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Relationship between Oral, Pharyngeal, and Esophageal Dysphagia

Erin Reedy
Medical University of South Carolina

RELATIONSHIP BETWEEN ORAL, PHARYNGEAL, AND ESOPHAGEAL DYSPHAGIA

BY

Erin Reedy, MS, CCC-SLP

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Approved by:

Chair, Project Committee	Heather Bonilha, PhD	8/2/2021 DATE
Member, Project Committee	Annie Simpson, PhD	8/2/2021 DATE
Member, Project Committee	Ashli O'Rourke, MD	7/31/21 DATE
Dean, College of Health Professions	Zoher Kopasi, PT, PhD MBA	8/2/2021 DATE

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CHAPTER 1:

INTRODUCTION

1.1 Background and Significance

Dysphagia is the medical term for disordered swallowing and affects approximately 15 million Americans per year with an additional 1 million diagnosed yearly (Carnaby & Harenberg, 2013) and costs over 540 billion dollars annually in government spending (Altman, Yu, Schaefer, 2010). Swallowing is a highly coordinated series of pressures generated by the 20+ muscles (Hosseini et al., 2019) which are involved in this complex process of swallowing; a process which exists in a reciprocal relationship with respiration. These muscles of the aerodigestive tract synchronously transform the oropharynx from a respiratory system to a deglutitive system where respiration ceases over the course of the approximately 1 second (Matsuo & Palmer, 2008) it takes for a bolus to traverse the pharynx. This transformation occurs so that the bolus is not easily misdirected into the airway (e.g., aspiration) and to ensure that the life-sustaining nutrients of the food or liquid being swallowed is adequately propelled into the upper gastrointestinal (GI) tract for digestion. Any impairment of bolus transit from the mouth, pharynx, or esophagus is considered a swallowing impairment, the pathophysiologic dysfunction of swallowing is referred to as dysphagia.

a. Dysphagia and stroke

Stroke is the fifth leading cause of mortality in the United States (Yang et al., 2017), impacting approximately 795,000 people and costs 34 billion dollars annually (Benjamin et al., 2017). Between 37-78% stroke survivors will experience post-stroke oropharyngeal dysphagia (Martino et al., 2005),11-31% of which will have chronic dysphagia (Gonzalez-Fernandez et al., 2013; Mann et al., 1999). And neurogenic diagnoses are the most common etiology for dysphagia (ASHA, n.d.). Complications from dysphagia can include pneumonia, dehydration, malnutrition, long-term feeding tube dependency, and a reduction in quality of life. Rates of pneumonia, mortality, and morbidity are higher in post-stroke patients who aspirate than for post-stroke patients without dysphagia (Cohen et al., 2016). Not surprisingly, healthcare costs for patients with dysphagia are higher than for those without dysphagia. The average adjusted cost of pneumonia-related hospitalizations in the post-stroke population is $27,633 (Wilson,

2012) and the one-year cost to Medicare for post-stroke patients with dysphagia is $4,510 greater than for post-stroke patients without dysphagia (Bonilha et al., 2014).

Despite the known risk for the acute onset of dysphagia in the post-stroke population, and with it the risk for silent aspiration (Cohen et al., 2016; Daniels et al., 1998; Galovic et al., 2013; Martino et al., 2005), respiratory phase changes (Catalá-Ripoll et al., 2020, Park G.W. et al., 2015) which may contribute to the risk for dysphagia, and the limited accuracy of clinical "bedside" swallow evaluations (Garand et al., 2020; O'Horo et al., 2015), there is no standard for the assessment of swallowing in this population. In fact, the *Recommendations for the Establishment of Stroke Systems of Care: A 2019 Update* from the American Heart Association (AHA) (Adoye et al., 2019) only includes limited references to rehabilitation efforts in the post-stroke population though does acknowledge that early interventions are key to maximal post-stroke rehabilitation.

Dysphagia in stroke is a complex phenomenon with multiple different presentations, owing to the complex neural network of the bilateral cortex, subcortical structures, cerebellum, and brainstem which informs swallowing. Lesions at any point within this network can result in altered swallowing ranging from mild to profound. Our understanding of the swallowing neural network, or connectome, continues to grow (Cola et al., 2010; Daniels et al., 2017; Flowers et al., 2017; May et al., 2017; Moon et al., 2012; Wilmskoetter et al., 2018; Wilmskoetter et al., 2019) and, with it our understanding of swallowing and swallowing disorders.

Although swallowing impairment primarily occurs in the acute phase of post-stroke recovery, for many patients disordered swallowing persists. Impairment in the oral and pharyngeal aspects of swallowing is well-identified in stroke; however, there is currently no research dedicated solely to esophageal impairment in stroke. Though, findings from a larger cohort (Miles et al., 2019) demonstrated that esophageal bolus transit time was 6 seconds longer in participants with a diagnosis of stroke than compared to healthy controls and that esophageal bolus transit time was statistically significantly associated with aspiration. The absence of

devoted research to esophageal impairment in the post-stroke population with dysphagia is contrary to the shared neurologic, anatomic, and physiologic characteristics of the oropharynx and esophagus. We hypothesize that these patients who do not improve with traditional swallowing interventions, focused on the oropharynx, may have an impairment that is, at least in part, due to esophageal dysfunction.

b. Dysphagia in Respiratory Disorders

Dysphagia is also a phenomenon known to occur in the context of respiratory disorders and/or respiratory compromise. There is a growing knowledge base investigating respiratory compromise and disorders/dysfunctions of the swallowing continuum. Disruptions in the normal respiratory-swallow coordination have been identified in Chronic Obstructive Pulmonary Disease (COPD) (Gross et al., 2009; Martin-Harris et al., 2015; Shaker et al., 1992) Pathophysiologic changes in COPD and swallowing have been identified to include laryngeal penetration and subglottic aspiration on instrumental assessment (Cassani et al., 2015; Cvejic et al., 2011; Garand et al., 2018; Good-Fraturelli, Curlee & Holle, 2000; Gross et al., 2009). This can create a cycle where the dysphagia itself can provoke a COPD exacerbation (Nagami et al., 2017; Steidl et al., 2015). These physiologic changes which elevate dysphagia and aspiration risk have been demonstrated in populations with respiratory compromise (Cassani et al., 2015; Clayton et al., 2012; Cvejic et al., 2011; Garand et al., 2018; Good-Fraturelli, Curlee & Holle, 2000, Nagami et al., 2017) and respiratory-swallow pattern alterations (Gross et al., 2009; Martin-Harris et al., 2015; Shaker et al., 1992). Esophageal function, or dysfunction, is also present in COPD and has been well-studied regarding gastroesophageal reflux disease (GERD) due to the acute concern for non-prandial aspiration of acidic reflux (Hamadan et al., 2016; Iliaz et al., 2016; Lin et al., 2018, Turbyville, 2009; Su et al., 2018).

Only a small body of research exists regarding oropharyngeal dysphagia in the post-lung transplant population (Atkins et al., 2007; Atkins et al., 2010; Baumann et al., 2017; Black et al., 2019; Miles et al., 2020). These patients are at risk of vagal injury during surgery and additionally at risk for post-extubation dysphagia and/or laryngeal trauma (Borders et al., 2019;

Brodsky, De, Chilkuri et al., 2018; Brodsky et al, 2014; Brodsky, Levy, Jedlanek et al., 2018; Skoretz, Flowers & Martino, 2010; Tikka & Hilmi, 2019). If high-flow nasal cannula if required post-lung transplant, there may be further changes to respiratory-swallow coordination (Eng et al., 2019; Jose Flores et al., 2019; Leder et al., 2016; Parke, McGuinness & Eccleston, 2009; Ward, 2013). And the evidence for esophageal dysphagia is persuasive (Cangemi et al., 2020; Ciriza de Los Ríos et al., 2018; Davis et al., 2010; Kayawake et al., 2018; Giulini et al., 2021; Grass et al., 2015; Griffin et al., 2013; Grass et al., 2015; Masuda et al., 2020; Masuda et al., 2019; Tangaroonsanti et al., 2019; Tangaroonsanti et al., 2017). However, there is currently no research which specifically identifies impairment of the swallowing continuum in a single cohort. We hypothesize that limiting assessments and interventions, focused solely on the oropharynx, may limit the diagnostic accuracy and treatment efficacy if the entire swallowing continuum is not evaluated and factored into the rehabilitative process.

c. Links Between Cohorts

Though these two cohorts may appear unrelated at first, they are linked by shared neurology, anatomy, and physiology. Despite the different etiologies, both groups are susceptible to disorders of the swallowing continuum. Neurologically, the main drivers for respiration, swallowing, and digestion lie in similar locations in the brainstem (pons, medulla). Anatomically, the nose, mouth, pharynx, larynx, bronchi, lungs, diaphragm, and esophagus form the multi-functional aerodigestive tract. Physiologically, the synchronized activity of the oral cavity, pharynx, esophagus, stomach, lungs, and diaphragm function as a swallowing continuum, one which exists in a reciprocal relationship with respiration.

Patients post-stroke may experience altered respiration (Catalá-Ripoll, Monsalve-Naharro & Hernández-Fernández, 2020, Park G.W. et al., 2015) and patients post-lung transplantation may experience neurologic sequela (Chan et al., 2016; Gamez et al., 2017; Mateen et al., 2010; Studer et al., 2004; Zivković et al., 2009). And, in fact, patients' post-stroke with comorbid COPD have been found to have worse swallowing outcomes including a higher incidence of pneumonia (Langmore et. al, 1998; Masiero et al., 2008).

1.2. Problem Statement

The oral cavity, pharynx, and esophagus form an aerodigestive tract from the mouth to the stomach where a disturbance in any part of the tract can cause a disruption in any or all other aspects of the swallowing mechanism (Triadafilopoulous et al., 1992; Gullung et al., 2012). It is growing increasingly evident that swallowing is not phasic but indeed a continuum involving anatomically contiguous and biomechanically interdependent elements (Gullung et al., 2012; Jones et al., 1985; Jones et al., 1987; Lever et al., 2007; Madhavan, Carnaby & Crary, 2015; Miles et al., 2017; Miles et al., 2019; Miles et al., 2015; O'Rourke et al., 2016; Ortiz et al., 2019; Triadafilopoulos, 1992; Reedy et al., 2021; Watts et al., 2019; Watts et al., 2021). Though it is understood that these interrelationships of swallowing exist the mechanisms of interplay and the clinical implications of the co-occurrences of oral, pharyngeal, and esophageal swallowing impairments are not well understood.

The assessments currently available for the investigation of swallowing fall into three diagnostic categories: fluoroscopic, endoscopic, and manometric. All these assessment methods have their own indications and contraindications and limitations to each exam, some of which are especially pertinent to consider in the swallowing assessment of patients with dysphagia (e.g., post-stroke and post-lung transplant). Radiographic fluoroscopy is used to demonstrate the anatomic and physiologic aspects of swallowing in real time and the Modified Barium Swallow Study (MBSS) is the "gold standard" for swallowing assessment (Martin-Harris & Jones, 2008). The Modified Barium Swallow Study Impairment Profile (MBSImP) (Martin-Harris et al., 2008) identifies the 17 physiologic components of swallowing, including esophageal visualization and is the only standardized, reliable, and validated protocol for the MBSS. Because of the division amongst providers (e.g., physicians) and clinicians (e.g., SLPs), there is a prevailing practice for the cervical esophagus to serve as the "end point" of the SLP's assessment. Though Martin-Harris, Michel, and Castell (2005) warn against "artificially separating the swallowing continuum into isolate phases."

A non-diagnostic visualization of the esophagus during the MBSS is of critical importance for all patients who can participate in this aspect of the exam, which involves turning the patient to view in the anterior-posterior (A-P) plane. There are many different interpretations as to what constitutes esophageal visualization during the MBSS including positioning, protocol (order of presentation, types of radio-opaque stimuli and under what conditions). Despite solid evidence to support esophageal visualization during the MBSS (Allen et al., 2012; Garand et al., 2020; Jones et al., 1987; Jones et al., 1985; Miles, 2017; Miles et al., 2019; Miles et al., 2016; Miles et al., 2015; Ortiz et al., 2019; Reedy et al., 2021; Watts et al., 2019; Watts et al., 2021) its inclusion remains somewhat controversial.

One unexplored aspect of esophageal visualization is the influence of deglutitive inhibition, or the normal cessation or attenuation of esophageal peristalsis for swallows which occur in quick succession (<20-30 seconds apart). Some current research includes the language for their visualization protocols, (Miles et al., 2019; Miles et al., 2016; Watts et al., 2021) intended to account for deglutitive inhibition, however, whether participants were able to follow the directions was not reported or factored into analysis. If deglutitive inhibition is unaccounted for in esophageal visualization practices, patients may be inaccurately judged to have abnormality where there is none.

1.3. Study Objectives

The goal of this dissertation is to investigate esophageal impairment in the post-stroke and post-lung transplant populations identified with oropharyngeal dysphagia. First, by identifying the proportion of patients in both cohorts with esophageal clearance abnormalities (as evidenced by abnormal MBSImP component 17 scores) during their MBSS. Second, for those patients who receive esophageal visualization as part of the MBSS, to look for correlations between the other MBSImP components, Penetration-Aspiration Scale (PAS) scores (Rosenbeck et al., 1996), Functional Oral Intake Scale (FOIS) scores (Crary, Mann & Groher, 2005), and oral intake recommendations in the form of the International Dysphagia Diet Standardization Initiative (IDDSI) functional diet scale (Steele et al., 2018) consistency levels. Lastly, to explore

the impact of cued vs. un-cued swallows in interpretation of esophageal clearance (MBSImP component 17 score).

Objective 1: Describe the population in the post-stroke and post-lung transplant populations with abnormal scores on MBSImP Component 17 (esophageal visualization).

Objective 2: Determine if associations exist between esophageal impairment and other measures of oropharyngeal impairment.

Objective 3: Ascertain if associations exist between judgements of esophageal clearance in un-cued vs. cued conditions to account for deglutitive inhibition.

1.4. Specific Aims

The goal of this dissertation is to investigate esophageal impairment in the post-stroke and post-lung transplant populations identified with oropharyngeal dysphagia and to identify the influence of cueing during the MBSS to account for normal physiologic factors. To achieve this goal, we will conduct two retrospective studies, the first relating to specific aims 1 and 2, the second correlating to specific aim 2. Study 1 (specific aims 1 and 2) is quantitative and will have commonality in patient recruitment, measurements, and metrics, as well as in statistical methods. A prospective experimental study has been included to explore the impact of cued vs. un-cued swallows on ratings of esophageal bolus clearance.

The findings from this study will help inform our understanding of swallowing and swallowing disorders, aid in planning future research and define further knowledge gaps. This research will contribute to public health in that it will inform the knowledge of disordered swallowing and the impact of including the esophagus in routine swallowing assessment. This will ultimately direct patient care, influencing how swallowing disorders are understood, diagnosed, and treated. With these findings, we will help to inform clinical best-practice, identify a need for more collaborative care for patients with dysphagia and, as a result, improve patient outcomes.

Specific Aim 1: Identify and describe the patients diagnosed with oropharyngeal dysphagia who have either co-occurring or primary esophageal dysphagia.

Hypothesis 1: Patients with oropharyngeal impairments will have co-occurring abnormal component 17 scores.

Rationale: The diagnosis for dysphagia invariably defaults to oropharyngeal in these populations, though shared neural innervation, anatomy, and physiology helps to illuminate that disordered swallowing crosses the arbitrary divide of the upper esophagus, especially in the context of stroke and lung transplantation. Current practice divides the assessment of swallowing amongst medial and clinical sub-specialties and the diagnostic assessments available follow the same arbitrary divides which separate the oropharyngeal from the esophageal aspects of swallowing. Because of the continuous nature of swallowing, it should be evaluated as such, and the aggregate components and contributions of each neuroanatomic aspect (and impairment) should be considered when determining the overall physiologic nature of post-stroke and post-lung transplant dysphagia. Without consideration of all aspects of the swallow, the disorder fails to be accurately diagnosed and treated.

Specific Aim 2: To identify associations between esophageal impairment and markers of oropharyngeal impairment as determined from the MBSS.

Hypothesis 2: Esophageal clearance abnormalities, evidenced during MBSS, will be positively correlated with markers of oropharyngeal impairment, aspiration, and altered oral intake.

Rationale: Existing studies support the interrelationship between all aspects of the swallowing continuum, but especially between the pharyngeal and esophageal aspects of the swallow. We will utilize component 17 data to analyze esophageal findings and to assess for relationships between known physiologic changes (represented by MBSImP and PAS scores) in post-stroke oropharyngeal dysphagia. Additionally, the outcomes of oral intake (in the form of FIOS and

IDDSI diet scale scores) will be used to determine if relationships between esophageal impairment and per oral (PO) recommendations exist.

Specific Aim 3: To analyze the proportion of patients identified with esophageal clearance abnormalities during cued vs. un-cued swallows.

Hypothesis 3: Judgements of esophageal clearance during the MBSS is more accurate when deglutitive inhibition is accounted for through patient instruction.

Rationale: Deglutitive inhibition is the cessation or alteration of peristalsis for swallows that are completed in quick succession. When provided with verbal cueing to swallow only once per bolus, visualization of the esophagus is more in-line with standardized esophageal testing.

CHAPTER 2: AIM 1

Manuscript 1:
Dysphagia Across the Swallowing Continuum in a Post-Stroke Cohort

TITLE: Abnormal Esophageal Clearance Identified During MBSS in a Post-Stroke Cohort

AUTHORS: Reedy, E.L., Simpson, A.N., O'Rourke, A.K., Bonilha, H.S.

ABSTRACT:

Background: Dysphagia impacts many post-stroke survivors with wide-ranging prevalence in the acute and chronic phases. One relatively unexplored manifestation of swallowing impairment is that of primary or co-occurring esophageal dysphagia. The incidence of esophageal dysphagia in this population is unknown despite the shared neuroanatomy and physiology with the oropharynx. We aimed to determine the presence of abnormal esophageal clearance in an acute post-stroke sample using the Modified Barium Swallow Impairment Profile (MBSImP™©) component 17 (esophageal clearance) as our outcome measure.

Methods: We performed a retrospective, cross-sectional, cohort study of 58 post-stroke patients with acute, first-ever, ischemic strokes. All participants received a Modified Barium Swallow Study (MBSS) as part of standard care during their acute hospitalization using the MBSImP™© protocol and scoring metric. Swallowing impairment was determined using a combination of MBSImP scores, Penetration-Aspiration Scale (PAS) scores, Functional Oral Intake Scale (FOIS) scores, International Dysphagia Diet Standardization Initiative (IDDSI) scores, and temporal variables (e.g., time from stroke to MBSS). We performed tests of association and logistic regression analysis to characterize variables and determine if statistically significant associations exist between MBSImP™© component 17 scores and other measures of swallowing impairment.

Results: In our study of post-stroke patients who received a Modified Barium Swallow Study (MBSS) as part of their care, abnormal esophageal clearance was identified in 57.89% of patients in the acute phase of post-stroke recovery. Statistically significant associations were also identified in measures of pharyngeal physiology (MBSImP scores) and swallowing outcome measures (IDDSI scores and alternate means of nutrition).

Conclusion: Abnormal esophageal clearance was identified in greater than half of our post-stroke patients. Given that swallowing occurs across a continuum (e.g., oral cavity, pharynx, esophagus) the evaluation of swallowing is incomplete if only certain aspects are visualized; and the esophageal contribution to dysphagia should not be ignored in the post-stroke population.

INTRODUCTION:

Stroke is the fifth leading cause of mortality in the United States (Yang et al., 2017), impacting approximately 795,000 people and costs 34 billion dollars annually (Benjamin et al., 2017). Between 37-78% of stroke survivors will experience post-stroke oropharyngeal swallowing impairment or dysphagia - the range can be explained by the various types of screening and assessment used to identify dysphagia (Martino et al., 2005). Dysphagia occurs primarily in the acute phase of post-stroke recovery, though for some patients disordered swallowing persists. Between 11-31 of those with post-stroke dysphagia will not have recovered 3-6 months post-stroke (Gonzalez-Fernandez et al., 2013; Mann et al., 1999). Patients with post-stroke dysphagia who aspirate are 3-11 times more likely to develop pneumonia and have higher rates of mortality and morbidity than post-stroke patients without dysphagia (Cohen et al., 2016). The average adjusted cost of pneumonia-related hospitalizations in the post-stroke population is $27,633 (Wilson, 2012). And the one-year cost to Medicare for post-stroke patients with dysphagia is $4,510 greater than for post-stroke patients without dysphagia (Bonilha et al., 2014). Attributable hospital costs for all patients with dysphagia have been calculated at over 540 billion dollars annually (Altman et al., 2010).

Swallowing occurs across a continuum of the oral cavity, pharynx, and esophagus. These structures form an aerodigestive tract from the mouth to the stomach where a disturbance in any part of the tract can disrupt any or all aspects of swallowing (Triadafilopoulous et al., 1992; Gullung et al., 2012). The vagus nerve, arising from the medulla, innervates much of the pharynx, and all of the larynx and esophagus. Under normal circumstances, swallowing is a highly coordinated series of pressures generated by the 20+ muscles (Hosseini et al., 2019) which are involved in this complex process of moving food and drink from the mouth into the gastric cavity. It is growing increasingly evident that swallowing is indeed a continuum (Gullung et al., 2012; Jones et al., 1985; Jones et al., 1987; Lever et al., 2007; Madhavan et al., 2015; Miles et al., 2015; Miles et al., 2019; Miles et al., 2017; O'Rourke et al., 2014; Ortiz et al., 2019; Reedy et al., 2021; Triadafilopoulos, 1992; Watts et al., 2019) involving anatomically contiguous and biomechanically interdependent elements. Despite this shared anatomy and physiology,

swallowing assessment remains divided at the upper esophageal sphincter (UES). Many studies have investigated post-stroke oropharyngeal dysphagia (Cohen et al., 2016; Cola et al., 2010; Daniels and Foundas, 1997; Daniels et al., 2017; Flowers et al., 2017; Kim et al.,2016; Leopold & Daniels, 2010; Martino et al., 2005; May et al., 2017; Moon, Pyon & Kwon, 2012; Robbins & Levine, 1988; Singh & Hamdy, 2006; Suntrup-Krueger, S., 2017; Wilmskoetter et al., 2018; Wilmskoetter et al., 2019), though none have explored esophageal impairment in this population. The shared vagal drivers for swallowing provide the critical neural link to identify that swallowing impairment crosses the arbitrary division of the UES and supports the investigation of swallowing across this continuum.

Dysphagia in stroke is a complex phenomenon with multiple different presentations, owing to the complex neural network of the bilateral cortex, subcortical structures, cerebellum, and brainstem which informs swallowing. Lesions at any point within this network can result in altered swallowing ranging from mild to profound. The complete neural network which informs swallowing is not yet known, though a growing body of research is helping to establish the swallowing connectome (Cola et al., 2010; Daniels et al., 2017; Flowers et al., 2017; May et al., 2017; Moon et al., 2012; Wilmskoetter et al., 2018; Wilmskoetter et al., 2019) and expand our understanding of swallowing and swallowing disorders. Despite this, the possibility for esophageal pathophysiology post-stroke is relatively unexplored. Miles et al. (2019) demonstrated a 6-second increase in mean esophageal bolus transit time in post-stroke participants when compared to normal controls. This finding provides early evidence of post-stroke changes to esophageal function and justifies further research. We hypothesize that esophageal dysfunction may contribute to the delay or lack of recovery in those patients with chronic dysphagia for which the complications include pneumonia, dehydration and/or malnutrition, long-term feeding tube dependency, and a reduction in quality of life.

Exploring the shared anatomic, neural, and physiologic connections is critical in the assessment of swallowing in stroke survivors who comprise the largest proportion of patients with dysphagia. Despite this, esophageal function is not commonly assessed in this population which

disregards the clear indication that our understanding of swallowing and swallowing disorders, as well as that patient outcomes could be improved. As a result, the proportion of post-stroke patients who may have primary or simultaneous esophageal deficits is not known. If our assessments of dysphagia do not include discerning the presence of an esophageal contribution, our patients may be inaccurately or incompletely diagnosed. Our recommendations or interventions may be ineffective or even deleterious if the primary source of impairment is not addressed.

We aimed to identify patients who are examined for oropharyngeal dysphagia and have either simultaneous or primary esophageal dysphagia owing to the shared neural, anatomic, and physiologic characteristics. We propose that investigating the swallow as a continuum will have a substantial impact on the post-stroke population. These patients are particularly susceptible to be incompletely diagnosed and treated because the diagnosis of dysphagia invariably defaults to oropharyngeal and the esophageal contribution to their symptoms is not routinely assessed.

METHODS:

Study Design

This study was approved by the Institutional Review Board (IRB). The study was performed retrospectively, sampling from a cross-sectional post-stroke cohort. Potential participants were identified via existing databases and/or the electronic health record (EHR), EPIC, at the Medical University of South Carolina (MUSC). A combination of ICD (9^{th} and 10^{th} editions: 433-34, 436 and I63.5* for stroke and 787.2* and R13.1* for dysphagia) and CPT codes (radiology-billed code 74230) was used to identify participants. An institutional request using this combination of ICD and CPT codes yielded a database of patients with identifiers from which the chart reviews were performed, and data was extracted.

Inclusion and Exclusion Criteria

Inclusion criteria were established to include adults (21+ years) who had a first-ever ischemic stroke confirmed by MRI or CT. The brain imaging had to be conducted at MUSC during acute stroke hospitalization. Those participants whose strokes were determined to be hemorrhagic (e.g., subarachnoid hemorrhage, intracerebral or subdural/epidural hematoma) were excluded. If a remote infarct or stroke was identified on CT or MR brain imaging, the participant was excluded. Potential participants were excluded if their past medical history included diseases known to impair swallow function (e.g., head and neck cancer, progressive neurologic disorders, diagnosed esophageal disorders [except gastroesophageal reflux disease]).

All eligible participants had a Modified Barium Swallow Study (MBSS) using the Modified Barium Swallow Impairment Profile (MBSImP™©) protocol and scoring metric. Those participants whose MBSS reports did not include any MBSImP scores or lacked an MBSImP component 17 (esophageal clearance) score were excluded. Penetration Aspiration Scale (PAS) scores (Rosenbek et al., 1996) were required. Functional Oral Intake Scale (FOIS) scores (Crary et al., 2005) and International Dysphagia Diet Standardization Initiative (IDDSI) scale (Steele et al., 2018) scores or enough information to determine scores from compatible pre-IDDSI consistencies were collected, but not required as some of the participants were identified from a database that pre-dated the information available in the EHR.

Modified Barium Swallow Studies

All patients received an MBSS during their acute post-stroke hospitalization as part of the standard of care. MBSS were performed at 30 pulses per second (pps) and were recorded at 30 frames per second (fps) according to best practices (Bonilha, Blair, Carnes, et al., 2013; Bonilha, Humphries, Blair, et al., 2013). All MBSS were conducted using the Modified Barium Swallow Impairment Profile (MBSImP) (Martin-Harris et al., 2008) which measures 17 distinct physiologic components of swallowing. The core protocol uses 12 swallows across varying liquid and solid consistencies, the initial 10 in the lateral view, the last 2 in the anterior-posterior view. Component 17, our outcome measure, is determined by the esophageal bolus clearance

patterns through the esophageal body and lower esophageal sphincter (LES) in the A-P view with 5 ml nectar and 5 ml pudding contrast. Standardized preparations of barium sulfate (Varibar®, Bracco Diagnostics Inc.) were used.

From these clinical MBSSs, data related to swallowing impairment and swallowing outcomes were extracted. Physiologic swallowing assessment in the form of MBSImP scores including component scores, and oral and pharyngeal total scores were collected as well as Penetration-Aspiration Scale (PAS) scores (Rosenbek et al., 1996), and the absence or presence of aspiration. Swallowing outcome measures in the form of Functional Oral Intake Scale (FOIS) scores (Crary et al., 2005) and International Dysphagia Diet Standardization Initiative (IDDSI) scores (Steele et al., 2018) were either collected directly from the medical record or were determined using a crosswalk of previous, compatible, consistencies. Due to the nature of IDDSI scores, typically reported as two scores one for liquids and one for solids, the IDDSI scores were separated into an "IDDSI Liquid" and an "IDDSI Solid" score. In the case of a single consistency recommendation, only one corresponding score was collected, and in the case of a recommendation for NPO (nil per os, “nothing by mouth”) no scores were recorded. Additional data was collecting regarding the absence or presence of alternate means of nutrition (e.g., feeding tube), alternate nutrition type (e.g., nasogastric vs. gastric tube), and the absence or presence of a recommendation for NPO. Data for "time to" events was also calculated for the time from stroke to clinical swallowing evaluation, time from stroke to MBSS, and days NPO before the MBSS.

Reliability

All MBSImP scores were determined by the clinicians who performed the study. All MUSC clinicians are MBSImP certified and have demonstrated 80% accuracy across all component scores as part of their training, which requires a re-certification process every 5 years (Martin-Harris, 2015; Martin-Harris et al., 2008).

Statistical Analysis

Data analysis was performed using SAS (v9.4, SAS Institute Inc., Cary, NC). Summary statistics were calculated for all variables collected (mean, median, the standard deviation for continuous variables and frequency, median, and mode for categorical variables). We hypothesized (H_0) that there was no difference in proportions between esophageal clearance abnormalities in this cohort compared to published estimates (Miles et al., 2015). This hypothesis was tested using a one-sample test of binomial proportions based upon limited pre-existing data, selecting from the only prospective applicable study (Miles et al., 2015) which demonstrated that 33% of patients whose MBSS included esophageal visualization had some type of esophageal abnormality. Fisher's exact tests were used to test for associations between categorical variables (e.g., MBSImP component scores) and measures of swallowing physiology and outcome measures. Our hypothesis (H_0) was that there were no statistically significant associations. As the data was non-parametric, Mann-Whitney U/Wilcoxon Rank Sum tests were used to test for differences in continuous variables (e.g., age). Logistic regression models with a binary outcome were created by dichotomizing the outcome variable MBSImP component 17 (esophageal clearance) scores into normal (C17 = 0 "complete clearance; esophageal coating") vs. abnormal (C17 ≥ 1 representing scores 1-3 for esophageal retention with or without retrograde flow, as well as a score [4] for minimal to absent clearance) groups. Logistic regression models were fit for each primary predictor of interests and were refined into the most parsimonious model, each of which examined associations with an outcome of abnormal esophageal clearance (C17 ≥1). Covariables which are known to influence stroke (e.g., age) and stroke-specific variables (location of stroke, National Institute of Health Stroke Severity [NIHSS] score, days from stroke to MBSS) were maintained in the model regardless of significance. Those variables which were not significant when tested were removed from the model included sex, race, and ethnicity. Relative risk was calculated for variables identified as statistically significant in our logistic regression, controlling for age, NIHSS score, and days from stroke to MBSS. Logistic regression models were checked for goodness of fit using the Hosmer and Lemeshow Test. Findings reflect the overall statistical significance and for all statistical analyses,

two-sided tests were performed with alpha set at 0.05 with P values of ≤ .05 indicating statistical significance.

RESULTS:

1. *Participants*

A total of 57 participants met the study inclusion and exclusion criteria. The average age of participants age was 70.12 years (range 38-97) with the cohort being 59.65% female. The greatest proportion of participants were black (48.28%) and none identified as Hispanic. See Table 1 for further detail.

Table 1. Demographic, Baseline, and Medical Characteristics of Post-Stroke Patients

Participant Characteristics	**Total** n = 57	**Normal Esophageal Clearance** n=24	**Abnormal Esophageal Clearance** n = 33	**P-value**
Age (mean, ±SD (95% CI)	70.12, ±12.57 (66.8, 73.46)	68.33, ±13.18 (62.77, 23.90)	71.42, ±12.14 (67.12, 75.73)	P = .6237
	n (%)	n (%)	n (%)	
Sex				P = .7883
Female	34 (59.65)	15 (62.5)	19 (57.58)	
Male	23 (40.35)	9 (37.5)	14 (42.42)	
Race				P = .3729
White	26 (45.61)	11 (45.83)	15 (45.45)	
Black	28 (49.12)	13 (54.17)	15 (45.45)	
Other	3 (5.26)	0 (0%)	3 (9.09)	
Ethnicity				P = 1.000
Non-Hispanic	56 (98.25)	24 (100)	32 (96.97)	
Not Specified	1 (1.75)	0 (0)	1 (3.03)	
Laterality				P = 1.000
Right	26 (46.43)	11 (47.83)	15 (45.45)	
Left	28 (50)	11 (47.83)	17 (51.52)	
Bilateral	2 (3.57)	1 (4.35)	1 (3.03)	
Stroke Location				P = .1183
Cortical	38 (66.67)	19 (79.17)	19 (57.58)	
Subcortical	10 (17.54)	1 (4.17)	9 (27.27)	
Cerebellar	6 (10.53)	3 (12.5)	3 (9.09)	
Brainstem	3 (5.26)	1 (4.17)	2 (6.06)	
tPA	11 (19.3)	4 (16.67)	7 (21.21)	P = .7449
Mechanical Thrombectomy	15 (27.27)	8 (34.78)	7 (21.21)	P = .3629

	mean, ±SD (95% CI)	mean, ±SD (95% CI	mean, ±SD (95% CI	
Initial NIH Stroke Score	12.34, ±6.95 (10.43, 14.25)	13.58, ±6.84 (10.70, 16.47)	11.31, ±6.98 (8.66, 13.97)	P = .1942
Days from CVA to MBSS	3.84, ±2.846 (3.08, 4.60)	4.58, ±3.01 (3.31, 5.85)	3.28, ±2.98 (2.33, 4.23)	P = .0701
Days from CSE to MBSS	2.89, ±2.69 (2.01, 3.78)	3.52, ±2.66 (2.37, 4.67)	1.93, ±2.52 (0.54, 3.33)	*P = .0484**
Days NPO Before MBSS	3.16, ±3.4 (2.09, 4.26)	3.65, ± 3.66 (2.07, 5.24)	2.53, ±2.98 (0.99, 4.06)	P = .3421

*P < .05 for Fisher's test of association (categorical variables), Wilcoxon Rank Sum/Mann-Whitney U test of association (continuous variables)

For participants with National Institutes of Health Stroke Scale (NIHSS) scores available, 17.31% had a minor stroke (NIHSS ≤4), 50% had a moderate stroke (NIHSS 5-15), 17.31% had a moderate-severe stroke (NIHSS 16-20), and 15.38% had a severe stroke (NIHSS ≥ 21). Stroke severity classifications were determined using NIHSS stroke severity rating (Brott et al., 1989; NIHSS Training, n.d.). Only a minority of participants were candidates for stroke interventions such as tPA or mechanical thrombectomy (19.3%, and 27.27%, respectively). The mean days from CVA to MBSS, from clinical swallowing evaluation (CSE) to MBSS, and days spent NPO prior to MBSS were all less than 4 days on average. See Table 1 for details.

2. MBSImP Component 17 (Esophageal Clearance) Scores

Abnormal esophageal clearance was identified in 57.89% (33/57) of this post-stroke cohort. Abnormal clearance was determined to be any MBSImP component 17 score greater than zero with abnormal esophageal clearance patterns ranging from esophageal retention with or without retrograde flow to minimal to no esophageal clearance. Specifically, 54.55% (18/33) had a score of 1 indicating "esophageal retention," 39.39% (13/33) had a score of 2 indicating "esophageal retention with retrograde flow below the PES [pharyngoesophageal segment]", and 6.06% (2/33) had a score of 3 indicating "esophageal retention with retrograde flow through the PES". No participants had a score of 4 for "minimal to no esophageal clearance."

Using a test of binomial proportions, we compared our findings against our pre-specified threshold of 33% from pre-existing data (Miles et al., 2015) which yielded a statistically significant result (P <.0001); thus we can conclude that in our sample, the proportion of

individuals with abnormal esophageal clearance patterns was different than 33%. The 95% exact confidence interval, around the proportion of post-stroke individuals with abnormal esophageal clearance patterns, would be expected to fall between 44.08% and 70.86%. In adjusted logistic regression models, after controlling for age, NIHSS score, and stroke location, only component 12 and component 14 were found to have a statistically significant association with abnormal component 17. Participants with abnormal pharyngeal stripping (component 12) (scores ≥ 1) had 2.06-fold greater risk of having abnormal esophageal clearance identified on their MBSS (adjusted RR=2.06, P = .0100) and participants with abnormal PES opening (component 14) (scores ≥1) had a 4.26 greater relative risk for abnormal esophageal clearance (adjusted RR=4.26, P = .0160).

3. MBSS Variables

3.1 MBSImP Component Scores

The most common abnormality in this cohort was in the initiation of the pharyngeal swallow, where 98.25% (56/57) of participants had scores greater than zero; indicating a swallow that was most frequently initiated past the posterior angle of the ramus of the mandible. This was followed by the abnormality in esophageal clearance where 57.89% of patients had scores greater than zero. There were several statistically significant associations between esophageal clearance and pharyngeal components (see Table 2).

Table 2. Associations Between MBSImP Component Scores and MBSImP Component 17

MBSImP Component Score Compared to Measures of MBSImP Component 17	**P-value**
MBSImP component 1 (lip closure) to component 17	P = .8642
MBSImP component 2 (tongue control during bolus hold) to component 17	P = .7845
MBSImP component 3 (bolus prep/mastication) to component 17	P = .2994
MBSImP component 4 (bolus transport/lingual motion) to component 17	P = .2539
MBSImP component 5 (oral residue) to component 17	P = .1180
MBSImP component 6 (initiation of pharyngeal swallow) to component 17	P = .7775
MBSImP component 7 (velar elevation) to component 17	P = .5786
MBSImP component 8 (laryngeal elevation) to component 17	P = .8142
MBSImP component 9 (anterior hyoid excursion) to component 17	*P = .0130**
MBSImP component 10 (epiglottic movement) to component 17	P = .4024
MBSImP component 11 (laryngeal vestibule closure) to component 17	P = .6333

MBSImP component 12 (pharyngeal stripping wave) to component 17	*P = .0126**
MBSImP component 13 (pharyngeal contraction) to component 17	P = .0726
MBSImP component 14 (pharyngoesophageal segment opening) to component 17	*P = .0008**
MBSImP component 15 (tongue base retraction) to component 17	P = .0504
MBSImP component 16 (pharyngeal residue) to component 17	P = .6210
MBSImP oral total scores to component 17	P = .0905
MBSImP pharyngeal total scores to component 17	P = .5273
Penetration-Aspiration Scale score to MBSImP component 17	P = .7786
Aspiration (presence/absence) to MBSImP component 17	P = .1476

*P <.05 for Fisher's test of association (categorical variables), Wilcoxon Rank Sum/Mann-Whitney U test of association (continuous variables)

Of the five oral component scores, there were no statistical associations when tested against component 17 (esophageal clearance) scores. The mean of MBSImP Oral Total (OT) scores was 11.57 (range 1-18) with a median of 13 and a mode of 14. The 95% confidence interval around the mean was calculated at 10.47 to 12.68. Of the 11 pharyngeal component scores, two demonstrated a statistical association when compared to component 17 (esophageal clearance) scores. Significant associations were found between MBSImP component 17 and component 12 (pharyngeal stripping wave) (P = .0143) and component 14 (pharyngoesophageal segment opening) (P = .0008). Component 12 (pharyngeal stripping wave) scores were abnormal (>1) in 59.65% (34/57) of participants with most (31/34) scores being a 1, or "present [but] diminished" pharyngeal constriction. Component 14 (pharyngoesophageal segment opening) scores were abnormal (>1) in 77.19% (44/57) of participants. Of those abnormal scores, 95.45% (42/44) were a score of 1, or "partial distention/partial duration; partial obstruction of flow." When compared to component 17 scores, component 14 (pharyngoesophageal segment opening) demonstrated the greatest statistical association of all components (P=.0008). Mean MBSImP Pharyngeal Total (PT) was 8.07 (range 0-15) with a median score of 8.5 and a mode of 9. The 95% confidence interval around the mean was calculated at 7.0 to 9.14. See Table 4 for MBSImP component score summaries.

3.2 Swallowing Impairment Severity

In our post-stroke cohort, 94.74% (54/57) had MBSImP oral total (OT) and pharyngeal total (PT) scores available. Beall et al. (2020) identified ranges of MBSImP OT and PT scores that account

for differences in swallowing impairment and provide a severity classification in their latent class analysis. Using this classification, we found that 37.04% (20/54) of this post-stroke cohort had a mild/functional oral impairment and 40.74% had a moderate oral impairment. Though not specified in their class analysis, using their framework 22.22% of participants could be classified as having a "mild to moderate" oral impairment. In our post-stroke cohort, 88.89% of participants had a mild/functional pharyngeal impairment. Using the Beall et al. (2020) severity framework, though again not specified in their classification, 11.11% of participants could be classified as having a "mild to moderate" pharyngeal impairment. Esophageal total scores are based on the single esophageal score (component 17) for which 57.89% of this post-stroke cohort demonstrated abnormal scores.

Component 17 scores in the mild-functional PT group ranged from 0-3. Normal clearance was seen in 41.67% (20/48) of participants with mild-functional PT scores. A score of 1 was seen in 33.33% (16/48) participants, indicating "esophageal retention." A score of 2 was identified in 20.83% (10/48) of participants in this group indication "esophageal retention with retrograde flow below the pharyngoesophageal segment (PES)." A score of 3, or "esophageal retention with retrograde flow through PES" was identified in 4.17% (2/48). Component 17 scores ranged from 0-2 for those participants in the mild-moderate PT group. A score of 0 or "complete clearance; esophageal coating" was seen in 33.33% (2/6) participants. A score of 1 or "esophageal retention" was seen in 16.67% (1/6) of this group. A score of 2 or "retention with retrograde flow below the PES" was seen in 50% (3/6) of those participants with mild-moderate PT scores.

