Characterizing Oropharyngeal Swallowing Following Single Lung Transplantation in Adults

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Swallowing is a physiologically complex kinematic process during which abnormal obstruction of bolus flow of incoordination can occur. Dysphagia, or a difficulty with swallowing, is a concern following single-lung transplantation (SLT) due to the high risk of recurrent laryngeal nerve damage, upper airway trauma secondary to orotracheal intubation, disruption of pulmonary sensorimotor circuits responsible for airway penetration, and the required levels of immunosuppression during and following surgery. Post-operatively, repetitive aspiration events are a major contributing factor in the long-term failure of lung allograft function. The goal of this descriptive, retrospective study is to quantitatively describe the characteristics of swallowing kinematic function through six durational measures in a group of 10 patients (age 49-68) following single-lung transplantation, describe airway protection ordinally through penetration-aspiration scale scores, and to compare findings from these patients to published norms for healthy adults. By explicitly describing the swallow physiology of a sample of patients with SLTs, clinically significant risk factors will be identified to help researchers and clinicians consider better treatment and safe swallowing strategies for future patients in order to mitigate adverse post-operative events, effectively increasing the functional lifespan of the transplant organ, and thusly decreasing morbidity and patient mortality.

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PREFACE

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1.0 INTRODUCTION

Lung transplantation is a radical surgical intervention used to manage end-stage pulmonary diseases such as idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease (Atkins et al., 2010). Given the relationship between the digestive and respiratory functions of the aerodigestive tract, postoperative disruption of swallowing function has been shown to be a relatively uncommon but clinically significant adverse outcome.

1.1 SWALLOWING

Swallowing is a physiologically complex, kinematic process involving intricately coordinated activity of more than 30 nerves and muscles.

1.1.1 Stages

Traditionally, swallowing is artificially broken down into four stages in order to discretely describe the numerous events taking place within one to two seconds. These stages, oral preparatory, oral transit, pharyngeal, and esophageal, are defined according to the location of the swallowed material (bolus) and the kinematic movements of various structures observed radiographically during the swallow (Matsuo & Palmer, 2009). After liquid enters the mouth via cup, spoon, or straw, the bolus is held in the anterior part of the mouth or on the superior tongue surface against the hard palate (Dodds et al., 1989, Mankekar, 2015). The oral cavity is sealed posteriorly by the soft palate and by the tongue to prevent the bolus from entering the oropharynx before the onset of the intentional transfer into the pharynx. At the onset of oral transit, the bolus is propelled posteriorly by the tongue, the tongue tip rises and progressively contacts the hard palate from anterior to posterior while the posterior portion of the tongue separates from the soft palate, allowing the bolus to enter the posterior oral cavity. The bolus then crosses the boundary defined by the faucial (or tonsillar) pillars, and a series of events ensues marking the onset of the pharyngeal stage (Coyle, 2012). The pharyngeal stage consists of a rapid sequence of kinematic events, occurring within a second, that has two crucial biological features: food/liquid passage toward the next segment of the digestive system and airway protection (Kim et al., 2005). First, the soft palate elevates and contacts the lateral and posterior walls of the pharynx, simultaneously closing the nasopharynx as the bolus head is propelled into the pharynx. The pharyngeal base of the tongue then descends and retracts, pushing the bolus against the pharyngeal walls. The three pharyngeal constrictor muscles contact sequentially from superior to inferior while lingual retraction continues, propelling the bolus toward the lower pharynx. Concurrently, the pharynx shortens vertically, reducing the volume of the pharyngeal cavity. Several airway protective mechanisms work to prevent aspiration of food or liquid into the airway during the swallow; the vocal folds seal the glottis and the arytenoids tilt forward to contact the epiglottic base prior to the opening of the upper esophageal sphincter (UES) (Kim et al., 2005). The suprahyoid muscles and the thyrohyoid muscles contract, pulling the hyoid bone and larynx forward and upward (Mankekar, 2015). This movement displaces the larynx under the base of the tongue and displaces the epiglottis backward and downward to seal the opening to the airway, the laryngeal vestibule (Kendall et al., 2004). Simultaneously, vagal inhibition causes the tonically contracted resting UES, to “relax” somewhat, which facilitates the effectiveness of muscular traction forces that pull the UES open during the pharyngeal stage, and reduces inertia within the UES during bolus flow. UES opening is crucial for bolus entry into the esophagus (Cook et al., 1989; Mendell & Logemann, 2007). The UES consists of the inferior pharyngeal constrictor muscles including its lower cricopharyngeal portion, and the most proximal portion of the esophagus (Kim et al., 2005). After the bolus tail passes through the opened UES, pharyngeal stage activity subsides, oropharyngeal structures return to their resting positions, and the esophageal stage begins, propelling the bolus toward the stomach.

Volume or viscosity of swallowed material can change the temporal aspects of the oropharyngeal swallow. Increasing the bolus volume has been linked with increased laryngeal closure, hyoid/laryngeal elevation, and UES opening diameter and duration while increased viscosity can lead to slower bolus transit times (Butler et al., 2004; Mendell & Logemann, 2007).

