measuring hyoid excursion across the life span: Anatomical scaling to control for variation. *Journal of Speech, Language, and Hearing Research: JSLHR*, *63*(1), 125–134. https://doi.org/10.1044/2019_JSLHR-19-00007

Caliskan, H., Mahoney, A. S., Coyle, J. L., & Sejdić, E. (2020, 20-24 July 2020). Automated Bolus Detection in Videofluoroscopic Images of Swallowing Using Mask-RCNN. 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC).

Carlson, D. A., & Pandolfino, J. E. (2015). High-resolution manometry in clinical practice. *Gastroenterology & Hepatology*, *11*(6), 374–384.

Cook, I. (2011). Cricopharyngeal bar and zenker diverticulum. *Gastroenterology & Hepatology*, *7*(8), 540.

Coyle, J. L., & Sejdić, E. (2020). High-resolution cervical auscultation and data science: New tools to address an old problem. *American Journal of Speech-language Pathology*, *29*(2S), 992–1000. https://doi.org/10.1044/2020_AJSLP-19-00155

Dodds, W. J., Taylor, A. J., Stewart, E. T., Kern, M. K., Logemann, J. A., & Cook, I. J. (1989). Tipper and dipper types of oral swallows. *American Journal of Roentgenology*, *153*(6), 1197–1199. https://doi.org/10.2214/ajr.153.6.1197

Donohue, C., Khalifa, Y., Perera, S., Sejdić, E., & Coyle, J. L. (2020). A preliminary investigation of whether HRCA signals can differentiate between swallows from healthy people and swallows from people with neurodegenerative diseases. *Dysphagia*, *36*(4), 635–643. https://doi.org/10.1007/s00455-020-10177-0

Donohue, C., Khalifa, Y., Perera, S., Sejdić, E., & Coyle, J. L. (2021). How closely do machine ratings of duration of UES opening during videofluoroscopy approximate clinician ratings using temporal kinematic analyses and the MBSImP?. *Dysphagia*, *36*(4), 707–718. https://doi.org/10.1007/s00455-020-10191-2

Donohue, C., Mao, S., Sejdić, E., & Coyle, J. L. (2021). Tracking hyoid bone displacement during swallowing without videofluoroscopy using machine learning of vibratory signals. *Dysphagia*, *36*(2), 259–269. https://doi.org/10.1007/s00455-020-10124-z

Eisenhuber, E., Schima, W., Schober, E., Pokieser, P., Stadler, A., Scharitzer, M., & Oschatz, E. (2002). Videofluoroscopic assessment of patients with dysphagia: Pharyngeal retention is a predictive factor for aspiration. *AJR. American journal of roentgenology*, *178*(2), 393–398. https://doi.org/10.2214/ajr.178.2.1780393

Ertekin, C., Aydoğdu, I., & Yüceyar, N. (1996). Piecemeal deglutition and dysphagia limit in normal subjects and in patients with swallowing disorders. *Journal of Neurology, Neurosurgery, and Psychiatry*, *61*(5), 491–496. https://doi.org/10.1136/jnnp.61.5.491

Garand, K. L., McCullough, G., Crary, M., Arvedson, J. C., & Dodrill, P. (2020). Assessment across the life span: The clinical swallow evaluation. *American Journal of Speech-Language Pathology*, *29*(2S), 919–933. https://doi.org/10.1044/2020_AJSLP-19-00063

Hendrix, T. R. (1993). Coordination of peristalsis in pharynx and esophagus. *Dysphagia*, *8*(2), 74–78. https://doi.org/10.1007/BF02266983

Hiiemae, K. M., & Palmer, J. B. (1999). Food transport and bolus formation during complete feeding sequences on foods of different initial consistency. *Dysphagia*, *14*(1), 31–42. https://doi.org/10.1007/PL00009582

Humbert, I. A., Sunday, K. L., Karagiorgos, E., Vose, A. K., Gould, F., Greene, L., Azola, A., Tolar, A., & Rivet, A. (2018). Swallowing kinematic differences across frozen, mixed, and ultrathin liquid boluses in healthy adults: Age, sex, and normal Variability. *Journal of Speech, Language, and Hearing Research: JSLHR*, *61*(7), 1544–1559. https://doi.org/10.1044/2018_JSLHR-S-17-0417

Jacob, P., Kahrilas, P. J., Logemann, J. A., Shah, V., & Ha, T. (1989). Upper esophageal sphincter opening and modulation during swallowing. *Gastroenterology*, *97*(6), 1469–1478. https://doi.org/10.1016/0016-5085(89)90391-0

Jean, A. (2001). Brain stem control of swallowing: Neuronal network and cellular mechanisms. *Physiological Reviews*, *81*(2), 929–969. https://doi.org/10.1152/physrev.2001.81.2.929

Kahrilas P. J. (1997). Upper esophageal sphincter function during antegrade and retrograde transit. *The American Journal of Medicine*, *103*(5A), 56S–60S. https://doi.org/10.1016/s0002-9343(97)00324-0

Kassambara A (2023). _ggpubr: 'ggplot2' Based Publication Ready Plots_. R package version 0.6.0, <https://CRAN.R-project.org/package=ggpubr>.