3.3 Measures of Bolus Airway Invasion

Penetration-Aspiration Scale (PAS) scores for this post-stroke cohort ranged from 1-8 (median score of 4, mode of 8) with 29.09% of the participants having silent aspiration (PAS score of 8) on their initial post-stroke MBSS. PAS scores within the reported ranges of normal (PAS 1-3) (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999) were seen in 49.09% of participants. Abnormal PAS (scores ≥ 4) were identified in 50.91% of participants. Overall,

43.64% of the participants were identified as aspirating on their initial post-stroke MBSS. And of those 24, 50% were identified as having abnormal esophageal clearance. However, no statistically significant association was identified between PAS and/or aspiration and MBSImP component 17 (esophageal clearance) scores. See Table 2.

4. MBSS Outcome Measures

Outcome measures from the MBSS were collected including the FOIS (Crary et al., 2005), the liquid and solid (as applicable) IDDSI (Steele et al., 2018) consistency recommendations, as well as the presence or absence of alternate means of nutrition. See Table 3 for details.

Table 3. Associations Between MBSImP Component 17 scores and MBSS Outcome Measures

MBSS Outcome Measures Score Compared to Measures of MBSImP Component 17	Median and Mode	Percent Abnormal	Association with MBSImP Component 17 scores (P-value)
FOIS Score	5, 5	87.72%	*P = .2747*
IDDSI Liquid Level	2, 0	71.93%	P = .2349
IDDSI Solid Level	5, 4	85.96%	*P = .0118**
Alternate Means Nutrition	-	-	*P = .0390**
Alt. Means Type	-	-	P = .2036

* P < .05 indicating statistical significance from Fisher's exact test of association

4.1 FOIS Scores

FOIS scores (Crary et al., 2005) were available for 73.68% of participants whose MBSS recommendations included P.O. intake. Scores represented the range of FOIS, except for a score of 3 (tube supplements with consistent oral intake) which was not seen in this sample. Most participants (59.52%) had a FOIS score of 5, or "total oral intake of multiple consistencies requiring special preparation." FOIS scores at the lowest (most restricted) end of the scale with a score of 1, or "no oral intake", were seen in 16.67% of participants. Scores at the highest end of the scale (7), or "total oral intake without restrictions", were identified in 16.67% of this post-stroke cohort. Scores of 2, 4, and 6 were each seen in a single participant, with each of these scores representing 2.38% of the sample. A statistically significant association was not seen between FOIS scores and component 17 scores. See Table 3.

4.2 IDDSI Scores

The outcome of oral intake was classified using IDDSI scores (Steele et al., 2018), one for solid consistencies and one for liquid viscosities. IDDSI scores were only available for 34 participants, or 60.34% of this sample. The most common IDDSI liquid score was a 0, or “thin” liquids in 47.06% (16/34) of participants. A score of 2 or “mildly”/nectar-thick liquid was seen in 38.24% (13/34) of participants and a score of 3 or “moderately”/honey-thick liquid was seen in 14.71% (5/34) of participants. The most common IDDSI solid score was a 4, or "pureed" solids in 44.12% (15/34) participants. The second most common was a score of 7 or "regular"/unaltered solids in 23.53% (8/34) participants. A score of 6 or "soft and bite-sized" solids was represented in 17.65% (6/34) of participants and, lastly, a score of 5 or "minced and moist" solids was seen in 14.71% (5/34) of participants. Only the IDDSI solid scores demonstrated a statistically significant association with MBSImP component 17 scores (P = .0118). See Table 3. When controlling for age, stroke location, time from stroke to MBSS, and NIHS score, there was no statistically significant association between abnormal component 17 and IDDSI solid scores.

4.3 Alternate Means of Nutrition

Data regarding the presence of alternate means of nutrition (e.g., small-bore feeding tube, gastric tube) was only available for 66.67% (38/57) of this post-stroke cohort. Of those 38 participants, only 26/38 EHR data contained information regarding the type of alternate access to nutrition. The most common alternate means of nutrition was a small-bore feeding tube (e.g., Dobhoff or Corpak) in 73.08% (19/26) and longer-term access (e.g., gastric tube) was seen in 11.54% of this post-stroke cohort which was not statistically significant. For those participants with alternate means of nutrition at the time of their MBSS, 18.42% (7/38) had abnormal component 17 scores, compared to 26.32% (10/38) without alternate means of nutrition with abnormal component 17 scores which was statistically significant (P = .0390); though the type of alternate means of nutrition was not. See Table 3. No statistically significant

association between abnormal component 17 and alternate means of nutrition when controlling for age, stroke location, time from stroke to MBSS, and NIHS score.

5. Subgroup Analysis: Abnormal Component 17 Scores

A subgroup analysis was performed on the data from those 33 participants who had abnormal component 17 scores (any score ≥ 1). For comparison, scores were dichotomized into "normal" vs. "abnormal" range. For MBSImP scores, a score greater than zero was the cutoff point except for components 1, 5, 15, and 16 for which a score of 1 is collapsed to a zero for aggregate "total" scores (Martin-Harris, 2015; Martin-Harris et al., 2017). For the PAS, scores of 1-3 were considered normal (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999). FOIS scores were categorized into 1, use of some degree of alternate means of nutrition (scores of 1-3), 2, significantly restricted PO intake (scores of 4-5), and 3, minimal to no PO restrictions (scores of 6-7). IDDSI scores for liquids were separated at a cutoff point of 0 for no restrictions and 1-3 for any degree of restriction/altered viscosity. IDDSI solids were separated at a cutoff point of 7 for no restrictions to 4-6 for any degree of restriction/altered texture. For comparison of variables, see Table 4.

The group with abnormal esophageal clearance (component 17) had a mean age of 71.42 years (range 49-97, standard deviation 12.14). Sex was distributed as 57.58% female and 42.42% male. Race was distributed as 45.45% (15/33) white, 45.45% (15/33) black, and 9.09% (3/33) identified as "other." Most participants were non-Hispanic (96.97%). Overall, MBSImP scores in this group were lower (indicating less impairment) across all components except for component 7 (velar elevation), component 13 (pharyngeal contraction), component 14 (pharyngoesophageal segment opening), and component 15 (base of tongue retraction). These four components demonstrated higher (worse) scores in this subgroup. A statistically significant association was seen in component 14 (PES opening) (P = .0008). Component 12 (pharyngeal stripping wave) also demonstrated statistical significance (P = .0143); however, most scores were zero (normal). A greater proportion of PAS scores within a normal range were seen in the abnormal component 17 group versus normal component 17 (57.58% and 41.67%,

respectively). Aspiration occurred less frequently in the abnormal component 17 group (36.36%) compared to the normal component 17 group (50%). See Table 4 for details.

Table 4. Comparison of Swallowing Impairment and Outcome Measures in Normal vs. Abnormal MBSImP Component 17 (Esophageal Clearance) Scores

Swallowing Impairment and Outcome Measures	**Full Cohort n = 57 n (%)**	**Normal Esophageal Clearance (MBSImP C17 = 0) n = 24 n (%)**	**Abnormal Esophageal Clearance (MBSImP C17 ≥1) n = 33 n (%)**	**P-value**
MBSImP component 1 (lip closure)				P= .4067
C1 ≤ 1	21 (36.84)	7 (29.17)	14 (42.42)	
C1 ≥ 2	36 (63.16)	17 (70.83)	19 (57.58)	
MBSImP component 2 (tongue control during bolus hold)				P = .2892
C2 = 0	9 (16.36)	2 (9.09)	7 (21.21)	
C2 ≥ 1	46 (83.84)	20 (90.91)	26 (78.79)	
MBSImP component 3 (bolus prep/mastication)				P = .2713
C3 = 0	9 (16.36)	2 (8.33)	7 (22.58)	
C3 ≥ 1	46 (83.64)	22 (91.67)	24 (77.42)	
MBSImP component 4 (bolus transport/lingual motion)				P = .2001
C4 = 0	13 (22.81)	3 (12.5)	10 (30.3)	
C4 ≥ 1	44 (77.19)	21 (87.5)	23 (69.7)	
MBSImP component 5 (oral residue) to component 17				P = .4462
C5 ≤ 1	8 (14.04)	2 (8.33)	6 (18.18)	
C5 ≥ 2	49 (85.96)	22 (91.67)	27 (81.82)	
MBSImP component 6 (initiation of pharyngeal swallow)				P = 1.000
C6 = 0	1 (1.75)	0 (0)	1 (3.03)	

C6 ≥ 1	56 (98.25)	24 (100)	32 (96.97)	
MBSImP component 7 (velar elevation)				P = .5241
C7 = 0	44 (77.19)	20 (83.33)	24 (72.73)	
C7 ≥ 1	13 (22.81)	4 (16.67)	9 (27.27)	
MBSImP component 8 (laryngeal elevation)				P = .4939
C8 = 0	10 (17.54)	3 (12.5)	7 (21.21)	
C8 ≥ 1	47 (82.46)	21 (87.5)	26 (78.79)	
MBSImP component 9 (anterior hyoid excursion)				P = .1606
C9 = 0	18 (31.58)	5 (20.83)	13 (39.39)	
C9 ≥ 1	39 (68.42)	19 (79.17)	20 (60.61)	
MBSImP component 10 (epiglottic movement)				P = .2889
C10 = 0	29 (50.88)	10 (41.67)	19 (57.58)	
C10 ≥ 1	28 (49.12)	14 (58.3)	14 (42.42)	
MBSImP component 11 (laryngeal vestibule closure)				P = .2614
C11 = 0	20 (35.09)	6 (25)	14 (42.42)	
C11 ≥ 1	37 (64.91)	18 (75)	19 (57.58)	
MBSImP component 12 (pharyngeal stripping wave)				*P = .0143**
C12 = 0	23 (40.35)	5 (20.83)	18 (54.55)	
C12 ≥ 1	34 (59.65)	19 (79.17)	15 (45.45)	
MBSImP component 13 (pharyngeal contraction)				P = .3587
C13 = 0	24 (51.06)	10 (62.5)	14 (45.16)	
C13 ≥ 1	23 (48.94)	6 (37.5)	17 (54.84)	
MBSImP component 14 (pharyngoesophageal segment opening)				*P =.0008**
C14 = 0	13 (22.81)	11 (45.83)	2 (6.06)	
C14 ≥ 1	44 (77.19)	13 (54.17)	31 (93.94)	
MBSImP component 15 (tongue base retraction)				P = .2762

C15 ≤ 1	23 (40.35)	12 (50)	11 (33.33)	
C15 ≥ 1	34 (59.65)	12 (50)	22 (66.67)	
MBSImP component 16 (pharyngeal residue)				P = 1.000
C16 ≤ 1	18 (31.58)	8 (33.33)	10 (30.3)	
C16 ≥ 1	39 (68.42)	16 (66.67)	23 (69.7)	
Penetration-Aspiration Scale (PAS) score				P = .2889
PAS ≤ 3	29 (50.88)	10 (41.67)	19 (57.58)	
PAS ≥ 4	28 (49.12)	14 (58.33)	14 (42.42)	
Presence of aspiration	24 (42.86)	12 (50)	12 (36.36)	P = .2810
Functional Oral Intake Scale (FOIS) score				P = .2561
FOIS 6-7	8 (19.05)	3 (13.04)	5 (26.32)	
FOIS 5-3	26 (61.9)	14 (60.87)	12 (63.16)	
FOIS 1-2	8 (19.05)	7 (26.09)	16 (48.48)	
International Dysphagia Diet (IDDSI) liquid score				P = .7319
IDDSI liquids = 0	16 (47.06)	9 (52.94)	7 (41.18)	
IDDSI liquids 2-3	18 (52.94)	8 (47.06)	10 (58.82)	
International Dysphagia Diet (IDDSI) solid score				P = .4462
IDDSI solids = 7	8 (14.04)	2 (8.33)	6 (18.18)	
IDDSI solids 4-6	49 (85.96)	22 (91.67)	27 (81.82)	
Presence of alternate means of nutrition	21 (56.76)	14 (66.67)	7 (43.75)	P = .1964
Initial NIHSS Score				P = .2669
NIHSS ≤ 4 (mild stroke)	9 (17.31)	4 (16.67)	5 (17.86)	
NIHSS 5-15 (moderate stroke)	26 (50)	9 (37.5)	17 (60.71)	
NIHSS 16-20 (moderate-severe)	9 (17.31)	6 (25)	3 (10.71)	
NIHSS ≥ 21 (severe stroke)	8 (15.38)	5 (20.83)	3 (10.71)	

*P <.05 for Fisher's test of association (categorical variables), Wilcoxon Rank Sum/Mann-Whitney U test of association (continuous variables)

We used the Beall et al. (2020) classification of oral (OT) and pharyngeal total (PT) severity levels for this subgroup. We identified that 50% had a functional/mild oral impairment, 15.6% had a mild-moderate oral impairment, and 34.4% had a moderate oral impairment; 87.5% had

a functional/mild pharyngeal impairment, 12.5% had a mild-moderate pharyngeal impairment. In this subgroup of participants with abnormal component 17 scores, all participants had an impairment in esophageal clearance with component 17 scores ranging from 1-3. Specifically, 54.55% had a score of 1, 39.39% had a score of 2, and 6.06% had a score of 3.

For measures of swallowing outcomes (FOIS, IDDSI, presence of alternate means nutrition), the abnormal component 17 group had more "normal" outcomes apart from IDDSI liquid recommendations. Participants in the abnormal component 17 group were less frequently recommended for thin liquids (41.18%) than in the normal component 17 group (52.94%). Though participants in the abnormal component 17 group were more likely to be recommended for regular solids (18.18%) compared to participants in the normal component 17 score group (8.33%). The group with abnormal component 17 scores demonstrated a lower frequency of alternate means of nutrition (43.75% compared to 66.67%). None of these associations demonstrated statistical significance. See Table 4.

There no statistically significant difference in NIHSS scores between normal and abnormal component 17 groups. The overall scores were less severe in the abnormal component 17 group compared to the normal component 17 group. For those participants with abnormal component 17 scores, 17.86% had a minor stroke (NIHSS ≤ 4), 60.71% had a moderate stroke (NIHSS 5-15), 10.7% had a moderate-severe stroke (NIHSS 16-20), and 10.7% had a severe stroke (NIHSS ≥ 21). See Table 4.

6. Post-Hoc Power Analysis

A post-hoc power analysis was completed on the data. The threshold was set at a conservative 33% based upon existing data (Miles et al., 2015). At this level, we met a power threshold of 95.9% for our test of binomial proportions answering the question, "Does our sample proportion of post-stroke patients with an abnormal component 17 score differ from what was observed in a previous study (33%)". However, when compared to an estimated higher proportion, based on a more heterogeneous sample (Reedy et al., 2021) of 48.67%, we failed to

meet adequate power, only yielding 25.3% power to find a difference between our sample (57.89%) and that of a previous study (48.67% from Reedy et al.). Thus, we would need a significantly larger sample to detect significance at this threshold.

DISCUSSION:

In post-stroke patients whose MBSS included esophageal visualization to determine esophageal bolus clearance (MBSImP component 17), 57.89% had abnormal scores. Though abnormal esophageal clearance was identified in most of this post-stroke cohort the true proportion of patients with abnormal clearance post-stroke is likely much higher. Our findings reflect only those patients whose swallowing was adequate to participate in the entire MBSImP protocol (including altering position for the A-P portion of the assessment), who were stable enough to leave the floor for an MBSS, and who were deemed safe enough for P.O. trials by their treating SLP. These patients, therefore, likely represent those with lesser oropharyngeal impairment.

Most post-stroke patients were found to have mild to functional impairment in both oral and pharyngeal MBSImP total scores in the abnormal component 17 group. Interestingly, patients in the abnormal component 17 group were less likely to receive clinical recommendations for thin liquids than for those with normal component 17 scores despite less severe oral and pharyngeal impairment. While the MBSImP and PAS are standardized, the outcome recommendations (FOIS, IDDSI, alternate means nutrition) are subjective and clinician dependent. Though statistically significant associations were seen in comparisons between component 17 and the swallowing outcome measures of IDDSI solids and alternate means nutrition there was no influence of component 17 on these individual outcomes. When controlling for age, NIHS, stroke location and time from stroke to MBSS there was no influence of component 17. In this cohort, component 17 does not appear to be driving recommendations for PO intake or influence judgements regarding alternate means of nutrition. It is important to highlight that swallowing is an incredibly complex act, and no one component should drive clinical recommendations. The extent to which component 17 influenced clinical judgements for P.O. intake is not known given the retrospective nature of our study. Future research into the

influence of component 17 or other esophageal visualization protocols on P.O. recommendations is needed.

Our study demonstrates a relationship between pressure driving and pressure modulating components and esophageal clearance particularly those vagally-dominated aspects in the pharynx. Most of the MBSImP physiologic components which demonstrated significant associations (components 9, 12, and 14) and those trending towards significance (components 13 and 15) with component 17 scores are innervated by the vagus nerve (CN X). The pharyngeal constrictors, represented by measures of pharyngeal stripping wave (component 12]) and pharyngeal contraction (component 13), receive motor and sensory input from the pharyngeal branch of the vagus nerve. Tongue base movement is modulated primarily by the hypoglossal nerve (CN XII) though the base of tongue is elevated by the palatoglossus which is innervated by the vagus (CNX). The trigeminal (CN V) and glossopharyngeal (CN IX) nerves are responsible for anterior hyoid excursion (component 9), which contributes to traction on the UES during opening; and UES function (pharyngoesophageal segment opening [component 14]) is regulated by the vagus nerve. All these components represent physiologic pharyngeal pressure driving (components 12,13, and 15) or pressure modulating forces (components 9 and 14). In fact, pharyngeal stripping (component 12) was normal (=0) in most participants with abnormal esophageal clearance which may demonstrate an “upstream” effect whereby the pharyngeal pressures increase in the context of esophageal abnormality. Furthermore, most participants with abnormal esophageal clearance had abnormal PES (component 14) function which may also demonstrate some type of compensation or reaction to altered esophageal physiology.

Unsurprisingly, the greatest association between MBSImP components was identified between component 14 (pharyngoesophageal segment [PES] opening) and component 17 (P= .0008). The pharyngoesophageal segment refers to the anatomical region where the inferior pharyngeal constrictors insert into the superior cricopharyngeal musculature posteriorly. The anterior PES consists of the cricoid cartilage and arytenoid and interarytenoid musculature (Sivarao & Goyal, 2000). Though primary UES structure comes from the crescent-shaped

cricopharyngeal musculature, the PES represents a high-pressure zone of 3-4 cm (Mittal, 2011). UES function is relative to its vagally-mediated tonic contraction at rest, with opening relative to pharyngeal intrabolus pressures and anterior hyoid excursion providing traction to the anterior UES. And alterations to PES maximal distention and duration of opening have been demonstrated in volitional pharyngeal swallowing maneuvers (Doeltgen et al., 2011; Hoffman et al., 2012; McCullough, 2012; Meyer et al., 2016; Molfenter et al., 2018). Abnormal PES function may provide an indication of esophageal dysfunction in those patients who cannot undergo A-P visualization or whose oropharyngeal function precludes further testing. This finding is analogous to the Jones et al. (1985) historical opinion that cricopharyngeal prominence should prompt a more dynamic pharyngoesophageal investigation.

The most common swallowing abnormality in this post-stroke cohort was in the initiation of the pharyngeal swallow, where 96.25% of participants had scores greater than zero. The pharyngeal swallow "trigger," initially thought to occur distinctly at or just beyond the faucial arches (Logemann, 1998), is now understood to have a much less stringent onset point and it has been demonstrated that the bolus head may be well into the pharynx at the onset of the pharyngeal swallow (Daggett et al., 2006; Ertkin & Aydogdu, 2003; Logemann et al., 2013; Martin-Harris et al, 2007; Matsuo & Palmer, 2008) and that this is a variant of normal swallow physiology. However, what is normal in healthy adults may be sufficient to result in impairment in the context of perturbation in the system, such as in stroke. However, if we account for these variations as normal swallowing physiology, then the most common abnormal finding in this post-stroke cohort is abnormal esophageal clearance. There is a dearth of prior data to which we can directly compare these esophageal findings. Only Miles et al. (2019) included those patients' post-stroke, however, was a heterogeneous sample and focused on measures of esophageal bolus transit time. They found that post-stroke patients, on average, had a 6 second longer transit time than healthy controls. This is likely indicative of both sensory and motor impairment in this population and, perhaps, a marker for disordered motility. However, the gold standard for motility testing is High-Resolution Manometry (HRM) with diagnostic criteria set forth by the Chicago Classification, now on its 4th version (CC v4.0) (Yadlapati et al., 2021).

Gullung et al. (2012) investigated the predictive value of MBSImP components to esophageal HRM with multichannel intraluminal impedance (MII) findings (using CC v 3.0, Kahrilas et al., 2015). They identified that 79% of participants with abnormal component 17 scores had abnormal HRM-MII. Overall, the sensitivity and specificity of component 17 and HRM-MII were calculated at 80% and 48%, respectively. For component 17 compared to MII alone, sensitivity was demonstrated at 79% with a specificity of 45%. Comparing component 17 to HRM alone demonstrated a sensitivity of 77% and a specificity of 40%. Gullung et al. (2012) also found a significant relationship between component 6 (initiation of pharyngeal swallow), component 11 (laryngeal vestibular closure) which were not identified in this study. This may be explained by the larger (n= 164), more heterogeneous sample in the Gullung et al. (2012) study. Our findings are, however, directly applicable to the post-stroke population with dysphagia.

It is important to acknowledge the contributions of individual physiologic components and not rely on gestalt findings, or reduce all swallowing impairments only to the absence or presence of aspiration. If we had only looked at MBSImP OT and PT scrores, we would have missed the associations between individual MBSImP components and measures of swallowing impairment, some of which were determined to have statistical significance. For example, associations between MBSImP components 9, 12 and 14 and in swallowing outcome measures such as IDDSI solids and the presence of alternate means of nutrition. Additionally, the absence of aspiration does not indicate the absence of aspiration risk. Multiple clinical and physiologic findings must be factored when determining an individual patient's risk.

Because of the contraindications for manometry (e.g., aspiration, cognitive impairment) may be prohibitive to its use in the post-stroke acute phase of recovery, we know little about esophageal function in this population. Pharyngeal maneuvers, however, have been demonstrated to impact esophageal body function. The effortful swallow maneuver has been found to increase esophageal peristaltic vigor (Lever et al., 2007; O'Rourke et al., 2014) demonstrating that oropharyngeal maneuvers generate increased intrabolus pressure in the pharynx have demonstrated an increase in esophageal peristalsis. Our data demonstrate the

inverse, where impaired pressure-driving forces in the pharynx are strongly associated with impairments in esophageal bolus clearance. However, most participants with MBSImP pharyngeal total scores in any PT impairment group (e.g., functional-mild, moderate, severe) had abnormal esophageal clearance. In fact, only a slightly higher proportion of patients with mild-moderate impairment had abnormal clearance compared to the mild-functional group (66.67% and 58.33% respectively).

In limiting our post-stroke swallowing assessments and, therefore, research we have failed to recognize the potential for co-occurring esophageal impairment in this population. Oropharyngeal impairments are not isolated to oropharyngeal manifestations as measures of physiologic pharyngeal pressure-driving (component 12) or pressure-modulating (component 14) components were demonstrated to be impaired in this study. Abnormal pharyngeal constriction (component 12) demonstrated a 2.06-fold increased risk of abnormal esophageal clearance. Abnormal PES function (component 14) demonstrated a 4.26-fold increased risk for abnormal esophageal clearance, both of which were statistically significant. Additionally, we know very little about the function of the striated musculature of the proximal (upper third) esophagus. There are no manometric normal values and, therefore, no diagnostic criteria for this region. It is unclear if findings related to cortical overdrive of the UES (Kahrilas et al., 1991; Nativ-Zeltzer et al., 2019) also apply to the proximal esophageal body beyond what we know about the effortful swallow (Lever et al., 2007; O'Rourke et al., 2014). And remains to be seen if pharyngeal pressures impact proximal esophageal pressures as these both consist of striated musculature, whereas the distal esophagus consists of smooth muscle.

Constraints to dedicated esophageal testing in this population relate to the acute concerns for aspiration. Esophageal clearance, as determined by the MBSImP, is a single score given to rate the clearance pattern of two viscous (5 ml nectar and 5 ml pudding Varibar®) boluses. Different textures, including increased viscosity, have demonstrated alterations on esophageal bolus transit times (Miles et al., 2016; Jou et al., 2006). However, the benefit of these specific consistencies used for esophageal visualization during the MBSImP protocol is that patients

who aspirate thin liquids can still have the length of the swallowing continuum visualized. All swallowing assessments involve swallowing some type of bolus and the risks vs. benefits of testing must always be considered with the paramount concern for patient safety. In the post-stroke population, there are also cognitive, language, and/or mobility limitations that may contraindicate certain testing (particularly devoted esophageal testing). While the determination of esophageal clearance on the MBSS is non-diagnostic, it does allow for visualization of the esophagus.

In summary, our findings indicate that in the stroke population, where the swallowing concern invariably defaults to oropharyngeal, we cannot ignore the potential for esophageal impairment. More specifically, we cannot disregard the potential for interactions between aspects of swallowing as swallowing is a highly coordinated series of pressures occurring along a continuum (oral cavity, pharynx, esophagus) and is not complete until the bolus enters the gastric cavity.

Limitations

This study has several limitations. First, the study has a small sample size and was performed retrospectively at a single site. The study was powered to detect a difference in proportions compared to a constant and not for associations between measures of swallowing impairment and outcome measures. Second, those patients who undergo the complete MBSImP protocol are likely less impaired than patient who do not. Patients who received scores on component 17 are appropriate for PO intake or trials, stable enough to leave the floor and participate in a MBSS and have sufficient swallow function that the clinicians are comfortable completing the full MBSImP protocol. Third, determination of esophageal clearance is not diagnostic; however, this work lays the foundation for future studies to explore the role of esophageal visualization during the MBSS as well as for other dedicated esophageal assessments for those patients who aspirate.

Given that a patient can have 20% failed swallows on HRM and still fall into the category of normal motility per CC v4.0 (Yadlapati et al., 2021), the two swallows administered during esophageal visualization may have limited sensitivity to identify a true abnormality. However, it is important to emphasize that the esophageal visualization of the MBSImP is non-diagnostic. As with the MBSS, it is a representation of swallowing physiology at a single point in time. The distinct 17 physiologic components scored across the administration of 12 bolus trials of various viscosities and textures provide a representative sample of swallowing. Abnormal component 17 scores, along with clinical correlation, can be an important consideration in recommending further diagnostic esophageal testing and/or referral to other specialties (e.g., gastroenterology, laryngology, etc.).

CONCLUSION:

Swallowing occurs along a continuum (oral cavity, pharynx, esophagus) and is not complete until the bolus enters the gastric cavity. Arbitrary divisions between the oropharynx and esophagus have limited our ability to fully diagnose and treat dysphagia in vulnerable populations, such as post-stroke. A significant proportion of post-stroke patients demonstrate abnormal esophageal clearance. The results of this study indicate that if we do not consider the esophageal contribution to the overall presentation of dysphagia, we fail to fully diagnose and treat our patients with post-stroke swallowing impairment.

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References:

1. Adeoye, O., Nyström, K. V., Yavagal, D. R., Luciano, J., Nogueira, R. G., Zorowitz, R. D., Khalessi, A. A., Bushnell, C., Barsan, W. G., Panagos, P., Alberts, M. J., Tiner, A. C., Schwamm, L. H., & Jauch, E. C. (2019). Recommendations for the Establishment of Stroke Systems of Care: A 2019 Update. Stroke, 50(7), e187–e210. https://doi.org/10.1161/STR.0000000000000173

2. Altman KW, Yu GP, Schaefer SD. Consequence of dysphagia in the hospitalized patient: Impact on prognosis and hospital resources. *Arch Otolaryngol Head Neck Surg*. 2010; Aug; 136(8):784-9. doi: 10.1001/archoto.2010.129.

3. Beall, J., Hill, E. G., Armeson, K., Garand, K., Davidson, K. H., & Martin-Harris, B. (2020). Classification of Physiologic Swallowing Impairment Severity: A Latent Class Analysis of Modified Barium Swallow Impairment Profile Scores. *American journal of speech-language pathology*, *29*(2S), 1001–1011. https://doi.org/10.1044/2020_AJSLP-19-00080

4. Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., de Ferranti, S. D., Floyd, J., Fornage, M., Gillespie, C., Isasi, C. R., Jiménez, M. C., Jordan, L. C., Judd, S. E., Lackland, D., Lichtman, J. H., Lisabeth, L., Liu, S., Longenecker, C. T., Mackey, R. H., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee (2017). Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation*, *135*(10), e146–e603. https://doi.org/10.1161/CIR.0000000000000485

5. Bonilha, H. S., Blair, J., Carnes, B., Huda, W., Humphries, K., McGrattan, K., Michel, Y., & Martin-Harris, B. (2013). Preliminary investigation of the effect of pulse rate on judgments of swallowing impairment and treatment recommendations. Dysphagia, 28(4), 528–538. https://doi.org/10.1007/s00455-013-9463-z

6. Bonilha, HS., Humphries, K., Hill, EG., McGrattan, K., Carnes, B., Huda, W., Martin-Harris, B. (2013). Radiation Exposure time during MBSS: influence of swallowing impairment severity, medical diagnosis, clinician experience, and standardized protocol use. Dysphagia, 28(1), 77-85. doi. 10.1007/s00455-012-9415-z.

7. Bonilha, H. S., Simpson, A. N., Ellis, C., Mauldin, P., Martin-Harris, B., & Simpson, K. (2014). The one-year attributable cost of post-stroke dysphagia. Dysphagia, 29(5), 545–552. https://doi.org/10.1007/s00455-014-9543-8

8. Brodsky, M. B., McFarland, D. H., Dozier, T. S., Blair, J., Ayers, C., Michel, Y., . . . Martin-Harris, B. (2010). Respiratory– swallow phase patterns and their relationship to swallowing impairment in patients treated for oropharyngeal cancer. *Journal of the*

Sciences and Specialties of the Head and Neck, 32(4), 481–489. https://doi.org/10.1002/hed.21209

9. Brott, T., Adams, H. P., Jr, Olinger, C. P., Marler, J. R., Barsan, W. G., Biller, J., Spilker, J., Holleran, R., Eberle, R., & Hertzberg, V. (1989). Measurements of acute cerebral infarction: a clinical examination scale. *Stroke*, *20*(7), 864–870. https://doi.org/10.1161/01.str.20.7.864

10. Catalá-Ripoll, J. V., Monsalve-Naharro, J. Á., & Hernández-Fernández, F. (2020). Incidence and predictive factors of diaphragmatic dysfunction in acute stroke. BMC neurology, 20(1), 79. https://doi.org/10.1186/s12883-020-01664-w

11. Cohen, D. L., Roffe, C., Beavan, J., Blackett, B., Fairfield, C. A., Hamdy, S., Havard, D., McFarlane, M., McLauglin, C., Randall, M., Robson, K., Scutt, P., Smith, C., Smithard, D., Sprigg, N., Warusevitane, A., Watkins, C., Woodhouse, L., & Bath, P. M. (2016). Post-stroke dysphagia: A review and design considerations for future trials. *International journal of stroke : official journal of the International Stroke Society*, *11*(4), 399–411. https://doi.org/10.1177/1747493016639057

12. Cola, M.G., Daniels, S.K., Corey, D.M., Lemen, L.C., Romero, M., Foundas, A.L. (2010). Relevance of subcortical stroke in dysphagia. *Stroke,* 41(3): 482-486. doi: 10.1161/STROKEAHA.109.566133

13. Crary, M., Carnaby Mann, G.D., Groher, M.E. (2005). Psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil, 86 (8): 1516-20. doi: 10.1016/j.apmr.2004.11.049

14. Daniels, S. K., Brailey, K., Priestly, D. H., Herrington, L. R., Weisberg, L. A., & Foundas, A. L. (1998). Aspiration in patients with acute stroke. Archives of physical medicine and rehabilitation, 79(1), 14–19. https://doi.org/10.1016/s0003-9993(98)90200-3

15. Daggett, A., Logemann, J., Rademaker, A., & Pauloski, B. (2006). Laryngeal penetration during deglutition in normal subjects of various ages. *Dysphagia*, *21*(4), 270–274. https://doi.org/10.1007/s00455-006-9051-6

16. Daniels, S. K., & Foundas, A. L. (1997). The role of the insular cortex in dysphagia. *Dysphagia, 12*(3), 146-156. doi:10.1007/PL00009529

17. Daniels, S., Pathak, S., Mukhi, S., Stach, C., Morgan, R., & Anderson, J. (2017). The relationship between lesion localization and dysphagia in acute stroke. *Dysphagia, 32*(6), 777-784. doi:10.1007/s00455-017-9824-0

18. Doeltgen, S. H., Ong, E., Scholten, I., Cock, C., & Omari, T. (2017). Biomechanical Quantification of Mendelsohn Maneuver and Effortful Swallowing on

Pharyngoesophageal Function. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *157*(5), 816–823. https://doi.org/10.1177/0194599817708173

19. Ertekin C., Aydogdu I. (2003). Neurophysiology of swallowing. *Clinical Neurophysiology*, 114, 2226-2244. doi: https://doi.org/10.1016/S1388-2457(03)00237-2

20. Flowers, H. L., AlHarbi, M. A., Mikulis, D., Silver, F. L., Rochon, E., Streiner, D., & Martino, R. (2017). MRI-based neuroanatomical predictors of dysphagia, dysarthria, and aphasia in patients with first acute ischemic stroke. *Cerebrovascular Diseases Extra, 7*(1), 21-34. doi:10.1159/000457810

21. Galovic M, Leisi N, Müller M, Weber J, Abela E, Kägi G, Weder B. (2013).Lesion location predicts transient and extended risk of aspiration after supratentorial ischemic stroke. *Stroke*,44(10):2760-7. doi: 10.1161/STROKEAHA.113.001690. Epub 2013 Jul 25. PMID: 23887840.

22. Garand, K., Hill, E. G., Amella, E., Armeson, K., Brown, A., & Martin-Harris, B. (2019). Bolus Airway Invasion Observed During Videofluoroscopy in Healthy, Non-dysphagic Community-Dwelling Adults. *The Annals of otology, rhinology, and laryngology*, *128*(5), 426–432. https://doi.org/10.1177/0003489419826141

23. Gonzalez-Fernandez, M., Ottenstein, L., Atanelov, L., Christian, A.B. (2013). Dysphagia after Stroke: an Overview. *Curr Phys Med Rehabil Rep*, 1(3) 187-196.

24. Gullung, J. L., Hill, E. G., Castell, D. O., & Martin-Harris, B. (2012). Oropharyngeal and esophageal swallowing impairments: Their association and the predictive value of the modified barium swallow impairment profile and combined multichannel intraluminal impedance-esophageal manometry. The Annals of Otology, Rhinology, and Laryngology, 121(11): 738-745. doi:10.1177/000348941212101107

25. Hoffman, M. R., Mielens, J. D., Ciucci, M. R., Jones, C. A., Jiang, J. J., & McCulloch, T. M. (2012). High-resolution manometry of pharyngeal swallow pressure events associated with effortful swallow and the Mendelsohn maneuver. *Dysphagia*, *27*(3), 418–426. https://doi.org/10.1007/s00455-011-9385-6

26. Hosseini, P., Tadavarthi, Y., Martin-Harris, B., & Pearson, W. G. (2019). Functional modules of pharyngeal swallowing mechanics. *Laryngoscope Investigative Otolaryngology, 4*(3), 341-346. doi:10.1002/lio2.273

27. Jones, B., Donner, M. W., Rubesin, S. E., Ravich, W. J., & Hendrix, T. R. (1987). Pharyngeal findings in 21 patients with achalasia of the esophagus. *Dysphagia*, 2(2), 87–92. https://doi.org/10.1007/BF02408139

28. Jones, B., Ravich, W. J., Donner, M. W., Kramer, S. S., & Hendrix, T. R. (1985). Pharyngoesophageal interrelationships: observations and working concepts. Gastrointestinal radiology, 10(3), 225–233. https://doi.org/10.1007/BF01893105

29. Jou, J., Radowsky, J., Gangnon, R., Sadowski, E., Kays, S., Hind, J., Gaumnitz, E., Taylor, A., & Robbins, J. (2009). Esophageal clearance patterns in normal older adults as documented with videofluoroscopic esophagram. *Gastroenterology research and practice*, *2009*, 965062.

30. Kahrilas, P. J., Bredenoord, A. J., Fox, M., Gyawali, C. P., Roman, S., Smout, A. J., Pandolfino, J. E., & International High Resolution Manometry Working Group (2015). The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, 27(2), 160–174. https://doi.org/10.1111/nmo.12477

31. Kahrilas, P. J., Logemann, J. A., Krugler, C., & Flanagan, E. (1991). Volitional augmentation of upper esophageal sphincter opening during swallowing. *The American journal of physiology*, *260*(3 Pt 1), G450–G456. https://doi.org/10.1152/ajpgi.1991.260.3.G450

32. Kim, B., Moon, W., Kim, H., Jung, E., & Lee, J. (2016). Association of dysphagia with supratentorial lesions in patients with middle cerebral artery stroke. *Annals of Rehabil Medicine, 40*(4), 637-646. doi:10.5535/arm.2016.40.4.637

33. Leopold, N.A, Daniels, S.K. (2010). Supranuclear control of swallowing. *Dysphagia,* 25:250-257. Doi: 10.1007//s00455-009-9249-5

34. Lever, T., Cox, K., T., Holbert, D., Shahrier, M., Hough, M., Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. *Dysphagia*, 22: 312-325. doi: 10.1007/s00455-007-9107-2

35. Logemann, J., Curro, F., Pauloski, B., & Gensler, G. (2013). Aging effects on oropharyngeal swallow and the role of dental care in oropharyngeal dysphagia. Oral Diseases, 19(8), 733-737. doi:10.1111/odi.12104

36. Logemann, J. A. (1998). Evaluation and treatment of swallowing disorders (2nd ed.). Austin, Texas: Pro-Ed.

37. Madhavan, A., Carnaby, G. D., & Crary, M. A. (2015). 'Food Sticking in My Throat': Videofluoroscopic Evaluation of a Common Symptom. Dysphagia, 30(3), 343–348. https://doi.org/10.1007/s00455-015-9605-6

38. Mann, G., Hankey, G. J., & Cameron, D. (1999). Swallowing function after stroke: prognosis and prognostic factors at 6 months. *Stroke*, *30*(4), 744–748. https://doi.org/10.1161/01.str.30.4.744

39. Martin-Harris, B., Brodsky, MB, Michel, Y., Castell, DO., Schleicher, M., Sandidge, J., Maxwell, R., Blair, J. (2008). MBS measurement tool for swallow impairment – MBSImp: establishing a standard. *Dysphagia,* 23(4): 392-405. doi: 10/1007/s00455-008-9185-9.

40. Martin-Harris, B., Brodsky, M. B., Michel, Y., Lee, F. S., & Walters, B. (2007). Delayed initiation of the pharyngeal swallow: normal variability in adult swallows. *Journal of speech, language, and hearing research : JSLHR*, *50*(3), 585–594. https://doi.org/10.1044/1092-4388(2007/041)

41. Martin-Harris, B., Humphries, K., Garand (Focht), K.L. (2017). The Modified Barium Swallow Impairment Profile (MBSImP) – Innovation, dissemination and implementation. Perspectives of the ASHA Special Interest Groups SIG 13, 2(4), 129-138. https://doi.org/10.1044/persp2.SIG13.129

42. Martin-Harris, B., Michel, Y., & Castell, D. O. (2005). Physiologic model of oropharyngeal swallowing revisited. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 133(2), 234–240. https://doi.org/10.1016/j.otohns.2005.03.059

43. Martino, R., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. (2005). Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. Stroke, 36(12), 2756–2763. https://doi.org/10.1161/01.STR.0000190056.76543.eb

44. 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–vii. https://doi.org/10.1016/j.pmr.2008.06.001

45. May, N.J., Pisegna, J.M, Marchina, S., Langmore, S.E., Kumar, S., Pearson, W.G. (2017). Pharyngeal swallowing mechanics secondary to hemispheric stroke. *J Stroke Cerebrovas Dis,* 26(5): 952-961. http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.11.001

46. McCullough, G. H., Kamarunas, E., Mann, G. C., Schmidley, J. W., Robbins, J. A., & Crary, M. A. (2012). Effects of Mendelsohn maneuver on measures of swallowing duration post stroke. *Topics in stroke rehabilitation*, *19*(3), 234–243. https://doi.org/10.1310/tsr1903-234

47. Meyer, J. P., Jones, C. A., Walczak, C. C., & McCulloch, T. M. (2016). Three-dimensional manometry of the upper esophageal sphincter in swallowing and nonswallowing tasks. *The Laryngoscope*, *126*(11), 2539–2545. https://doi.org/10.1002/lary.25957

48. Miles, A., Bennett, K., & Allen, J. (2019). Esophageal Transit Times Vary with Underlying Comorbid Disease. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *161*(5), 829–834. https://doi.org/10.1177/0194599819874342

49. Miles, A., Clark, S., Jardine, M., & Allen, J. (2016). Esophageal Swallowing Timing Measures in Healthy Adults During Videofluoroscopy. *The Annals of otology, rhinology, and laryngology*, *125*(9), 764–769. https://doi.org/10.1177/0003489416653410

50. Miles, A., McMillan, J., Ward, K., & Allen, J. (2015). Esophageal visualization as an adjunct to the videofluoroscopic study of swallowing. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 152(3), 488–493. https://doi.org/10.1177/0194599814565599

51. Mittal RK. Motor Function of the Pharynx, Esophagus, and its Sphincters. San Rafael (CA): Morgan & Claypool Life Sciences; 2011. Upper Esophageal Sphincter

52. Molfenter, S. M., Hsu, C. Y., Lu, Y., & Lazarus, C. L. (2018). Alterations to Swallowing Physiology as the Result of Effortful Swallowing in Healthy Seniors. *Dysphagia*, *33*(3), 380–388. https://doi.org/10.1007/s00455-017-9863-6

53. Moon, H.I., Nam, J-S., Leem, M.J., Kim, K.H. (2017). Periventricular white matter lesions as a prognostic factor of swallowing function in older patients with mild stroke. *Dysphagia,* 32: 480-486. Doi: 10.1007//s00455-017-9788-0

54. Moon, H.I., Pyun, S.B., Kwon, H.K. (2012). Correlation between location of brain lesion and cognitive function and findings of videofluoroscopic study. *Ann Rehabil Med,* 36: 347-355. Doi: http://dx.doi.org/10.5535/arm.2012.36.3.347

55. Nativ-Zeltzer, N., Belafsky, P. C., Bayoumi, A., & Kuhn, M. A. (2019). Volitional control of the upper esophageal sphincter with high-resolution manometry driven biofeedback. *Laryngoscope investigative otolaryngology*, *4*(2), 264–268. https://doi.org/10.1002/lio2.255

56. NIH Stroke Scale Training, Part 2. Basic Instruction. Department of Health and Human Services, National Institute of Neurological Disorders and Stroke. The National Institute of Neurological Disorders and Stroke (NINDS) Version 2.0

57. O'Horo, J. C., Rogus-Pulia, N., Garcia-Arguello, L., Robbins, J., & Safdar, N. (2015). Bedside diagnosis of dysphagia: a systematic review. Journal of hospital medicine, 10(4), 256–265. https://doi.org/10.1002/jhm.2313

58. O'Rourke, A., Morgan, L.B., Coss-Adame, E., Morrison, M., Weinberger, P., Postma, G. (2014). The effect of voluntary pharyngeal swallowing maneuvers on esophageal swallowing physiology. *Dysphagia*, 2: 262-268. doi: 10.1007//s00455-013-9595-6

59. Reedy, E. L., Herbert, T. L., & Bonilha, H. S. (2021). Visualizing the Esophagus During Modified Barium Swallow Studies: A Systematic Review. *American journal of speech-language pathology*, *30*(2), 761–771. https://doi.org/10.1044/2020_AJSLP-20-00255

60. Robbins, J.A., Coyle J., Rosenbek J, Roecker E, Wood J. (1999). Differentiation of Normal and Abnormal Airway Protection during Swallowing Using the Penetration-Aspiration Scale. *Dysphagia,*14: 228-232.