1.1.2 Dysphagia

During a disordered swallow, abnormal obstruction of bolus flow or incoordination can occur, leading to varying degrees of dysphagia, or difficulty with swallowing (Coyle, 2012). “Oropharyngeal” is one classification of dysphagia and is often characterized by the complaint of difficulty initiating a swallow, transitioning the bolus into the esophagus, meal-induced coughing/choking, and the sensation of “food getting stuck” immediately after swallowing (Ferguson & DeVault, 2004, Kotloff & Thabut, 2011). The transportation of the bolus from the oral cavity to the esophagus through the pharynx is a typically synchronized sequence but damage to central sensorimotor processing centers, sensory or motor signals via the cranial nerves, other peripheral nerves, or anatomical abnormalities can result in the partial or total disruption of the process that can disable efficient transfer of swallowed material into the digestive system (Kim & McCullough, 2008; Coyle, 2008). As a result, dysphagia may lead to serious complications including dehydration and malnutrition. It can also enable abnormal transfer of swallowed material into the airway and lungs, or “aspiration”, which leads to large or small airway obstruction and pulmonary consequences associated with alveolar trauma and inflammation (Marik, 2001; Matsuo & Palmer, 2009). Current treatments to alleviate dysphagia or its symptoms are mainly focused on volitional augmentation of swallowing through postural change/compensatory maneuvers that exploit sensorimotor strengths while mitigating sensorimotor impairments, dietary modifications, and restorative interventions designed to restore and rehabilitate impaired function.

1.2 LUNG TRANSPLANTATION

Lung transplantation has become the standard of care for patients with advanced or end-stage, intractable lung diseases such as idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, and other lung diseases of nonmalignant etiologies (Atkins et al., 2010). The first successful lung transplantation occurred in 1963 and was followed by a cohort of successful transplants in the 1980s (Floreth & Bhorade, 2010). Since then, significant research advances into the modern lung transplantation have led to improvements in surgical techniques, treatment of infectious diseases, and immunotherapies that reduce rejection of the newly transplanted allograft organ (Kotloff & Thabut, 2011). Additionally, selection criteria for implantation have become less restrictive, broadening the range of patients eligible for transplantation. Single-lung transplantation (SLT) and double-lung transplantation (DLT) make up over 97% of the lung-related thoracic procedures performed worldwide (Kotloff & Thabut, 2011). SLT offers a more efficient use of the limited donor pool and is better tolerated than DLT by medically frail patients, but it also results in less functional reserve than DLT (Floreth & Bhorade, 2010). In choosing between SLT and DLT, the underlying disease necessitating lung transplantation is a major determinant of the chosen procedure and of the overall prognosis (Kotloff & Thabut, 2011).

1.2.1 Transplantation: Complications and Aspiration

Previous research has identified swallowing disorders as a typical concern following lung transplantation (Atkins et al., 2007). Despite recent technological and surgical advances, lung transplantation success rates still fall behind other solid organ transplant rates (Floreth & Bhorade, 2010). Significant constraints on long-term survival are still prevalent; the average survival rate stands at 5.7 years (Kotloff & Thabut, 2011).

Primary graft dysfunction, infection from pneumonia, and bronchiolitis obliterans syndrome are common complications encountered by the lung transplant recipient and are major impediments to long-term survival. Primary graft dysfunction (PGD) describes a form of acute allograft injury characterized by development of noncardiogenic pulmonary edema within 72 hours of transplantation in the absence of identifiable secondary causes (Kotloff & Thabut, 2011).

Bacterial pneumonia is the most frequently encountered infection, with a peak incidence in the first post-transplant month. The passive transfer of occult infection from the donor is a concern, however, factors such as high levels of immunosuppression for maximum graft tolerance, need for prolonged mechanical ventilator support, blunted cough due to post-operative pain and weakness, surgical disruption of lymphatic system, impaired mucociliary clearance associated with airway ischemic injury and other factors related to the recipient are more likely responsible for the increased risk (Estenne & Kotloff, 2005; Kotloff & Thabut, 2011). In addition to these pneumonia risk factors, aspiration related to postoperative dysphagia contributes significantly to the inoculation of the immunocompromised allograft lung with oral pathogens and caustic food products (Marik, 2001; Atkins et al., 2007).

Oropharyngeal dysphagia is associated with increased post-operative complications, such as pneumonia, leading to respiratory complications that can result in overall increased post-operative mortality (Atkins et al., 2007). Bacterial infections, in the form of purulent bronchitis, bronchiectasis, and pneumonia reemerge as a late complication among patients who develop Bronchiolitis Obliterans Syndrome (BOS) (Estenne & Kotloff, 2005). Chronic allograft dysfunction due to BOS represents the major impediment to long-term graft integrity and patient survival (Atkins et al., 2010). Bronchiolitis obliterans is a fibroproliferative process that narrows and ultimately obliterates the lumens of small airways, resulting in progressive and largely irreversible obstruction of airflow to and from the alveoli. Approximately 50% of lung transplant recipients develop BOS by 5 years and 75% by 10 years (Kotloff & Thabut, 2011). Previous treatment research has focused on strategies to reduce immunosuppression, but the benefits of such approaches are questionable as the risk of infection is considerably high (Kotloff & Thabut, 2011).