Kessler, J. P., & Jean, A. (1985). Identification of the medullary swallowing regions in the rat. *Experimental Brain Research*, *57*(2), 256–263. https://doi.org/10.1007/BF00236530

Lang, I. M., & Shaker, R. (1997). Anatomy and physiology of the upper esophageal sphincter. *The American Journal of Medicine*, *103*(5A), 50S-55S. https://doi.org/10.1016/s0002-9343(97)00323-9

Lang, I. M., & Shaker, R. (2000). An overview of the upper esophageal sphincter. *Current Gastroenterology Reports*, *2*(3), 185-190. https://doi.org/10.1007/s11894-000-0059-z

Langmore, S. E., Schatz, K., & Olsen, N. (1988), Fiberoptic endoscopic examination of swallowing safety: A new procedure. *Dysphagia*, *2*(4), 216-9.

Law, R., Katzka, D. A., & Baron, T. H. (2014). Zenker's diverticulum. *Clinical Gastroenterology and Hepatology*, *12*(11), 1773–1782. https://doi.org/10.1016/j.cgh.2013.09.016

Leonard, R., Kendall, K., & McKenzie, S. (2004). UES opening and cricopharyngeal bar in nondysphagic elderly and nonelderly adults. *Dysphagia*, *19*(3), 182–191. https://doi.org/10.1007/s00455-004-0005-6

Logemann J. A. (1988). Swallowing physiology and pathophysiology. *Otolaryngologic Clinics of North America*, *21*(4), 613–623.

Martin-Harris, B., Brodsky, M. B., Michel, Y., Castell, D. O., Schleicher, M., Sandidge, J., Maxwell, R., & Blair, J. (2008). MBS measurement tool for swallow impairment--MBSImp: Establishing a standard. *Dysphagia*, *23*(4), 392–405. https://doi.org/10.1007/s00455-008-9185-9

Matsuo, K., & Palmer, J. B. (2008). Anatomy and physiology of feeding and swallowing- normal and abnormal. *Physical Medicine and Rehabilitation Clinics of North America*, *19*(4), 691-707. https://doi.org/10.1016/j.pmr.2008.06.001

Matsuo, K., & Palmer, J. B. (2009). Coordination of mastication, swallowing and breathing. *The Japanese Dental Science Review*, *45*(1), 31–40. https://doi.org/10.1016/j.jdsr.2009.03.004

McCarty, E. B., & Chao, T. N. (2021). Dysphagia and swallowing disorders. *Medical Clinics of North America*, *105*(5), 939–954. https://doi.org/10.1016/j.mcna.2021.05.013

Mendelsohn, M. S., & McConnel, F. M. (1987). Function in the pharyngoesophageal segment. *The Laryngoscope*, *97*(4), 483-489. https://doi.org/10.1288/00005537-198704000-00014

Molfenter, S. M., & Steele, C. M. (2013). Variation in temporal measures of swallowing: Sex and volume effects. *Dysphagia*, *28*(2), 226–233. https://doi.org/10.1007/s00455-012-9437-6

Pearson, W. G., Hindson, D. F., Langmore, S. E., & Zumwalt, A. C. (2013). Evaluating swallowing muscles essential for hyolaryngeal elevation by using muscle functional magnetic resonance imaging. *International Journal of Radiation Oncology, Biology, Physics, 85*(3), 735-740. https://doi.org/10.1016/j.ijrobp.2012.07.2370

Pearson, W. G., Langmore, S. E., Yu, L. B., & Zumwalt, A. C. (2012). Structural analysis of muscles elevating the hyolaryngeal complex. *Dysphagia, 27*(4), 445-451. https://doi.org/10.1007/s00455-011-9392-7

Perlman, A. L., Booth, B. M., Grayhack, J. P. (1994) Videofluoroscopic predictors of aspiration in patients with oropharyngeal dysphagia. *Dysphagia, 9*(2), 90-95. https://doi.org/10.1007/BF00714593

Posit team (2023). RStudio: Integrated Development Environment for R. Posit Software, PBC, Boston, MA. URL http://www.posit.co/.