61. Robbins, J., & Levin, R. L. (1988). Swallowing after unilateral stroke of the cerebral cortex: Preliminary experience. *Dysphagia, 3*(1), 11-17. doi:10.1007/BF02406275

62. Rosenbek, J., Robbins, J.A., Roecker, E.B., Coyle, J.L., Wood, J.L. (1996). A penetration-aspiration scale. *Dysphagia,* 11(2): 93-98. Doi: 10.1007/bf00417897

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

64. Singh, S., Hamdy, S. (2006). Dysphagia in stroke patients. *Postgrad Med,* 82(968): 383-391. Doi: 10.1136/pgmj.2005.043281.

65. Steele, C. M., Alsanei, W. A., Ayanikalath, S., Barbon, C. E., Chen, J., Cichero, J. A., Coutts, K., Dantas, R. O., Duivestein, J., Giosa, L., Hanson, B., Lam, P., Lecko, C., Leigh, C., Nagy, A., Namasivayam, A. M., Nascimento, W. V., Odendaal, I., Smith, C. H., & Wang, H. (2015). The influence of food texture and liquid consistency modification on swallowing physiology and function: a systematic review. Dysphagia, 30(1), 2–26. https://doi.org/10.1007/s00455-014-9578-x

66. Steele CM, Molfenter SM, Peladeau-Pigeon M, Delacco R, Yee C. Variations in Tongue-Palate Swallowing Pressures When Swallowing Xanthan Gum-Thickened Liquids. *Dysphagia.* 2014; 29(6): 678-684.

67. Steele, C. M., Namasivayam-MacDonald, A. M., Guida, B. T., Cichero, J. A., Duivestein, J., Hanson, B., Lam, P., & Riquelme, L. F. (2018). Creation and Initial Validatioxn of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale. Archives of physical medicine and rehabilitation, 99(5), 934–944. https://doi.org/10.1016/j.apmr.2018.01.012

68. Suntrup-Krueger, S., Kemmling, A., Warnecke, T., Hamacher, C., Oelenberg, S., Niederstadt, T., . . . Dziewas, R. (2017). The impact of lesion location on dysphagia

incidence, pattern and complications in acute stroke. part 2: Oropharyngeal residue, swallow and cough response, and pneumonia. *European Journal of Neurology, 24*(6), 867-874. doi:10.1111/ene.13307

Teismann, I. K., Suntrup, S., Warnecke, T., Steinsträter, O., Fischer, M., Flöel, A., . . . Dziewas, R. (2011). Cortical swallowing processing in early subacute stroke. *BMC Neurology, 11*(1), 34. doi:10.1186/1471-2377-11-34

69. Wheeler Hegland, K., Huber, J. E., Pitts, T., Davenport, P. W., & Sapienza, C. M. (2011). Lung volume measured during sequential swallowing in healthy young adults. *J Sp Lang Hear*, Research, 54(3), 777–786. https://doi. org/10.1044/1092-4388(2010/09-0237)

70. Wilmskoetter, J., Bonilha, L., Martin-Harris, M., Elm, J.J., Horn, J., Bonilha, H.S. (2019). Mapping acute lesions to physiological swallow impairments after stroke. *NeuroImage Clin,* 22:101685. doi: 10.1016/j.nicl.2019.101685.

71. Wilmskoetter, J., Martin-Harris, B., Pearson, W.G., Bonilha, L., Elm, J.J., Horn, J., Bonilha, H.S. (2018). Differences in swallow physiology in patients with left and right hemispheric strokes. *Phys Behavior,* 194" 144-152. Doi: https://doi.org/10.1016/j.physceh.2018.05.010

72. Wilson R. D. (2012). Mortality and cost of pneumonia after stroke for different risk groups. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association, 21(1), 61–67. https://doi.org/10.1016/j.jstrokecerebrovasdis.2010.05.002

73. Wilson-Pauwels, L., Akesson, E.J., Stewart, P.A. (1988). *Cranial Nerves: Anatomy and Clinical Comments*. Toronto: BC Decker.

74. Wilson R. D. (2012). Mortality and cost of pneumonia after stroke for different risk groups. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association, 21(1), 61–67. https://doi.org/10.1016/j.jstrokecerebrovasdis.2010.05.002

75. Wilson-Pauwels, L., Akesson, E.J., Stewart, P.A. (1988). *Cranial Nerves: Anatomy and Clinical Comments*. Toronto: BC Decker.

76. Yadlapati, R., Kahrilas, P. J., Fox, M. R., Bredenoord, A. J., Prakash Gyawali, C., Roman, S., Babaei, A., Mittal, R. K., Rommel, N., Savarino, E., Sifrim, D., Smout, A., Vaezi, M. F., Zerbib, F., Akiyama, J., Bhatia, S., Bor, S., Carlson, D. A., Chen, J. W., Cisternas, D., … Pandolfino, J. E. (2021). Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *33*(1), e14058. https://doi.org/10.1111/nmo.14058

77. Yang, Q., Tong, X., Schieb, L., Vaughan, A., Gillespie, C., Wiltz, J. L., King, S. C., Odom, E., Merritt, R., Hong, Y., & George, M. G. (2017). Vital Signs: Recent Trends in Stroke Death Rates - United States, 2000-2015. *MMWR. Morbidity and mortality weekly report*, *66*(35), 933–939. https://doi.org/10.15585/mmwr.mm6635e1

CHAPTER 3: AIM 2

Manuscript 2: Esophageal Dysphagia in Acute Post-Lung Transplantation

TITLE: Esophageal Clearance Abnormalities in Acute Post-Lung Transplantation

AUTHORS: Reedy, E.L., Simpson, A.N., O'Rourke, A.K., Khalaf, M.H., Whelan, T.P.M., Bonilha, H.S.

ABSTRACT:

Background: Dysphagia, or difficulty swallowing, is a possible complication in the post-lung transplant population. Much of the literature has focused solely on the presence of atypical laryngeal penetration and/or aspiration or on post-transplant esophageal testing. However, no literature has explored dysphagia across the swallowing continuum (e.g., oral cavity, pharynx, esophagus) within a single cohort. Esophageal impairment post-lung transplantation may go overlooked during the acute phase of recovery given the immediate concern for oropharyngeal dysphagia and its consequences (e.g., aspiration, pneumonia), and the potential for allograft (donor) injury.

Methods: We performed a retrospective, cross-sectional, cohort study of 28 post-lung transplant patients. All participants received a Modified Barium Swallow Study (MBSS) as part of standard care during their acute hospitalization using the Modified Barium Swallow Impairment Profile (MBSImP™©) protocol and scoring metric. Swallowing impairment was determined using a combination of MBSImP scores, Penetration-Aspiration Scale (PAS) scores, Functional Oral Intake Scale (FOIS) scores, International Dysphagia Diet Standardization Initiative (IDDSI) scores, and temporal variables (e.g., time from stroke to MBSS). We performed tests of association to determine if statistically significant associations exist between MBSImP™© component 17 scores and other measures of swallowing impairment.

Results: In this post-lung transplant cohort, 85.71% had abnormal esophageal clearance identified in their first post-transplant MBSS which was the most common form of swallowing impairment. Further analysis revealed that all patients identified as aspirating on their post-transplant MBSS had abnormal esophageal clearance.

Conclusion: Swallowing occurs across a continuum (e.g., oral cavity, pharynx, esophagus) and the assessment of dysphagia in the post-lung transplant population is incomplete if limited solely to concerns for oropharyngeal impairment. It is critical to consider the interactions between physiologic components of swallowing across the swallowing continuum.

INTRODUCTION:

Dysphagia, or difficulty swallowing, is a possible postoperative complication after lung transplantation. This population may be particularly susceptible to dysphagia given the multiple pre-morbid dysphagia risk factors in the end-stage lung disease (ESLD) population (Cassani et al., 2015; Cvejic et al., 2011; Garand et al., 2018; Good-Fraturelli et al., 2000; Gross et al., 2009; Martin-Harris & McFarland, 2013; Martin-Harris et al., 2015; Shaker et al., 1992) as well as surgical risk factors for dysphagia related to post-extubation dysphagia and/or laryngeal injury (Borders et al., 2019; Brodsky, De, Chilkuri, et al., 2018; Brodsky et al., 2014; Brodsky, Levy, Jedlanek, et al., 2018; Krisciunas et al., 2020; Miles et al., 2018; Nguyen et al., 2016; Plowman et al., 2021; Skoretz et al., 2010; Tikka & Hilmi, 2019) and the vulnerability of the intrathoracic vagal nerve and its branches injury during surgery (Grote et al., 2019; Studer et al., 2004). Prandial aspiration, or abnormal bolus passage into the trachea during swallowing, is one concerning factor in the acute phase of recovery post-lung transplant. Avoidance of allograft (donor tissue) injury is of paramount concern and aspiration could be one mechanism of injury. However, there is limited literature to date regarding acute dysphagia in this population, and no current studies that report findings across the swallowing continuum (e.g., oral, pharyngeal, and esophageal aspects of swallowing) in a single cohort despite the evidence that swallowing as a continuum and not a three-phase act (Gullung et al., 2012; Jones et al., 1985; Jones et al., 1987; Lever et al., 2007; Madhavan, Carnaby & Crary, 2015; Miles et al., 2017; Miles et al., 2019; Miles et al., 2015; O'Rourke et al., 2016; Ortiz et al., 2019; Reedy et al., 2021; Triadafilopoulos, 1992; Watts et al., 2019). The interactions between or across aspects of the swallowing impairment might be especially pertinent in the post-lung transplant population.

According to the United Network for Organ Sharing (UNOS), there were 2,714 lung transplants in 2019 representing a 7.3% increase from 2018 - a trend that is expected to continue (UNOS, n.d.). Lung transplantation, typically performed via thoracotomy or median sternotomy (Meyers et al., 1999), may render certain branches of the vagus nerve vulnerable in the surgical field. The nerves which innervate the larynx nerves may be particularly vulnerable from both intubation and the surgical manipulation. The internal branch of the superior laryngeal nerves

supplies all sensory input above the vocal folds. The external branch of the superior laryngeal nerve provides motor input to the cricothyroid. The recurrent laryngeal nerves (RLN) provide bilateral motor and sensory input at and below the level of the vocal folds. The left recurrent laryngeal nerve initially courses downward and around the aortic arch before traveling upwards to innervate the left vocal fold, whereas the right travels downward and around the subclavian artery before coursing upwards to innervate the right vocal fold (Saran, Georgakopoulos, Bordoni, 2020). The main anterior and posterior thoracic vagus nerve are also at-risk during lung transplantation, as its branches, situated in the mediastinum, travel through the esophageal hiatus of the diaphragm (Studer et al., 2004). Pulmonary denervation, without a suggestion for reinnervation post-lung transplant (Lumb, 2017), is considered a surgical consequence of lung transplantation as the pulmonary autonomic nerves are completely transected at the distal trachea (Studer et al., 2004). Intubation, a necessary aspect of general anesthesia, may result in laryngeal injury and/or dysphagia upon extubation (Borders et al., 2019; Brodsky, De, Chilukuri, et al., 2018; Brodsky et al., 2014; Brodsky, Levy, Jedlanek, et al., 2018; Krisciunas et al., 2020; Plowman et al., 2021; Skoretz, Flowers & Martino, 2010; Tikka & Hilmi, 2019). Intubation involves passing a rigid endotracheal tube through the oropharynx and laryngeal vestibule, between the vocal folds, and into the trachea. These tubes are measured in French which reflects the inner diameter and ranges from 2.5 to 9.0 French (Gupta & Gupta, 2019). Both Krisciunas et al. (2020) and Plowman et al. (2021) identified endotracheal tube (ETT) sizes of 8.0 or greater as an independent risk factor for laryngeal injury and dysphagia in their cohorts of recently extubated patients (respiratory failure, and post-cardiothoracic surgery, respectively).

The oropharynx is a multi-functional anatomic space, unique to the human body, critical for respiration, deglutition, and phonation which have both involuntary (brainstem) and voluntary (cortical) controls. The central pattern generators for respiration, swallowing and digestion all reside within the medulla and are predominantly vagally mediated. Swallowing is a complex act requiring the highly synchronized transformation of the oropharynx from a respiratory system to a deglutitive (swallowing) system where respiration briefly ceases. Under normal

circumstances, respiration and swallowing exist in a reciprocal relationship – one cannot occur in the context of the other. This relationship has been studied with a typical pattern of an exhale-swallow-exhale pattern, where swallowing is “bracketed” by expiratory airflow at mid to low lung volumes (Brodsky et al, 2010; Hopkins-Rossabi, 2019; Martin-Harris, 2008; Martin-Harris et al., 2003, Martin-Harris et al., 2005; McFarland et al., 2016; Wheeler-Hegland et al., 2011). The swallow requires inhibition of breathing, or apneic period, during the glottal closure reflex lasting from 0.5-1.5 seconds (Matsuo & Palmer, 2008). Eating, therefore, involves a high level of coordination of mastication, respiration, and swallowing which can be especially taxing in the respiratory compromised population (Martin-Harris & McFarland, 2013, p.26-27). There is compelling evidence that respiratory compromise changes the normal respiratory-swallow coordination (Gross et al., 2009; Martin-Harris et al., 2015; Shaker et al., 1992). Pathophysiologic changes in swallowing have been identified in the Chronic Obstructive Pulmonary Disease (COPD) population including laryngeal penetration and subglottic aspiration (Cassani et al., 2015; Cvejic et al., 2011; Garand et al., 2018; Good-Fraturelli et al., 2000; Gross et al., 2009) on instrumental assessment. This can create a cycle where the dysphagia itself can provoke COPD exacerbation (Nagami et al., 2017; Steidl et al., 2015).

Bronchiolitis Obliterans Syndrome (BOS) is a significant post-lung transplant risk factor for allograft (donor tissue) dysfunction. BOS is one of the greatest limiting factors to lung transplant success and long-term survival rates (Boehler, 1998; Estenne et al., 2002; Tejwani et al., 2016; Studer et al., 2004; Verleden, 2000; Verleden et al., 2004, pg 19-30). Gastroesophageal Reflux Disease (GERD) is an indirect contributor to the development and progression of BOS (Bobadilla et al., 2010; Burton et al., 2009; Cantu et al., 2004; Hadjiliadis et al., 2003; King et al., 2009; Lau et al, 2002; Parada, Alba, & Sepúlveda, 2010; Shah et al., 2010) due to the risk of aspiration of acidic reflux (Effros et al., 2000; Miyagawa-Hayashino, Wain & Mark, 2005). Though GERD is a concern and may factor into allograft injury or failure, it is not a contraindication to surgery. The American Transplant Society (ATS) "International Guidelines for the Selection of Lung Transplant Candidates" (Maurer et al., 1998) and the 2006 update to these guidelines (Orens et al., 2006) outline transplant candidacy indications and

contraindications as well as testing that should be done to determine eligibility. Orens et al. (2006) highlight the "primary importance" of optimal candidate selection for "favorable long-term outcomes." Both iterations of these guidelines fail to mention the possibility of pre-and/or post-lung transplant dysphagia or reflux as factors to consider. More currently, Adegunsoye et al. (2017) outline the comprehensive care for lung transplant patients with updated indications, contraindications, testing, and post-transplant risk factors. However, there is no acknowledgment of dysphagia as a potential risk factor for pre- or post-lung transplant recipients. Girgis and Khaghani (2016), however, include "upper deglutition problems resulting in aspiration, severe esophageal dysmotility, gastroparesis, [and] severe GERD that will not be amenable to fundoplication" (p. 5) as relative contraindications for LTX candidacy in their “Global Perspective of Lung Transplantation”. The article also outlines the components of pre-lung transplant evaluation which includes an esophagram on all candidates with consideration of 24-hour pH monitoring plus impedance, and esophageal manometry, gastric emptying study, and GI consultation.

Opportunistic infections are a source of post-lung transplant complications particularly from a gram-negative bacterium. Post-lung transplant patients are pharmacologically immunocompromised to prevent rejection (Studer et al., 2004) and are particularly at risk for pseudomonas, non-tuberculosis mycobacterium, cytomegalovirus, pneumocystis jiroveci, and Aspergillus (Studer et al., 2004; Tejwani et al., 2016). Given the dearth of evidence regarding post-lung transplant dysphagia, it is unclear if there is a causal relationship between chronic aspiration and/or aspiration pneumonia and allograft injury or transplant failure. While Posner et al. (2018) advocate for a more comprehensive pre-transplant assessment, their recommendations are limited to diagnostics of the esophagus. Notably absent is an assessment of the oral and pharyngeal aspects of the swallow, or an evaluation of the swallowing as a continuum.

The literature investigating oropharyngeal dysphagia in the post-lung transplant population is limited. Atkins et al. (2007) identified abnormal swallowing in 70.95% of their post-lung

transplant cohort with aspiration identified in 63.8% on instrumental assessment (Fiberoptic Endoscopic Evaluation of Swallowing [FEES] or Modified Barium Swallow Study [MBSS]). They also reported that approximately 25% of their participants whose assessments included FEES (87.9% of their sample received an instrumental assessment), had vocal fold paresis/injury. Baumann et al. (2017) reported dysphagia in 67% of their post-lung transplant cohort with 62% having deep laryngeal penetration and/or aspiration. Other work by Black et al. (2019) identified dysphagia in 88% of their cohort which encompassed both post-lung and post-heart and lung transplant recipients though only 11.78% of their sample received an instrumental assessment. More recently, Miles et al. (2020) reported that of the post-lung transplant patients who underwent FEES (64.35% of the sample), 75% demonstrated aspiration, 63% of which was silent aspiration. Vocal fold paralysis was diagnosed in 34% of those patients who received an ENT referral.

Gastrointestinal dysfunction recognized in the form of gastroesophageal reflux disease (GERD) has been well-established in the pre-and post-lung transplant population. Though other disorders of the esophagus are less well-studied. While High-Resolution Manometry (HRM) is considered a standard aspect of pre-transplant evaluation, post-transplant HRM is less common. Those studies which assessed esophageal function post-lung transplant demonstrated GERD, disorders of motility, and disorders of the gastroesophageal junction (GEJ). Davis et al. (2010) assessed post-lung transplant participants with HRM+MII, 24-hour pH monitoring, EGD, barium swallow, and gastric emptying studies. They found evidence of GERD in 51% of their post-lung transplant participants, all with normal lower esophageal sphincter (LES) findings. Ineffective Esophageal Motility (IEM) was present in 36% of participants with GERD compared to 6% without GERD. Patients with GERD demonstrated delayed esophageal bolus transit more frequently, as well as more prolonged episodes of reflux and slower acid clearance. Gadel et al. (2012) found manometric evidence of esophageal pathophysiology in 55% of their post-lung transplant participants. They identified that 65% of their participants had a hypotensive UES and 52.2% of participants had a hypotensive LES. Pathological acidic reflux was demonstrated in 35% of participants. In their cohort of post-lung transplant patients,

Griffin et al. (2013) found abnormal esophageal motility on HRM in 44% of participants, distal esophageal reflux on 24-hour pH monitoring with impedance in 71% of participants. Grass et al. (2015) reported that GI complications post-lung transplant occurred in 62% of their sample with GERD being the most common (22.9%). They also found that double-lung transplantation was an independent risk factor for developing post-transplantation GI complications. By Chicago Classification v3.0 (CC v3.0) (Kahrilas et al., 2015) standards, Tangaroonsanti et al. (2017) identified abnormal esophageal motility in 72% of their participants post-lung transplant, esophagogastric junction outflow obstruction without hypercontractility (achalasia) in 8%, hypercontractility in 24%, EGJOO with hyper-contractility in 8%, and hypocontractility in 14%. Interestingly, when comparing the prior version of the classification (v2.0), more participants would have been identified as having abnormal findings. Additionally, those participants with EGJOO were more likely to develop obstructive chronic lung allograft dysfunction (o-CLAD), although they were less likely to demonstrate the atypical frequency of reflux and had an overall reduction in reflux exposure time when compared to those with normal manometric findings. Ciriza de Los Ríos et al. (2018) identified post-transplant esophageal motility disorders of any type in 49.1% in their study of post-lung transplant recipients. Masuda et al. (2019) compared pre-and post-lung transplant participants via HRM, 24-hour impedance monitoring, EGD, and gastric emptying studies. Motility abnormalities were identified in 55.1% of pre-lung transplant participants and in 45.8% of post-lung transplant participants. There was a change in diagnostic category for 51.4% of those participants comparing pre-and post-transplant studies per the Chicago Classification (CC v 3.0). Gastric emptying studies were performed in 80.37% of the pre-lung transplant and 88.79% of the post-lung groups with delayed gastric emptying had worsened function or were newly identified post-lung transplantation. Additionally, gastroparesis appears to be a common neurogastroenterologic sequelae of lung transplantation (Gamez et al., 2017, Gasper et al., 2008; Grass et al., 2015; Hirji et al., 2017; Kayawake et al., 2018, Lidor et al., 2014). In their 2019 study, Tangaroonsanti et al. identified abnormal esophageal motility in 72.92% of their post-lung transplant cohort. Though only investigating for a single manometric abnormality, Cangemi et al. (2020) identified hypercontractility or, “jackhammer” esophagus in 18.8% (CC v3.0) of their post-lung transplant participants. Gouynou

et al. (2020) demonstrated that esophageal manometric abnormality of any type was seen in 38.1% (CC v3.0) of their post-lung transplant cohort. Masuda et al. (2020) reported HRM-confirmed esophageal motor disorders in 65.5% of their post-lung transplant cohort and that 31% of those with a motility disorder post-transplant had findings that differed from pre-transplant HRM testing. In their 2021 study of patients with aperistalsis pre-transplant, Giulini et al. (2021) reported improved esophageal peristaltic function in 65.52% of their post-lung transplant cohort. In their small sample, they identified that patients with pulmonary hypertension or obstructive lung diseases were more likely than patients with restrictive lung diseases to have improved peristalsis post-transplant.

To our knowledge, there are no studies that investigate dysphagia across the swallowing continuum in a single cohort. Our primary goal was to identify those post-lung transplant patients examined for acute oropharyngeal dysphagia who have either simultaneous or primary esophageal dysphagia owing to the shared neural, anatomic, and physiologic characteristics. We propose that investigating the swallow as a continuum will have a substantial impact in the post-lung transplant population.

METHODS:

Study Design

This retrospective, cross-sectional cohort study was conducted at the Medical University of South Carolina (MUSC). Between January 1, 2016, and January 1, 2021, a total of 78 patients received lung transplants. Potential participants were identified using a database of lung transplant recipients maintained by the MUSC lung transplant team, part of the Department of Pulmonology. All electronic health records (EHR) were reviewed for eligibility.

Inclusion and Exclusion Criteria

Inclusion criteria were established as adults (21+ years) who received a single or bilateral lung transplant for ESLD. Potential participants were excluded if their past medical history included

diseases known to impair oropharyngeal swallow function outside of their respiratory disorder (e.g., head and neck cancer, progressive neurologic disorders, history of stroke).

All eligible participants had a Modified Barium Swallow Study (MBSS) using the MBS Impairment Profile (MBSImP™©) (Martin-Harris et al., 2008) protocol and scoring system. Those participants whose MBSS reports did not include MBSImP scores or did not have an MBSImP component 17 (esophageal clearance) score were excluded. Penetration Aspiration Scale (PAS) scores (Rosenbek et al., 1996) were required. Both Functional Oral Intake Scale (FOIS) scores (Crary et al., 2005) and International Dysphagia Diet Standardization Initiative (IDDSI) scale (Steele et al., 2018) scores or enough information in the EHR to determine both were required for study inclusion.

Modified Barium Swallow Studies

As part of the standard of care, all participants received an MBSS during their acute post-lung transplant hospitalization. All MBSSs were performed at 30 pulses per second (pps) and were recorded at 30 frames per second (fps) according to best practices (Bonilha, Blair, Carnes, et al., 2013; Bonilha, Humphries, Blair, et al., 2013). All MBSSs were conducted using the Modified Barium Swallow Impairment Profile (MBSImP™©) (Martin-Harris et al., 2008) which measures 17 distinct physiologic components of swallowing. The base protocol consists of 12 swallows of varying liquid and solid consistencies, the initial 10 in the lateral view, the last 2 in the anterior-posterior view. Component 17, our primary outcome measure, is determined by the esophageal bolus clearance patterns through the esophageal body and lower esophageal sphincter (LES) in the A-P view with 5 ml nectar and 5 ml pudding contrast. Standard barium sulfate preparations (Varibar®, Bracco Diagnostics Inc.) were used.

From these clinical MBSSs, data related to swallowing impairment and swallowing outcomes were extracted. Physiologic swallowing assessment in the form of MBSImP scores including component, and oral and pharyngeal total scores were collected as well as Penetration-Aspiration Scale (PAS) scores (Rosenbek et al., 1996), and the absence or presence of

aspiration. Swallowing outcome measures in the form of Functional Oral Intake Scale (FOIS) scores (Crary et al., 2005) and International Dysphagia Diet Standardization Initiative (IDDSI) scores (Steele et al., 2018) were either collected directly from the medical record. For those participants whose MBSS were performed prior to the transition to IDDSI standards, levels were determined using a crosswalk of previous, compatible, consistencies (e.g., “mechanical soft” is comparable to IDDSI level 6). Due to the nature of IDDSI scores, typically reported as two scores, the IDDSI scores were separated into an "IDDSI Liquid" and an "IDDSI Solid" score. In the case of a single consistency recommendation, only one corresponding score was collected, and in the case of a recommendation for NPO (nil per os, “nothing by mouth”) no scores were recorded. The presence of alternate means of nutrition (e.g., feeding tube), alternate nutrition type (e.g., nasogastric vs. gastric tube), and the absence or presence of a recommendation for NPO were also collected. Data for "time to" events was calculated for the time from lung transplant to clinical swallowing evaluation, time from lung transplant to MBSS, and days spent NPO before the MBSS.

Reliability

All MBSSs were performed, and MBSImP scores were determined, by the treating clinician (speech-language pathologist). All MUSC clinicians are MBSImP certified and have, therefore, demonstrated 80% accuracy across all component scores as part of their training, which requires recertification every 5 years to maintain eligibility (Martin-Harris, 2015; Martin-Harris et al., 2008).

Statistical Analysis

Summary statistics were calculated (e.g., mean, median, mode, and standard deviation for continuous variables; median, mode, and frequency for categorical variables). Our null hypothesis (H_0) was that there was no difference in the proportion of esophageal abnormalities in this cohort compared with published estimates (Miles et al., 2015). Only one applicable prospective study (Miles et al., 2015) was available for comparison which demonstrated that 33% of patients whose MBSS included esophageal visualization had some type of esophageal

abnormality. This hypothesis was investigated using a test of binomial proportions. Given the small sample size, the data was separated into two component 17 groups for analysis – those with normal component 17 (C17 =0) and with abnormal component 17 (C17 >1). MBSImP Component 17 (esophageal clearance) was dichotomized into normal (C17 = 0 "complete clearance; esophageal coating") vs. abnormal (C17 ≥ 1 representing scores 1-3 for esophageal retention with or without retrograde flow, as well as a score of 4 for minimal to absent clearance) scores. Fisher's exact tests were used to describe categorical variables (e.g., MBSImP component scores) and determine if associations exist between measures of swallowing physiology and outcome measures. As the data was determined to be non-parametric, Mann-Whitney U/Wilcoxon Rank Sum tests were used to test for differences in continuous variables (e.g., age). Our hypothesis (H_0) was that there were no statistically significant associations between these variables and component 17. A subgroup analysis of summary statistics, associations between variables, and relative risk was performed for those patients who were determined to be aspirating on their MBSS. Given the small, heterogeneous sample, logistic regression could not be performed. Therefore, unadjusted relative risks were calculated for significant variables with the outcome of abnormal (C17 ≥1). Findings reflect the overall statistical significance and for all statistical analyses, two-sided tests were performed with the alpha set at 0.05 with P values of ≤ .05 indicating statistical significance. All analysis was performed using SAS (v9.4, SAS Institute Inc., Cary, NC).

RESULTS:

1. *Participants*

Between January 1, 2016, and January 1, 2021, 78 patients underwent lung transplantation at the Medical University of South Carolina (MUSC). Only 28 patients met specified inclusion and exclusion criteria and were enrolled in the study. The mean age was 57.25 years (range 27-70) with a 95% confidence limit around the mean of 53.2-61.3. Half (50%) of the participants were female. The majority of participants were white (71.43%) and none of the participants identified as Hispanic. All patients who undergo lung transplantation have some form of end-stage lung disease (ESLD). Most participants in this cohort had Idiopathic Pulmonary Fibrosis

(IPF) (32.14%), followed by COPD (25%), Interstitial Lung Disease (ILD) (21.43%), sarcoidosis (14.29%), and Cystic Fibrosis (CF) (7.14%). Surgical data was collected with almost all transplants being bilateral (96.43%) via clamshell thoracotomy (53.57%). Variables related to ventilation were also collected with most participants receiving cardiopulmonary bypass (60.71%) during transplantation. All participants whose charts included intubation data (20/28) reported that intubation was achieved with an endotracheal tube (ETT) of 8 or larger (100%). See Table 1.

Table 1. Demographic, Baseline, and Surgical Characteristics of Post-Lung Transplant Recipients

n	28
Age (mean, ±SD, 95% CI)	57.25, ±10.44 (53.20, 61.3)
Sex	
Female	14 (50%)
Race	
White	20 (71.43%)
Black	8 (28.57%)
Ethnicity	
Non-Hispanic	28 (100%)
End-Stage Lung Disease Type	
Cystic Fibrosis (CF)	2 (7.14%)
Chronic Obstructive Pulmonary Disease (COPD)	7 (25%)
Idiopathic Pulmonary Fibrosis (IPF)	9 (32.14%)
Interstitial Lung Disease (ILD)	6 (21.43%)
Sarcoidosis	4 (14.29%)
Transplant Type	
Single Lung	1 (3.57%)
Bilateral Lung	27 (96.43%)
Surgical Approach	
Median Sternotomy	12 (42.86%)
Clamshell Thoracotomy	15 (53.57%)
Thoracotomy	1 (3.57%)
Ventilation Type	
Single-lung mechanical ventilation	1 (3.57%)
Cardiopulmonary bypass	17 (60.71%)
Extracorporeal Membrane Oxygenation (ECMO)	10 (35.71%)
Endotracheal Tube (ETT) Size	n = 20
<8.0	0 (0%)
8.0	17 (85%)
>8.0	3 (15%)
Days from transplant to MBSS (mean, standard deviation, 95% CI)	13.14, ±23.15 (4.17, 22.12)

Most participants underwent pre-transplant esophageal testing with 26/28 (92.86%) having High-Resolution Esophageal Manometry (HRM), 24/28 (85.71%) had ambulatory 24-hour pH Multichannel Intraluminal Impedance (pH-MII), and only 7/28 (25%) had a pre-transplant barium esophagram. Abnormal HRM was identified in 22/28 (84.62%) of pre-transplant studies. All studies were analyzed using the Chicago Classification v3.0 (Kahrilas et al., 2015). Under this classification, 19/26 (73.08%) patients were diagnosed with ineffective esophageal motility (IEM), 3/36 (11.54%) were diagnosed with distal esophageal spasm (DES), and 6/26 (23.08%) were diagnosed with gastroesophageal junction (GEJ) dysfunction. However, version 4.0 has since been published (Yadlapati et al., 2021) with changes to many diagnostic classifications. Therefore, the individual manometric findings are reported in Table 2. Abnormal pH-MII was seen in 11/28 indicating the presence of reflux in 45.83% of pre-lung transplant studies. Abnormal results were reported in 6/7 (85.71%) of our cohort's pre-transplant barium esophagram studies. See Table 2 for a full profile of pre-lung transplant esophageal testing.

Table 2. Pre-Lung Transplant Esophageal Testing Profile

High-Resolution Esophageal Manometry (HRM)*	n = 26
Normal study	4 (15.38%)
Any study abnormality	22 (84.62%)
5-7 weak swallows	10 (38.46%)
8 or more weak swallows or 5 failed swallows	9 (34.62%)
Hypercontractility (DCI > 8000) in 20% of swallows	0 (0%)
Elevated LES IRP	3 (11.54%)
Hypertensive LES	3 (11.54%)
Hypotensive LES	2 (7.7%)
Hypertensive UES	5 (19.23%)
Hypotensive UES	0 (0%)
Premature contractions (DL < 4.5) in 20% of swallows	3 (11.54%)
Abnormal Impedance	13 (50%)
Days from HRM to lung transplant (mean, ± SD, 95% CI)	406.38, ± 400.14 (244.77, 568.0)
24-Hour pH Impedance Monitoring (MII-pH)	n = 24
Abnormal results	11 (45.83%)
Days from pH-MII to lung transplant (mean, ± SD, 95% CI)	419.17, ±461.86 (244.14, 614.19)
Barium Esophagram	n = 7
Normal study	1 (14.29%)
Impression of dysmotility	5 (71.43%)
Web, stricture, or ring	0 (0%)
Hiatal Hernia	3 (42.86%)

Gastroesophageal junction abnormality	1 (14.29%)
Observed gastroesophageal reflux	3 (42.86%)
Days from barium esophagram to lung transplant (mean, ± SD, 95% CI)	240, ±206.47 (49.05, 430.95)

2. MBSImP Component 17 (Esophageal Clearance) Scores

In this post-lung transplant cohort, abnormal esophageal clearance was seen in 85.71% of participants. Abnormal clearance was established as any MBSImP component 17 score greater than zero where abnormal esophageal clearance ranged from esophageal retention with or without retrograde flow to minimal to no esophageal clearance. Abnormal scores ranged from 1-4 in this cohort with 9/28 (32.14%) having a score of 1 or "esophageal retention." The most common score was a 2, or "esophageal retention below [the] pharyngoesophageal segment (PES)" in 11/28 (39.29%) participants. A score of 3 or, "esophageal retention with retrograde flow through [the] PES" was seen in 3/28 (10.71%) participants. One participant (3.57%) had a score of 4, or "minimal to no esophageal clearance."

Using a test of binomial proportions, we compared our findings (85.71%) against our pre-specified threshold of 33% from pre-existing data (Miles et al., 2015) which yielded a statistically significant result (P <.0001); thus, we can conclude that in our sample, the proportion of individuals with abnormal esophageal clearance patterns was different than 33%. The 95% exact confidence interval, around the proportion of post-lung transplant individuals with abnormal esophageal clearance patterns, would be expected to fall between 67.33% and 95.97%. We identified that participants had a 44% (unadjusted RR = 1.444) increased risk for abnormal component 9 (anterior hyoid excursion) when component 17 was abnormal (≥1). Additionally, those participants with abnormal esophageal clearance were 57% (unadjusted RR = 1.571) more likely to have a recommendation for altered solids based on IDDSI classifications.

7. MBSS Variables

3.4 MBSImP Component Scores

The most common abnormality in this post-lung transplant cohort was a lower bolus head at the onset of the pharyngeal swallow (component 6) identified in 92.86% of participants. The

second most common abnormality was abnormal esophageal clearance (component 17) in 85.71% of participants. Both laryngeal elevation (component 8) and laryngeal vestibular closure (component 11) were abnormal in 60.71% of participants.

Table 3. Unadjusted Association Between Component 17 Scores: MBSImP Scores and Other Measures of Swallowing Impairment

MBSImP Component Score Compared to Measures of MBSImP Component 17	P-value
MBSImP component 1 (lip closure)	P = .3039
MBSImP component 2 (tongue control during bolus hold)	P = .1606
MBSImP component 3 (bolus prep/mastication)	P = .4053
MBSImP component 4 (bolus transport/lingual motion	P = .8242
MBSImP component 5 (oral residue)	P = .3494
MBSImP component 6 (initiation of pharyngeal swallow)	P = 1.0000
MBSImP component 7 (velar elevation)	P = 1.0000
MBSImP component 8 (laryngeal elevation)	P = 1.0000
MBSImP component 9 (anterior hyoid excursion)	*P = .0349**
MBSImP component 10 (epiglottic movement)	P = .4719
MBSImP component 11 (laryngeal vestibule closure)	P = .3690
MBSImP component 12 (pharyngeal stripping wave)	P = .6659
MBSImP component 13 (pharyngeal contraction)	P = .6659
MBSImP component 14 (pharyngoesophageal segment opening)	P = .3723
MBSImP component 15 (tongue base retraction)	P = .8286
MBSImP component 16 (pharyngeal residue)	P = .1949
MBSImP oral total (OT) scores	P = .3156
MBSImP pharyngeal total (PT) scores	P = .5784
Penetration-Aspiration Scale score	P = .3039
Aspiration (presence/absence)	P = .1606

**P <0.05 Fisher's exact test of association for categorical variables, Wilcoxon Rank Sum/Mann Whitney-U test of association for continuous variables*

Of the five MBSImP oral component scores, no statistical associations were identified when compared against component 17 scores. Of the eleven pharyngeal component scores, only component 9 (anterior hyoid excursion) demonstrated a statistically significance association with component 17 scores (P = .0349). See Table 3. The majority of participants (53.57%) had a score of 1, or "partial anterior movement". All other (46.43%) participants had a score of 0 indicating "complete anterior movement."

3.1 Swallowing Impairment Severity

Beall et al. (2020) identified ranges of oral total (OT) and pharyngeal total (PT) scores that account for differences in swallowing impairment in their latent class analysis of MBSImP OT and PT scores. Using this range, our post-lung transplant cohort was overwhelmingly identified as having either functional physiology (minimal changes not considered to be impairment) or mild swallowing impairment for both the OT (89.29%) and PT (96.43%) scores. Esophageal total scores are comprised of the single component 17 score, yielding a normal result in only 14.29% of participants.

3.1 Measures of Bolus Airway Invasion

The full range of Penetration-Aspiration Scale (PAS) scores (1-8) was observed in this post-lung transplant cohort except for a score of 5. The median PAS score was 2, or "material enters airway, remains above the [vocal] folds, and is ejected from the airway". PAS scores representing variations of normal swallow physiology (scores 1-3) (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999) were seen in 20/28 (71.43%) of participants. Atypical laryngeal penetration, represented by a score of 4 was seen in 1/28 (3.57%) of participants. Aspiration, as indicated by PAS scores of 6-8, was identified in 7/28 (25%) of participants. Of those patients who aspirated, 5/7 (71.43%) did so silently (PAS score of 8).

8. MBSS Outcome Measures

MBSS outcome measures were collected in the form of FOIS (Crary et al., 2005), the liquid and solid (as applicable) IDDSI (Steele et al., 2018) consistency recommendations, and the use of alternate means of nutrition. See Table 4 for details.

Table 4. Association Between MBSS Outcome Measures and Esophageal Clearance (Component 17) Scores

	P-value
Functional Oral Intake Scale (FOIS) Score	P = .6813
International Dysphagia Diet (IDDSI) Solid Level	P = .4764
International Dysphagia Diet (IDDSI) Liquid Level	P = .2283
Recommendation for Alternate Means of Nutrition	P = .6011

**P <0.05 Fisher's exact test of association*

4.1 FOIS Scores

The full range of FOIS scores (Crary et al., 2005) except for a score of 4 (total intake of a single consistency) was seen in this sample. Most participants (13/28, 46.43%) had a score of 7 or "total oral intake with no restrictions," followed by a score of 5 in 4/28 (14.29%) indicating "total oral intake of multiple consistencies requiring special preparation." A score of 6 or "total oral intake with no special preparation but must avoid specific food and liquid items" was seen in 2/28 (7.14%) of participants. Mid-range scores of 2 and 3 were each seen in 3 participants (10.71% respectively) indicating alternate means of nutrition with some degree of oral intake. A score of 1 or no oral intake was seen in 3 participants (10.71%). No statistical significance was seen in tests of association between FIOS scores and dichotomized component 17 (esophageal clearance) scores. See Table 4.

4.2 IDDSI Scores

IDDSI scores were only available for those participants whose recommendations included oral intake (25/28). Oral intake was classified using IDDSI scale scores (Steele et al., 2018) with scores for liquid and solid consistency recommendations. The most common IDDSI liquid consistency recommendation was for thin liquids (score of 0) in 16/25 (64%) of participants. "Mildly thick" (nectar-thick) liquids (score of 2) were recommended in 8/25 (32%) of participants. One participant (4%) was recommended for "moderately thick" (honey-thick) liquids (score of 3). The most common IDDSI solid recommendation was for regular solids in 11/22 (50%) of participants. A score of 6 or "soft and bite-sized" solids was recommended in 7/22 (31.82%) of participants. "Minced and moist" solids (score of 5) were recommended for one (4.54%) participant. Three (13.64%) participants were recommended for pureed solids (score of 4). No statistical significance was demonstrated between either IDDSI liquid or solid scores and the dichotomized component 17 (esophageal clearance) scores. See Table 4.

4.3 Alternate Means of Nutrition

Information for the presence of alternate means of nutrition was only available in 23 (85.19%) of post-lung transplant participants. The majority (65.22%) of participants had an alternate

means of nutrition, all had a small-bore feeding tube (e.g., Dobhoff or Corpak) present at the time of MBSS. See Table 4.

9. Sub-Group Analysis for Patients with Aspiration on MBSS

A subgroup analysis was performed for those seven patients (25%) who were identified as aspirating on their MBSS. The mean age for this group was 54.43 years (range 27-67). This group was predominantly male 6/7 (85.71%) and all participants identified as white. ESLD types were distributed as: 14.29% (1/7) with COPD, 28.57% (2/7) with CF, 28.57% (2/7) with IPF, and 28.57% (2/7) with ILD. Most participants (5/7, 71.43%) in this sub-group were surgically approached with a clamshell thoracotomy and 2/7 (28.57%) underwent a median sternotomy. Mean days from HRM was 421.5 (range 11-1881 days) compared to 548.6 days (range 11-2184) for pH-MII. Mean days from esophagram to lung transplant was 97.67 days (range 4-299). Mean days to MBSS post-transplant was 14.08 days (range 3-15) with a 95% confidence interval around the mean of 1.88 to 9.83 days.

Scores were dichotomized for comparison into "normal" vs. "abnormal" categories. For all MBSImP component scores, a score greater than zero was the threshold with the exceptions of components 1, 5, 15, and 16 for which a score of 1 is collapsed to a zero for aggregate “total” scores (Martin-Harris, 2015; Martin-Harris, 2017). PAS scores of 1-3 were considered normal (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999). FOIS scores were dichotomized into severely restricted oral intake (scores of 1-5) vs. full oral intake with minimal to no restrictions (scores of 6-7). IDDSI scores for liquids were separated at a cutoff point of 0 for no restrictions and 1-3 for any degree of restriction/altered viscosity. IDDSI solids were separated at a cutoff point of 7 for no restrictions to 4-6 for any degree of restriction/altered texture. See Table 5 For a full comparison of variables.

Table 5. Comparison of Swallowing Impairment and Outcome Measures in Patients with and without Aspiration

Swallowing Impairment and Outcome Measures	Full Cohort n = 28 n (%)	No Aspiration n =21 n (%)	Aspiration n =7 n (%)	Association (P-value)
MBSImP component 1 (lip closure)				P= 0.2883
C1 ≤ 1	22 (78.57)	15 (71.43)	7 (100)	
C1 ≥ 2	6 (21.43)	6 (28.57)	0 (0)	
MBSImP component 2 (tongue control during bolus hold)				P = 1.000
C2 = 0	18(66.67)	14 (66.67)	4 (66.67)	
C2 ≥ 1	9 (33.33)	7 (33.33)	2 (33.33)	
MBSImP component 3 (bolus prep/mastication)				P = 1.000
C3 = 0	11 (45.83)	9 (45)	2 (50)	
C3 ≥ 1	13 (54.17)	11 (55)	2 (50)	
MBSImP component 4 (bolus transport/lingual motion)				P = .6618
C4 = 0	16 (57.14)	11 (52.38)	5 (71.43)	
C4 ≥ 1	12 (42.86)	10 (47.62)	2 (28.57)	
MBSImP component 5 (oral residue) to component 17				P = 1.000
C5 ≤ 1	12 (42.86)	9 (42.86)	3 (42.86)	
C5 ≥ 2	16 (57.14)	12 (57.14)	4 (57.14)	
MBSImP component 6 (initiation of pharyngeal swallow)				P = 1.000
C6 = 0	2 (7.14)	2 (9.52)	0 (0)	
C6 ≥ 1	26 (92.86)	19 (90.48)	7 (100)	
MBSImP component 7 (velar elevation)				P = 1.000
C7= 0	27 (96.43)	20 (95.24)	7 (100)	
C7 ≥ 1	1 (3.57)	1 (4.76)	0 (0)	
MBSImP component 8 (laryngeal elevation)				*P = .0233**
C8 = 0	11 (39.29)	11 (52.39)	0 (0)	

C8 ≥ 1	17 (60.71)	10 (47.62)	7 (100)	
MBSImP component 9 (anterior hyoid excursion)				P = .0836
C9 = 0	13 (46.43)	12 (57.14)	1 (14.29)	
C9 ≥ 1	15 (53.57)	9 (42.86)	6 (85.71)	
MBSImP component 10 (epiglottic movement)				P = .0627
C10 = 0	18 (64.29)	16 (76.19)	2 (28.57)	
C10 ≥ 1	10 (35.71	5 (23.81)	5 (71.43)	
MBSImP component 11 (laryngeal vestibule closure)				*P = .0233**
C11 = 0	11 (39.29)	11 (52.38)	0 (0)	
C11 ≥ 1	17 (60.71)	10 (47.62)	7 (100)	
MBSImP component 12 (pharyngeal stripping wave)				P = .0764
C12 = 0	17 (60.71)	15 (71.43)	2 (28.57)	
C12 ≥ 1	11 (39.29)	6 (28.57)	5 (71.43)	
MBSImP component 13 (pharyngeal contraction)				P = 1.000
C13 = 0	20 (90.91)	15 (88.24)	5 (100)	
C13 ≥ 1	2 (9.09)	2 (11.76)	0 (0)	
MBSImP component 14 (pharyngoesophageal segment opening)				P = .6774
C14 = 0	18 (64.29)	14 (66.67)	4 (57.14)	
C14 ≥ 1	10 (35.71)	7 (33.33)	3 (42.86)	
MBSImP component 15 (tongue base retraction)				P = 1.000
C15 ≤ 1	17 (60.71)	13 (61.9)	4 (57.14)	
C15 ≥ 2	11 (39.29)	8 (38.1)	3 (42.86)	
MBSImP component 16 (pharyngeal residue)				P = 1.000
C16 ≤ 1	12 (42.86)	9 (42.86)	3 (42.86)	
C16 ≥ 2	16 (57.14)	12 (57.14)	4 (57.14)	

MBSImP component 17 (esophageal clearance)				P = .5453
C17 = 0	4 (14.29)	4 (19.05)	0 (0)	
C17 ≥ 1	24 (85.71)	17 (80.95)	7 (100)	
MBSImP Oral Total (OT) (mean, ± SD, 95% CI)	5.86, ± 3.36 (4.55, 7.16)	6.14, ± 3.8 (4.41, 7.87)	5.0, 1.29 (3.81, 619)	P = .5105
MBSImP Pharyngeal Total (PT) (mean, ± SD, 95% CI)	5.25, ±3.93 (3.73, 6.77)	4.57, ±3.82 (2.83, 6.31)	7.29, ±3.82 (3.76, 10.82)	P = .0986
Penetration-Aspiration Scale (PAS) score				*P < .0001*
PAS 1-3	20 (71.43)	20 (95.24)	0 (0)	
PAS ≥ 4	8 (28.57)	1 (4.76)	7 (100)	
Functional Oral Intake Scale (FOIS) score				*P = .0101**
FOIS ≥ 6	17 (53.57)	14 (66.67)	1 (14.29)	
FOIS 5-3	7 (25)	5 (23.81)	2 (28.57)	
FOIS ≤ 2	6 (21.43)	2 (9.52)	4 (57.14)	
International Dysphagia Diet (IDDSI) liquid score				P = .1162
IDDSI liquid score = 0	16 (64)	15 (71.43)	1 (25)	
IDDSI liquid score 1-3	9 (36)	6 (28.57)	3(75)	
International Dysphagia Diet (IDDSI) solid score				P = .1914
IDDSI solid score = 7	11 (39.29)	10 (47.62)	1 (14.29)	
IDDSI solid score = 4-6	17 (60.71)	11 (52.38)	6 (85.71)	
Presence of alternate means of nutrition	15 (65.22)	10 (58.82)	5 (83.33)	P = .3690

**P < 0.05 Fisher's exact test of association for categorical variables, Wilcoxon Rank Sum/Mann Whitney-U test of association for continuous variables*

Compared to those participants who did not aspirate, the group that aspirated had more abnormal individual MBSImP pharyngeal component scores. Specifically, component 8 (laryngeal elevation) P = .0233, component 9 (anterior hyoid excursion) P = .0836, component 10 (epiglottic movement) P = 0.627, component 11 (laryngeal vestibule closure) P = .0233, and component 12 (pharyngeal stripping wave) P = .0764 although all did not reach statistical significance, as seen in Table 5. All participants in this subgroup had a lower bolus head at the onset of the pharyngeal swallow (component 6). Reduced laryngeal elevation at the height of

the swallow (component 8) was seen with 100% of this group having a score of 1 or, “partial superior movement of thyroid cartilage/partial approximation of arytenoids to epiglottic petiole.” All participants in this subgroup demonstrated reduced laryngeal vestibular closure (component 11) with 100% having a score of 1 or, “incomplete; narrow column of air/contrast in laryngeal vestibule.” All component 17 scores were abnormal and were distributed as 42.86% (3/7) having a score of 1, 42.86% (3/7) having a score of 2, and 14.29% (1/7) having a score of 3. See Table 5 for further detail.

We determined the swallowing severity of this subgroup using the Beall et al. (2020) severity classification for MBSImP oral and pharyngeal totals. Both oral total (OT) and pharyngeal total (PT) impairments fell into the functional-mild classification for all participants who were identified as aspirating, compared to 85.71% of those participants who did not aspirate having a functional-mild OT and 95.24% had a functional-mild PT. PAS scores demonstrated a statistically significant difference between normal and abnormal component 17 groups ($P < .0001$) with normal being scores of 1-3 and abnormal being scores of 4 or more (see Table 5). Because this subgroup consists of patients who aspirated, PAS scores were all abnormal and ranged from 6-8 with 14.29% having a PAS score of 6, 14.29% having a PAS score of 7, and 71.43% having a PAS score of 8. Meaning that for most participants who aspirated, they did so silently. All participants who were identified as aspirating had abnormal esophageal clearance. See Table 5.

Swallowing outcome measures in the form of FOIS and IDDIS score indicated more restricted PO consistencies in this group with a higher proportion receiving alternate means of nutrition. FOIS scores in this subgroup were lower (more restrictive) and when compared to component 17 scores yielded statistical significance ($P = .0101$). See Table 5. Only one participant (14.29%) had a FOIS of 7 or “total oral intake with no restrictions.” The most common FOIS score in this group was a 1, or “no oral intake” in 3/7 (42.86%). Scores of 2 or 3 were each seen in one participant, indicating a combination of alternate means of nutrition and oral intake in 28.58%. A score of 5, or “total oral intake of multiple consistencies requiring special preparation” was seen in one participant (14.29%). IDDSI scores were higher for liquids and lower for solids

demonstrating more restrictive consistencies for this group. Only 4/7 (57.14%) of participants had liquid recommendations and only 3/7 (42.86%) had solid recommendations owing to recommendations for nothing by mouth (nil per os, NPO). Of these, only one participant (25%) had a recommendation for thin liquids, the remaining 75% were recommended for IDDSI level 2 “mildly thick”, or nectar-thick, liquids. One participant (33.33%) was recommended for IDDSI level 7 or “regular” solids. One participant (33.33%) had a recommendation for IDDSI level 6 “soft and bite-sized” solids. One participant (33.33%) had a recommendation for IDDSI level 4 “pureed” solids. Most (83.33%) had alternate means of nutrition at the time of the MBSS in the form of a small-bore feeding tube (e.g., Dobhoff or Corpak). See Table 5 for details.

Regarding pre-transplant esophageal assessments, 66.67% of those participants who aspirated had an abnormal pre-transplant HRM study. Two-thirds (66.67%) of those participants who were identified as aspirating had an abnormal pre-transplant pH-MII study. Only 7 participants had a pre-transplant barium esophagram with 6 (85.71%) being abnormal. Of those with abnormal pre-transplant barium esophagram findings, 2/6 (33%) were later identified as aspirating on their post-lung transplant MBSS.

10. Sensitivity Analysis

We found that 85.71% of this population had abnormal esophageal clearance that was statistically different ($P < .0001$) from our pre-specified value (33%) from a prior study. However, we performed a sensitivity analysis to examine if this proportion differed at higher thresholds of 48.67% (Reedy et al., 2021) and 63.41% (Gullung et al., 2012), our findings remained statistically significant ($P < .0001$ and $P = .0143$, respectively). A post-hoc power analysis was completed at the pre-specified threshold of 33% (Miles et al., 2015) which demonstrated power of >99.9% power to find the difference. A power analysis at the higher threshold of 48.67% (Reedy et al., 2021) yielded a power of 98.7%. However, the power at the highest threshold of 63.41% was insufficient for our sample size, yielding a power of 0.629.

DISCUSSION:

Abnormal esophageal clearance patterns were identified on the MBSS of 85.71% of post-lung transplant participants. Abnormalities were identified in both pharyngeal and esophageal aspects of swallowing, however, the most common finding amongst these post-lung transplant patients was abnormal MBSImP component 17 (esophageal clearance) scores. This is contradictory to our pre-study hypothesis that post-lung transplant patients would have an acute, primarily oropharyngeal impairment given the risks for oropharyngeal dysphagia in this population. The esophageal contribution to the overall pathophysiology and clinical presentation of dysphagia should not be overlooked in the post-lung transplant population.

Concern for Aspiration Post-Lung Transplantation

Earlier research in the post-lung transplant population only reported laryngeal penetration and aspiration without other measures for physiologic impairment. Atkins et al. (2007) and Miles et al. (2020) reported aspiration occurring in 63.8% and 75% of their post-lung transplant cohorts, respectively. Baumann et al., (2017) reported aspiration and/or deep laryngeal penetration equivocally in 62% of their post-lung transplant cohort making interpretation challenging as some degree of laryngeal penetration is a normal variation of swallow physiology (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999). And, beyond that, what may be normal physiology in healthy individuals may represent a disadvantage in those same persons in the context of illness. We identified a lower incidence of aspiration in our cohort (25%) compared to previous findings. The significantly lower incidence of aspiration in our cohort may be explained by the fact that only a subgroup of previous studies' cohorts received an instrumental assessment. Those participants who did undergo instrumental assessment in previous studies likely had a greater risk of aspiration and/or more overt signs and symptoms of dysphagia on a clinical swallowing evaluation (CSE). Whereas our entire post-lung transplant cohort received an MBSS. Given these findings, instrumental swallowing assessments should not be delayed with the assumption of poor swallow function post-transplant. Rather, much of this cohort was initiated on P.O. relatively soon after transplant.

It should be noted that prandial aspiration from oropharyngeal swallowing impairment is just one form of aspiration. Post-prandial aspiration can occur as a consequence of esophageal pathophysiology (e.g., GEJ obstruction, reflux). In our cohort, 39.29% of participants with abnormal clearance were identified as having retrograde flow. An additional 10.17% had retrograde flow which exited the esophageal body through UES into the pharynx. For patients who maintain an upright posture without spinal deformations, most pulmonary manifestations of aspiration are in the gravity-dependent lung zones. All aspiration implies abnormal airway invasion via the larynx and trachea. The trachea descends through the neck and into the chest where the airway then begins its hierarchical divide, starting with the bifurcation at the carina, dividing into the two mainstem bronchi. The separation is not symmetric, however, and the less acute angle of the right mainstem bronchus accounts for the preference of aspirated contents to enter the right lung (Lumb, 2017). Though the physical manifestations of aspiration (e.g., pneumonia) can be determined radiographically, the appearance of "aspiration pneumonia" on a chest x-ray can be equivocal for prandial and post-prandial aspiration that occurs in the upright patient. The same can be said for non-prandial aspiration that occurs in the upright position, as with the aspiration of tube feeds.

Allograft injury is of paramount concern post-lung transplant though the influence of dysphagia and the role of aspiration is just beginning to be explored. Concerns for aspiration frequently default to prandial aspiration as related to primary oropharyngeal dysphagia. However, in this population, we identified that all participants who aspirated had abnormal esophageal clearance patterns. Dedicated esophageal testing in the post-lung transplant population is often limited, due to the acute concerns for aspiration, as all swallowing assessments involve ingesting some type of bolus.

Clinical Implications for Post-Lung Transplant Assessment of Swallowing

In this population, with pre-and post-transplant dysphagia risks, a clinical swallowing evaluation (CSE) alone is inadequate to make recommendations for P.O. intake, assess physiology, and plan interventions. A CSE is insufficient given the lack of standardization and inability to rule out silent aspiration (Garand et al., 2020; O'Horo et al., 2016). Most patients (71.43%) in our study

that were identified as aspirating did so silently. This is in line with previous findings of silent aspiration in earlier studies ranging from 63 to 77.6% (Atkins et al., 2007; Miles et al., 2020). An instrumental assessment (FEES vs. MBSS) is not optional in this population and a FEES may be preferable as the first-line instrumental assessment. Ideally, a FEES would precede the MBSS in this population given the fact that these patients are in critical care post-transplant and the potential for laryngeal injury. An MBSS should follow shortly thereafter given the likelihood of impairment across the swallowing continuum. Though, minimally, an MBSS should be standard of care in this population to determine impairments across the 17 physiologic components identifiable on fluoroscopy (Martin-Harris et al., 2008) and make the most appropriate recommendations.

One consideration in the assessment, and potentially intervention, for dysphagia is the unexplored role of respiratory assessment as a standard part of a post-lung transplant evaluation. Assessing respiratory-swallow coordination post-transplant may provide additional, critical information regarding the unique interactions between the aerodigestive systems. Respiratory-swallow training has proven both feasible (Hopkins-Rossabi, 2020) and beneficial in many populations (Anthukorala et al., 2014; Curtis et al., 2020; Martin-Harris, McFarland, Hill, et al., 2015) as has respiratory muscle strength training (Arnold & Bausek, 2020; Brooks et al., 2019; Eom et al., 2017; Hegland et al., 2016; Hutcheson et al., 2018; Plowman et al., 2018) though both are unexplored in this population (pre-and post-lung transplant). However, these interventions and assessments are unexplored in this population. For post-transplant patients, treating SLPs should work closely with the pulmonary transplant team to determine RMST and cough testing candidacy which will be unique in every patient case. To date, respiratory-swallow coordination research outcomes have been limited to the oropharynx (Brodsky et al, 2010; Hopkins-Rossabi, 2019; Martin-Harris, 2008; Martin-Harris et al, 2003, Martin-Harris et al, 2005; Martin-Harris, Michel & Castell, 2005; McFarland et al., 2016; Wheeler-Hegland et al., 2011), thereby limiting our understanding of the impact of respiratory-swallow coordination on esophageal pathophysiology and the swallowing continuum. The lower esophageal sphincter (LES) is dependent upon, and external structure is provided by, the crural aspect of the

diaphragm. Intrathoracic pressures related to respiration impact on the esophagus: the maintenance of the esophagus as collapsed at rest is related to negative intrathoracic pressures, which become more negative upon inspiration (Turbyville, 2009). These pressures provide traction on the aerodigestive continuum, specifically to the larynx, trachea, and esophagus (McFarland et al., 2016). Another pulmonary consideration is the inclusion of standardized cough testing in the post-lung transplant patient. The cough strength to clear sputum has been identified at ≥ 160 L/min (Bach & Saporito, 1996). Adequate cough strength at this threshold has been associated with a lower re-intubation risk compared to ≤ 59 L/min being associated with re-intubation in recently extubated patients (Jiang et al., 2017). Handheld cough testing has been investigated in other populations with a 90.9% sensitivity, 80% specificity to predict dysphagia at a threshold of 42.5 L/min (Curtis & Troche, 2020). This might be an especially important assessment for post-lung transplant patients even before initiating any trials of oral intake. And is an important factor to assess, particularly whose instrumental swallowing assessments may be borderline for PO intake.

Measures of Swallowing Impairment and Abnormal Esophageal Clearance

Interestingly, only the association between the dichotomized component 17 (esophageal clearance) (normal C17 = 0, abnormal C17 ≥ 1) and component 9 (anterior hyoid excursion) demonstrated statistical significance. The unarticulated, crescent-shaped hyoid bone is one structure of the hyolaryngeal complex. Anchored to the base of tongue via the suprahyoid muscles, the stylohyoid ligament attaches to the styloid process of the temporal bone bilaterally (AlJulaih & Menezes, 2019). Inferiorly, the thyroid ligament and thyrohyoid connect to the superior aspects of the larynx to the hyoid. The mylohyoid, which constitutes much of the floor or mouth elevates the hyoid and tongue via the trigeminal nerve (V). The posterior belly of the digastric functions to elevate the hyoid superiorly. The stylohyoid, innervated by the facial nerve (VII) lifts and retracts the hyoid bone, thereby elevating the base of tongue and elongating the floor of the mouth. Humbert et al. (2013) identified adaptive motor learning when electrical stimulation was used to provide resistance against the hyolaryngeal elevators in healthy adult participants. Given that anterior hyoid excursion is one of the mechanisms for

opening of the upper esophageal sphincter, whether these study findings are related to some maladaptive compensation remains to be seen. The significance of only this single component likely reflects the small sample size. Using the OT and PT MBSImP severity classification (Beall et al., 2020), the oral and pharyngeal totals were vastly within ranges for functional swallowing to mild impairment at 89.29% and 96.43%, respectively compared to the low proportion of patients that had normal esophageal clearance (14.29%).

Pre-Lung Transplant Clinical Considerations:

Despite the evidence for dysphagia in this population, there is no standardized pre-transplant workup that includes the swallowing continuum in its entirety. Partly because there is no single test that evaluates swallowing as a whole and that, despite the evidence to support dysphagia in the end-stage lung disease population (Cassani et al., 2015; Cvejic et al., 2011; Garand et al., 2018; Good-Fraturelli et al., 2000; Gross et al., 2009; Martin-Harris & McFarland, 2013; Martin-Harris et al., 2015; Shaker et al., 1992), instrumental assessment of swallowing may only occur for these patients during acute ESLD exacerbations or during other acute hospitalizations. Given the nature of swallowing and swallowing disorders, it may be useful to incorporate MBSS and esophagram as standard tests in the pre-transplant workup. Despite the concern for the development of allograft-threatening Bronchiolitis Obliterans Syndrome (BOS) in this population, there is currently no research that directly investigates the potential link between dysphagia-related aspiration and BOS post-lung transplant.

There can be an expected increase in pre-lung transplant barium esophagrams in this population related to the change in diagnostic criteria in the latest version of the Chicago Classification (v.40) (Yadlapati et al., 2021). Now, certain diagnoses will require or rely more heavily on symptoms and secondary testing (e.g., barium esophagram) for a confirmation of certain diagnoses. The latest version (v4.0) includes recommendations for “supportive measures,” as with the Multiple Rapid Swallow (MRS) challenge, in addition to the standard protocol of single 10 mL swallows. This adjunct to the base protocol may help to better identify those patients with certain esophageal pathophysiology (Fornari et al., 2009; Leopold et al.,

2019) which might be especially pertinent in pre-lung transplant manometry. Despite the strength of HRM testing with a standardized protocol and periodically updated classification criteria, the question remains as to how long HRM results remain valid in this population. In other words, there is no threshold for when repeat testing would be indicated. This consideration is especially pertinent in the ESLD progression would likely result in more abnormal intrathoracic pressures. Our cohort demonstrated a vast range of times from HRM completion to transplantation (mean 406.35 days, range 11-1,881). Given the nature of allograft transplantation, standardizing a timing threshold for pre-transplant studies would be difficult, if not impossible. However, establishing thresholds at which repeat testing is indicated would be a valuable step in refining pre-transplant swallowing diagnostic guidelines.

Another important factor in pre-transplant workup may be to enhance surgical considerations as with intubation, yielding a more tailored approach. Plowman et al. (2021) demonstrated three-fold greater odds for developing laryngeal injury and/or dysphagia with ETT of 8.0 or greater in their post-cardiothoracic surgery cohort. Krisciunas et al. (2020) identified that patients with an ETT of 8.0 or greater had a statistically significantly greater incidence of aspiration and development of granulation tissue in their cohort of patients with respiratory failure. Both studies evaluated patients within 72 hours of extubation and used Fiberoptic Endoscopic Evaluation of Swallowing (FEES). Interestingly, none of our cohort was found to have been intubated with any ETT smaller than 8.0 French tube, although 8 participants had missing values for this variable as it was absent from the electronic health record.

Without comparative, standardized, pre-and post-transplant testing we are left without critical information on the expected post-transplant course for these patients. Work towards standardizing swallowing assessments pre- and post-lung transplant including a protocol for readiness, order of assessments (e.g., FEES vs. MBSS first which may depend on facility availability), and routine cough testing would be advantageous. A larger, more heterogeneous post-lung transplant sample would be beneficial to expand our understanding of dysphagia in this population. With continued research in this unique population, we may be able to glean

practical clinical considerations based on pre-lung transplant risk factors for dysphagia, risk factors based on end-stage lung disease type, as well as surgical factors that may increase the likelihood for laryngeal injury and dysphagia. A pre-transplant MBSS is a critical piece to pre-transplant assessment to determine the pre-transplant presence of dysphagia and/or risk of aspiration. Currently, the proportion of pre-lung transplant candidates with dysphagia is unexplored. In the head and neck cancer population, SLPs routinely provide pre-surgical (e.g., pre-laryngectomy) counseling. Pre-lung transplant SLP consultations would facilitate the initiation of pre-habilitative dysphagia intervention for lung transplant patients. Pre-transplant SLP consultation would also allow for educating patients and families (familiarizing with anatomy, the concept of dysphagia, etc.). Skill or strength-based dysphagia exercises might be introduced for familiarity, or to practice in the case of dysphagia identified on a pre-transplant MBSS.

Clinical Implications of Omitting Esophageal Considerations:

Dysphagia across the swallowing continuum was identified in our post-lung transplant cohort. Although the most commonly occurring swallowing abnormality in this cohort was that of abnormal esophageal clearance seen in 87.51% of participants. Esophageal pathophysiology may be expected in the post-lung transplant population - especially for those patients having abnormal esophageal testing pre-transplant. However, a worsening of esophageal function and/or a difference in manometric classification has been demonstrated post-transplant (Cangemi et al., 2020; Ciriza de Los Ríos, 2018; Masuda et al., 2019; Masuda et al., 2020; Tangaroonsanti et al., 2017). In fact, an acute esophageal decompensation might be expected owing to intubation, surgical manipulation of the thoracic cavity, vulnerability of the vagus nerve and its branches during surgery, post-operative edema, and physiologic adjustment to the allograft. Though what type of esophageal recovery can be expected, and in which patients, is unknown as research investigating post-lung transplant esophageal function has only come out in recent years (Cangemi et al., 2020; Ciriza de los Ríos et al., 2018; Gouynou et al., 2020; Masuda et al. 2018; Masuda et al., 2019; Masuda et al., 2020; Miele et al., 2016; Posner et al.,2019; Tangaroonsanti et al., 2017; Tangaroonsanti et al., 2019).

Though swallowing occurs in a “top down” manner, we cannot ignore the possible esophageal contribution with “bottom up” manifestations. This interrelationship has been established as early as 1985 with historic expert opinion (Jones et al., 1985; Jones et al., 1987; Triadafilopoulos, 1992) and, more recently the scientific evidence base continues to grow (Gullung et al., 2012; Lever et al., 2007; Madhavan et al., 2015; Miles et al., 2015; Miles et al., 2019; Miles et al., 2017; O’Rourke et al., 2014; Ortiz et al., 2019; Reedy et al., 2021; Watts et al., 2019). For all appropriate patients, esophageal visualization should be performed during the MBSS. In a systematic review, we identified abnormal esophageal clearance on MBSS in 48.67% of participants (Reedy et al., 2021). Abnormal clearance (component 17) has been identified as high as 63.41% (Gullung et al., 2012) in a heterogeneous sample. And, though non-diagnostic, esophageal visualization may provide insights into the potential for esophageal pathophysiology, especially in those patients whose swallowing may preclude dedicated esophageal testing (e.g., HRM, barium esophagram). In their study 2012 study, Gullung et al. demonstrated that when compared to abnormalities identified via HRM with Multichannel Intraluminal Impedance (HRM+MII) component 17 scores ≥ 1 demonstrated statistical significance ($P < .001$). Abnormal component 17 scores compared to HRM+MII (CC v2.0), yielded a sensitivity of 80% and a specificity of 48%. As outlined in our earlier work (Reedy et al., 2021), non-diagnostic esophageal visualization during the MBSS is feasible, within the scope of the SLP, and is a critical portion of the MBSS. Clinicians (e.g., SLP, pulmonologists, gastroenterologists, laryngologists) cannot underestimate the impact of esophageal abnormality in this population. And, given that all patients who aspirated had abnormal esophageal clearance, this may be an especially pertinent factor in determining candidacy for PO intake in these patients. Additionally, the presence of oral and/or pharyngeal abnormalities should not be presumed to be isolated to the oropharynx.

Future Considerations:

Work to standardize a more comprehensive swallowing assessment pre- and post-lung transplant is needed. This would include a protocol for readiness, order of assessments (e.g., FEES vs. MBSS first which may depend on facility availability), cough testing, and more

comprehensive consideration of the swallowing continuum when considering readiness for PO intake. With continued research in this unique population, we may be able to glean practical clinical considerations based on pre-lung transplant risk factors for dysphagia, risk factors based on end-stage lung disease type, as well as surgical factors that may increase the likelihood for laryngeal injury and dysphagia.

Appropriately trained speech pathologists are uniquely poised to bridge the gaps between diagnostics and service delivery resulting from the divide between assessments of the oropharynx vs. the esophagus. Speech-language pathologists (SLP) should be considered a vital part of the pre-and post-lung transplant interdisciplinary team with a unique perspective on respiration and swallowing. These skills are especially pertinent when considering the medical sub-specialties these functions span (e.g., pulmonology, laryngology, gastroenterology, neurology). However, it should be noted that this would be a sub-specialty and the benefit of additional training for the knowledge and skills required to work in this population cannot be undervalued.

Limitations:

This study has several limitations. First, as with all data extraction from electronic health records, it is subject to human error and missingness. The study has a small sample size and was performed retrospectively at a single site. The study was powered to detect a difference in proportions compared to a constant and not for associations between measures of swallowing impairment and outcome measures. Second, esophageal visualization to determine esophageal clearance is not diagnostic; however, work towards dedicated esophageal assessments for those patients who aspirate is critical, especially in this population.

Despite the benefit of a standardized MBSS protocol and assessment, in the form of the MBSImP, there is Inherent subjectivity related to clinician decision-making for outcome measures. FOIS, IDDSI levels, and the recommendation for alternate means of nutrition are

clinician dependent. The clinical decision-making regarding abnormal esophageal clearance identified on the MBSS and recommendations for P.O. intake is unexplored.

CONCLUSION:

There is a high proportion of post-lung transplant patients who will develop dysphagia in the acute phase of their recovery. This study found that 85.71% of post-lung transplant patients had abnormal esophageal clearance identified during their MBSS; and that all participants who aspirated on their MBSS had some form of abnormal esophageal clearance. Though acute dysphagia may be anticipated in this population, our understanding of the influence of dysphagia across the swallowing continuum is limited. These post-lung transplant patients are particularly susceptible to be incompletely diagnosed and treated because the diagnosis of dysphagia in the acute phase of recovery invariably defaults to oropharyngeal, related to surgical and intubation risks, and the esophageal contribution to their symptoms is not routinely assessed post-transplant and may go overlooked as biomedical orthodoxy continues to perpetuate swallowing as a three-phase act. The assessment of dysphagia in this population requires instrumental assessment, and the esophageal contribution to overall swallowing impairment in this population cannot be underestimated.

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References:

1. Adegunsoye, A., Strek, M. E., Garrity, E., Guzy, R., & Bag, R. (2017). Comprehensive Care of the Lung Transplant Patient. Chest, 152(1), 150–164. https://doi.org/10.1016/j.chest.2016.10.001

2. Ahya, V. N., & Diamond, J. M. (2019). Lung Transplantation. The Medical clinics of North America, 103(3), 425–433. https://doi.org/10.1016/j.mcna.2018.12.003

3. Altman, K. W., Yu, G. P., & Schaefer, S. D. (2010). Consequence of dysphagia in the hospitalized patient: impact on prognosis and hospital resources. *Archives of otolaryngology--head & neck surgery*, *136*(8), 784–789. https://doi.org/10.1001/archoto.2010.129

4. Athukorala, R. P., Jones, R. D., Sella, O., & Huckabee, M. L. (2014). Skill training for swallowing rehabilitation in patients with Parkinson's disease. Archives of Physical Medicine and Rehabilitation, 95(7), 1374–1382. https://doi.org/10.1016/j.apmr.2014.03.001

5. Arnold, R. J., & Bausek, N. (2020). Effect of respiratory muscle training on dysphagia in stroke patients-A retrospective pilot study. *Laryngoscope investigative otolaryngology*, *5*(6), 1050–1055. https://doi.org/10.1002/lio2.483

6. Atkins, B. Z., Petersen, R. P., Daneshmand, M. A., Turek, J. W., Lin, S. S., & Davis, R. D., Jr (2010). Impact of oropharyngeal dysphagia on long-term outcomes of lung transplantation. *The Annals of thoracic surgery*, *90*(5), 1622–1628. https://doi.org/10.1016/j.athoracsur.2010.06.089

7. Atkins, B. Z., Trachtenberg, M. S., Prince-Petersen, R., Vess, G., Bush, E. L., Balsara, K. R., Lin, S. S., & Davis, R. D., Jr (2007). Assessing oropharyngeal dysphagia after lung transplantation: altered swallowing mechanisms and increased morbidity. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation*, *26*(11), 1144–1148. https://doi.org/10.1016/j.healun.2007.07.038

8. Au, J., Hawkins, T., Venables, C., Morritt, G., Scott, C. D., Gascoigne, A. D., Corris, P. A., Hilton, C. J., & Dark, J. H. (1993). Upper gastrointestinal dysmotility in heart-lung transplant recipients. *The Annals of thoracic surgery*, *55*(1), 94–97. https://doi.org/10.1016/0003-4975(93)90480-6

9. Bach, J. R., & Saporito, L. R. (1996). Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. *Chest*, *110*(6), 1566–1571. https://doi.org/10.1378/chest.110.6.1566

10. Baumann, B., Byers, S., Wasserman-Wincko, T., Smith, L., Hathaway, B., Bhama, J., Shigemura, N., Hayanga, J., D'Cunha, J., & Johnson, J. T. (2017). Postoperative Swallowing Assessment After Lung Transplantation. *The Annals of thoracic surgery*, *104*(1), 308–312. https://doi.org/10.1016/j.athoracsur.2017.01.080

11. Black, R. J., Bogaardt, H., McCabe, P., Glanville, A. R., MacDonald, P., & Madill, C. (2019). Clinical predictors for oropharyngeal dysphagia and laryngeal dysfunction after lung and heart transplantation. *International journal of language & communication disorders*, *54*(6), 894–901. https://doi.org/10.1111/1460-6984.12492

12. Black, R., McCabe, P., Glanville, A., Bogaardt, H., MacDonald, P., & Madill, C. (2020). Oropharyngeal dysphagia and laryngeal dysfunction after lung and heart transplantation: A systematic review. *Disability and rehabilitation*, *42*(15), 2083–2092. https://doi.org/10.1080/09638288.2018.1552326

13. Brodsky, M. B., McFarland, D. H., Dozier, T. S., Blair, J., Ayers, C., Michel, Y., Gillespie, M. B., Day, T. A., & Martin-Harris, B. (2010). Respiratory-swallow phase patterns and their relationship to swallowing impairment in patients treated for oropharyngeal cancer. Head & neck, 32(4), 481–489. https://doi.org/10.1002/hed.21209

14. Brooks, M., McLaughlin, E., & Shields, N. (2019). Expiratory muscle strength training improves swallowing and respiratory outcomes in people with dysphagia: A systematic review. *International journal of speech-language pathology*, *21*(1), 89–100. https://doi.org/10.1080/17549507.2017.1387285

15. Cangemi, D. J., Flanagan, R., Bailey, A., Staller, K., & Kuo, B. (2020). Jackhammer Esophagus After Lung Transplantation: Results of a Retrospective Multicenter Study. *Journal of clinical gastroenterology*, *54*(4), 322–326. https://doi.org/10.1097/MCG.0000000000001254

16. Cassiani, R. A., Santos, C. M., Baddini-Martinez, J., & Dantas, R. O. (2015). Oral and pharyngeal bolus transit in patients with chronic obstructive pulmonary disease. International journal of chronic obstructive pulmonary disease, 10, 489–496. https://doi.org/10.2147/COPD.S74945

17. Ciriza de Los Ríos, C., Canga Rodríguez-Valcárcel, F., de Pablo Gafas, A., Castel de Lucas, I., Lora Pablos, D., & Castellano Tortajada, G. (2018). Esophageal motor disorders are frequent during pre and post lung transplantation. Can they influence lung rejection?. *Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva*, *110*(6), 344–351. https://doi.org/10.17235/reed.2018.5263/2017

18. Crary, M., Carnaby Mann, G.D., Groher, M.E. (2005). Psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil, 86 (8): 1516-20. doi: 10.1016/j.apmr.2004.11.049

19. Curtis, J. A., & Troche, M. S. (2020). Handheld Cough Testing: A Novel Tool for Cough Assessment and Dysphagia Screening. *Dysphagia*, *35*(6), 993–1000. https://doi.org/10.1007/s00455-020-10097-z

20. Curtis, J. A., Dakin, A. E., & Troche, M. S. (2020). Respiratory-Swallow Coordination Training and Voluntary Cough Skill Training: A Single-Subject Treatment Study in a Person With Parkinson's Disease. *Journal of speech, language, and hearing research : JSLHR*, *63*(2), 472–486. https://doi.org/10.1044/2019_JSLHR-19-00207

21. Cvejic, L., Harding, R., Churchward, T., Turton, A., Finlay, P., Massey, D., Bardin, P. G., & Guy, P. (2011). Laryngeal penetration and aspiration in individuals with stable COPD. Respirology (Carlton, Vic.), 16(2), 269–275. https://doi.org/10.1111/j.1440-1843.2010.01875.x

22. da Rosa, F. B., Pasqualoto, A. S., Steele, C. M., & Mancopes, R. (2020). Oral and oropharyngeal sensory function in adults with chronic obstructive pulmonary disease. American journal of speech-language pathology, 29(2), 864–872. https://doi.org/10.1044/2019_AJSLP-19-00095

23. Daggett A, Logemann J, Rademaker A, Pauloski B. (2006). Laryngeal penetration during deglutition in normal subjects of various ages. Dysphagia, 270-274. doi: 10.1007/s00455-006-9051-6

24. Davis, C. S., Shankaran, V., Kovacs, E. J., Gagermeier, J., Dilling, D., Alex, C. G., Love, R. B., Sinacore, J., & Fisichella, P. M. (2010). Gastroesophageal reflux disease after lung transplantation: pathophysiology and implications for treatment. Surgery, 148(4), 737–745. https://doi.org/10.1016/j.surg.2010.07.011

25. Eom, M. J., Chang, M. Y., Oh, D. H., Kim, H. D., Han, N. M., & Park, J. S. (2017). Effects of resistance expiratory muscle strength training in elderly patients with dysphagic stroke. *NeuroRehabilitation*, *41*(4), 747–752. https://doi.org/10.3233/NRE-172192

26. Estenne, M., Maurer, J. R., Boehler, A., Egan, J. J., Frost, A., Hertz, M., Mallory, G. B., Snell, G. I., & Yousem, S. (2002). Bronchiolitis obliterans syndrome 2001: an update of the diagnostic criteria. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation*, 21(3), 297–310. https://doi.org/10.1016/s1053-2498(02)00398-4

27. Fisichella, P. M., & Jalilvand, A. (2014). The role of impaired esophageal and gastric motility in end-stage lung diseases and after lung transplantation. *The Journal of surgical research*, *186*(1), 201–206. https://doi.org/10.1016/j.jss.2013.09.023

28. Garand, K., 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

29. Garand, K. L., Strange, C., Paoletti, L., Hopkins-Rossabi, T., & Martin-Harris, B. (2018). Oropharyngeal swallow physiology and swallowing-related quality of life in underweight patients with concomitant advanced chronic obstructive pulmonary disease. International journal of chronic obstructive pulmonary disease, 13, 2663–2671. https://doi.org/10.2147/COPD.S165657

30. Gasper, W. J., Sweet, M. P., Golden, J. A., Hoopes, C., Leard, L. E., Kleinhenz, M. E., Hays, S. R., & Patti, M. G. (2008). Lung transplantation in patients with connective tissue disorders and esophageal dysmotility. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus*, *21*(7), 650–655. https://doi.org/10.1111/j.1442-2050.2008.00828.x

31. Giulini, L., Mittal, S. K., Masuda, T., Razia, D., Csucska, M., Walia, R., Smith, M. A., & Bremner, R. M. (2021). Factors associated with esophageal motility improvement after bilateral lung transplant in patients with an aperistaltic esophagus. *The Journal of thoracic and cardiovascular surgery*, S0022-5223(21)00027-1. Advance online publication. https://doi.org/10.1016/j.jtcvs.2020.12.130

32. Good-Fratturelli, M. D., Curlee, R. F., & Holle, J. L. (2000). Prevalence and nature of dysphagia in VA patients with COPD referred for videofluoroscopic swallow examination. *Journal of communication disorders*, *33*(2), 93–110. https://doi.org/10.1016/s0021-9924(99)00026-x

33. Gouynou, C., Philit, F., Mion, F., Tronc, F., Sénéchal, A., Giai, J., Rabain, A. M., Mornex, J. F., & Roman, S. (2020). Esophageal Motility Disorders Associated With Death or Allograft Dysfunction After Lung Transplantation? Results of a Retrospective Monocentric Study. *Clinical and translational gastroenterology*, *11*(3), e00137. https://doi.org/10.14309/ctg.0000000000000137

34. Grass, F., Schäfer, M., Cristaudi, A., Berutto, C., Aubert, J. D., Gonzalez, M., Demartines, N., Ris, H. B., Soccal, P. M., & Krueger, T. (2015). Incidence and Risk Factors of Abdominal Complications After Lung Transplantation. *World journal of surgery*, *39*(9), 2274–2281. https://doi.org/10.1007/s00268-015-3098-1

35. Gross, R., Atwood Jr., C.W., Ross, S.B., Olszewski, J.W., Eichhorn, K.A. (2009). The coordination of breathing and swallowing in chronic obstructive pulmonary disease. Am J Resp Crit Care Med, 179:559-545. Doi: 10.1164/rccm.200807-11390C

36. Gullung, J. L., Hill, E. G., Castell, D. O., & Martin-Harris, B. (2012). Oropharyngeal and esophageal swallowing impairments: their association and the predictive value of the modified barium swallow impairment profile and combined multichannel intraluminal impedance-esophageal manometry. *The Annals of otology, rhinology, and laryngology*, *121*(11), 738–745. https://doi.org/10.1177/000348941212101107

37. Gupta, B., & Gupta, L. (2019). Significance of the outer diameter of an endotracheal tube: a lesser-known parameter. *Korean journal of anesthesiology*, *72*(1), 72–73. https://doi.org/10.4097/kja.d.18.00056

38. Hegland, K. W., Davenport, P. W., Brandimore, A. E., Singletary, F. F., & Troche, M. S. (2016). Rehabilitation of Swallowing and Cough Functions Following Stroke: An Expiratory Muscle Strength Training Trial. Archives of physical medicine and rehabilitation, 97(8), 1345–1351. https://doi.org/10.1016/j.apmr.2016.03.027

39. Hopkins-Rossabi, T., Curtis, P., Temenak, M., Miller, C., Martin-Harris, B. (2019). Respiratory phase and lung volume patterns during swallowing in healthy adults: A systematic review and meta-analysis*. J Sp Lang Hear Res,* 62: 868-882. https://doi.org/10.1044/2018_JSLHR-S-18-0323.