Prisman, E., & Genden, E. M. (2013). Zenker diverticulum. *Otolaryngologic Clinics of North America*, *46*(6), 1101–1111. https://doi.org/10.1016/j.otc.2013.08.011

R Core Team (2023). _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/

Robbins, J., & Levine R. (1993). Swallowing after lateral medullary syndrome plus. *Clin Comm Disord*, *3*(4), 45-55.

Rosenbek, J. C., Robbins, J. A., Roecker, E. B., Coyle, J. L., & Wood, J. L. (1996). A penetration-aspiration scale. *Dysphagia*, *11*(2), 93–98. https://doi.org/10.1007/BF00417897

Sabry, A., Mahoney, A. S., Mao, S., Khalifa, Y., Sejdić, E., & Coyle, J. L. (2020). Automatic estimation of laryngeal vestibule closure duration using high-resolution cervical auscultation signals. *Perspectives of the ASHA Special Interest Groups*, *5*(6), 1647–1656. https://doi.org/10.1044/2020_persp-20-00073

Saitoh, E., Shibata, S., Matsuo, K., Baba, M., Fujii, W., & Palmer, J. B. (2007). Chewing and food consistency: Effects on bolus transport and swallow initiation. *Dysphagia*, *22*(2), 100–107. https://doi.org/10.1007/s00455-006-9060-5

Sasaki, C. T., & Isaacson, G. (1988). Functional anatomy of the larynx. *Otolaryngologic Clinics of North America*, *21*(4), 595–612.

Schwertner, R. W., Garand, K. L., & Pearson, W. G., Jr. (2016). A novel imaging analysis method for capturing pharyngeal constriction during swallowing. *Journal of Imaging Science*, *1*(1), http://www.ommegaonline.org/admin/journalassistance/publishimages/A-Novel-Imaging-Analysis-Method-for-Capturing-Pharyngeal-Constriction-During-Swallowing.pdf.

Shaw, S., & Martino, R. (2013). The normal swallow: Muscular and neurophysiological control. *Otolaryngologic Clinics of North America*, *46*(6), 937–956. https://doi.org/10.1016/j.otc.2013.09.006

Singh, S., & Hamdy, S. (2005) The upper oesophageal sphincter. *Neurogastroenterology and Motility, 17*(1), 3-12. https://doi.org/10.1111/j.1365-2982.2005.00662.x

Sivarao, D .V., & Goyal R. K. (2000). Functional anatomy and physiology of the upper esophageal sphincter. *The American Journal of Medicine, 108*(4A), 27S-37S. https://doi.org/10.1016/s0002-9343(99)00337-x

Torchiano M (2020). _effsize: Efficient Effect Size Computation_. doi:10.5281/zenodo.1480624 <https://doi.org/10.5281/zenodo.1480624>, R package version 0.8.1, https://CRAN.R-project.org/package=effsize

Vandaele, D. J., Perlman, A. L., & Cassell, M. D. (1995). Intrinsic fibre architecture and attachment of the human epiglottis and their contributions to the mechanism of deglutition. *Journal of Anatomy, 186,* 1-15.

Vose, A. K., Kesneck, S., Sunday, K., Plowman, E., & Humbert, I. (2018). A Survey of clinician decision making when identifying swallowing impairments and determining treatment. *Journal of Speech, Language, and Hearing Research*, *61*(11), 2735–2756. https://doi.org/10.1044/2018_JSLHR-S-17-0212

Wickham H, Averick M, Bryan J, Chang W, McGowan LD, François R, Grolemund G, Hayes A, Henry L, Hester J, Kuhn M, Pedersen TL, Miller E, Bache SM, Müller K, Ooms J, Robinson D, Seidel DP, Spinu V, Takahashi K, Vaughan D, Wilke C, Woo K, Yutani H (2019). "Welcome to the tidyverse." Journal of Open Source Software, *4*(43), 1686. doi:10.21105/joss.01686 https://doi.org/10.21105/joss.01686

Wickham H, François R, Henry L, Müller K, Vaughan D (2023). _dplyr: A Grammar of Data Manipulation_. R package version 1.1.2, https://CRAN.R-project.org/package=dplyr

Zhang, J., Zhou, Y., Wei, N., Yang, B., Wang, A., Zhou, H., Zhao, X., Wang, Y., Liu, L., Ouyoung, M., Villegas, B., & Groher, M. (2016). Laryngeal elevation velocity and aspiration in acute ischemic stroke patients. *PLOS One, 11*(9). https://doi.org/10.1371/journal.pone.0162257

Zhang, Z., Mao, S., Coyle, J., & Sejdić, E. (2021). Automatic annotation of cervical vertebrae in videofluoroscopy images via deep learning. *Medical Image Analysis, 74*, 102218. https://doi.org/https://doi.org/10.1016/j.media.2021.102218