40. Hopkins-Rossabi, T., Rowe, M., McGrattan, K., Rossabi, S., & Martin-Harris, B. (2020). Respiratory-Swallow Training Methods: Accuracy of Automated Detection of Swallow Onset, Respiratory Phase, Lung Volume at Swallow Onset, and Real-Time Performance Feedback Tested in Healthy Adults. *American journal of speech-language pathology*, *29*(2S), 1012–1021. https://doi.org/10.1044/2020_AJSLP-19-00201

41. Hirji, S. A., Gulack, B. C., Englum, B. R., Speicher, P. J., Ganapathi, A. M., Osho, A. A., Shimpi, R. A., Perez, A., & Hartwig, M. G. (2017). Lung transplantation delays gastric motility in patients without prior gastrointestinal surgery-A single-center experience of 412 consecutive patients. *Clinical transplantation*, *31*(10), 10.1111/ctr.13065. https://doi.org/10.1111/ctr.13065

42. Hutcheson, K. A., Barrow, M. P., Plowman, E. K., Lai, S. Y., Fuller, C. D., Barringer, D. A., Eapen, G., Wang, Y., Hubbard, R., Jimenez, S. K., Little, L. G., & Lewin, J. S. (2018). Expiratory muscle strength training for radiation-associated aspiration after head and neck cancer: A case series. *The Laryngoscope*, *128*(5), 1044–1051. https://doi.org/10.1002/lary.26845

43. Jiang, C., Esquinas, A., & Mina, B. (2017). Evaluation of cough peak expiratory flow as a predictor of successful mechanical ventilation discontinuation: a narrative review of the literature. *Journal of intensive care*, *5*, 33. https://doi.org/10.1186/s40560-017-0229-9

44. Jones, B., Ravich, W. J., Donner, M. W., Kramer, S. S., & Hendrix, T. R. (1985). Pharyngoesophageal interrelationships: observations and working concepts. *Gastrointestinal radiology*, *10*(3), 225–233. https://doi.org/10.1007/BF01893105

45. Jones, B., Donner, M. W., Rubesin, S. E., Ravich, W. J., & Hendrix, T. R. (1987). Pharyngeal findings in 21 patients with achalasia of the esophagus. *Dysphagia*, *2*(2), 87–92. https://doi.org/10.1007/BF02408139

46. Jou, J., Radowsky, J., Gangnon, R., Sadowski, E., Kays, S., Hind, J., Gaumnitz, E., Taylor, A., & Robbins, J. (2009). Esophageal clearance patterns in normal older adults as documented with videofluoroscopic esophagram. *Gastroenterology research and practice*, *2009*, 965062.

47. Kahrilas, P. J., Bredenoord, A. J., Fox, M., Gyawali, C. P., Roman, S., Smout, A. J., Pandolfino, J. E., & International High Resolution Manometry Working Group (2015). The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *27*(2), 160–174. https://doi.org/10.1111/nmo.12477

48. Kayawake, H., Chen-Yoshikawa, T. F., Motoyama, H., Hamaji, M., Nakajima, D., Aoyama, A., & Date, H. (2018). Gastrointestinal complications after lung transplantation in Japanese patients. *Surgery today*, *48*(9), 883–890. https://doi.org/10.1007/s00595-018-1666-3

49. King, B. J., Iyer, H., Leidi, A. A., & Carby, M. R. (2009). Gastroesophageal reflux in bronchiolitis obliterans syndrome: a new perspective. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, 28(9), 870–875. https://doi.org/10.1016/j.healun.2009.05.040

50. Kotloff, R. M., & Thabut, G. (2011). Lung transplantation. *American journal of respiratory and critical care medicine*, *184*(2), 159–171. https://doi.org/10.1164/rccm.201101-0134CI

51. Krisciunas, G. P., Langmore, S. E., Gomez-Taborda, S., Fink, D., Levitt, J. E., McKeehan, J., McNally, E., Scheel, R., Rubio, A. C., Siner, J. M., Vojnik, R., Warner, H., White, S. D., & Moss, M. (2020). The Association Between Endotracheal Tube Size and Aspiration (During Flexible Endoscopic Evaluation of Swallowing) in Acute Respiratory Failure

Survivors. *Critical care medicine*, *48*(11), 1604–1611. https://doi.org/10.1097/CCM.0000000000004554

52. Levine, M. S., & Trenkner, S. W. (2011). Training the next generation in luminal gastrointestinal radiology: a call to arms. *AJR. American journal of roentgenology*, *196*(2), 362–366. https://doi.org/10.2214/AJR.10.4917

53. Lever, T., Cox, K.,T., Holbert, D., Shahrier, M., Hough, M., Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. *Dysphagia*, 22: 312-325. doi: 10.1007/s00455-007-9107-2

54. Lumb, A. B. (2017). Nunns applied respiratory physiology. Edinburgh: Elsevier.

55. Madhavan, A., Carnaby, G. D., & Crary, M. A. (2015). 'Food Sticking in My Throat': Videofluoroscopic Evaluation of a Common Symptom. Dysphagia, 30(3), 343–348. https://doi.org/10.1007/s00455-015-9605-6

56. Martin-Harris B. (2008). Clinical implications of respiratory-swallowing interactions. Current opinion in otolaryngology & head and neck surgery, 16(3), 194–199. https://doi.org/10.1097/MOO.0b013e3282febd4b

57. Martin-Harris, B., (2015). Standardized training in swallow physiology – evidence-based assessment using the modified barium swallow impairment profile (MBSImP) approach. Gaylord, MI, Northern Speech Services.

58. Martin-Harris, B., Brodsky, MB, Michel, Y., Castell, DO., Schleicher, M., Sandidge, J., Maxwell, R., Blair, J. (2008). MBS measurement tool for swallow impairment – MBSImp: establishing a standard. *Dysphagia,* 23(4): 392-405. doi: 10/1007/s00455-008-9185-9.

59. Martin-Harris, B., Brodsky, M. B., Price, C. C., Michel, Y., & Walters, B. (2003). Temporal coordination of pharyngeal and laryngeal dynamics with breathing during swallowing: single liquid swallows. Journal of applied physiology (Bethesda, Md. : 1985), 94(5), 1735–1743. https://doi.org/10.1152/japplphysiol.00806.2002

60. Martin-Harris, B., & McFarland, D. (2013). Coordination of deglutition and respiration. *Principles of deglutition* (2013th ed., pp. 25-34). New York, NY: Springer New York. doi:10.1007/978-1-4614-3794-9_3

61. Martin-Harris, B., McFarland, D., Hill, E. G., Strange, C. B., Focht, K. L., Wan, Z., Blair, J., & Mcgrattan, K. (2015). Respiratory–swallow training in patients with head and neck cancer. Archives of Physical Medicine and Rehabilitation, 96(5), 885–893. https://doi.org/10.1016/j.apmr.2014.11.022

62. Martino, R ., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. (2005). Dysphagia after stroke: Incidence, diagnosis, and pulmonary complications. *Stroke, 36,* 2756–2763.

63. Masuda, T., Mittal, S. K., Csucska, M., Kovacs, B., Walia, R., Huang, J. L., Smith, M. A., & Bremner, R. M. (2020). Esophageal aperistalsis and lung transplant: Recovery of peristalsis after transplant is associated with improved long-term outcomes. *The Journal of thoracic and cardiovascular surgery*, *160*(6), 1613–1626. https://doi.org/10.1016/j.jtcvs.2019.12.120

64. Masuda, T., Mittal, S. K., Kovacs, B., Smith, M., Walia, R., Huang, J., & Bremner, R. M. (2018). Thoracoabdominal pressure gradient and gastroesophageal reflux: insights from lung transplant candidates. *Diseases of the esophagus: official journal of the International Society for Diseases of the Esophagus*, *31*(10), 10.1093/dote/doy025. https://doi.org/10.1093/dote/doy025

65. Masuda, T., Mittal, S. K., Kovács, B., Smith, M. A., Walia, R., Huang, J. L., & Bremner, R. M. (2019). Foregut function before and after lung transplant. *The Journal of thoracic and cardiovascular surgery*, *158*(2), 619–629. https://doi.org/10.1016/j.jtcvs.2019.02.128

66. Mateen, F. J., Dierkhising, R. A., Rabinstein, A. A., van de Beek, D., & Wijdicks, E. F. (2010). Neurological complications following adult lung transplantation. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 10(4), 908–914. https://doi.org/10.1111/j.1600-6143.2009.02998.x

67. Matsuo, K., Palmer, J.B. (2009). Coordination of mastication, swallowing and breathing. *J Dent Sci Rev,* 45(1): 31-40. Doi: 10.1016/j.jdsr.2009.04.004

68. Maurer, J. R., Frost, A. E., Estenne, M., Higenbottam, T., & Glanville, A. R. (1998). International guidelines for the selection of lung transplant candidates. The International Society for Heart and Lung Transplantation, the American Thoracic Society, the American Society of Transplant Physicians, the European Respiratory Society. *Transplantation*, 66(7), 951–956. https://doi.org/10.1097/00007890-199810150-00033

69. McFarland, D. H., & Lund, J. P. (1995). Modification of mastication and respiration during swallowing in the adult human. Journal of neurophysiology, 74(4), 1509–1517. https://doi.org/10.1152/jn.1995.74.4.1509

70. McFarland, D.H., Martin-Harris, B., Fortin, A., Humphries, K., Hill, E., & Armeson, K. (2016). Respiratory-swallowing coordination in normal subjects: Lung volume at swallowing initiation. Respiratory Physiology & Neurobiology, 234, 89-96. doi:10.1016/j.resp.2016.09.004

71. Miles, A., Barua, S., McLellan, N., & Brkic, L. (2020). Dysphagia and medicine regimes in patients following lung transplant surgery: A retrospective review. *International journal of speech-language pathology*, 1–10. Advance online publication. https://doi.org/10.1080/17549507.2020.1807051

72. Miles, A., Bennett, K., & Allen, J. (2019). Esophageal Transit Times Vary with Underlying Comorbid Disease. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *161*(5), 829–834. https://doi.org/10.1177/0194599819874342

73. Miles, A., Clark, S., Jardine, M., & Allen, J. (2016). Esophageal Swallowing Timing Measures in Healthy Adults During Videofluoroscopy. *The Annals of otology, rhinology, and laryngology*, *125*(9), 764–769. https://doi.org/10.1177/0003489416653410

74. Miles, A., McMillan, J., Ward, K., & Allen, J. (2015). Esophageal visualization as an adjunct to the videofluoroscopic study of swallowing. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *152*(3), 488–493. https://doi.org/10.1177/0194599814565599

75. Miles, A., McLellan, N., Machan, R., Vokes, D., Hunting, A., McFarlane, M., Holmes, J., & Lynn, K. (2018). Dysphagia and laryngeal pathology in post-surgical cardiothoracic patients. Journal of critical care, 45, 121–127. https://doi.org/10.1016/j.jcrc.2018.01.027

76. *National Data*, Organ Procurement and Transplantation Network U.S. Department of Health & Human Services. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

77. Nguyen, S., Zhu, A., Toppen, W., Ashfaq, A., Davis, J., Shemin, R., Mendelsohn, A. H., & Benharash, P. (2016). Dysphagia after Cardiac Operations Is Associated with Increased Length of Stay and Costs. The American surgeon, 82(10), 890–893.

78. NIH Stroke Scale Training, Part 2. Basic Instruction. Department of Health and Human Services, National Institute of Neurological Disorders and Stroke. The National Institute of Neurological Disorders and Stroke (NINDS) Version 2.0

79. O'Horo, J. C., Rogus-Pulia, N., Garcia-Arguello, L., Robbins, J., & Safdar, N. (2015). Bedside diagnosis of dysphagia: a systematic review. Journal of hospital medicine, 10(4), 256–265. https://doi.org/10.1002/jhm.2313

80. Orens, J. B., Estenne, M., Arcasoy, S., Conte, J. V., Corris, P., Egan, J. J., Egan, T., Keshavjee, S., Knoop, C., Kotloff, R., Martinez, F. J., Nathan, S., Palmer, S., Patterson, A., Singer, L., Snell, G., Studer, S., Vachiery, J. L., Glanville, A. R., & Pulmonary Scientific

Council of the International Society for Heart and Lung Transplantation (2006). International guidelines for the selection of lung transplant candidates: 2006 update--a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, 25(7), 745–755. https://doi.org/10.1016/j.healun.2006.03.011

81. Ortiz, A. S., Lawton, A., Rives, E., Gutierrez, G., & Dion, G. R. (2019). Correlating videofluoroscopic swallow study findings with subjective globus location. *The Laryngoscope*, *129*(2), 335–338. https://doi.org/10.1002/lary.27536

82. Parada, M. T., Alba, A., & Sepúlveda, C. (2010). Bronchiolitis obliterans syndrome development in lung transplantation patients. *Transplantation proceedings*, *42*(1), 331–332. https://doi.org/10.1016/j.transproceed.2009.11.037

83. Plowman, E. K., Anderson, A., York, J. D., DiBiase, L., Vasilopoulos, T., Arnaoutakis, G., Beaver, T., Martin, T., & Jeng, E. I. (2021). Dysphagia after cardiac surgery: Prevalence, risk factors, and associated outcomes. *The Journal of thoracic and cardiovascular surgery*, S0022-5223(21)00405-0. Advance online publication. https://doi.org/10.1016/j.jtcvs.2021.02.087

84. Plowman, E. K., Tabor-Gray, L., Rosado, K. M., Vasilopoulos, T., Robison, R., Chapin, J. L., Gaziano, J., Vu, T., & Gooch, C. (2019). Impact of expiratory strength training in amyotrophic lateral sclerosis: Results of a randomized, sham-controlled trial. *Muscle & nerve*, *59*(1), 40–46. https://doi.org/10.1002/mus.26292

85. Posner, S., Zheng, J., Wood, R. K., Shimpi, R. A., Hartwig, M. G., Chow, S. C., & Leiman, D. A. (2018). Gastroesophageal reflux symptoms are not sufficient to guide esophageal function testing in lung transplant candidates. *Diseases of the esophagus: official journal of the International Society for Diseases of the Esophagus*, *31*(5), 10.1093/dote/dox157. https://doi.org/10.1093/dote/dox157

86. Reedy, E. L., Herbert, T. L., & Bonilha, H. S. (2021). Visualizing the Esophagus During Modified Barium Swallow Studies: A Systematic Review. *American journal of speech-language pathology*, *30*(2), 761–771. https://doi.org/10.1044/2020_AJSLP-20-00255

87. Schmidt Leuenberger, J. M., Hoksch, B., Luder, G., Schmid, R. A., Verra, M. L., & Dorn, P. (2019). Early Assessment and Management of Dysphagia After Lung Resection: A Randomized Controlled Trial. *The Annals of thoracic surgery*, *108*(4), 1059–1064. https://doi.org/10.1016/j.athoracsur.2019.04.067

88. Seccombe, J., Mirza, F., Hachem, R., & Gyawali, C. P. (2013). Esophageal motor disease and reflux patterns in patients with advanced pulmonary disease undergoing lung transplant evaluation. *Neurogastroenterology and motility : the official journal of the*

European Gastrointestinal Motility Society, *25*(8), 657–663. https://doi.org/10.1111/nmo.12135

89. Shah, N., Force, S. D., Mitchell, P. O., Lin, E., Lawrence, E. C., Easley, K., Qian, J., Ramirez, A., Neujahr, D. C., Gal, A., Leeper, K., & Pelaez, A. (2010). Gastroesophageal reflux disease is associated with an increased rate of acute rejection in lung transplant allografts. Transplantation proceedings, 42(7), 2702–2706. https://doi.org/10.1016/j.transproceed.2010.05.155

90. Shaker, R., Li, Q., Ren, J., Townsend, W. F., Dodds, W. J., Martin, B. J., Kern, M. K., & Rynders, A. (1992). Coordination of deglutition and phases of respiration: effect of aging, tachypnea, bolus volume, and chronic obstructive pulmonary disease. The American journal of physiology, 263(5 Pt 1), G750–G755. https://doi.org/10.1152/ajpgi.1992.263.5.G750

91. Steele, C. M., Namasivayam-MacDonald, A. M., Guida, B. T., Cichero, J. A., Duivestein, J., Hanson, B., Lam, P., & Riquelme, L. F. (2018). Creation and Initial Validation of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale. Archives of physical medicine and rehabilitation, 99(5), 934–944. https://doi.org/10.1016/j.apmr.2018.01.012

92. Steidl, E., Ribeiro, C. S., Gonçalves, B. F., Fernandes, N., Antunes, V., & Mancopes, R. (2015). Relationship between Dysphagia and Exacerbations in Chronic Obstructive Pulmonary Disease: A Literature Review. International archives of otorhinolaryngology, 19(1), 74–79. https://doi.org/10.1055/s-0034-1376430

93. Stephen, J. R., Taves, D. H., Smith, R. C., & Martin, R. E. (2005). Bolus location at the initiation of the pharyngeal stage of swallowing in healthy older adults. *Dysphagia*, *20*(4), 266–272. https://doi.org/10.1007/s00455-005-0023-z

94. Studer, S. M., Levy, R. D., McNeil, K., & Orens, J. B. (2004). Lung transplant outcomes: a review of survival, graft function, physiology, health-related quality of life and cost-effectiveness. The European respiratory journal, 24(4), 674–685. https://doi.org/10.1183/09031936.04.00065004

95. Tangaroonsanti, A., Lee, A. S., Vela, M. F., Crowell, M. D., Erasmus, D., Keller, C., Mallea, J., Alvarez, F., Almansa, C., DeVault, K. R., & Houghton, L. A. (2019). Unilateral Versus Bilateral Lung Transplantation: Do Different Esophageal Risk Factors Predict Chronic Allograft Failure?. *Journal of clinical gastroenterology*, *53*(4), 284–289. https://doi.org/10.1097/MCG.0000000000001015

96. Tangaroonsanti, A., Lee, A. S., Crowell, M. D., Vela, M. F., Jones, D. R., Erasmus, D., Keller, C., Mallea, J., Alvarez, F., Almansa, C., DeVault, K. R., & Houghton, L. A. (2017). Impaired Esophageal Motility and Clearance Post-Lung Transplant: Risk For Chronic

Allograft Failure. *Clinical and translational gastroenterology*, *8*(6), e102. https://doi.org/10.1038/ctg.2017.30

97. Tangaroonsanti, A., Vela, M. F., Crowell, M. D., DeVault, K. R., & Houghton, L. A. (2018). Esophageal dysmotility according to Chicago classification v3.0 vs v2.0: Implications for association with reflux, bolus clearance, and allograft failure post-lung transplantation. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *30*(6), e13296. https://doi.org/10.1111/nmo.13296

98. Triadafilopoulos, G., Hallstone, A., Nelson-Abbott, H., & Bedinger, K. (1992). Oropharyngeal and esophageal interrelationships in patients with nonobstructive dysphagia. *Digestive diseases and sciences*, *37*(4), 551–557. https://doi.org/10.1007/BF01307579

99. United Network for Organ Sharing (UNOS). (n.d.) Transplant Trends. https://unos.org/data/transplant-trends/

100. Watts, S., Gaziano, J., Jacobs, J., & Richter, J. (2019). Improving the Diagnostic Capability of the Modified Barium Swallow Study Through Standardization of an Esophageal Sweep Protocol. *Dysphagia*, *34*(1), 34–42. https://doi.org/10.1007/s00455-018-09966-5

101. Wheeler Hegland, K., Huber, J. E., Pitts, T., Davenport, P. W., & Sapienza, C. M. (2011). Lung volume measured during sequential swallowing in healthy young adults. *Journal of speech, language, and hearing research : JSLHR*, 54(3), 777–786. https://doi.org/10.1044/1092-4388(2010/09-0237)

102. Yadlapati, R., Kahrilas, P. J., Fox, M. R., Bredenoord, A. J., Prakash Gyawali, C., Roman, S., Babaei, A., Mittal, R. K., Rommel, N., Savarino, E., Sifrim, D., Smout, A., Vaezi, M. F., Zerbib, F., Akiyama, J., Bhatia, S., Bor, S., Carlson, D. A., Chen, J. W., Cisternas, D., … Pandolfino, J. E. (2021). Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *33*(1), e14058. https://doi.org/10.1111/nmo.14058

103. Zivković, S. A., Jumaa, M., Barisić, N., & McCurry, K. (2009). Neurologic complications following lung transplantation. *Journal of the neurological sciences*, 280(1-2), 90–93. https://doi.org/10.1016/j.jns.2009.02.308

CHAPTER 4: AIM 3

Manuscript 3: A Pilot Study Investigating the Influence of Cueing on Impressions of Esophageal Clearance During the Modified Barium Swallow Study

TITLE: A Pilot Study Investigating the Influence of Cueing on Impressions of Esophageal Clearance During the Modified Barium Swallow Study

AUTHORS: Reedy, E.L., O'Rourke, A.K., Simpson, A.N., Khalaf, M.H., Bonilha, H.S.

ABSTRACT:

Background: Esophageal visualization is an important aspect of the Modified Barium Swallow Study (MBSS). This is especially true as we learn more about the relationship between oropharyngeal and esophageal swallow function. One consideration in esophageal visualization is the influence of deglutitive inhibition, or the cessation or alteration of esophageal peristalsis, in the context of multiple swallows. If multiple swallows trigger deglutitive inhibition, this may cause the impression of impaired esophageal clearance. We aimed to determine if the visualization of esophageal clearance is altered in cued versus un-cued conditions to ascertain the potential impact of deglutitive inhibition.

Methods: We performed a prospective cohort study with 36 participants referred for an outpatient MBSS as part of standard of care. All MBSS were performed using the Modified Barium Swallow Impairment Profile (MBSImP™©). In the standard MBSImP condition, participants were instructed to hold the bolus in their mouths and were only given the direction to "swallow." In the experimental condition, participants were instructed to hold the bolus in their mouth and then to "swallow once and only once, focus on your breathing and don't swallow again." Swallowing impairment was determined using a combination of MBSImP scores and penetration-Aspiration Scale (PAS) scores. Swallowing outcomes were determined using Functional Oral Intake Scale (FOIS) scores International Dysphagia Diet Standardization Initiative (IDDSI) scores. We performed tests of association to determine if statistically significant associations existed between measures of swallowing impairment and MBSImP component 17 scores under two conditions.

Results: Esophageal clearance scores changed in 38.89% of participants when comparing standard MBSImP protocol versus the cued condition. Of those participants with a change in scores, 50% had an increase in scores (decreased esophageal clearance) and 50% had a

decrease (improved esophageal clearance) in scores. There were no statistically significant associations between cued vs. un-cued scores.

Conclusion: When participants were provided a specific cue to "swallow only once" compared to a cue only to "swallow," impressions of esophageal clearance changed in 39.89% of participants. Our results illuminate the need for further study into the influence of cueing and the effect of deglutitive inhibition on the visualization of esophageal clearance.

INTRODUCTION:

The Modified Barium Swallow (MBSS) study has long been considered the gold standard assessment tool (Martin-Harris & Jones, 2008) by most clinicians working in the field of dysphagia. The MBSS allows for a multi-plane view of the oral, pharyngeal, and esophageal domains of the swallow and is performed by a speech-language pathologist (SLP) and Radiologist or Radiology Technician (ASHA, 2004). The MBSS study traditionally involves examination of the swallowing continuum (e.g., oral, pharyngeal, esophageal domains) with various liquid viscosities and food textures with the patient seated or standing, unless positioning techniques are being trialed (Martin-Harris et al., 2020).

Historic expert opinion and early work identified interrelationships between aspects of the swallowing continuum, oropharyngeal and esophageal, as early as 1985 (Jones et al., 1987; Jones et al., 1985; Triadafilopoulous et al., 1992). More recently, the scientific evidence that supports incorporating esophageal visualization into standard MBSS practice continues to grow (Allen et al., 2012; Miles, 2017; Miles et al., 2015; Miles et al., 2019; Reedy et al., 2020; Watts et al., 2019; Watts et al., 2021); though practices regarding fluoroscopic visualization of the esophagus vary significantly in the literature (Belafsky et al., 2008; Bogstrom et al., 1998; Ekberg & Feinberg, 1991; Feinberg & Ekberg, 1991; Gullung et al., 2012; Jones et al., 1987; Jones et al., 1985; Madhavan et al., 2015; Miles et al., 2017; Miles et al., 2019; Ortiz et al., 2019; Triadafilopoulous et al., 1992; Scharitzer et al., 2002; Watts et al., 2019; Watts et al., 2021).

A non-diagnostic visualization of the esophagus falls within the scope of practice for speech-language pathologists (SLP) according to both the American College of Radiology (ACR) (ACR, 2017) as well as the American Speech-Language Hearing Association (ASHA) (ASHA, 2003; ASHA, 2004a; ASHA, 2004b). Miles et al. (2017) demonstrated that SLPs trained in their esophageal screening protocol were able to identify abnormal esophageal bolus transit time with perfect agreement (kappa = 1.0), and the presence of stasis, abnormal bolus flow, and need for further assessment (e.g., GI referral) with substantial (kappa = .61-.80) agreement. Whereas Watts et al. (2021) reported almost perfect agreement (kappa = 0.86) between SLP raters trained in their screening protocol on impressions of esophageal anatomic abnormality and dysmotility. Research supports the routine inclusion of non-diagnostic esophageal visualization during an MBSS to improve the gestalt impression of swallowing (Allen et al., 2012; Gullung et al. 2012; Madhavan, Carnaby & Crary, 2015; Miles, 2017; Miles et al., 2015; Ortiz et al., 2019; Reedy et al., 2021; Watts et al., 2019; Watts et al., 2021). Currently, the MBSImP (Martin-Harris et al., 2008) is the only standardized, reliable, and validated protocol for the MBSS. The MBSImP (Martin-Harris et al., 2008) identifies 17 different physiologic components of swallowing, including the determination of esophageal clearance (component 17). For the judgement of esophageal clearance, the MBSImP protocol includes two swallows in the anterior-posterior plane with 5mL of nectar-thick barium sulfate (Varibar) and 5mL pudding consistency barium sulfate. Per the standard MBSImP protocol, the patient is instructed to perform an oral bolus hold and then to “swallow when you’re ready” (Martin-Harris et al., 2017). The bolus is then followed fluoroscopically through the lower esophageal sphincter (LES) and esophageal clearance is judged. MBSImP component 17 (esophageal clearance) score has five possible scores: 0, or “complete clearance; esophageal coating,” 1, or “esophageal retention,” 2, or “esophageal retention without retrograde flow through the pharyngoesophageal segment (PES)”, 3, or “esophageal retention with retrograde flow through [the] PES,” and 4, “minimal to no esophageal clearance.” Though esophageal visualization is non-diagnostic, scores are hierarchical meaning that a score of 4 implies less abnormality than a score of 4. In the MBSImP protocol, the patient receives no instruction other than to hold the

bolus in the oral cavity until directed to “swallow when ready;” therefore, the patient could perform multiple or single swallows while ingesting the single test bolus.

During swallowing, a bolus is propelled through the oropharynx and into the esophagus. Once a bolus enters the esophagus, it is driven by a primary esophageal peristaltic wave where pressure is applied to the tail of the bolus as it moves through the length of the esophageal body into the stomach (Goyal & Chaudhury, 2008). Primary peristalsis is only initiated by deglutition, with a bolus that passes through the upper esophageal sphincter (UES). If this first wave is ineffective at clearing the bolus, a secondary peristaltic wave should be initiated to help clear the bolus through the esophageal body and into the stomach. A secondary wave is triggered by esophageal distention and mediated by intrinsic esophageal neuromuscular reflexes. Non-propulsatile, often retrograde contractions of the esophagus are referred to as tertiary contractions if seen radiographically.

Deglutitive inhibition is a normal phenomenon that results in the cessation or alteration of peristalsis in the case of multiple or sequential swallows (Hightower, 1955; Shi et al., 2003; Sifrim & Jafari 2012; Tutuian, Jalil, Katz & Castell, 2004). Meyer et al. (1985) identified 20-30 seconds as the refractory period required for the distal esophagus to “recover.” Deglutitive inhibition functions as a mechanism to promote more efficient bolus transit in the context of multiple swallows. Sequential esophageal peristaltic waves following every swallow originating in the oropharynx would result in a bolus or boluses to become “trapped” or misdirected between peristaltic waves. Not all swallows which follow less than 20-30 seconds after an initial swallow will result in inhibition, but rather an attenuation (Meyer et al., 1985; Pandolfino et al., 2005; Shi et al., 2003). If only two oropharyngeal swallows occur, there may be no significant esophageal consequence (inhibition or alteration of peristalsis) in healthy adults (Hollenstein et al., 2017).

Therefore, we sought to investigate the potential impact of deglutitive inhibition in esophageal visualization during the MBSS. We hypothesized that specific cueing to swallow only once,

would decrease the incidence of deglutitive inhibition, and thus would result in a different determination of esophageal clearance compared to an un-cued condition in which participants may be more likely to perform multiple or sequential swallows.

METHODS:

Study Design

Between April 1, 2021, and June 4, 2021, participants were recruited from the Medical University of South Carolina (MUSC) clinics where MBSS are performed. All participants were referred for an MBSS by a provider for an assessment of swallowing as per the standard of care. Informed consent procedures were completed within all ethical standards and written consent was obtained prior to participation in study procedures. This study was approved by the Institutional Review Board.

Inclusion and Exclusion Criteria

Inclusion criteria were established to include adults (18+ years) who were referred for an outpatient MBSS for an assessment of swallowing function as a standard of care. Those participants with any past medical history for altered oral, pharyngeal, and/or esophageal anatomy (e.g., tongue resection, laryngectomy, or fundoplication) were excluded. Though participants with a history of head and neck cancer without resection, participants post-anterior cervical surgeries were included. Participants who were unable to follow or execute the instructions for the experimental (cued) condition were excluded.

All eligible participants had a Modified Barium Swallow Study (MBSS) using the MBS Impairment Profile (MBSImP™©) base protocol. Those participants whose MBSS reports did not include any MBSImP scores or lacked an MBSImP component 17 (esophageal clearance) score under both conditions were excluded. Penetration Aspiration Scale (PAS) scores (Rosenbek et al., 1996), Functional Oral Intake Scale (FOIS) scores (Crary et al., 2005), and International Dysphagia Diet Standardization Initiative (IDDSI) scale (Steele et al., 2018) scores were required

where applicable (e.g., patients who are not recommended for per oral (P.O.) intake do not have IDDSI scores).

Modified Barium Swallow Study

All participants were referred for an MBSS as part of the standard of care for patients with complaints of, or concerns for, dysphagia. MBSS were performed at 30 pulses per second (pps) and were recorded at 30 frames per second (fps) according to best practices (Bonilha, Blair, Carnes, et al., 2013; Bonilha, Humphries, Blair, et al., 2013). All MBSS were conducted using the Modified Barium Swallow Impairment Profile protocol (Martin-Harris et al., 2008). The core protocol uses 12 swallows across varying liquid and solid consistencies, the initial 10 in the lateral view, the last 2 in the anterior-posterior view. The standard MBSImP component 17, our outcome measure, is determined by the esophageal bolus clearance patterns through the esophageal body and lower esophageal sphincter (LES) in the A-P view with 5 ml nectar and 5 ml pudding barium sulfate contrast (Varibar®, Bracco Diagnostics Inc.). Per the standard MBSImP protocol, the patient is instructed to "hold this in your mouth until I ask you to swallow," and then, to "swallow when you're ready" (Martin-Harris et al., 2017). In the experimental condition, the participant was prompted by the clinician saying, "for these next two swallows I want you to swallow only one time." For each bolus provision the participant was instructed to hold the bolus in their mouths until directed to "swallow once and only once, focus on your breathing and don't swallow again." A period of 30 seconds was provided between the 5ml nectar and 5ml pudding boluses in the experimental condition. The standardized score was recorded in the MBSImP database and in the electronic health record (EHR), and the experimental score was recorded only in the MBSS EHR documentation and separately from other MBSImP scores.

Statistical Analysis

Analysis was performed using SAS (v9.4, Cary, NC). Summary statistics were calculated for all variables collected (mean, median, the standard deviation for continuous variables and frequency, median, and mode for categorical variables). Our statistical hypothesis (H_0) was that

there would be no statistically significant differences in MBSImP component 17 (esophageal clearance) scores in un-cued (standard MBSImP) vs. cued (experimental) conditions. Fisher's exact tests were used to test for associations between categorical variables (e.g., MBSImP component scores) and determine if associations exist between measures of swallowing physiology and outcome measures. A McNemar test of association was used to perform a paired (case-control) analysis on our two component 17 conditions with each participant serving as their own control. Our hypothesis (H_0) was that there were no statistically significant associations. As the data was non-parametric, Mann-Whitney U/Wilcoxon Rank Sum tests were used to test for differences in continuous variables (e.g., age). Findings reflect the overall statistical significance and for all statistical analyses, two-sided tests were performed with alpha set at 0.05 with P values of ≤ .05 indicating statistical significance.

RESULTS:

1. *Participants*

A total of 36 participants met study inclusion and exclusion criteria. The average age was 64.01 (range 33-94 years). The majority (55.56%) of participants were female. Most participants were white (83.33%), and none identified as Hispanic. Most of the participants were referred by laryngology (52.94%), followed by primary care (17.65%). While only 27.78% of participants' medical records included a diagnosis of gastroesophageal reflux disease, 61.11% of participants were on a proton pump inhibitor (PPI) (e.g., omeprazole) and 33.33% were on an H2-receptor antagonist (e.g., famotidine). Of these patients, 9/25 (36%) were on both a PPI and an H2-receptor antagonist. Only 11/36 (30.56%) participants were not on either medication. The most common participant reported symptom was dysphagia to solids (55.56%), followed by coughing with eating (44.44%), dysphagia to pills (36.11%), and globus sensation (27.78%). See Table 1 for further detail.

Given that some participants had a change in component 17 scores in our two conditions, demographics, participant characteristics, and baseline data, including presenting symptoms and medications were tested for statistical associations between the groups. Participants were

dichotomized, for the purpose of analysis, into a “no change in esophageal clearance” group and a “change in esophageal clearance” group. There were no statistical differences found between groups (Table 1).

Table 1: Patient Demographics, Characteristics, and Baseline Data by Influence of Cueing on MBSImP Component 17 (esophageal clearance) Score

	Total n = 36 n (%)	**No Change in Esophageal Clearance n = 22 n (%)**	**Change in Esophageal Clearance n = 14 n (%)**	**P-value**
Age mean, SD (95% CI)	64.01 ± 14.07 (60.05, 69.57)	64.59 ± 15.15 (57.88, 71.31)	65.14 ± 12.73 (57.79, 72.49)	P = .8718
Sex				P = 1.000
Female	20 (55.56)	12 (54.55)	8 (57.14)	
Male	16 (44.44)	10 (45.45)	6 (42.86)	
Race				P = .7722
White	30 (83.33)	17 (77.27)	13 (92.86)	
Black	5 (13.89)	4 (18.18)	1 (7.14)	
Other	1 (2.78)	1 (4.55)	0 (0)	
Ethnicity				
Non-Hispanic	37 (100)	22 (100)	14 (100)	-
PAST MEDICAL HISTORY:				
Pulmonary Disease	9 (25)	6 (27.27)	3 (21.43)	P = 1.000
Diabetes	8 (21.62)	6 (27.27)	3 (21.43)	P = 1.000
Thyroid Disease	9 (25)	4 (18.18)	5 (35.71)	P = .2667
Gastroesophageal Reflux Disease	10 (27.78)	9 (40.91)	1 (7.14)	P = .0536
Other GI Disorder, Not Esophageal	11 (30.56)	9 (40.91)	2 (14.29)	P = .1419
Stroke	3 (8.33)	2 (9.09)	1 (7.14)	P = 1.000
Neurodegenerative Disease	3 (8.33)	2 (9.09)	1 (7.14)	P = 1.000
Seizure Disorder or Seizure History	2 (5.56)	0 (0)	2 (14.29)	P = .1444
Migraine	5 (14.29)	3 (13.64)	2 (15.38)	P = 1.000
Psychiatric Disorder	6 (16.67)	4 (18.18)	2 (14.29)	P = 1.000

Autoimmune Disorder	5 (13.89)	2 (9.09)	3 (21.43)	P = .3566
MEDICATIONS:				
Proton Pump Inhibitor (PPI)	22 (61.11)	15 (68.18)	7 (50)	P= .3142
H2-Receptor Antagonist	12 (33.33)	7 (31.82)	5 (35.71)	P = 1.000
H1-Receptor Antagonist	6 (16.67)	3 (13.64)	3 (21.43)	P = .6582
Gabapentin (Neurontin)	11 (30.56)	7 (31.82)	4 (28.57)	P = 1.000
Opioid	8 (22.22)	5 (22.73)	3 (21.43)	P = 1.000
Vitamin D	16 (44.44)	12 (54.44)	4 (28.57)	P = .1760
REFERRAL SOURCE:				P = .0921
Primary Care	6 (17.65)	5 (35)	1 (7.14)	
Laryngology	18 (52.94)	10 (50)	8 (57.14)	
General ENT	5 (4.71)	1 (5)	4 (28.57)	
Gastroenterology	1 (2.94)	1 (5)	0 (0)	
Neurology	1 (2.94)	0 (0)	1 (7.14)	
REPORT OF SYMPTOMS:				
Dysphagia to Liquids	15 (41.67)	12 (54.55)	3 (21.43)	P = .0833
Dysphagia to Solids	20 (55.56)	15 (68.18)	5 (35.71)	P = .0874
Dysphagia to Pills	13 (36.11)	9 (40.91)	4 (28.57)	P = .5013
Coughing with Eating/Drinking	16 (44.44)	9 (40.91)	7 (50)	P =.7343
Globus Sensation	10 (27.78)	6 (27.27)	4 (28.57)	P = 1.000
Odynophagia	5 (13.89)	4 (18.18)	1 (7.14)	P = .6283
Eructation	2 (5.41)	1 (4.55)	1 (7.14)	P = 1.000
Gagging	2 (5.56)	1 (4.55)	1 (7.14)	P = 1.000
Regurgitation/Vomiting	2 (5.56)	2 (9.09)	0 (0)	P = .5111
EAT-10 scores mean, SD (95% CI)	15.47, ± 11.18 (10.08, 20.86)	14.69, ± 9.49 (8.96, 20.43)	17.17, ± 15.13 (1.29, 33.05)	P = .8965

2. Impressions of Esophageal Clearance Under Two Conditions

Component 17 (esophageal clearance) scores under the standard MBSImP protocol (un-cued) ranged from 0 to 4. Component 17 (esophageal clearance) scores changed between the standard and experimental conditions in 38.89% (14/36) of participants. For those with a change in component 17 scores, half (7/14) had a decrease and half (7/14) had an increase in scores. A statistically significant association was not identified for component 17 scores in the

standard vs. experimental condition (P = .6547). In fact, a kappa coefficient was calculated and determined fair agreement (Kappa = .4643) between the two scores. See Table 2.

Table 2. Component 17 (Esophageal Clearance) Scores Under Two Conditions

Component 17 Score	Standard Condition n (%)	Experimental Condition n (%)
0 – Complete clearance, esophageal coating	6 (16.67)	5 (13.89)
1 – Esophageal retention	16 (44.44)	20 (55.56)
2 – Esophageal retention with retrograde flow below the PES	10 (27.78)	6 (16.67)
3 - Esophageal retention with retrograde flow through the PES	0 (0)	0 (0)
4 – Minimal to no esophageal clearance	4 (11.11)	5 (13.89)

11. MBSS Variables

Given that some participants experienced a change in component 17 scores in the standard condition vs. the experimental condition, we sought to investigate if there were statistically significant associations between other measures of swallowing physiology and/or impairment.

3.5 MBSImP Component Scores

The most common physiologic abnormality for this cohort was a lower bolus head at the onset of the pharyngeal swallow (component 6) which was abnormal in 88.89%. The second most common finding was abnormal esophageal clearance (component 17) in the experimental condition identified in 86.11% of participants. Abnormal esophageal clearance (component 17) in the standard condition was the third most common abnormality seen in 83.33% of participants (See Table 3). Only one participant had a score of zero (normal) for both component 6 and the standard component 17. Three participants (8.33%) had a score of zero for component 17 under both conditions (cued vs. un-cued). There were no statistically

significant associations between component 17 conditions and other measures of swallowing physiology or swallowing outcome measures. See Table 3 for details.

TABLE 3. Comparison of Swallowing Impairment and Outcome Measures in Unchanged vs. Changed Component 17 (Esophageal Clearance) Scores Given Cueing

Swallowing Impairment and Outcome Measures	**Total n = 36 (%)**	**No Change in Component 17 scores n = 22 n (%)**	**Change in Component 17 scores n = 14 n (%)**	**P-value**
MBSImP component 1 (lip closure)				P = 1.000
C1 ≤ 1	32 (88.89)	19 (86.36)	13 (92.86)	
C1 ≥ 2	4 (10.81)	3 (13.64)	1 (7.14)	
MBSImP component 2 (tongue control during bolus hold)				P = .7272
C2 = 0	24 (66.67)	14 (63.64)	10 (71.43)	
C2 ≥ 1	12 (33.33)	8 (36.36)	4 (28.57)	
MBSImP component 3 (bolus prep/mastication)				P = .4267
C3 = 0	25 (73.53)	14 (66.67)	11 (84.62)	
C3 ≥ 1	9 (26.47)	7 (33.33)	2 (15.38)	
MBSImP component 4 (bolus transport/lingual motion)				P = 1.000
C4 = 0	28 (77.78)	17 (77.27)	11 (78.57)	
C4 ≥ 1	8 (22.22)	5 (22.73)	3 (21.43)	
MBSImP component 5 (oral residue) to component 17				
C5 ≤ 1	17 (47.22)	12 (54.55)	5 (35.71)	P = .3217
C5 ≥ 2	19 (52.78)	10 (45.45)	9 (64.29)	
MBSImP component 6 (initiation of pharyngeal swallow)				P = .6340
C6 = 0	4 (11.11)	2 (9.09)	2 (14.29)	
C6 ≥ 1	32 (88.89)	20 (90.91)	12 (85.71)	

MBSImP component 7 (velar elevation)				-
C7 = 0	35 (100)	21 (100)	14 (100)	
C7 ≥ 1	0 (0)	0 (0)	0 (0)	
MBSImP component 8 (laryngeal elevation)				P = 1.000
C8 = 0	24 (68.57)	14 (66.67)	10 (71.43)	
C8 ≥ 1	11 (31.43)	7 (33.33)	4 (28.57)	
MBSImP component 9 (anterior hyoid excursion)				P = .2100
C9 = 0	27 (79.41)	15 (71.43)	12 (92.31)	
C9 ≥ 1	7 (20.59)	6 (28.57)	1 (7.69)	
MBSImP component 10 (epiglottic movement)				P = .4619
C10 = 0	26 (72.22)	17 (77.27)	9 (64.29)	
C10 ≥ 1	10 (27.78)	5 (22.73)	5 (35.71)	
MBSImP component 11 (laryngeal vestibule closure)				P = .4307
C11 = 0	27 (77.14)	15 (71.43)	12 (85.71)	
C11 ≥ 1	8 (22.86)	6 (28.57)	2 (14.29)	
MBSImP component 12 (pharyngeal stripping wave)				P = .2925
C12 = 0	23 (65.71)	16 (72.73)	7 (53.85)	
C12 ≥ 1	12 (34.29)	6 (27.27)	6 (46.15)	
MBSImP component 13 (pharyngeal contraction)				P = .2074
C13 = 0	26 (72.22)	17 (77.27)	9 (64.29)	
C13 ≥ 1	10 (27.78)	5 (22.73)	5 (35.71)	
MBSImP component 14 (pharyngoesophageal segment opening)				P = .4813
C14 = 0	17 (50)	12 (57.14)	5 (38.46)	
C14 ≥ 1	17 (50)	9 (42.86)	8 (61.54)	
MBSImP component 15 (tongue base retraction)				P = .0967
C15 ≤ 1	17 (47.22)	13 (59.09)	4 (28.57)	
C15 ≥ 1	19 (52.78)	9 (40.91)	10 (71.43)	
MBSImP component 16 (pharyngeal residue)				P = .4847
C16 ≤ 1	14 (38.89)	10 (45.45)	4 (28.57)	
C16 ≥ 1	22 (61.11)	12 (54.55)	10 (71.43)	
Penetration-Aspiration Scale (PAS) score				P = 1.000
PAS ≤ 3	32 (88.89)	19 (86.36)	13 (92.86)	
PAS ≥ 4	4 (11.11)	3 (13.64)	1 (7.14)	

Presence of aspiration	4 (11.11)	3 (13.64)	1 (7.14)	P = 1.000
Functional Oral Intake Scale (FOIS) score				P = 1.000
FOIS 6-7	35 (97.22)	21 (95.45)	14 (100)	
FOIS 5-3	1 (2.78)	1 (4.55)	0 (0)	
FOIS 1-2	0 (0)	0 (0)	0 (0)	
International Dysphagia Diet (IDDSI) liquid score				-
IDDSI liquids = 0	34 (100)	21 (100)	13 (100)	
IDDSI liquids 2-3	0 (0)	0 (0)	0 (0)	
International Dysphagia Diet (IDDSI) solid score				
IDDSI solids = 7	33 (91.67)	21 (95.45)	12 (85.71)	P = .5471
IDDSI solids 4-6	3 (8.33)	1 (4.55)	2 (14.29)	

*P value < .05

Of the five oral component scores, there were no statistical associations when tested against component 17 (esophageal clearance) scores. The mean of MBSImP Oral Total (OT) scores was 5.36 (range 0-18, standard deviation ± 3.59). The 95% confidence interval around the mean was 4.15 to 6.57. There were no statistically significant associations between the 11 pharyngeal component scores and component 17 scores. Mean MBSImP Pharyngeal Total (PT) scores was 4.78 (range 0-13, standard deviation ± 3.61). The 95% confidence interval around the mean was 3.56 to 6.0.

3.6 Swallowing Impairment Severity

Beall et al. (2020) identified ranges of OT and PT scores that account for differences in swallowing impairment and provided a classification framework. Using this classification, we found that 34/36 (94.44%) of participants had an oral classification of “mild/functional”. Using the Beall et al. (2020) framework, though not directly specified in the classification, one (2.78%) participant could be classified as having a “mild-moderate” oral impairment and one (2.87%) participant was classified as having a “moderate” oral impairment. All participants were classified in the “mild/functional” pharyngeal impairment category.

3.7 Measures of Bolus Airway Invasion

Penetration-Aspiration Scale (PAS) (Rosenbek et al., 1996) scores for this cohort ranged from 1-8, though no scores of 5 were seen. The majority (61.11%) of participants had PAS of 1 or, contrast "material does not enter the airway" and remains entirely out of the laryngeal vestibule. Ten (27.78%) participants had a PAS of 2, or "material enters the airway, remains above the vocal folds, and is ejected from the airway." A score of 4 or, "material enters the airway, contacts the vocal folds, and is ejected from the airway" was seen in one (2.87%) participant. Scores representing aspiration were seen in 3/36 (8.33%) of participants. A score of 6 or, "material enters the airway, passes below the vocal folds and is ejected into the larynx or out of the airway" was seen in one participant. A score of 7 or, "material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort" was seen in one participant. A score of 8 or, "material enters the airway, passes below the vocal folds, and no effort is made to eject," or silent aspiration, was seen in one participant. PAS scores of 1-2 have been identified as a range of normal for healthy participants (Daggett et al., 2006; Garand et al., 2019; Robbins et al., 1999) which was seen in 88.89% of our cohort.

3.8 MBSS Outcome Measures

Swallowing outcome measures were collected from MBSS recommendations including the FOIS (Crary et al., 2005), and the liquid and solid (as applicable) IDDSI (Steele et al., 2018) consistency recommendations. See Table 4 for details.

Table 4. Associations Between Component 17 (Esophageal Clearance) scores and MBSS Outcome Measures

MBSS Outcome Measures Score Compared to Measures of MBSImP Component 17	Median and Mode	Percent Abnormal	Association with Standard Component 17 scores (P-value)	Association with Experimental Component 17 scores (P-value)
FOIS Score	7, 7	2.78%	P = .8095	P = 1.000
IDDSI Liquid Level	0, 0	0%	-	-
IDDSI Solid Level	7, 7	5.71%	P = .5714	P = 1.000

4.1 Measures of Oral Intake

Functional Oral Intake Scale (FOIS) (Crary et al., 2005) scores ranged from 4-7 in our sample. Specifically, 33 (91.67%) of participants had a score of 7 indicating "total oral intake with no restrictions." One (2.78%) participant had a score of 6 or, "total oral intake with no special preparation, but must avoid specific food and liquid items." And one (2.78%) participant had a score of 4 or, "total intake of a single consistency." International Dysphagia Diet Standardization Initiative (IDDSI) (Steele et al., 2018) scores for solids ranged from 6-7. There were 33/36 (94.29%) of participants recommended for regular solids (IDDSI score 7) and 2/36 (5.41) recommended for "soft and bite sized" (IDDSI score 7) solids. Of the participants recommended to consume liquids (35/36) all had an IDDSI score of 0 or thin liquids. See Table 4.

5. Sub-Group Analysis of Participants with a Change in Component 17 (Esophageal Clearance) Scores Given Cueing

Fourteen participants were identified as having a change in component 17 scores in the cued (experimental) vs. un-cued (standard) condition. The mean age for participants with a change in scores was 65.14 years (range 36-84, standard deviation ± 12.73). The majority of participants with a score change were female (57.14%) and almost all (92.86%) were white. See Table 5.

No statistically significant differences were seen between any of the other MBSImP components or swallowing outcome measures. However, results from comparisons with components 12 (pharyngeal stripping wave) and 14 (pharyngoesophageal segment opening) might indicate a trend toward significance. See Table 5.

Table 5. Subgroup Analysis for Participants with a Change in Component 17 (Esophageal Clearance) Given Cueing

Swallowing Impairment and Outcome Measures	**Total** **n = 14** **(%)**	**Decrease in Component 17 score** **n = 7** **n (%)**	**Increase in Component 17 score** **n = 7** **n (%)**	**P-value**

MBSImP component 1 (lip closure)				P = 1.000
C1 ≤ 1	13 (92.86)	7 (100)	6 (85.71)	
C1 ≥ 2	1 (7.14)	0 (0)	1 (14.29)	
MBSImP component 2 (tongue control during bolus hold)				P = 1.000
C2 = 0	10 (71.43)	5 (71.43)	5 (71.43)	
C2 ≥ 1	4 (28.57	2 (28.57)	2 (28.57)	
MBSImP component 3 (bolus prep/mastication)				P = .4615
C3 = 0	11 (84.62)	5 (71.43)	6 (100)	
C3 ≥ 1	2 (15.38)	2 (28.57)	0 (0)	
MBSImP component 4 (bolus transport/lingual motion)				P = 1.000
C4 = 0	11 (78.57)	5 (71.43)	6 (85.71)	
C4 ≥ 1	3 (21.43)	2 (28.57)	1 (14.29)	
MBSImP component 5 (oral residue) to component 17				P = 1.000
C5 ≤ 1	5 (35.71)	2 (28.57)	3 (42.86)	
C5 ≥ 2	9 (64.29)	5 (71.43)	4 (57.14)	
MBSImP component 6 (initiation of pharyngeal swallow)				P = 1.000
C6 = 0	2 (14.29)	1 (14.29)	1 (14.29)	
C6 ≥ 1	12 (85.71)	6 (85.71)	6 (85.71)	
MBSImP component 7 (velar elevation)				N/A
C7 = 0	14 (100)	7 (100)	7 (100)	
C7 ≥ 1	0 (0)	0 (0)	0 (0)	
MBSImP component 8 (laryngeal elevation)				P = .5594
C8 = 0	10 (71.43)	6 (85.71)	4 (57.14)	
C8 ≥ 1	4 (28.57)	1 (14.29)	3 (42.86)	
MBSImP component 9 (anterior hyoid excursion)				P = .4615
C9 = 0	12 (92.31)	7 (100)	5 (83.33)	
C9 ≥ 1	1 (7.69)	0 (0)	1 (16.67)	
MBSImP component 10 (epiglottic movement)				P = 1.000
C10 = 0	9 (64.29)	4 (57.14)	5 (71.43)	
C10 ≥ 1	5 (35.71)	3 (42.86)	2 (28.57)	
MBSImP component 11 (laryngeal vestibule closure)				P = .4615

C11 = 0	12 (85.71)	7 (100)	5 (71.43)	
C11 ≥ 1	2 (14.29)	0 (0)	2 (28.57)	
MBSImP component 12 (pharyngeal stripping wave)				P = .1026
C12 = 0	7 (53.85)	2 (28.57)	5 (83.33)	
C12 ≥ 1	6 (46.15)	5 (71.43)	1 (16.67)	
MBSImP component 13 (pharyngeal contraction)				P = 1.000
C13 = 0	9 (64.29)	4 (57.14)	5 (71.43)	
C13 ≥ 1	5 (35.71)	3 (42.86)	2 (28.57)	
MBSImP component 14 (pharyngoesophageal segment opening)				P = .1026
C14 = 0	5 (38.46)	1 (14.29)	4 (66.67)	
C14 ≥ 1	8 (61.54)	6 (85.71)	2 (33.33)	
MBSImP component 15 (tongue base retraction)				P = .5594
C15 ≤ 1	4 (28.57)	1 (14.29)	3 (42.86)	
C15 ≥ 1	10 (71.43)	6 (85.71)	4 (57.14)	
MBSImP component 16 (pharyngeal residue)				P = .5594
C16 ≤ 1	4 (28.57)	1 (14.29)	3 (42.86)	
C16 ≥ 1	10 (71.43)	6 (85.71)	4 (57.14)	
MBSImP component 17 (esophageal clearance) **				P = .1923
C17 = 0	3 (21.43)	0 (0)	3 (42.86)	
C17 ≥ 1	11 (78.57)	7 (100)	4 (57.14)	
Penetration-Aspiration Scale (PAS) score				P = 1.000
PAS ≤ 3	13 (92.86)	7 (100)	6 (85.71)	
PAS ≥ 4	1 (7.14)	0 (0)	1 (14.29)	
Presence of aspiration	1 (7.14)	0 (0)	1 (14.29)	P = 1.000
Functional Oral Intake Scale (FOIS) score				
FOIS 6-7	14 (100)	7 (100)	7 (100)	N/A
FOIS 5-3	0 (0)	0 (0)	0 (0)	

FOIS 1-2	0 (0)	0 (0)	0 (0)	
International Dysphagia Diet (IDDSI) liquid score				
IDDSI liquids = 0	13 (100)	6 (100)	7 (100)	N/A
IDDSI liquids 2-3	0 (0)	0 (0)	0 (0)	
International Dysphagia Diet (IDDSI) solid score				P = 1.000
IDDSI solids = 7	12 (85.71)	6 (85.71)	6 (85.71)	
IDDSI solids 4-6	2 (14.29)	1 (14.29)	1 (14.29)	

*P <.05 for Fisher's test of association
**Standard MBSImP condition

5.1 Decrease in Component 17 Scores

Seven participants were found to have a decrease in component 17 scores in our two study conditions. The mean age for participants who were found to have a decrease in component 17 scores was 67.57 years (range 53-84, standard deviation ± 11.31). Most, 5/7, (71.43%) participants in this subgroup of decreased scores were female and all were white. See Table 5.

The most common score change was from a score of 2 to a score of 1 seen in 4 (28.57%) participants. This was also the most common change of any of the score change types overall (increase or decrease). Two (14.29%) participants went from a score of 1 to a score of 0. And one (7.14%) participant went from a score of 4 to a score of 1. This last change type representing the most "dramatic" of score changes (e.g., widest score change range) of this subgroup, and the largest change (3 "points") overall.

5.2 Increase in Component 17 Scores

Seven participants were found to have an increase in component 17 scores between the standard and experimental conditions. The mean age for participants with an increase in component 17 scores was 62.71 years (range 36-76, standard deviation ± 14.47). Slightly less participants (3/7, 42.86%), in this subgroup of participants with an increase in scores, were female and almost all (6/7, 85.71%) were white. See Table 5.

A change from 0 to one was seen in 3 (21.43%) participants. This was the second most common score change of any of the score change types overall (increase or decrease). Two participants (14.29%) demonstrated a change from a score of 1 to a score of 2. And two participants (14.29%) changed from a score of 2 to a score of 4. This last change type representing the most "dramatic" of score changes (e.g., widest score change range) of this subgroup. See Table 5.

DISCUSSION:

To account for deglutitive inhibition, when participants were provided a specific cue to swallow only once, impressions of esophageal clearance (component 17) changed in 39.89% of participants. Half (7/14) participants had an increase in scores and half (7/14) had a decrease in scores which contradicted our pre-study hypothesis that cueing would result in an overall reduction (improvement) in impression of esophageal clearance (component 17). Our results, therefore, highlight the need for further study into the influence of cueing and the effect of deglutitive inhibition on impressions of esophageal clearance. As well as pose an important question as to the best, most effective practices for esophageal visualization during the MBSS.

Our cohort had very mild oral or pharyngeal swallowing impairments which may have influenced our findings of esophageal clearance. Most participants were classified with MBSImP oral total scores that indicated a mild/functional impairment and all participants had pharyngeal scores that were classified as mild/functional. PAS, FOIS, and IDDSI scores were overwhelmingly normal for participants in this study. As swallowing is a continuum of highly coordinated series of pressures driven by biomechanically interdependent events, our cohort of participants with relatively "normal" oropharyngeal swallow function may not demonstrate meaningful relationships between oropharyngeal measures and component 17 scores in our two conditions. More significant findings may be identified in a more heterogeneous sample representing a wider range of swallowing impairments.

There evidence for co-occurring esophageal abnormalities identified during MBSSs is mounting.

Reported esophageal abnormalities range from 26% (Watts et al., 2019) to 100% (Belafsky et al., 2008) in the literature. In our systematic review (Reedy et al., 2021), which included many of the studies referenced here (Gullung et al., 2012; Madhavan et al., 2015; Miles et al., 2015; Ortiz et al., 2019; Watts et al., 2019), we identified that when esophageal visualization was completed during the MBSS, 48.67% of participants had some type of esophageal abnormality. In the current study, abnormal esophageal clearance was identified in both the standard and experimental conditions (83.33% and 86.11%, respectively). The high proportion of esophageal findings may reflect that many patients referred for an MBSS, particularly outpatients, may have a primary esophageal etiology for their complaints of dysphagia. It should be acknowledged that the participant-reported symptoms in our cohort could be primarily esophageal in nature. The majority of participants reported dysphagia to solids (55.56%), followed by coughing with eating (44.44%), dysphagia to pills (36.11%), and globus sensation (27.78%). Studies attempting to study patient localization of dysphagia symptoms, specifically globus and a "sticking" sensation, have found poor correlation. Madhavan et al. (2015) identified esophageal abnormality in 69.5% of their participants presenting with globus sensation. Ortiz et al. (2019) found that in 90% of participants with globus sensation had retained contrast in the esophageal body. When patient symptoms were grouped into "above the thyroid notch" to "below the thyroid notch", however, there was poor symptom location correlation to fluoroscopic findings. They also found that participants who localized above the thyroid notch had more evidence for distal esophageal abnormalities, whereas participants who localized symptoms substernally had more oropharyngeal abnormalities. Ashraf et al. (2017) reported that the nature of anatomic abnormality or physiologic impairment also influences localization. For example, participants with an obstructive pathology in the proximal esophagus were the most accurate (81.7%) at identifying the level of their dysphagia. Overall, participants were determined to have an accuracy of 48.2% in identifying the level of their dysphagia.

The esophageal visualization portion of the MBSS is non-diagnostic, though may provide relevant information to be correlated clinically to help determine those patients who would

benefit from dedicated esophageal testing. There are multiple physiologic oral and pharyngeal components that constitute the composite oral impairment total and pharyngeal impairment total scores of the MBSImP, whereas the only determination for esophageal body function is in the categorization of esophageal clearance (e.g., retention, retrograde flow, absence of clearance) (Martin-Harris, 2015; Martin-Harris et al., 2008; Martin-Harris et al., 2017). It is also important to acknowledge that an abnormal component 17 score may not be indicative of a disorder. Only Gullung et al. (2012) has compared MBSImP findings against a gold-standard for esophageal assessment by comparing MBSImP scores to high resolution esophageal manometry. It should be acknowledged that the study did not focus on this finding alone and did not further investigate findings by score, rather, by a dichotomized normal vs. abnormal component 17 score. And the Gullung et al. (2012) study pre-dates the current Chicago Classification (v4.0) (Yadlapati et al., 2021) which has more stringent classification requirements for some diagnoses.

There is limited research that compares esophageal visualization to the standards of dedicated esophageal testing (e.g., barium esophagram, high-resolution esophageal manometry). In their study comparing an esophageal screening protocol to a barium esophagram, Allen et al. (2012) reported a 62.8% specificity, 100% sensitivity, though both reported 95% confidence intervals had a range greater than 20%. They also report a positive predictive value of 100%. Gullung et al. (2012) identified abnormal component 17 (esophageal clearance) scores (Martin-Harris et al., 2008) in 63.4% of their participants which correlated to a 78% sensitivity for detecting abnormality when compared to the standard of high-resolution esophageal manometry with impedance (HRM-MII). No confidence intervals were reported. Watts et al. (2019) reported a 100% agreement of abnormality identified during esophageal visualization when compared to dedicated esophageal testing (HRM, timed barium esophagram, esophagogastroduodenoscopy [EGD]), though only for a subset (52.5%) of their sample. More recently, Watts et al. (2021) reported a sensitivity of 83.7% and specificity of 73.7% when their Robust Esophageal Screening Test (REST) was compared against HRM or a timed barium esophagram. Though the 95% confidence intervals reported were greater than 20% sensitivity and greater than 30% for

specificity. They reported a positive predictive value of 82% and a negative predictive value of 76%.

There are many different factors that may influence esophageal visualization during the MBSS including positioning, protocol (e.g., order of presentation, types of barium stimuli used, and under what conditions). Despite evidence to support esophageal visualization during the MBSS (Allen et al., 2012; Jones et al., 1987; Jones et al., 1985; Miles et al., 2015; Ortiz et al., 2019; Reedy et al., 2021; Watts et al., 2019; Watts et al., 2021) there is little agreement on protocol. Deglutitive inhibition is relatively unexplored in visualization protocols. Both of Miles et al.'s (2016 and 2019) studies on esophageal bolus transit time report a patient directive to swallow a 20 ml bolus "all in one go" to address deglutitive inhibition. The Miles et al. (2019) protocol specified a cue of "try hard not to swallow a second time," and Watts et al. (2021) protocol included a cue to "only swallow one time." Though cueing was included, the patient's ability to follow-through was not recorded. To our knowledge, our study is the first of its kind investigating the influence of multiple swallows on impressions of esophageal clearance.

Limitations

This study has several limitations. First, as a pilot study no threshold was set for participant recruitment, and we only achieved a small sample size for this cohort. We did not address cognition as a potential influence on the participants' ability to follow directions. The number of swallows in the standard (un-cued) condition was not counted and, therefore, we were unable to compare if multiple swallows occurred in the un-cued condition. And, if more than one swallow did occur, the time between swallows was not measured.

Future Considerations:

Future research into the influence of cueing on impressions of esophageal clearance should consider patient factors and refine the assessment of swallowing under both conditions. Standardized cognitive screening tests such as the Mini Mental Status Exam (MMSE) (Folstein et al., 1975) should be considered in protocols where cognition may influence outcome. The

process by which data regarding swallowing and the number of swallows collected should be refined, such as by including sEMG which would register submental and laryngeal activity related to oropharyngeal swallowing. Lastly, the scoring of component 17 under both conditions should be rated by a second, blinded, rater to account for bias as the clinicians performing the MBSS provided the standard and experimental component 17 scores in the current study. Ultimately, our findings compel further research into the influence of cueing in a more rigorous manner.

CONCLUSION:

This study contributes to our knowledge about esophageal visualization and determinations of clearance during the MBSS. This study found that 38.89% of participants had a change in scores when provided a verbal cue to swallow only one time to account for deglutitive inhibition. However, half of those with a change in scores demonstrated an increase and half had a decrease in component 17 scores in our experimental condition. Our findings highlight the importance of future work investigating the influence of cueing to account for the effect of deglutitive inhibition on impressions of esophageal clearance.

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REFERENCES:

1. Abrahao, L., Jr, Bhargava, V., Babaei, A., Ho, A., & Mittal, R. K. (2011). Swallow induces a peristaltic wave of distension that marches in front of the peristaltic wave of contraction. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *23*(3), 201–e110. https://doi.org/10.1111/j.1365-2982.2010.01624.x

2. Allen, J. E., White, C., Leonard, R., & Belafsky, P. C. (2012). Comparison of esophageal screen findings on videofluoroscopy with full esophagram results. *Head & Neck,* 34(2), 264-269. doi:10.1002/hed.21727

3. American College of Radiology (ACR). (2017). ACR-SPR Practice Parameter for the Performance of the Modified Barium Swallow. Retrieved from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Modified-Ba-Swallow.pdf

4. American College of Radiology (ACR). (2019). ACR-SPR Practice Parameter for the Performance of Esophagrams and upper gastrointestinal examinations in adults. Retrieved from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/UpperGIAdults.pdf

5. American Speech-Language Hearing Association (ASHA). (2004a) Knowledge and Skills Needed by Speech-Language Pathologists Performing Videofluoroscopic Swallowing Studies. Retrieved from: www.asha.org/policy

6. American Speech-Language Hearing Association (ASHA). (2004b) Preferred Practice Patterns for the Profession of Speech-Language Pathology. Retrieved from: www.asha.org/policy

7. American Speech-Language-Hearing Association. (2004c). Guidelines for speech-language pathologists performing videofluoroscopic swallowing studies. *ASHA Supplement 24*, 77–92.

8. Ashraf, H. H., Palmer, J., Dalton, H. R., Waters, C., Luff, T., Strugnell, M., & Murray, I. A. (2017). Can patients determine the level of their dysphagia?. *World journal of gastroenterology*, *23*(6), 1038–1043. https://doi.org/10.3748/wjg.v23.i6.1038

9. Barbon, C., & Steele, C. M. (2019). Characterizing the Flow of Thickened Barium and Non-barium Liquid Recipes Using the IDDSI Flow Test. *Dysphagia*, *34*(1), 73–79. https://doi.org/10.1007/s00455-018-9915-6

10. Behar, J., & Biancani, P. (1993). Pathogenesis of simultaneous esophageal contractions in patients with motility disorders. *Gastroenterology*, *105*(1), 111–118. https://doi.org/10.1016/0016-5085(93)90016-6

11. Belafsky, P. C., Rees, C. J., Rodriguez, K., Pryor, J. S., & Katz, P. O. (2008). Esophagopharyngeal reflux. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *138*(1), 57–61. https://doi.org/10.1016/j.otohns.2007.09.006

12. Blonski, W., Hila, A., Jain, V., Freeman, J., Vela, M., & Castell, D. O. (2007). Impedance manometry with viscous test solution increases detection of esophageal function defects compared to liquid swallows. *Scandinavian journal of gastroenterology*, *42*(8), 917–922. https://doi.org/10.1080/00365520701245702

13. Blonski, W., Vela, M., Hila, A., & Castell, D. O. (2008). Normal values for manometry performed with swallows of viscous test material. *Scandinavian journal of gastroenterology*, *43*(2), 155–160. https://doi.org/10.1080/00365520701679603

14. Bonilha, H. S., Blair, J., Carnes, B., Huda, W., Humphries, K., McGrattan, K., Michel, Y., & Martin-Harris, B. (2013). Preliminary investigation of the effect of pulse rate on judgments of swallowing impairment and treatment recommendations. *Dysphagia,* 28(4), 528–538. https://doi.org/10.1007/s00455-013-9463-z

15. Bonilha, HS., Humphries, K., Hill, EG., McGrattan, K., Carnes, B., Huda, W., Martin-Harris, B. (2013). Radiation Exposure time during MBSS: influence of swallowing impairment severity, medical diagnosis, clinician experience, and standardized protocol use. *Dysphagia,* 28(1), 77-85. doi. 10.1007/s00455-012-9415-z.

16. Bonilha, H. S., Wilmskoetter, J., Tipnis, S., Horn, J., Martin-Harris, B., & Huda, W. (2019). Relationships Between Radiation Exposure Dose, Time, and Projection in Videofluoroscopic Swallowing Studies. *American journal of speech-language pathology*, 28(3), 1053–1059. https://doi.org/10.1044/2019_AJSLP-18-0271

17. Bonilha, H. S., Huda, W., Wilmskoetter, J., Martin-Harris, B., & Tipnis, S. V. (2019). Radiation Risks to Adult Patients Undergoing Modified Barium Swallow Studies. *Dysphagia,* 34(6), 922–929. https://doi.org/10.1007/s00455-019-09993-w

18. Bracco Diagnostics. (2016). Varibar. Retrieved from: https://imaging.bracco.com/sites/braccoimaging.com/files/technica_sheet_pdf/us-en-2018-07-27-brochure-varibar.pdf

19. Crary, M., Carnaby Mann, G.D., Groher, M.E. (2005). Psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Arch Phys Med Rehabil*, 86 (8): 1516-20. doi: 10.1016/j.apmr.2004.11.049

20. Daggett A, Logemann J, Rademaker A, Pauloski B. (2006). Laryngeal penetration during deglutition in normal subjects of various ages. *Dysphagia*, 270-274. doi: 10.1007/s00455-006-9051-6

21. Ekberg O., Feinberg, M.J. (1991). Altered swallowing function in elderly patients without dysphagia: Radiographic findings in 56 cases. *AJR AM J Roentgenol*. 156 (6): 1181-1184. doi: 10.2214/ajr/156.6.2028863

22. Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, *12*(3), 189–198. https://doi.org/10.1016/0022-3956(75)90026-6

23. Fornari, F., Bravi, I., Penagini, R., Tack, J., & Sifrim, D. (2009). Multiple rapid swallowing: a complementary test during standard oesophageal manometry. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *21*(7), 718–e41. https://doi.org/10.1111/j.1365-2982.2009.01273.x

24. Fox, M. R., Sweis, R., Yadlapati, R., Pandolfino, J., Hani, A., Defilippi, C., Jan, T., & Rommel, N. (2021). Chicago classification version 4.0©technical review: Update on standard high-resolution manometry protocol for the assessment of esophageal motility. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *33*(4), e14120. https://doi.org/10.1111/nmo.14120

25. Garand, K., Culp, L., Wang, B., Davidson, K., & Martin-Harris, B. (2020). Aging Effects on Esophageal Transit Time in the Upright Position During Videofluoroscopy. *The Annals of otology, rhinology, and laryngology*, *129*(6), 618–624. https://doi.org/10.1177/0003489420903332

26. Garand, K. L., Hill, E. G., Amella, E., Armeson, K., Brown, A., & Martin-Harris, B. (2019). Bolus airway invasion observed during videofluoroscopy in healthy, non-dysphagic community-dwelling adults. Annals of Otology, Rhinology & Laryngology, 128(5), 426-432. doi:10.1177/0003489419826141

27. Gidda, J. S., & Goyal, R. K. (1985). Regional gradient of initial inhibition and refractoriness in esophageal smooth muscle. *Gastroenterology*, *89*(4), 843–851. https://doi.org/10.1016/0016-5085(85)90582-7

28. Goyal, R. K., & Chaudhury, A. (2008). Physiology of normal esophageal motility. *Journal of clinical gastroenterology*, *42*(5), 610–619. https://doi.org/10.1097/MCG.0b013e31816b444d

29. Goyal, R.K., Mashimo, H. (2006). Physiology of oral, pharyngeal, and esophageal motility. *GI Motil online*. doi: 10.1038/gimo1

30. Gullung, J. L., Hill, E. G., Castell, D. O., & Martin-Harris, B. (2012). Oropharyngeal and esophageal swallowing impairments: Their association and the predictive value of the modified barium swallow impairment profile and combined multichannel intraluminal

impedance-esophageal manometry. *The Annals of Otology, Rhinology, and Laryngology*, 121(11): 738-745. doi:10.1177/000348941212101107

31. Hightower, N. C., Jr (1955). Esophageal motility in health and disease. *Diseases of the chest,* 28(2), 150–169. https://doi.org/10.1378/chest.28.2.150

32. Hollenstein, M., Thwaites, P., Bütikofer, S., Heinrich, H., Sauter, M., Ulmer, I., Pohl, D., Ang, D., Eberli, D., Schwizer, W., Fried, M., Distler, O., Fox, M., & Misselwitz, B. (2017). Pharyngeal swallowing and oesophageal motility during a solid meal test: a prospective study in healthy volunteers and patients with major motility disorders. *The lancet. Gastroenterology & hepatology*, *2*(9), 644–653. https://doi.org/10.1016/S2468-1253(17)30151-6

33. Hollis, J. B., & Castell, D. O. (1975). Effect of dry swallows and wet swallows of different volumes on esophageal peristalsis. *Journal of applied physiology*, *38*(6), 1161–1164. https://doi.org/10.1152/jappl.1975.38.6.1161

34. Holloway, R.H. (2006). Esophageal Manometry. *GI Motil Online*. Doi: 10.1038/gimo39

35. Jones, B., Donner, M. W., Rubesin, S. E., Ravich, W. J., & Hendrix, T. R. (1987). Pharyngeal findings in 21 patients with achalasia of the esophagus. *Dysphagia*, 2(2), 87–92. https://doi.org/10.1007/BF02408139

36. Jones, B., Ravich, W. J., Donner, M. W., Kramer, S. S., & Hendrix, T. R. (1985). Pharyngoesophageal interrelationships: observations and working concepts. *Gastrointestinal radiology,* 10(3), 225–233. https://doi.org/10.1007/BF01893105

37. Jou, J., Radowsky, J., Gangnon, R., Sadowski, E., Kays, S., Hind, J., Gaumnitz, E., Taylor, A., & Robbins, J. (2009). Esophageal clearance patterns in normal older adults as documented with videofluoroscopic esophagram. *Gastroenterology research and practice*, *2009*, 965062. https://doi.org/10.1155/2009/965062

38. Kharilas, P.J., Logemann, J.A., Lin, S., Ergun, G.A. (1992). Pharyngeal clearance during swallowing: a combined manometric and videofluoroscopic study. *Gastroenterology,* 103: 128-136.

39. Leopold, A., Yu, D., Bhuta, R., Kataria, R., Lu, X., Jehangir, A., Harrison, M., Friedenberg, F., Malik, Z., Schey, R., & Parkman, H. P. (2019). Multiple Rapid Swallows (MRS) Complements Single-Swallow (SS) Analysis for High-Resolution Esophageal Manometry (HREM). *Digestive diseases and sciences*, *64*(8), 2206–2213. https://doi.org/10.1007/s10620-019-05545-2

40. Lever, T. E., Cox, K. T., Holbert, D., Shahrier, M., Hough, M., & Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. *Dysphagia,* 22(4), 312–325. https://doi.org/10.1007/s00455-007-9107-2

41. Levine, M. S., & Rubesin, S. E. (2017). History and Evolution of the Barium Swallow for Evaluation of the Pharynx and Esophagus. *Dysphagia,* 32(1), 55–72. https://doi.org/10.1007/s00455-016-9774-y

42. Levine, M. S., & Trenkner, S. W. (2011). Training the next generation in luminal gastrointestinal radiology: a call to arms. AJR. *American journal of roentgenology*, 196(2), 362–366. https://doi.org/10.2214/AJR.10.4917

43. Lin, Z., Yim, B., Gawron, A., Imam, H., Kahrilas, P. J., & Pandolfino, J. E. (2014). The four phases of esophageal bolus transit defined by high-resolution impedance manometry and fluoroscopy. *American journal of physiology. Gastrointestinal and liver physiology*, *307*(4), G437–G444. https://doi.org/10.1152/ajpgi.00148.2014

44. Logemann, J. A., & Larsen, K. (2012). Oropharyngeal dysphagia: Pathophysiology and diagnosis for the anniversary issue of diseases of the esophagus. *Diseases of the Esophagus,* 25(4), 299-304. doi:10.1111/j.1442-2050.2011.01210.x

45. Madhavan, A., Carnaby, G. D., & Crary, M. A. (2015). 'Food Sticking in My Throat': Videofluoroscopic Evaluation of a Common Symptom. *Dysphagia,* 30(3), 343–348. https://doi.org/10.1007/s00455-015-9605-6

46. Martin-Harris, B., (2015). Standardized training in swallow physiology – evidence-based assessment using the modified barium swallow impairment profile (MBSImP) approach. Gaylord, MI, Northern Speech Services.

47. Martin-Harris, B., Brodsky, MB, Michel, Y., Castell, DO., Schleicher, M., Sandidge, J., Maxwell, R., Blair, J. (2008). MBS measurement tool for swallow impairment – MBSImp: establishing a standard. *Dysphagia,* 23(4): 392-405. doi: 10/1007/s00455-008-9185-9.

48. Martin-Harris, B., Canon, C. L., Bonilha, H. S., Murray, J., Davidson, K., & Lefton-Greif, M. A. (2020). Best Practices in Modified Barium Swallow Studies. *American journal of speech-language pathology*, *29*(2S), 1078–1093. https://doi.org/10.1044/2020_AJSLP-19-00189

49. Martin-Harris, B., Humphries, K., Garand (Focht), K.L. (2017). The Modified Barium Swallow Impairment Profile (MBSImP) – Innovation, dissemination and implementation. Perspectives of the ASHA Special Interest Groups SIG 13, 2(4), 129-138. https://doi.org/10.1044/persp2.SIG13.129

50. Martin-Harris, B., & Jones, B. (2008). The videofluorographic swallowing study. *Physical medicine and rehabilitation clinics of North America*, 19(4), 769–viii. https://doi.org/10.1016/j.pmr.2008.06.004

51. Martin-Harris, B., Logemann, J. A., McMahon, S., Schleicher, M., & Sandidge, J. (2000). Clinical utility of the modified barium swallow. *Dysphagia,* 15(3), 136–141. https://doi.org/10.1007/s004550010015

52. Maurer A. H. (2016). Gastrointestinal Motility, Part 1: Esophageal Transit and Gastric Emptying. *Journal of nuclear medicine technology*, 44(1), 1–11. https://doi.org/10.2967/jnumed.112.114314

53. Meyer, G. W., Gerhardt, D. C., & Castell, D. O. (1981). Human esophageal response to rapid swallowing: muscle refractory period or neural inhibition? *The American journal of physiology*, *241*(2), G129–G136. https://doi.org/10.1152/ajpgi.1981.241.2.G129

54. Miles A. (2017). Inter-rater reliability for speech-language therapists' judgement of oesophageal abnormality during oesophageal visualization. *International journal of language & communication disorders,* 52(4), 450–455. https://doi.org/10.1111/1460-6984.12283

55. Miles, A., Bennett, K., & Allen, J. (2019). Esophageal Transit Times Vary with Underlying Comorbid Disease. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, 161(5), 829–834. https://doi.org/10.1177/0194599819874342

56. Miles, A., Clark, S., Jardine, M., & Allen, J. (2016). Esophageal Swallowing Timing Measures in Healthy Adults During Videofluoroscopy. *The Annals of otology, rhinology, and laryngology*, *125*(9), 764–769. https://doi.org/10.1177/0003489416653410

57. Miles, A., McMillan, J., Ward, K., & Allen, J. (2015). Esophageal visualization as an adjunct to the videofluoroscopic study of swallowing. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery,* 152(3), 488–493. https://doi.org/10.1177/0194599814565599

58. Mittal, R. K., Muta, K., Ledgerwood-Lee, M., & Zifan, A. (2020). Relationship between distension-contraction waveforms during esophageal peristalsis: effect of bolus volume, viscosity, and posture. *American journal of physiology. Gastrointestinal and liver physiology*, *319*(4), G454–G461. https://doi.org/10.1152/ajpgi.00117.2020

59. O'Rourke, A. K., Lazar, A., Murphy, B., Castell, D. O., & Martin-Harris, B. (2016). Utility of Esophagram versus High-Resolution Manometry in the Detection of Esophageal Dysmotility. *Otolaryngology--head and neck surgery : official journal of American*

Academy of Otolaryngology-Head and Neck Surgery, 154(5), 888–891. https://doi.org/10.1177/0194599816629379

60. O'Rourke, A., Morgan, L. B., Coss-Adame, E., Morrison, M., Weinberger, P., & Postma, G. (2014). The effect of voluntary pharyngeal swallowing maneuvers on esophageal swallowing physiology. *Dysphagia,* 29(2), 262–268. https://doi.org/10.1007/s00455-013-9505-6

61. Parada, M. T., Alba, A., & Sepúlveda, C. (2010). Bronchiolitis obliterans syndrome development in lung transplantation patients. *Transplantation proceedings,* 42(1), 331–332. https://doi.org/10.1016/j.transproceed.2009.11.037

62. Pandolfino, J. E., Shi, G., Zhang, Q., & Kahrilas, P. J. (2005). Absence of a deglutitive inhibition equivalent with secondary peristalsis. *American journal of physiology. Gastrointestinal and liver physiology*, *288*(4), G671–G676. https://doi.org/10.1152/ajpgi.00388.2004

63. Popa Nita, S., Murith, M., Chisholm, H., & Engmann, J. (2013). Matching the rheological properties of videofluoroscopic contrast agents and thickened liquid prescriptions. *Dysphagia*, *28*(2), 245–252. https://doi.org/10.1007/s00455-012-9441-x

64. Pouderoux, P., Shi, G., Tatum, R. P., & Kahrilas, P. J. (1999). Esophageal solid bolus transit: studies using concurrent videofluoroscopy and manometry. *The American journal of gastroenterology*, *94*(6), 1457–1463. https://doi.org/10.1111/j.1572-0241.1999.01126.x

65. Reedy, E. L., Herbert, T. L., & Bonilha, H. S. (2021). Visualizing the Esophagus During Modified Barium Swallow Studies: A Systematic Review. *American journal of speech-language pathology*, *30*(2), 761–771. https://doi.org/10.1044/2020_AJSLP-20-00255

66. Robbins, J., Coyle, J., Rosenbek, J., Roecker, E., & Wood, J. (1999). Differentiation of normal and abnormal airway protection during swallowing using the penetration-aspiration scale. *Dysphagia,* 14(4), 228–232. https://doi.org/10.1007/PL00009610

67. 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

68. Savarino, E., di Pietro, M., Bredenoord, A. J., Carlson, D. A., Clarke, J. O., Khan, A., Vela, M. F., Yadlapati, R., Pohl, D., Pandolfino, J. E., Roman, S., & Gyawali, C. P. (2020). Use of the Functional Lumen Imaging Probe in Clinical Esophagology. *The American journal of gastroenterology*, *115*(11), 1786–1796. https://doi.org/10.14309/ajg.0000000000000773

69. Scharitzer, M., Lenglinger, J., Schima, W., Weber, M., Ringhofer, C., & Pokieser, P. (2017). Comparison of videofluoroscopy and impedance planimetry for the evaluation of oesophageal stenosis: a retrospective study. *European radiology*, *27*(4), 1760–1767. https://doi.org/10.1007/s00330-016-4516-y

70. Shi, G., Pandolfino, J. E., Zhang, Q., Hirano, I., Joehl, R. J., & Kahrilas, P. J. (2003). Deglutitive inhibition affects both esophageal peristaltic amplitude and shortening. *American journal of physiology. Gastrointestinal and liver physiology*, *284*(4), G575–G582. https://doi.org/10.1152/ajpgi.00311.2002

71. Sifrim, D., & Jafari, J. (2012). Deglutitive inhibition, latency between swallow and esophageal contractions and primary esophageal motor disorders. *Journal of neurogastroenterology and motility,* 18(1), 6–12. https://doi.org/10.5056/jnm.2012.18.1.6

72. Sifrim, D. A., & Janssens, J. P. (1999). The 'artificial high pressure zone'. A non-invasive method to study in man the effect of the inhibitory innervation to the oesophagus. Validation study using a combined manometric-barostat technique. *European journal of gastroenterology & hepatology*, *11*(2), 165–169. https://doi.org/10.1097/00042737-199902000-00017

73. Sifrim, D., Janssens, J., & Vantrappen, G. (1994). Failing deglutitive inhibition in primary esophageal motility disorders. *Gastroenterology*, *106*(4), 875–882. https://doi.org/10.1016/0016-5085(94)90745-5

74. Sifrim, D., Janssens, J., & Vantrappen, G. (1992). A wave of inhibition precedes primary peristaltic contractions in the human esophagus. *Gastroenterology*, *103*(3), 876–882. https://doi.org/10.1016/0016-5085(92)90020-y

75. Snyder, D. L., Valdovinos, L. R., Horsley-Silva, J., Crowell, M. D., Valdovinos, M. A., & Vela, M. F. (2020). Opioids Interfere With Deglutitive Inhibition Assessed by Response to Multiple Rapid Swallows During High-Resolution Esophageal Manometry. *The American journal of gastroenterology*, *115*(7), 1125–1128. https://doi.org/10.14309/ajg.0000000000000682

76. Steele, C. M., Alsanei, W. A., Ayanikalath, S., Barbon, C. E., Chen, J., Cichero, J. A., Coutts, K., Dantas, R. O., Duivestein, J., Giosa, L., Hanson, B., Lam, P., Lecko, C., Leigh, C., Nagy, A., Namasivayam, A. M., Nascimento, W. V., Odendaal, I., Smith, C. H., & Wang, H. (2015). The influence of food texture and liquid consistency modification on swallowing physiology and function: a systematic review. *Dysphagia,* 30(1), 2–26. https://doi.org/10.1007/s00455-014-9578-x

77. Steele, C.M., Martin-Harris, B., Gosa, M., Allen, S.E. (2021). Applications in Contrast Imaging: Diagnosis and Management of Swallowing Physiology: Standardized Contrast,

the MBSImPTM, & the IDDSI Framework. *Applied Radiology.* Retrieved from: https://www.appliedradiology.org/courses/4294%2FPDF%2FBracco_05-21_IDDSI_CE_FNL040221.pdf

78. Steele, C. M., Namasivayam-MacDonald, A. M., Guida, B. T., Cichero, J. A., Duivestein, J., Hanson, B., Lam, P., & Riquelme, L. F. (2018). Creation and Initial Validation of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale. *Archives of physical medicine and rehabilitation,* 99(5), 934–944. https://doi.org/10.1016/j.apmr.2018.01.012

79. Tutuian, R., Jalil, S., Katz, P. O., & Castell, D. O. (2004). Effect of interval between swallows on oesophageal pressures and bolus movement in normal subjects - Studies with combined multichannel intraluminal impedance and oesophageal manometry. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society,* 16(1), 23–29. https://doi.org/10.1046/j.1365-2982.2003.00460.x

80. Watts, S., Gaziano, J., Jacobs, J., & Richter, J. (2019). Improving the Diagnostic Capability of the Modified Barium Swallow Study Through Standardization of an Esophageal Sweep Protocol. *Dysphagia*, 34(1), 34–42. https://doi.org/10.1007/s00455-018-09966-5

81. Watts, S., Gaziano, J., Kumar, A., & Richter, J. (2021). Diagnostic Accuracy of an Esophageal Screening Protocol Interpreted by the Speech-Language Pathologist. *Dysphagia*, 10.1007/s00455-020-10239-3. Advance online publication. https://doi.org/10.1007/s00455-020-10239-3

82. Yadlapati, R., Furuta, G. T., & Menard-Katcher, P. (2019). New Developments in Esophageal Motility Testing. *Current treatment options in gastroenterology*, *17*(1), 76–88. https://doi.org/10.1007/s11938-019-00218-5

83. Yadlapati, R., Kahrilas, P. J., Fox, M. R., Bredenoord, A. J., Prakash Gyawali, C., Roman, S., Babaei, A., Mittal, R. K., Rommel, N., Savarino, E., Sifrim, D., Smout, A., Vaezi, M. F., Zerbib, F., Akiyama, J., Bhatia, S., Bor, S., Carlson, D. A., Chen, J. W., Cisternas, D., … Pandolfino, J. E. (2021). Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, *33*(1), e14058. https://doi.org/10.1111/nmo.14058

CHAPTER 5:
CONCLUSION

Our research identified that esophageal clearance abnormalities identified during the MBSS was not a rare event – even in populations where the suspected risk for oropharyngeal manifestations of dysphagia were higher (e.g., post-stroke and post-lung transplant). In fact, we found that any degree of pharyngeal impairment, but specifically reduced pharyngeal constriction, was significantly associated with abnormal esophageal clearance in post-stroke patients. Whereas this was not seen in the post-lung transplant cohort, most patients had abnormal esophageal clearance regardless of oropharyngeal impairment, though findings might owe to a smaller sample size. In a small cohort of outpatients referred for an MBSS the vast majority were identified with having abnormal esophageal clearance patterns with and without cueing to alter the impact of deglutitive inhibition. It is becoming increasingly clear that arbitrary divisions between assessments of the oropharynx and esophagus is contradictory to the physiologic interrelationships of the swallowing continuum. Swallowing is not phasic, rather, a highly synchronous coordination of pressures generated by biomechanically interdependent events.

Future Considerations:

Assessment practices should follow the growing body of evidence which supports not only swallowing as a continuum (Gullung et al., 2012; Jones et al., 1987; Jones et al., 1985; Lever et al., 2007; Madhavan, Carnaby & Crary, 2015; Miles et al., 2015; Miles et al., 2019; Miles et al., 2017; O'Rourke et al., 2016; Ortiz et al., 2019; Reedy et al., 2021; Triadafilopoulos, 1992; Watts et al., 2019; Watts et al., 2021), but also that swallowing and respiration are inextricably linked (Brodsky et al, 2010; Hopkins-Rossabi, 2019; Martin-Harris, 2008; Martin-Harris et al, 2003, Martin-Harris et al, 2005; Mastuo & Palmer, 2009; Martin-Harris & McFarland, 2013; McFarland et al., 2016; McFarland & Lund, 1995; Wheeler-Hegland et al., 2011). Treatment should target these shared neurophysiologic components to utilize the entire aerodigestive system to recruit the maximum amount of musculature and activate or aim to stimulate the most nerves. Since the systems are linked, so too should the interventions (when the patients are appropriate and able to engage in such dynamic therapies). Therapy which targets the respiratory system, such as respiratory muscle strength training (RMST), demonstrates improved swallowing function for

the post-stroke population (Eom et al., 2017; Gomes-Neto et al., 2016; Hegland et al., 2016). Utilizing this therapeutic technique in the pre-lung transplant population has demonstrated promise (Pehlivan et al., 2018) and could be an encouraging intervention to explore in the post-lung transplant population as well. RMST has the benefit of addressing more than dysphagia with potential to target the breathing, coughing, and speech functions of the aerodigestive tract (Arnold & Bausek, 2020; Brooks et al., 2019; Eom et al., 2017; Hegland et al., 2016; Hutcheson et al., 2018; Plowman et al., 2018; Sapienza & Wheeler, 2006). And the influence of respiratory training and/or respiratory-swallow training on those patients with primary disorders of the esophagus is relatively unexplored.

References

1. Adegunsoye, A., Strek, M. E., Garrity, E., Guzy, R., & Bag, R. (2017). Comprehensive Care of the Lung Transplant Patient. Chest, 152(1), 150–164. https://doi.org/10.1016/j.chest.2016.10.001

2. Adeoye, O., Nyström, K. V., Yavagal, D. R., Luciano, J., Nogueira, R. G., Zorowitz, R. D., Khalessi, A. A., Bushnell, C., Barsan, W. G., Panagos, P., Alberts, M. J., Tiner, A. C., Schwamm, L. H., & Jauch, E. C. (2019). Recommendations for the Establishment of Stroke Systems of Care: A 2019 Update. Stroke, 50(7), e187–e210. https://doi.org/10.1161/STR.0000000000000173

3. Ahya, V. N., & Diamond, J. M. (2019). Lung Transplantation. The Medical clinics of North America, 103(3), 425–433. https://doi.org/10.1016/j.mcna.2018.12.003

4. AlJulaih, G. H., & Menezes, R. G. (2020). Anatomy, Head and Neck, Hyoid Bone. In StatPearls. StatPearls Publishing.

5. Allaix, M. E., Rebecchi, F., Morino, M., Schlottmann, F., & Patti, M. G. (2017). Gastroesophageal Reflux and Idiopathic Pulmonary Fibrosis. World journal of surgery, 41(7), 1691–1697. https://doi.org/10.1007/s00268-017-3956-0

6. Allen, J. E., White, C., Leonard, R., & Belafsky, P. C. (2012). Comparison of esophageal screen findings on videofluoroscopy with full esophagram results. Head & Neck, 34(2), 264-269. doi:10.1002/hed.21727

7. Altman KW, Yu GP, Schaefer SD. Consequence of dysphagia in the hospitalized patient: Impact on prognosis and hospital resources. Arch Otolaryngol Head Neck Surg. 2010; Aug; 136(8):784-9. doi: 10.1001/archoto.2010.129.

8. American College of Radiology (ACR). (2017). ACR-SPR Practice Parameter for the Performance of the Modified Barium Swallow. Retrieved from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Modified-Ba-Swallow.pdf

9. American College of Radiology (ACR). (2019). ACR-SPR Practice Parameter for the Performance of Esophagrams and upper gastrointestinal examinations in adults. Retrieved from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/UpperGIAdults.pdf

10. American Speech-Language Hearing Association (ASHA). (n.d.). Adult Dysphagia: Incidence and prevalence. Retrieved from: https://www.asha.org/PRPSpecificTopic.aspx?folderid=8589942550&section=Incidence_and_Prevalence

11. American Speech-Language Hearing Association (ASHA). (2004a) Knowledge and Skills Needed by Speech-Language Pathologists Performing Videofluoroscopic Swallowing Studies. Retrieved from: www.asha.org/policy

12. American Speech-Language Hearing Association (ASHA). (2004b) Preferred Practice Patterns for the Profession of Speech-Language Pathology. Retrieved from: www.asha.org/policy

13. American Speech-Language-Hearing Association. (2004c). Guidelines for speech-language pathologists performing videofluoroscopic swallowing studies. *ASHA Supplement 24*, 77–92.

14. Anderson, T. M., Garcia, A. J., 3rd, Baertsch, N. A., Pollak, J., Bloom, J. C., Wei, A. D., Rai, K. G., & Ramirez, J. M. (2016). A novel excitatory network for the control of breathing. Nature, 536(7614), 76–80. https://doi.org/10.1038/nature18944

15. Atkins, B. Z., Petersen, R. P., Daneshmand, M. A., Turek, J. W., Lin, S. S., & Davis, R. D., Jr (2010). Impact of oropharyngeal dysphagia on long-term outcomes of lung transplantation. The Annals of thoracic surgery, 90(5), 1622–1628. https://doi.org/10.1016/j.athoracsur.2010.06.089

16. Atkins, B. Z., Trachtenberg, M. S., Prince-Petersen, R., Vess, G., Bush, E. L., Balsara, K. R., Lin, S. S., & Davis, R. D., Jr (2007). Assessing oropharyngeal dysphagia after lung transplantation: altered swallowing mechanisms and increased morbidity. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, 26(11), 1144–1148. https://doi.org/10.1016/j.healun.2007.07.038

17. Au, J., Hawkins, T., Venables, C., Morritt, G., Scott, C. D., Gascoigne, A. D., Corris, P. A., Hilton, C. J., & Dark, J. H. (1993). Upper gastrointestinal dysmotility in heart-lung transplant recipients. The Annals of thoracic surgery, 55(1), 94–97. https://doi.org/10.1016/0003-4975(93)90480-6

18. Bacak, B. J., Kim, T., Smith, J. C., Rubin, J. E., & Rybak, I. A. (2016). Mixed-mode oscillations and population bursting in the pre-Bötzinger complex. eLife, 5, e13403. https://doi.org/10.7554/eLife.13403

19. Barha, C.K., Nagamatsu, L.S., Liu-Ambrose, T. (2016). Basics of neuroanatomy and physiology. *Handbook of clinical neurology*, (138, p.p. 53-68), https://doi.org/10.1016/B978-0-12-802973-2.00004-5

20. Basseri, B., Conklin, J.L., Pimentel, M., Tabrizi R., Phillips, E.H., Simsir, S.A., …, Soukiasian, H.J. (2010). Esophageal motor dysfunction and gastroesophageal reflux are present in

lung transplant candidates. *J Thorac Surg*, 90: 1630-36. doi: 10.1016/j.athoracsur.2010.06.104

21. Baumann, B., Byers, S., Wasserman-Wincko, T., Smith, L., Hathaway, B., Bhama, J., Shigemura, N., Hayanga, J., D'Cunha, J., & Johnson, J. T. (2017). Postoperative Swallowing Assessment After Lung Transplantation. *The Annals of thoracic surgery*, *104*(1), 308–312. https://doi.org/10.1016/j.athoracsur.2017.01.080

22. Belafsky, P. C., Postma, G. N., & Koufman, J. A. (2001). The validity and reliability of the reflux finding score (RFS). *The Laryngoscope*, 111(8), 1313–1317. https://doi.org/10.1097/00005537-200108000-00001

23. Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., de Ferranti, S. D., Floyd, J., Fornage, M., Gillespie, C., Isasi, C. R., Jiménez, M. C., Jordan, L. C., Judd, S. E., Lackland, D., Lichtman, J. H., Lisabeth, L., Liu, S., Longenecker, C. T., Mackey, R. H., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee (2017). Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation,* 135(10), e146–e603. https://doi.org/10.1161/CIR.0000000000000485

24. Bhatnagar, S. C. (2008). Neuroscience for the study of communicative disorders (3rd ed.). Baltimore, MD: Wolters Kluwer Health, Lippincott Williams & Wilkins.

25. Blondeau, K., Mertens, V., Vanaudenaerde, B. A., Verleden, G. M., Van Raemdonck, D. E., Sifrim, D., & Dupont, L. J. (2009). Nocturnal weakly acidic reflux promotes aspiration of bile acids in lung transplant recipients. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation*, 28(2), 141–148. https://doi.org/10.1016/j.healun.2008.11.906

26. Bobadilla, J. L., Jankowska-Gan, E., Xu, Q., Haynes, L. D., Munoz del Rio, A., Meyer, K., Greenspan, D. S., De Oliveira, N., Burlingham, W. J., & Maloney, J. D. (2010). Reflux-induced collagen type v sensitization: potential mediator of bronchiolitis obliterans syndrome. Chest, 138(2), 363–370. https://doi.org/10.1378/chest.09-2610

27. Boehler A, Kesten S, Weder W, Speich R. (1998). Bronchiolitis obliterans after lung transplantation: a review. Chest, 114:1411–26.

28. Bonilha, H. S., Blair, J., Carnes, B., Huda, W., Humphries, K., McGrattan, K., Michel, Y., & Martin-Harris, B. (2013). Preliminary investigation of the effect of pulse rate on judgments of swallowing impairment and treatment recommendations. Dysphagia, 28(4), 528–538. https://doi.org/10.1007/s00455-013-9463-z

29. Bonilha, HS., Humphries, K., Hill, EG., McGrattan, K., Carnes, B., Huda, W., Martin-Harris, B. (2013). Radiation Exposure time during MBSS: influence of swallowing impairment severity, medical diagnosis, clinician experience, and standardized protocol use. Dysphagia, 28(1), 77-85. doi. 10.1007/s00455-012-9415-z.

30. Bonilha, H. S., Simpson, A. N., Ellis, C., Mauldin, P., Martin-Harris, B., & Simpson, K. (2014). The one-year attributable cost of post-stroke dysphagia. Dysphagia, 29(5), 545–552. https://doi.org/10.1007/s00455-014-9543-8

31. Bonilha, H. S., Wilmskoetter, J., Tipnis, S., Horn, J., Martin-Harris, B., & Huda, W. (2019). Relationships Between Radiation Exposure Dose, Time, and Projection in Videofluoroscopic Swallowing Studies. American journal of speech-language pathology, 28(3), 1053–1059. https://doi.org/10.1044/2019_AJSLP-18-0271

32. Bonilha, H. S., Huda, W., Wilmskoetter, J., Martin-Harris, B., & Tipnis, S. V. (2019). Radiation Risks to Adult Patients Undergoing Modified Barium Swallow Studies. Dysphagia, 34(6), 922–929. https://doi.org/10.1007/s00455-019-09993-w

33. Borders, J. C., Fink, D., Levitt, J. E., McKeehan, J., McNally, E., Rubio, A., Scheel, R., Siner, J. M., Taborda, S. G., Vojnik, R., Warner, H., White, S. D., Langmore, S. E., Moss, M., & Krisciunas, G. P. (2019). Relationship Between Laryngeal Sensation, Length of Intubation, and Aspiration in Patients with Acute Respiratory Failure. Dysphagia, 34(4), 521–528. https://doi.org/10.1007/s00455-019-09980-1

34. Bracco Diagnostics. (2016). Varibar. Retrieved from: https://imaging.bracco.com/sites/braccoimaging.com/files/technica_sheet_pdf/us-en-2018-07-27-brochure-varibar.pdf

35. Bredenoord, A. J., Fox, M., Kahrilas, P. J., Pandolfino, J. E., Schwizer, W., Smout, A. J., & International High Resolution Manometry Working Group (2012). Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 24 Suppl 1(Suppl 1), 57–65. https://doi.org/10.1111/j.1365-2982.2011.01834.x

36. Brodsky, M. B., De, I., Chilukuri, K., Huang, M., Palmer, J. B., & Needham, D. M. (2018). Coordination of Pharyngeal and Laryngeal Swallowing Events During Single Liquid Swallows After Oral Endotracheal Intubation for Patients with Acute Respiratory Distress Syndrome. Dysphagia, 33(6), 768–777. https://doi.org/10.1007/s00455-018-9901-z

37. Brodsky, M. B., Gellar, J. E., Dinglas, V. D., Colantuoni, E., Mendez-Tellez, P. A., Shanholtz, C., Palmer, J. B., & Needham, D. M. (2014). Duration of oral endotracheal intubation is associated with dysphagia symptoms in acute lung injury patients. Journal of critical care, 29(4), 574–579. https://doi.org/10.1016/j.jcrc.2014.02.015

38. Brodsky, M. B., Levy, M. J., Jedlanek, E., Pandian, V., Blackford, B., Price, C., Cole, G., Hillel, A. T., Best, S. R., & Akst, L. M. (2018). Laryngeal injury and upper airway symptoms after oral endotracheal intubation with mechanical ventilation during critical care: A systematic review. Critical care medicine, 46(12), 2010–2017. https://doi.org/10.1097/CCM.0000000000003368

39. Brodsky, M. B., McFarland, D. H., Dozier, T. S., Blair, J., Ayers, C., Michel, Y., Gillespie, M. B., Day, T. A., & Martin-Harris, B. (2010). Respiratory-swallow phase patterns and their relationship to swallowing impairment in patients treated for oropharyngeal cancer. Head & neck, 32(4), 481–489. https://doi.org/10.1002/hed.21209

40. Burton PR, Button B, Brown W, et al. Medium-term outcome of fundoplication after lung transplantation. Dis Esophagus. 2009;22(8):642-648. doi:10.1111/j.1442-2050.2009.00980.x

41. Cantu, E., 3rd, Appel, J. Z., 3rd, Hartwig, M. G., Woreta, H., Green, C., Messier, R., Palmer, S. M., & Davis, R. D., Jr (2004). J. Maxwell Chamberlain Memorial Paper. Early fundoplication prevents chronic allograft dysfunction in patients with gastroesophageal reflux disease. The Annals of thoracic surgery, 78(4), 1142–1151. https://doi.org/10.1016/j.athoracsur.2004.04.044

42. Carnaby, G., Harenberg, L. (2013). What is “usual care” in dysphagia rehabilitation: A survey of USA dysphagia practice patterns. Dysphagia, 28: 567-574. doi: 10.1007/s00455-013-9467-8

43. Cassiani, R. A., Santos, C. M., Baddini-Martinez, J., & Dantas, R. O. (2015). Oral and pharyngeal bolus transit in patients with chronic obstructive pulmonary disease. International journal of chronic obstructive pulmonary disease, 10, 489–496. https://doi.org/10.2147/COPD.S74945

44. Catalá-Ripoll, J. V., Monsalve-Naharro, J. Á., & Hernández-Fernández, F. (2020). Incidence and predictive factors of diaphragmatic dysfunction in acute stroke. BMC neurology, 20(1), 79. https://doi.org/10.1186/s12883-020-01664-w

45. Chan, E. G., Bianco, V., 3rd, Richards, T., Hayanga, J. W., Morrell, M., Shigemura, N., Crespo, M., Pilewski, J., Luketich, J., & D'Cunha, J. (2016). The ripple effect of a complication in lung transplantation: Evidence for increased long-term survival risk. The Journal of thoracic and cardiovascular surgery, 151(4), 1171–1179. https://doi.org/10.1016/j.jtcvs.2015.11.058

46. Clayton, N. A., Carnaby, G. D., Peters, M. J., & Ing, A. J. (2014). Impaired laryngopharyngeal sensitivity in patients with COPD: the association with swallow

function. International journal of speech-language pathology, 16(6), 615–623. https://doi.org/10.3109/17549507.2014.882987

47. Cohen, D. L., Roffe, C., Beavan, J., Blackett, B., Fairfield, C. A., Hamdy, S., Havard, D., McFarlane, M., McLauglin, C., Randall, M., Robson, K., Scutt, P., Smith, C., Smithard, D., Sprigg, N., Warusevitane, A., Watkins, C., Woodhouse, L., & Bath, P. M. (2016). Post-stroke dysphagia: A review and design considerations for future trials. *International journal of stroke : official journal of the International Stroke Society*, *11*(4), 399–411. https://doi.org/10.1177/1747493016639057

48. Cola, M.G., Daniels, S.K., Corey, D.M., Lemen, L.C., Romero, M., Foundas, A.L. (2010). Relevance of subcortical stroke in dysphagia. Stroke, 41(3): 482-486. doi: 10.1161/STROKEAHA.109.566133.

49. Cole, A. P., & Trinh, Q. D. (2017). Secondary data analysis: techniques for comparing interventions and their limitations. Current opinion in urology, 27(4), 354–359. https://doi.org/10.1097/MOU.0000000000000407

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

51. Cranial Nerves. (nd). Cranial Nerves, n.d.; http://what-when-how.com/wp-content/uploads/2012/04/tmp15F29.jpg)

52. Crary, M., Carnaby Mann, G.D., Groher, M.E. (2005). Psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil, 86 (8): 1516-20. doi: 10.1016/j.apmr.2004.11.049

53. Cvejic, L., Harding, R., Churchward, T., Turton, A., Finlay, P., Massey, D., Bardin, P. G., & Guy, P. (2011). Laryngeal penetration and aspiration in individuals with stable COPD. Respirology (Carlton, Vic.), 16(2), 269–275. https://doi.org/10.1111/j.1440-1843.2010.01875.x

54. da Rosa, F. B., Pasqualoto, A. S., Steele, C. M., & Mancopes, R. (2020). Oral and oropharyngeal sensory function in adults with chronic obstructive pulmonary disease. American journal of speech-language pathology, 29(2), 864–872. https://doi.org/10.1044/2019_AJSLP-19-00095

55. Daggett A, Logemann J, Rademaker A, Pauloski B. (2006). Laryngeal penetration during deglutition in normal subjects of various ages. Dysphagia, 270-274. doi: 10.1007/s00455-006-9051-6

56. Daniels, S. K., Brailey, K., Priestly, D. H., Herrington, L. R., Weisberg, L. A., & Foundas, A. L. (1998). Aspiration in patients with acute stroke. Archives of physical medicine and rehabilitation, 79(1), 14–19. https://doi.org/10.1016/s0003-9993(98)90200-3

57. Daniels, S. K., & Foundas, A. L. (1997). The role of the insular cortex in dysphagia. Dysphagia, 12(3), 146-156. doi:10.1007/PL00009529

58. Daniels, S., Pathak, S., Mukhi, S., Stach, C., Morgan, R., & Anderson, J. (2017). The relationship between lesion localization and dysphagia in acute stroke. Dysphagia, 32(6), 777-784. doi:10.1007/s00455-017-9824-0

59. Davis, C. S., Shankaran, V., Kovacs, E. J., Gagermeier, J., Dilling, D., Alex, C. G., Love, R. B., Sinacore, J., & Fisichella, P. M. (2010). Gastroesophageal reflux disease after lung transplantation: pathophysiology and implications for treatment. Surgery, 148(4), 737–745. https://doi.org/10.1016/j.surg.2010.07.011

60. Effros, R.M. (2006). Anatomy, development, and physiology of the lungs. GI Motil. Doi: 10.1038/gimo73

61. Effros, R. M., Jacobs, E. R., Schapira, R. M., & Biller, J. (2000). Response of the lungs to aspiration. The American journal of medicine, 108 Suppl 4a, 15S–19S. https://doi.org/10.1016/s0002-9343(99)00290-9

62. Ekberg O., Feinberg, M.J. (1991). Altered swallowing function in elderly patients without dysphagia: Radiographic findings in 56 cases. AJR AM J Roentgenol. 156 (6): 1181-1184. doi: 10.2214/ajr/156.6.2028863

63. Eng, K., Jose Flores, M., Gerrity, E., Sinha, N., Imbeau, K., Erbele, L., Yeh, C. (2019). Evaluation of swallow function on healthy adults while using high-flow nasal cannula. Perspectives of the ASHA Special Interest Groups, 4(6), 1516
64. -1524. https://doi.org/10.1044/2019_PERS-SIG13-2019-0013

65. Eom, M. J., Chang, M. Y., Oh, D. H., Kim, H. D., Han, N. M., & Park, J. S. (2017). Effects of resistance expiratory muscle strength training in elderly patients with dysphagic stroke. *NeuroRehabilitation*, 41(4), 747–752. https://doi.org/10.3233/NRE-172192

66. Ertekin, C., (2011). Voluntary versus spontaneous swallowing in man. *Dysphagia,* 26(2), 183-192. doi: 10.1007/s00455-010-9319-8

67. Ertekin C., Aydogdu I. (2003). Neurophysiology of swallowing. *Clinical Neurophysiology*, 114, 2226-2244. doi: https://doi.org/10.1016/S1388-2457(03)00237-2

68. Estenne, M., Maurer, J. R., Boehler, A., Egan, J. J., Frost, A., Hertz, M., Mallory, G. B., Snell, G. I., & Yousem, S. (2002). Bronchiolitis obliterans syndrome 2001: an update of

the diagnostic criteria. *The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation*, 21(3), 297–310. https://doi.org/10.1016/s1053-2498(02)00398-4

69. Fahim, A., Crooks, M., & Hart, S. P. (2011). Gastroesophageal reflux and idiopathic pulmonary fibrosis: a review. Pulmonary medicine, 2011, 634613. https://doi.org/10.1155/2011/634613

70. Ferreira, J. N., & Hoffman, M. P. (2013). Interactions between developing nerves and salivary glands. Organogenesis, 9(3), 199-205. doi:10.4161/org.25224

71. Fife, T. A., Butler, S. G., Langmore, S. E., Lester, S., Wright, S. C., Jr, Kemp, S., Grace-Martin, K., & Lintzenich, C. R. (2015). Use of topical nasal anesthesia during flexible endoscopic evaluation of swallowing in dysphagic patients. *The Annals of otology, rhinology, and laryngology*, 124(3), 206–211. https://doi.org/10.1177/0003489414550153

72. Flowers, H. L., AlHarbi, M. A., Mikulis, D., Silver, F. L., Rochon, E., Streiner, D., & Martino, R. (2017). MRI-Based Neuroanatomical Predictors of Dysphagia, Dysarthria, and Aphasia in Patients with First Acute Ischemic Stroke. *Cerebrovascular diseases extra*, 7(1), 21–34. https://doi.org/10.1159/000457810

73. Gadel, A. A., Mostafa, M., Younis, A., & Haleem, M. (2012). Esophageal motility pattern and gastro-esophageal reflux in chronic obstructive pulmonary disease. *Hepato-gastroenterology*, 59(120), 2498–2502. https://doi.org/10.5754/hge10433

74. Galmiche, J. P., & des Varannes, S. B. (2001). Endoscopy-negative reflux disease. *Current gastroenterology reports*, 3(3), 206–214. https://doi.org/10.1007/s11894-001-0023-6

75. Galovic M, Leisi N, Müller M, Weber J, Abela E, Kägi G, Weder B. (2013).Lesion location predicts transient and extended risk of aspiration after supratentorial ischemic stroke. *Stroke*,44(10):2760-7. doi: 10.1161/STROKEAHA.113.001690. Epub 2013 Jul 25. PMID: 23887840.

76. Gamez, J., Salvado, M., Martinez-de La Ossa, A., Deu, M., Romero, L., Roman, A., Sacanell, J., Laborda, C., Rochera, I., Nadal, M., Carmona, F., Santamarina, E., Raguer, N., Canela, M., & Solé, J. (2017). Influence of early neurological complications on clinical outcome following lung transplant. *PloS one*, 12(3), e0174092. https://doi.org/10.1371/journal.pone.0174092

77. Gao, F., Hobson, A. R., Shang, Z. M., Pei, Y. X., Gao, Y., Wang, J. X., & Huang, W. N. (2015). The prevalence of gastro-esophageal reflux disease and esophageal dysmotility in Chinese patients with idiopathic pulmonary fibrosis. BMC gastroenterology, 15, 26. https://doi.org/10.1186/s12876-015-0253-y

78. Garand, K. L., Hill, E. G., Amella, E., Armeson, K., Brown, A., & Martin-Harris, B. (2019). Bolus airway invasion observed during videofluoroscopy in healthy, non-dysphagic community-dwelling adults. Annals of Otology, Rhinology & Laryngology, 128(5), 426-432. doi:10.1177/0003489419826141

79. Garand, K., 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

80. Garand, K. L., Strange, C., Paoletti, L., Hopkins-Rossabi, T., & Martin-Harris, B. (2018). Oropharyngeal swallow physiology and swallowing-related quality of life in underweight patients with concomitant advanced chronic obstructive pulmonary disease. International journal of chronic obstructive pulmonary disease, 13, 2663–2671. https://doi.org/10.2147/COPD.S165657

81. Gasper, W. J., Sweet, M. P., Golden, J. A., Hoopes, C., Leard, L. E., Kleinhenz, M. E., Hays, S. R., & Patti, M. G. (2008). Lung transplantation in patients with connective tissue disorders and esophageal dysmotility. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus*, 21(7), 650–655. https://doi.org/10.1111/j.1442-2050.2008.00828.x

82. Gavini, S., Borges, L. F., Finn, R. T., Lo, W. K., Goldberg, H. J., Burakoff, R., Feldman, N., & Chan, W. W. (2017). Lung disease severity in idiopathic pulmonary fibrosis is more strongly associated with impedance measures of bolus reflux than pH parameters of acid reflux alone. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*, 29(5), 10.1111/nmo.13001. https://doi.org/10.1111/nmo.13001

83. Gavini, S., Finn, R. T., Lo, W. K., Goldberg, H. J., Burakoff, R., Feldman, N., & Chan, W. W. (2015). Idiopathic pulmonary fibrosis is associated with increased impedance measures of reflux compared to non-fibrotic disease among pre-lung transplant patients. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 27(9), 1326–1332. https://doi.org/10.1111/nmo.12627

84. Gaziano, J., Watts, S. (2018). Screening for Esophageal Dysphagia: Enhancing the Clinical Utility of the Modified Barium Swallow. Perspectives of the ASHA Special Interest Groups, SIG 13. 3 (2): 67-74. https://doi.org/10.1044/persp3.SIG13.67

85. Girgis, R. E., & Khaghani, A. (2016). A global perspective of lung transplantation: Part 1 - Recipient selection and choice of procedure. Global cardiology science & practice, 2016(1), e201605. https://doi.org/10.21542/gcsp.2016.5

86. Glaser, B. G., Strauss, A. L., & Strutzel, E. (1968). The discovery of grounded theory; strategies for qualitative research. Nursing research, 17(4), 364.

87. Good-Fratturelli, M. D., Curlee, R. F., & Holle, J. L. (2000). Prevalence and nature of dysphagia in VA patients with COPD referred for videofluoroscopic swallow examination. *Journal of communication disorders*, 33(2), 93–110. https://doi.org/10.1016/s0021-9924(99)00026-x

88. Gomes-Neto, M., Saquetto, M. B., Silva, C. M., Carvalho, V. O., Ribeiro, N., & Conceição, C. S. (2016). Effects of respiratory muscle training on respiratory function, respiratory muscle strength, and exercise tolerance in patients poststroke: A systematic review with meta-analysis. Archives of physical medicine and rehabilitation, 97(11), 1994–2001. https://doi.org/10.1016/j.apmr.2016.04.018

89. González-Fernández, M., Ottenstein, L., Atanelov, L., & Christian, A. B. (2013). Dysphagia after stroke: an overview. Current physical medicine and rehabilitation reports, 1(3), 187–196. https://doi.org/10.1007/s40141-013-0017-y

90. Goyal, R.K., Mashimo, H. (2006). Physiology of oral, pharyngeal, and esophageal motility. GI Motil online. doi: 10.1038/gimo1

91. Grass, F., Schäfer, M., Cristaudi, A., Berutto, C., Aubert, J. D., Gonzalez, M., Demartines, N., Ris, H. B., Soccal, P. M., & Krueger, T. (2015). Incidence and Risk Factors of Abdominal Complications After Lung Transplantation. World journal of surgery, 39(9), 2274–2281. https://doi.org/10.1007/s00268-015-3098-1

92. Griffin, S.M., Robertson, A.G.N., Bredenoord, .J., Brownlee, I.A., Stovold, R., Brodlie, M., …, Ward, C. (2013). Aspiration and allograft injury secondary to gastroesophageal reflux occur in the immediate post-lung transplantation period (prospective clinical trial). Ann Surg, 258(5): 705-712. Doi: 10.1097/SLA.0b013e3182a6589b

93. Gross, R., Atwood Jr., C.W., Ross, S.B., Olszewski, J.W., Eichhorn, K.A. (2009). The coordination of breathing and swallowing in chronic obstructive pulmonary disease. Am J Resp Crit Care Med, 179:559-545. Doi: 10.1164/rccm.200807-11390C

94. Gullung, J. L., Hill, E. G., Castell, D. O., & Martin-Harris, B. (2012). Oropharyngeal and esophageal swallowing impairments: Their association and the predictive value of the modified barium swallow impairment profile and combined multichannel intraluminal impedance-esophageal manometry. The Annals of Otology, Rhinology, and Laryngology, 121(11): 738-745. doi:10.1177/000348941212101107

95. Hadjiliadis, D., Duane Davis, R., Steele, M. P., Messier, R. H., Lau, C. L., Eubanks, S. S., & Palmer, S. M. (2003). Gastroesophageal reflux disease in lung transplant recipients. Clinical transplantation, 17(4), 363–368. https://doi.org/10.1034/j.1399-0012.2003.00060.x

96. Hamdan, A. L., Ziade, G., Turfe, Z., Beydoun, N., Sarieddine, D., & Kanj, N. (2016). Laryngopharyngeal symptoms in patients with chronic obstructive pulmonary disease. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery, 273(4), 953–958. https://doi.org/10.1007/s00405-015-3830-3

97. Hegland, K. W., Davenport, P. W., Brandimore, A. E., Singletary, F. F., & Troche, M. S. (2016). Rehabilitation of Swallowing and Cough Functions Following Stroke: An Expiratory Muscle Strength Training Trial. Archives of physical medicine and rehabilitation, 97(8), 1345–1351. https://doi.org/10.1016/j.apmr.2016.03.027

98. Hightower, N. C., Jr (1955). Esophageal motility in health and disease. Diseases of the chest, 28(2), 150–169. https://doi.org/10.1378/chest.28.2.150

99. Hirji, S. A., Gulack, B. C., Englum, B. R., Speicher, P. J., Ganapathi, A. M., Osho, A. A., Shimpi, R. A., Perez, A., & Hartwig, M. G. (2017). Lung transplantation delays gastric motility in patients without prior gastrointestinal surgery-A single-center experience of 412 consecutive patients. Clinical transplantation, 31(10), 10.1111/ctr.13065. https://doi.org/10.1111/ctr.13065

100. Holloway, R.H. (2006). Esophageal Manometry. *GI Motil Online*. Doi: 10.1038/gimo39

101. Hoppo, T., Komatsu, Y., & Jobe, B. A. (2014). Gastroesophageal reflux disease and patterns of reflux in patients with idiopathic pulmonary fibrosis using hypopharyngeal multichannel intraluminal impedance. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus, 27(6), 530–537. https://doi.org/10.1111/j.1442-2050.2012.01446.x

102. Hosseini, P., Tadavarthi, Y., Martin-Harris, B., & Pearson, W. G. (2019). Functional modules of pharyngeal swallowing mechanics. *Laryngoscope Investigative Otolaryngology*, 4(3), 341-346. doi:10.1002/lio2.273

103. Humbert, I. A., Christopherson, H., Lokhande, A., German, R., Gonzalez-Fernandez, M., & Celnik, P. (2013). Human hyolaryngeal movements show adaptive motor learning during swallowing. *Dysphagia*, 28(2), 139–145. https://doi.org/10.1007/s00455-012-9422-0

104. Iliaz, S., Iliaz, R., Onur, S. T., Arici, S., Akyuz, U., Karaca, C., Demir, K., Besisik, F., Kaymakoglu, S., & Akyuz, F. (2016). Does gastroesophageal reflux increase chronic obstructive pulmonary disease exacerbations?. *Respiratory medicine*, 115, 20–25. https://doi.org/10.1016/j.rmed.2016.04.005

105. Jones, B., Donner, M. W., Rubesin, S. E., Ravich, W. J., & Hendrix, T. R. (1987). Pharyngeal findings in 21 patients with achalasia of the esophagus. *Dysphagia*, 2(2), 87–92. https://doi.org/10.1007/BF02408139

106. Jones, B., Ravich, W. J., Donner, M. W., Kramer, S. S., & Hendrix, T. R. (1985). Pharyngoesophageal interrelationships: observations and working concepts. Gastrointestinal radiology, 10(3), 225–233. https://doi.org/10.1007/BF01893105

107. Jose Flores, M., Eng, K., Gerrity, E., Sinha, N. (2019). Initiation of Oral Intake in Patients Using High-Flow Nasal Cannula: A Retrospective Analysis. Perspectives of the ASHA Special Interest Groups, 4, 522-531. https://doi.org/10.1044/2019_PERS-SIG13-2018-2019.

108. Kao, C. C., & Parulekar, A. D. (2019). Postoperative management of lung transplant recipients. Journal of thoracic disease, 11(Suppl 14), S1782–S1788. https://doi.org/10.21037/jtd.2019.05.60

109. Kayawake, H., Chen-Yoshikawa, T. F., Motoyama, H., Hamaji, M., Nakajima, D., Aoyama, A., & Date, H. (2018). Gastrointestinal complications after lung transplantation in Japanese patients. Surgery today, 48(9), 883–890. https://doi.org/10.1007/s00595-018-1666-3

110. Kahrilas, P. J., Logemann, J. A., Krugler, C., & Flanagan, E. (1991). Volitional augmentation of upper esophageal sphincter opening during swallowing. *The American journal of physiology*, *260*(3 Pt 1), G450–G456. https://doi.org/10.1152/ajpgi.1991.260.3.G450

111. Kahrilas, P. J., Logemann, J. A., Lin, S., & Ergun, G. A. (1992). Pharyngeal clearance during swallowing: a combined manometric and videofluoroscopic study. *Gastroenterology*, *103*(1), 128–136. https://doi.org/10.1016/0016-5085(92)91105-d

112. Khan, M. Q., Alaraj, A., Alsohaibani, F., Al-Kahtani, K., Jbarah, S., & Al-Ashgar, H. (2014). Diagnostic Utility of Impedance-pH Monitoring in Refractory Non-erosive Reflux Disease. Journal of neurogastroenterology and motility, 20(4), 497–505. https://doi.org/10.5056/jnm14038

113. Kim, B., Moon, W., Kim, H., Jung, E., & Lee, J. (2016). Association of dysphagia with supratentorial lesions in patients with middle cerebral artery stroke. Annals of Rehabilitation Medicine, 40(4), 637-646. doi:10.5535/arm.2016.40.4.637

114. King, B. J., Iyer, H., Leidi, A. A., & Carby, M. R. (2009). Gastroesophageal reflux in bronchiolitis obliterans syndrome: a new perspective. The Journal of heart and lung

transplantation : the official publication of the International Society for Heart Transplantation, 28(9), 870–875. https://doi.org/10.1016/j.healun.2009.05.040

115. Kotloff, R. M., & Thabut, G. (2011). Lung transplantation. American journal of respiratory and critical care medicine, 184(2), 159–171. https://doi.org/10.1164/rccm.201101-0134CI

116. Krause, M., German, P. W., Taha, S. A., & Fields, H. L. (2010). A pause in nucleus accumbens neuron firing is required to initiate and maintain feeding. The Journal of neuroscience : the official journal of the Society for Neuroscience, 30(13), 4746–4756. https://doi.org/10.1523/JNEUROSCI.0197-10.2010

117. Langmore S. E. (2017). History of Fiberoptic Endoscopic Evaluation of Swallowing for Evaluation and Management of Pharyngeal Dysphagia: Changes over the Years. Dysphagia, 32(1), 27–38. https://doi.org/10.1007/s00455-016-9775-x

118. Langmore, S. E., Terpenning, M. S., Schork, A., Chen, Y., Murray, J. T., Lopatin, D., & Loesche, W. J. (1998). Predictors of aspiration pneumonia: how important is dysphagia?. Dysphagia, 13(2), 69–81. https://doi.org/10.1007/PL00009559

119. Lau, C. L., Palmer, S. M., Howell, D. N., McMahon, R., Hadjiliadis, D., Gaca, J., Pappas, T. N., Davis, R. D., & Eubanks, S. (2002). Laparoscopic antireflux surgery in the lung transplant population. Surgical endoscopy, 16(12), 1674–1678. https://doi.org/10.1007/s00464-001-8251-2

120. Leder, S. B., Siner, J. M., Bizzarro, M. J., McGinley, B. M., & Lefton-Greif, M. A. (2016). Oral Alimentation in Neonatal and Adult Populations Requiring High-Flow Oxygen via Nasal Cannula. Dysphagia, 31(2), 154–159. https://doi.org/10.1007/s00455-015-9669-3

121. Leopold, N. A., & Daniels, S. K. (2010). Supranuclear control of swallowing. Dysphagia, 25(3), 250–257. https://doi.org/10.1007/s00455-009-9249-5

122. Lever, T. E., Cox, K. T., Holbert, D., Shahrier, M., Hough, M., & Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. Dysphagia, 22(4), 312–325. https://doi.org/10.1007/s00455-007-9107-2

123. Levine, M. S., & Rubesin, S. E. (2017). History and Evolution of the Barium Swallow for Evaluation of the Pharynx and Esophagus. Dysphagia, 32(1), 55–72. https://doi.org/10.1007/s00455-016-9774-y

124. Levine, M. S., & Trenkner, S. W. (2011). Training the next generation in luminal gastrointestinal radiology: a call to arms. AJR. American journal of roentgenology, 196(2), 362–366. https://doi.org/10.2214/AJR.10.4917

125. Lidor, A. O., Ensor, C. R., Sheer, A. J., Orens, J. B., Clarke, J. O., & McDyer, J. F. (2014). Domperidone for delayed gastric emptying in lung transplant recipients with and without gastroesophageal reflux. Progress in transplantation (Aliso Viejo, Calif.), 24(1), 27–32. https://doi.org/10.7182/pit2014823

126. Lin, Y. H., Tsai, C. L., Tsao, L. I., & Jeng, C. (2019). Acute exacerbations of chronic obstructive pulmonary disease (COPD) experiences among COPD patients with comorbid gastrooesophageal reflux disease. Journal of clinical nursing, 28(9-10), 1925–1935. https://doi.org/10.1111/jocn.14814

127. Logemann, J. A., & Larsen, K. (2012). Oropharyngeal dysphagia: Pathophysiology and diagnosis for the anniversary issue of diseases of the esophagus. Diseases of the Esophagus, 25(4), 299-304. doi:10.1111/j.1442-2050.2011.01210.x

128. Logemann, J., Curro, F., Pauloski, B., & Gensler, G. (2013). Aging effects on oropharyngeal swallow and the role of dental care in oropharyngeal dysphagia. Oral Diseases, 19(8), 733-737. doi:10.1111/odi.12104

129. Logemann, J. A. (1998). Evaluation and treatment of swallowing disorders (2nd ed.). Austin, Texas: Pro-Ed.

130. Logemann, J. A., Pauloski, B. R., Rademaker, A. W., Colangelo, L. A., Kahrilas, P. J., & Smith, C. H. (2000). Temporal and biomechanical characteristics of oropharyngeal swallow in younger and older men. Journal of Speech, Language, and Hearing Research, 43(5), 1264-1274. doi:10.1044/jslhr.4305.1264

131. Logemann, J. A., Pauloski, B. R., Rademaker, A. W., & Kahrilas, P. J. (2002). Oropharyngeal swallow in younger and older women: Videofluoroscopic analysis. Journal of Speech, Language, and Hearing Research, 45(3), 434-445. doi:10.1044/1092-4388(2002/034)

132. Lohia, A., & McKenzie, J. (2020). Neuroanatomy, Pyramidal Tract Lesions. In StatPearls. StatPearls Publishing.

133. Ludlow C. L. (2015). Central Nervous System Control of Voice and Swallowing. Journal of clinical neurophysiology : official publication of the American Electroencephalographic Society, 32(4), 294–303. https://doi.org/10.1097/WNP.0000000000000186

134. Lui, F., Tadi, P., & Anilkumar, A. C. (2020). Wallenberg Syndrome. In StatPearls. StatPearls Publishing.

135. Lumb, A. B. (2017). Nunns applied respiratory physiology. Edinburgh: Elsevier.

136. Madhavan, A., Carnaby, G. D., & Crary, M. A. (2015). 'Food Sticking in My Throat': Videofluoroscopic Evaluation of a Common Symptom. Dysphagia, 30(3), 343–348. https://doi.org/10.1007/s00455-015-9605-6

137. Mahabadi, N., Goizueta, A. A., & Bordoni, B. (2020). Anatomy, Thorax, Lung Pleura And Mediastinum. In StatPearls. StatPearls Publishing.

138. Malandraki, G., Robbins, J.A. (2013). Dysphagia. Handbook of Clinical Neurology, Neurological Rehabilitation. (pp.255-271). Elselvier; Amsterdam, The Netherlands. https://doi.org/10.1016/B978-0-444-52901-5.00021-6

139. Martin, R. (2019). Lecture: Introduction to logistic regression [PowerPoint slides]. Medical University of South Carolina, BMTRY 701-01 Biostatistical Methods II.

140. Martin-Harris B. (2008). Clinical implications of respiratory-swallowing interactions. Current opinion in otolaryngology & head and neck surgery, 16(3), 194–199. https://doi.org/10.1097/MOO.0b013e3282febd4b

141. Martin-Harris, B., (2015). Standardized training in swallow physiology – evidence-based assessment using the modified barium swallow impairment profile (MBSImP) approach. Gaylord, MI, Northern Speech Services.

142. Martin-Harris, B., Brodsky, M. B., Michel, Y., Ford, C. L., Walters, B., & Heffner, J. (2005). Breathing and swallowing dynamics across the adult lifespan. Archives of otolaryngology--head & neck surgery, 131(9), 762–770. https://doi.org/10.1001/archotol.131.9.762

143. Martin-Harris, B., Brodsky, MB, Michel, Y., Castell, DO., Schleicher, M., Sandidge, J., Maxwell, R., Blair, J. (2008). MBS measurement tool for swallow impairment – MBSImp: establishing a standard. Dysphagia, 23(4): 392-405. doi: 10/1007/s00455-008-9185-9.

144. Martin-Harris, B., Brodsky, M. B., Michel, Y., Lee, F. S., & Walters, B. (2007). Delayed initiation of the pharyngeal swallow: normal variability in adult swallows. Journal of speech, language, and hearing research : JSLHR, 50(3), 585–594. https://doi.org/10.1044/1092-4388(2007/041)

145. Martin-Harris, B., Brodsky, M. B., Price, C. C., Michel, Y., & Walters, B. (2003). Temporal coordination of pharyngeal and laryngeal dynamics with breathing during swallowing: single liquid swallows. Journal of applied physiology (Bethesda, Md. : 1985), 94(5), 1735–1743. https://doi.org/10.1152/japplphysiol.00806.2002

146. Martin-Harris, B., & Jones, B. (2008). The videofluorographic swallowing study. Physical medicine and rehabilitation clinics of North America, 19(4), 769–viii. https://doi.org/10.1016/j.pmr.2008.06.004

147. Martin-Harris, B., Logemann, J. A., McMahon, S., Schleicher, M., & Sandidge, J. (2000). Clinical utility of the modified barium swallow. Dysphagia, 15(3), 136–141. https://doi.org/10.1007/s004550010015

148. Martin-Harris, B., & McFarland, D. (2013). Coordination of deglutition and respiration. Principles of deglutition (2013th ed., pp. 25-34). New York, NY: Springer New York. doi:10.1007/978-1-4614-3794-9_3

149. Martin-Harris, B., McFarland, D., Hill, E. G., Strange, C. B., Focht, K. L., Wan, Z., Blair, J., & McGrattan, K. (2015). Respiratory-swallow training in patients with head and neck cancer. Archives of physical medicine and rehabilitation, 96(5), 885–893. https://doi.org/10.1016/j.apmr.2014.11.022

150. Martin-Harris, B., Michel, Y., & Castell, D. O. (2005). Physiologic model of oropharyngeal swallowing revisited. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 133(2), 234–240. https://doi.org/10.1016/j.otohns.2005.03.059

151. Martino, R., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. (2005). Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. Stroke, 36(12), 2756–2763. https://doi.org/10.1161/01.STR.0000190056.76543.eb

152. Masiero, S., Pierobon, R., Previato, C., & Gomiero, E. (2008). Pneumonia in stroke patients with oropharyngeal dysphagia: a six-month follow-up study. Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 29(3), 139–145. https://doi.org/10.1007/s10072-008-0925-2

153. Masuda, T., Mittal, S. K., Kovacs, B., Smith, M., Walia, R., Huang, J., & Bremner, R. M. (2018). Thoracoabdominal pressure gradient and gastroesophageal reflux: insights from lung transplant candidates. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus, 31(10), 10.1093/dote/doy025. https://doi.org/10.1093/dote/doy025

154. Masuda, T., Mittal, S.K., Kovacs, B., Smith, M.A., Walia, R., Huang, J.L., Bremner, R.M. (2019). Foregut function before and after lung transplant. J Thor Cardiovas Surg, 158(2): 619-629. https://doi.org/10.1016/j.jtcvs.2019.02.128

155. 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–vii. https://doi.org/10.1016/j.pmr.2008.06.001

156. Mateen, F. J., Dierkhising, R. A., Rabinstein, A. A., van de Beek, D., & Wijdicks, E. F. (2010). Neurological complications following adult lung transplantation. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 10(4), 908–914. https://doi.org/10.1111/j.1600-6143.2009.02998.x

157. 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

158. Maurer A. H. (2016). Gastrointestinal Motility, Part 1: Esophageal Transit and Gastric Emptying. *Journal of nuclear medicine technology*, 44(1), 1–11. https://doi.org/10.2967/jnumed.112.114314

159. Maurer, J. R., Frost, A. E., Estenne, M., Higenbottam, T., & Glanville, A. R. (1998). International guidelines for the selection of lung transplant candidates. The International Society for Heart and Lung Transplantation, the American Thoracic Society, the American Society of Transplant Physicians, the European Respiratory Society. *Transplantation*, 66(7), 951–956. https://doi.org/10.1097/00007890-199810150-00033

160. May, N. H., Pisegna, J. M., Marchina, S., Langmore, S. E., Kumar, S., & Pearson, W. G., Jr (2017). Pharyngeal Swallowing Mechanics Secondary to Hemispheric Stroke. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*, 26(5), 952–961. https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.11.001

161. McCullough, G. (2014). One Step Back and Two Steps Up and Forward: The Superior Movements of Research Defining the Utility of the Mendelsohn Maneuver for Improving UES Function. *Perspectives on Swallowing and Swallowing Disorders (Dysphagia)*. doi: 23. 5. 10.1044/sasd23.1.5.

162. McFarland, D. H., & Lund, J. P. (1995). Modification of mastication and respiration during swallowing in the adult human. Journal of neurophysiology, 74(4), 1509–1517. https://doi.org/10.1152/jn.1995.74.4.1509

163. McFarland, D.H., Martin-Harris, B., Fortin, A., Humphries, K., Hill, E., & Armeson, K. (2016). Respiratory-swallowing coordination in normal subjects: Lung volume at swallowing initiation. Respiratory Physiology & Neurobiology, 234, 89-96. doi:10.1016/j.resp.2016.09.004

164. Methacholine challenge test. (2020). American Academy of Allergy Asthma & Immunology. Retrieved from: https://www.aaaai.org/

165. Meyers, B. F., Sundaresan, R. S., Guthrie, T., Cooper, J. D., & Patterson, G. A. (1999). Bilateral sequential lung transplantation without sternal division eliminates posttransplantation sternal complications. The Journal of thoracic and cardiovascular surgery, 117(2), 358–364. https://doi.org/10.1016/S0022-5223(99)70434-4

166. Miles, A., Barua, S., McLellan, N., & Brkic, L. (2020). Dysphagia and medicine regimes in patients following lung transplant surgery: A retrospective review. *International journal of speech-language pathology*, 1–10. Advance online publication. https://doi.org/10.1080/17549507.2020.1807051

167. Miles, A., Bennett, K., & Allen, J. (2019). Esophageal Transit Times Vary with Underlying Comorbid Disease. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *161*(5), 829–834. https://doi.org/10.1177/0194599819874342

168. Miles, A., Clark, S., Jardine, M., & Allen, J. (2016). Esophageal Swallowing Timing Measures in Healthy Adults During Videofluoroscopy. *The Annals of otology, rhinology, and laryngology*, *125*(9), 764–769. https://doi.org/10.1177/0003489416653410

169. Miles, A., McMillan, J., Ward, K., & Allen, J. (2015). Esophageal visualization as an adjunct to the videofluoroscopic study of swallowing. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery*, *152*(3), 488–493. https://doi.org/10.1177/0194599814565599

170. Miles, A., McLellan, N., Machan, R., Vokes, D., Hunting, A., McFarlane, M., Holmes, J., & Lynn, K. (2018). Dysphagia and laryngeal pathology in post-surgical cardiothoracic patients. Journal of critical care, 45, 121–127. https://doi.org/10.1016/j.jcrc.2018.01.027

171. Miller, M. R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C. P., Gustafsson, P., Jensen, R., Johnson, D. C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O. F., Pellegrino, R., Viegi, G., Wanger, J., & ATS/ERS Task Force (2005). Standardisation of spirometry. The European respiratory journal, 26(2), 319–338. https://doi.org/10.1183/09031936.05.00034805

172. Mittal R. K. (1993). The sphincter mechanism at the lower end of the esophagus: an overview. Dysphagia, 8(4), 347–350. https://doi.org/10.1007/BF01321777

173. Miyagawa-Hayashino, A., Wain, J. C., & Mark, E. J. (2005). Lung transplantation biopsy specimens with bronchiolitis obliterans or bronchiolitis obliterans organizing

pneumonia due to aspiration. Archives of pathology & laboratory medicine, 129(2), 223–226. https://doi.org/10.1043/1543-2165(2005)129<223:LTBSWB>2.0.CO;2

174. Morgan, L.B. (2017). Exercise-based dysphagia rehabilitation: Past, present, and future. Perspectives on Swallowing and Swallowing Disorders (Dysphagia), 2(1): 36-43. doi: https://doi.org/10.1044/persp2.SIG13.36

175. Moon, H. I., Nam, J. S., Leem, M. J., & Kim, K. H. (2017). Periventricular White Matter Lesions as a Prognostic Factor of Swallowing Function in Older Patients with Mild Stroke. Dysphagia, 32(4), 480–486. https://doi.org/10.1007/s00455-017-9788-0

176. Moon, H. I., Pyun, S. B., & Kwon, H. K. (2012). Correlation between Location of Brain Lesion and Cognitive Function and Findings of Videofluoroscopic Swallowing Study. Annals of rehabilitation medicine, 36(3), 347–355. https://doi.org/10.5535/arm.2012.36.3.347

177. Moore, K. L., Dalley, A. F., & Agur, A. M. R. (2018). Clinically oriented anatomy, 8th Edition. Philadelphia: Wolters Kluwer.

178. Murray, J., Langmore, S. E., Ginsberg, S., & Dostie, A. (1996). The significance of accumulated oropharyngeal secretions and swallowing frequency in predicting aspiration. Dysphagia, 11(2), 99–103. https://doi.org/10.1007/BF00417898

179. Nagami, S., Oku, Y., Yagi, N., Sato, S., Uozumi, R., Morita, S., Yamagata, Y., Kayashita, J., Tanimura, K., Sato, A., Takahashi, R., & Muro, S. (2017). Breathing-swallowing discoordination is associated with frequent exacerbations of COPD. BMJ open respiratory research, 4(1), e000202. https://doi.org/10.1136/bmjresp-2017-000202

180. National Data, Organ Procurement and Transplantation Network U.S. Department of Health & Human Services. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

181. National Heart, Lung, and Blood Institute (NHLBI). (nd). COPD. Retrieved from: https://www.nhlbi.nih.gov/health-topics/copd

182. Nativ-Zeltzer, N., Belafsky, P. C., Bayoumi, A., & Kuhn, M. A. (2019). Volitional control of the upper esophageal sphincter with high-resolution manometry driven biofeedback. Laryngoscope investigative otolaryngology, 4(2), 264–268. https://doi.org/10.1002/lio2.255

183. Netter, F. H. (2006). Atlas of human anatomy (4th ed.). Philadelphia, PA: Saunders Elsevier.

184. Nguyen, S., Zhu, A., Toppen, W., Ashfaq, A., Davis, J., Shemin, R., Mendelsohn, A. H., & Benharash, P. (2016). Dysphagia after Cardiac Operations Is Associated with Increased Length of Stay and Costs. The American surgeon, 82(10), 890–893.

185. O'Horo, J. C., Rogus-Pulia, N., Garcia-Arguello, L., Robbins, J., & Safdar, N. (2015). Bedside diagnosis of dysphagia: a systematic review. Journal of hospital medicine, 10(4), 256–265. https://doi.org/10.1002/jhm.2313

186. Omari, T. I., Ciucci, M., Gozdzikowska, K., Hernández, E., Hutcheson, K., Jones, C., Maclean, J., Nativ-Zeltzer, N., Plowman, E., Rogus-Pulia, N., Rommel, N., & O'Rourke, A. (2020). High-Resolution Pharyngeal Manometry and Impedance: Protocols and Metrics-Recommendations of a High-Resolution Pharyngeal Manometry International Working Group. Dysphagia, 35(2), 281–295. https://doi.org/10.1007/s00455-019-10023-y

187. Orens, J. B., Estenne, M., Arcasoy, S., Conte, J. V., Corris, P., Egan, J. J., Egan, T., Keshavjee, S., Knoop, C., Kotloff, R., Martinez, F. J., Nathan, S., Palmer, S., Patterson, A., Singer, L., Snell, G., Studer, S., Vachiery, J. L., Glanville, A. R., & Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation (2006). International guidelines for the selection of lung transplant candidates: 2006 update--a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation, 25(7), 745–755. https://doi.org/10.1016/j.healun.2006.03.011

188. O'Rourke, A.K. (2019, January 18-19). Course: The Charleston pharyngoesophageal manometry training program. Medical University of South Carolina, Charleston, SC.

189. O'Rourke, A. K., Lazar, A., Murphy, B., Castell, D. O., & Martin-Harris, B. (2016). Utility of Esophagram versus High-Resolution Manometry in the Detection of Esophageal Dysmotility. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery, 154(5), 888–891. https://doi.org/10.1177/0194599816629379

190. O'Rourke, A., Morgan, L. B., Coss-Adame, E., Morrison, M., Weinberger, P., & Postma, G. (2014). The effect of voluntary pharyngeal swallowing maneuvers on esophageal swallowing physiology. Dysphagia, 29(2), 262–268. https://doi.org/10.1007/s00455-013-9505-6

191. Parada, M. T., Alba, A., & Sepúlveda, C. (2010). Bronchiolitis obliterans syndrome development in lung transplantation patients. Transplantation proceedings, 42(1), 331–332. https://doi.org/10.1016/j.transproceed.2009.11.037

192. Parada, M. T., Alba, A., & Sepúlveda, C. (2010). Bronchiolitis obliterans syndrome development in lung transplantation patients. *Transplantation proceedings*, *42*(1), 331–332. https://doi.org/10.1016/j.transproceed.2009.11.037

193. Park, G. Y., Kim, S. R., Kim, Y. W., Jo, K. W., Lee, E. J., Kim, Y. M., & Im, S. (2015). Decreased diaphragm excursion in stroke patients with dysphagia as assessed by M-mode sonography. Archives of physical medicine and rehabilitation, 96(1), 114–121. https://doi.org/10.1016/j.apmr.2014.08.019

194. Park, G. W., Kim, S. K., Lee, C. H., Kim, C. R., Jeong, H. J., & Kim, D. K. (2015). Effect of chronic obstructive pulmonary disease on swallowing function in stroke patients. Annals of rehabilitation medicine, 39(2), 218–225. https://doi.org/10.5535/arm.2015.39.2.218

195. Parke, R. L., Eccleston, M. L., & McGuinness, S. P. (2011). The effects of flow on airway pressure during nasal high-flow oxygen therapy. Respiratory care, 56(8), 1151–1155. https://doi.org/10.4187/respcare.01106

196. Patejdl, R., Kästner, M., Kolbaske, S., & Wittstock, M. (2017). Clinical nutrition and gastrointestinal dysfunction in critically ill stroke patients. Neurological research, 39(11), 959–964. https://doi.org/10.1080/01616412.2017.1367545

197. Patti, M. G., Tedesco, P., Golden, J., Hays, S., Hoopes, C., Meneghetti, A., Damani, T., & Way, L. W. (2005). Idiopathic pulmonary fibrosis: how often is it really idiopathic?. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract, 9(8), 1053–1058. https://doi.org/10.1016/j.gassur.2005.06.027

198. Patti, M. G., Vela, M. F., Odell, D. D., Richter, J. E., Fisichella, P. M., & Vaezi, M. F. (2016). The Intersection of GERD, Aspiration, and Lung Transplantation. Journal of laparoendoscopic & advanced surgical techniques. Part A, 26(7), 501–505. https://doi.org/10.1089/lap.2016.0170

199. Pearson, W. G., Jr, 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

200. Pehlivan, E., Mutluay, F., Balcı, A., & Kılıç, L. (2018). The effects of inspiratory muscle training on exercise capacity, dyspnea and respiratory functions in lung transplantation candidates: a randomized controlled trial. *Clinical rehabilitation*, 32(10), 1328–1339. https://doi.org/10.1177/0269215518777560

201. Peters, D. (2009). Course: Advanced (Gross) Anatomy of Speech/Hearing Mechanism [PowerPoint slides]. New York Medical College, SLPM 6004: Advanced Anatomy of Speech/Hearing Mechanism.

202. Pinto, V. L., & Sharma, S. (2020). Continuous Positive Airway Pressure (CPAP). In StatPearls. StatPearls Publishing.

203. Posner, S., Zheng, J., Wood, R. K., Shimpi, R. A., Hartwig, M. G., Chow, S. C., & Leiman, D. A. (2018). Gastroesophageal reflux symptoms are not sufficient to guide esophageal function testing in lung transplant candidates. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus*, 31(5), 10.1093/dote/dox157. https://doi.org/10.1093/dote/dox157

204. Rangarathnam, B., Kamarunas, E., & McCullough, G. H. (2014). Role of cerebellum in deglutition and deglutition disorders. Cerebellum (London, England), 13(6), 767–776. https://doi.org/10.1007/s12311-014-0584-1

205. Reedy, E. L., Herbert, T. L., & Bonilha, H. S. (2021). Visualizing the Esophagus During Modified Barium Swallow Studies: A Systematic Review. *American journal of speech-language pathology*, *30*(2), 761–771. https://doi.org/10.1044/2020_AJSLP-20-00255

206. Reflex [Def 2]. (n.d.). Merriam Webster Online. Retrieved from: https://www.merriam-webster.com/dictionary/reflex?src=search-dict-hed.

207. Regan, J., Lawson, S., & De Aguiar, V. (2017). The Eating Assessment Tool-10 Predicts Aspiration in Adults with Stable Chronic Obstructive Pulmonary Disease. Dysphagia, 32(5), 714–720. https://doi.org/10.1007/s00455-017-9822-2

208. Riquelme, L. (2009). Course: Dysphagia [PowerPoint slides]. New York Medical College, SLPM 6014: Dysphagia.

209. Robbins, J., Coyle, J., Rosenbek, J., Roecker, E., & Wood, J. (1999). Differentiation of normal and abnormal airway protection during swallowing using the penetration-aspiration scale. Dysphagia, 14(4), 228–232. https://doi.org/10.1007/PL00009610

210. Robbins, J., & Levin, R. L. (1988). Swallowing after unilateral stroke of the cerebral cortex: Preliminary experience. Dysphagia, 3(1), 11-17. doi:10.1007/BF02406275

211. 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

212. Saleem, F., & M Das, J. (2020). Lateral Medullary Syndrome. In StatPearls. StatPearls Publishing.

213. Sapienza, C. M., & Wheeler, K. (2006). Respiratory muscle strength training: functional outcomes versus plasticity. Seminars in speech and language, 27(4), 236–244. https://doi.org/10.1055/s-2006-955114

214. Saran, M., Georgakopoulos, B., & Bordoni, B. (2020). Anatomy, Head and Neck, Larynx Vocal Cords. In StatPearls. StatPearls Publishing.

215. Sasegbon, A., & Hamdy, S. (2017). The anatomy and physiology of normal and abnormal swallowing in oropharyngeal dysphagia. Neurogastroenterology & Motility, 29(11), e13100-n/a. doi:10.1111/nmo.13100

216. Savarino, E., Carbone, R., Marabotto, E., Furnari, M., Sconfienza, L., Ghio, M., Zentilin, P., & Savarino, V. (2013). Gastro-oesophageal reflux and gastric aspiration in idiopathic pulmonary fibrosis patients. The European respiratory journal, 42(5), 1322–1331. https://doi.org/10.1183/09031936.00101212

217. Schmidt Leuenberger, J. M., Hoksch, B., Luder, G., Schmid, R. A., Verra, M. L., & Dorn, P. (2019). Early Assessment and Management of Dysphagia After Lung Resection: A Randomized Controlled Trial. The Annals of thoracic surgery, 108(4), 1059–1064. https://doi.org/10.1016/j.athoracsur.2019.04.067

218. Seccombe, J., Mirza, F., Hachem, R., & Gyawali, C. P. (2013). Esophageal motor disease and reflux patterns in patients with advanced pulmonary disease undergoing lung transplant evaluation. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 25(8), 657–663. https://doi.org/10.1111/nmo.12135

219. Shah, N., Force, S. D., Mitchell, P. O., Lin, E., Lawrence, E. C., Easley, K., Qian, J., Ramirez, A., Neujahr, D. C., Gal, A., Leeper, K., & Pelaez, A. (2010). Gastroesophageal reflux disease is associated with an increased rate of acute rejection in lung transplant allografts. Transplantation proceedings, 42(7), 2702–2706. https://doi.org/10.1016/j.transproceed.2010.05.155

220. Shahid, Z., & Burns, B. (2020). Anatomy, Abdomen and Pelvis, Diaphragm. In StatPearls. StatPearls Publishing.

221. Shaker, R., Li, Q., Ren, J., Townsend, W. F., Dodds, W. J., Martin, B. J., Kern, M. K., & Rynders, A. (1992). Coordination of deglutition and phases of respiration: effect of aging, tachypnea, bolus volume, and chronic obstructive pulmonary disease. The American journal of physiology, 263(5 Pt 1), G750–G755. https://doi.org/10.1152/ajpgi.1992.263.5.G750

222. Shelly, M. P., & Nightingale, P. (1999). ABC of intensive care: respiratory support. BMJ (Clinical research ed.), 318(7199), 1674–1677. https://doi.org/10.1136/bmj.318.7199.1674

223. Shi, L. (2008). Health services research methods (2nd ed.). Clifton Park, NY: Delmar Cengage Learning.

224. Siebert, T. A., & Rugonyi, S. (2008). Influence of liquid-layer thickness on pulmonary surfactant spreading and collapse. Biophysical journal, 95(10), 4549–4559. https://doi.org/10.1529/biophysj.107.127654

225. Sifrim, D., & Jafari, J. (2012). Deglutitive inhibition, latency between swallow and esophageal contractions and primary esophageal motor disorders. Journal of neurogastroenterology and motility, 18(1), 6–12. https://doi.org/10.5056/jnm.2012.18.1.6

226. Singh, S., & Hamdy, S. (2006). Dysphagia in stroke patients. Postgraduate medical journal, 82(968), 383–391. https://doi.org/10.1136/pgmj.2005.043281

227. Sivit, C. J., Curtis, D. J., Crain, M., Cruess, D. F., & Winters, C., Jr (1988). Pharyngeal swallow in gastroesophageal reflux disease. Dysphagia, 2(3), 151–155. https://doi.org/10.1007/BF02424933

228. Skoretz, S. A., Flowers, H. L., & Martino, R. (2010). The incidence of dysphagia following endotracheal intubation: a systematic review. Chest, 137(3), 665–673. https://doi.org/10.1378/chest.09-1823

229. Smith, J. A., & Houghton, L. A. (2013). The oesophagus and cough: laryngo-pharyngeal reflux, microaspiration and vagal reflexes. Cough (London, England), 9(1), 12. https://doi.org/10.1186/1745-9974-9-12

230. Soli-Borey, M. (2013). Dealing with missing data: Key assumptions and methods for applied analysis. Technical Report No.4. Boston University School of Public Health: Department of Health Policy & Management. Retrieved from: /https://www.bu.edu/sph/files/2014/05/Marina-tech-report.pdf/

231. Steele, C. M., Alsanei, W. A., Ayanikalath, S., Barbon, C. E., Chen, J., Cichero, J. A., Coutts, K., Dantas, R. O., Duivestein, J., Giosa, L., Hanson, B., Lam, P., Lecko, C., Leigh, C., Nagy, A., Namasivayam, A. M., Nascimento, W. V., Odendaal, I., Smith, C. H., & Wang, H. (2015). The influence of food texture and liquid consistency modification on swallowing physiology and function: a systematic review. Dysphagia, 30(1), 2–26. https://doi.org/10.1007/s00455-014-9578-x

232. Steele, C. M., & Miller, A. J. (2010). Sensory input pathways and mechanisms in swallowing: a review. Dysphagia, 25(4), 323–333. https://doi.org/10.1007/s00455-010-9301-5

233. Steele, C. M., Namasivayam-MacDonald, A. M., Guida, B. T., Cichero, J. A., Duivestein, J., Hanson, B., Lam, P., & Riquelme, L. F. (2018). Creation and Initial Validation of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale. Archives of physical medicine and rehabilitation, 99(5), 934–944. https://doi.org/10.1016/j.apmr.2018.01.012

234. Steidl, E., Ribeiro, C. S., Gonçalves, B. F., Fernandes, N., Antunes, V., & Mancopes, R. (2015). Relationship between Dysphagia and Exacerbations in Chronic Obstructive Pulmonary Disease: A Literature Review. International archives of otorhinolaryngology, 19(1), 74–79. https://doi.org/10.1055/s-0034-1376430

235. Studer, S. M., Levy, R. D., McNeil, K., & Orens, J. B. (2004). Lung transplant outcomes: a review of survival, graft function, physiology, health-related quality of life and cost-effectiveness. The European respiratory journal, 24(4), 674–685. https://doi.org/10.1183/09031936.04.00065004

236. Suntrup-Krueger, S., Kemmling, A., Warnecke, T., Hamacher, C., Oelenberg, S., Niederstadt, T., Heindel, W., Wiendl, H., & Dziewas, R. (2017). The impact of lesion location on dysphagia incidence, pattern and complications in acute stroke. Part 2: Oropharyngeal residue, swallow and cough response, and pneumonia. European journal of neurology, 24(6), 867–874. https://doi.org/10.1111/ene.13307

237. Sweet, M. P., Herbella, F. A., Leard, L., Hoopes, C., Golden, J., Hays, S., & Patti, M. G. (2006). The prevalence of distal and proximal gastroesophageal reflux in patients awaiting lung transplantation. Annals of surgery, 244(4), 491–497. https://doi.org/10.1097/01.sla.0000237757.49687.03

238. Sweet, M. P., Patti, M. G., Leard, L. E., Golden, J. A., Hays, S. R., Hoopes, C., & Theodore, P. R. (2007). Gastroesophageal reflux in patients with idiopathic pulmonary fibrosis referred for lung transplantation. The Journal of thoracic and cardiovascular surgery, 133(4), 1078–1084. https://doi.org/10.1016/j.jtcvs.2006.09.085

239. Su, V. Y., Liao, H. F., Perng, D. W., Chou, Y. C., Hsu, C. C., Chou, C. L., Chang, Y. L., Yen, J. C., Chen, T. J., & Chou, T. C. (2018). Proton pump inhibitors use is associated with a lower risk of acute exacerbation and mortality in patients with coexistent COPD and GERD. International journal of chronic obstructive pulmonary disease, 13, 2907–2915. https://doi.org/10.2147/COPD.S157761

240. Suárez-Quintanilla, J., Fernández Cabrera, A., & Sharma, S. (2020). Anatomy, Head and Neck, Larynx. In StatPearls. StatPearls Publishing.

241. Tack, J., & Fass, R. (2004). Review article: approaches to endoscopic-negative reflux disease: part of the GERD spectrum or a unique acid-related disorder?. Alimentary pharmacology & therapeutics, 19 Suppl 1, 28–34. https://doi.org/10.1111/j.0953-0673.2004.01835.x

242. Teismann, I. K., Suntrup, S., Warnecke, T., Steinsträter, O., Fischer, M., Flöel, A., Ringelstein, E. B., Pantev, C., & Dziewas, R. (2011). Cortical swallowing processing in early subacute stroke. BMC neurology, 11, 34. https://doi.org/10.1186/1471-2377-11-34

243. Tangaroonsanti, A., Vela, M. F., Crowell, M. D., DeVault, K. R., & Houghton, L. A. (2018). Esophageal dysmotility according to Chicago classification v3.0 vs v2.0: Implications for association with reflux, bolus clearance, and allograft failure post-lung transplantation. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 30(6), e13296. https://doi.org/10.1111/nmo.13296

244. Tejwani, V., Panchabhai, T. S., Kotloff, R. M., & Mehta, A. C. (2016). Complications of Lung Transplantation: A Roentgenographic Perspective. Chest, 149(6), 1535–1545. https://doi.org/10.1016/j.chest.2015.12.019

245. Thabut, G., & Mal, H. (2017). Outcomes after lung transplantation. Journal of thoracic disease, 9(8), 2684–2691. https://doi.org/10.21037/jtd.2017.07.85

246. Tikka, T., & Hilmi, O. J. (2019). Upper airway tract complications of endotracheal intubation. British journal of hospital medicine (London, England : 2005), 80(8), 441–447. https://doi.org/10.12968/hmed.2019.80.8.441

247. Triadafilopoulos, G., Hallstone, A., Nelson-Abbott, H., & Bedinger, K. (1992). Oropharyngeal and esophageal interrelationships in patients with nonobstructive dysphagia. Digestive diseases and sciences, 37(4), 551–557. https://doi.org/10.1007/BF01307579

248. Turbyville J. C. (2010). Applying principles of physics to the airway to help explain the relationship between asthma and gastroesophageal reflux. Medical hypotheses, 74(6), 1075–1080. https://doi.org/10.1016/j.mehy.2009.12.030

249. Tutuian, R., Jalil, S., Katz, P. O., & Castell, D. O. (2004). Effect of interval between swallows on oesophageal pressures and bolus movement in normal subjects - Studies with combined multichannel intraluminal impedance and oesophageal manometry. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 16(1), 23–29. https://doi.org/10.1046/j.1365-2982.2003.00460.x

250. United Network for Organ Sharing (UNOS). (n.d.) Transplant Trends. https://unos.org/data/transplant-trends/

251. Verleden G. M. (2000). Bronchiolitis obliterans syndrome after lung transplantation: medical treatment. *Monaldi archives for chest disease*, 55(2), 140–145.

252. Verleden, G.M., Bankier A., Boehler A., Corris P., Dupont LJ, Estenne, S., Fishcer, T., Lerut, H., Reichenspurner, H., and other co-authors of Working Group 1. (2004). Bronchiolitis obliterans syndrome after lung transplantation: diagnosis and treatment In Verleden G.M., Van Raemdonck, D., Lerut, T., Demedts., M. *Surgery for non-neoplastic disorders of the chest: A clinical update.* Pg 19-30. European Respiratory Society Monographs: United Kingdom. DOI: 10.1183/1025448x.erm2904

253. Volin, R. Course Lectures: Neuroscience [PowerPoint slides]. New York Medical College, SLPM 6032: Neuroscience.

254. Ward J. J. (2013). High-flow oxygen administration by nasal cannula for adult and perinatal patients. *Respiratory care*, 58(1), 98–122. https://doi.org/10.4187/respcare.01941

255. Watts, S., Gaziano, J., Jacobs, J., & Richter, J. (2019). Improving the Diagnostic Capability of the Modified Barium Swallow Study Through Standardization of an Esophageal Sweep Protocol. *Dysphagia*, 34(1), 34–42. https://doi.org/10.1007/s00455-018-09966-5

256. Watts, S., Gaziano, J., Kumar, A., & Richter, J. (2021). Diagnostic Accuracy of an Esophageal Screening Protocol Interpreted by the Speech-Language Pathologist. *Dysphagia*, 10.1007/s00455-020-10239-3. Advance online publication. https://doi.org/10.1007/s00455-020-10239-3

257. West, J. B., & Luks, A. (2016). *Wests respiratory physiology: the essentials*. Philadelphia: Wolters Kluwer.

258. Wheeler Hegland, K., Huber, J. E., Pitts, T., Davenport, P. W., & Sapienza, C. M. (2011). Lung volume measured during sequential swallowing in healthy young adults. *Journal of speech, language, and hearing research : JSLHR*, 54(3), 777–786. https://doi.org/10.1044/1092-4388(2010/09-0237)

259. Wilmskoetter, J., Bonilha, L., Martin-Harris, B., Elm, J. J., Horn, J., & Bonilha, H. S. (2019). Mapping acute lesion locations to physiological swallow impairments after stroke. *NeuroImage. Clinical*, 22, 101685. https://doi.org/10.1016/j.nicl.2019.101685

260. Wilmskoetter, J., Martin-Harris, B., Pearson, W.G., Bonilha, L., Elm, J.J., Horn, J., Bonilha, H.S. (2018). Differences in swallow physiology in patients with left and right hemispheric strokes. *Phys Behavior*, 194" 144-152. Doi: https://doi.org/10.1016/j.physceh.2018.05.010

261. Wilson R. D. (2012). Mortality and cost of pneumonia after stroke for different risk groups. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association, 21(1), 61–67. https://doi.org/10.1016/j.jstrokecerebrovasdis.2010.05.002

262. Wilson-Pauwels, L., Akesson, E.J., Stewart, P.A. (1988). *Cranial Nerves: Anatomy and Clinical Comments*. Toronto: BC Decker.

263. Yalcin, N. G., Choong, C. K., & Eizenberg, N. (2013). Anatomy and pathophysiology of the pleura and pleural space. *Thoracic surgery clinics*, 23(1), 1–v. https://doi.org/10.1016/j.thorsurg.2012.10.008

264. Yang, Q., Tong, X., Schieb, L., Vaughan, A., Gillespie, C., Wiltz, J. L., King, S. C., Odom, E., Merritt, R., Hong, Y., & George, M. G. (2017). Vital Signs: Recent Trends in Stroke Death Rates - United States, 2000-2015. *MMWR. Morbidity and mortality weekly report*, *66*(35), 933–939. https://doi.org/10.15585/mmwr.mm6635e1

265. Zivković, S. A., Jumaa, M., Barisić, N., & McCurry, K. (2009). Neurologic complications following lung transplantation. *Journal of the neurological sciences*, 280(1-2), 90–93. https://doi.org/10.1016/j.jns.2009.02.308