Additionally, oropharyngeal dysphagia (OPD) often occurs after various types of thoracic surgery due to the high risk of recurrent laryngeal nerve damage (Harrington et al., 1998). Oropharyngeal dysphagia is often overlooked on clinical examination but is very common following lung transplantation (Atkins et al., 2010). The anatomical position of the lungs exposes several peripheral nerves innervating pharyngeal, laryngeal and respiratory muscles and sensory receptors to damage during transplantation (Atkins et al., 2007). Such damage negatively impacts the muscles needed to control the typical swallow sequence and swallow-respiratory coordination depending on the site of lesion. The recurrent laryngeal nerve, the most inferior branch of the proximal vagus, innervates all intrinsic laryngeal muscles except cricothyroid, in addition to the cricopharyngeal portion of the inferior constrictor muscle and the sensory receptors of the trachea (Zemlin, 1998). Intrinsic laryngeal muscles are responsible for adducting the vocal folds, which in swallowing prevents foreign matter from entering the lower airway and the lungs (Mendell & Logemann, 2007). Interarytenoids (transverse and oblique) and lateral cricoarytenoids aid in the adduction of the vocal folds. The inferior constrictor is not only responsible for the final propulsion of the swallowed food into the digestive system, but its most inferior cricopharyngeal portion is part of the upper esophageal sphincter which allows flow into the esophagus and then prevents retrograde flow of swallowed material from the esophagus back into the pharynx or upper airway (Zemlin, 1998). Phrenic nerve injury is also a potential postoperative complication. Diaphragmatic paralysis leads to lower tidal volumes per respiratory cycle, which in turn increases respiratory rate to compensate for the necessary minute volume of inspired air needed to maintain adequate gas exchange. This increased respiratory rate leads to impaired coordination of ventilation and swallowing, which in the healthy system is characterized by post-swallow exhalation after most swallows (Martin-Harris, 2008; Troche et al., 2011; Leslie et al., 2005). Damage to any of these muscles or their sensorimotor innervations can result in oropharyngeal dysphagia, putting patients at high risk for aspiration (Zemlin, 1998).

1.3 VIDEOFLUOROSCOPY

The videofluoroscopic swallowing examination (VFSS) is accepted as the gold standard for evaluation of disordered oropharyngeal swallowing. VFSS provides real-time x-ray imaging of the oral and pharyngeal stages that can be recorded and analyzed frame-by-frame, second-by-second, through digital image processing software programs. This precision allows clinicians and researchers to pinpoint specific physiologic events that occur during the swallow. Additionally, judgments of bolus flow and misdirection can be made.

1.3.1 Modified Barium Swallow Study

The evaluation of the oropharyngeal swallow using videofluoroscopy is called a modified barium swallow study (MBSS) (Lof & Robbins, 1990). Over the past 35+ years, research using MBSS data has produced a substantial normative database that has formed the basis for judgments of impairment in clinical settings. This study uses controlled amounts of radiopaque substances that are swallowed by the patient, to accurately diagnose swallowing difficulties with different volumes and consistencies (Kim et al., 2005). MBSS is often part of the routine post-operative evaluation for patients who have undergone a single-lung transplant (Atkins et al., 2010).

1.3.2 Swallow Kinematic Assessment

Analysis of the recorded swallows from the MBSS involves measurement of the durations of various kinematic swallowing events and their timing in relation to one another. Measurements of event durations require noting the time when the barium or bolus reached specific anatomical landmarks or when oropharyngeal structures initiated, reached, or terminated maximal movements during the swallow (Lof & Robbins, 1990). Several of these durations have been used in dysphagia research to characterize typical swallowing patterns and to assess pathological changes in swallowing function in disease states, and have been defined by Lof and Robbins (1990) and others.

1.3.2.1 Durations

Duration of stage transition (DST) is the measure of the coupling of the voluntary oral stage to the involuntary pharyngeal stage and a common index of the duration of delay in the onset of the pharyngeal stage, and is measured by observing the time it takes the patient to transition from the oral preparatory stage to the pharyngeal swallow stage. The duration is calculated by subtracting the time at which the hyoid bone begins its maximal pharyngeal-stage related excursion from time the first bolus head enters the pharynx as indicated by crossing the radiographic shadow of the mandibular ramus (Lof & Robbins, 1990).

The *pharyngeal transit duration* (PTD) is the duration in which the swallowed material travels through the pharynx and is measured by subtracting the time at which the bolus tail passes through the upper esophageal sphincter from the time at which the first bolus head crosses the mandibular ramus (Lof & Robbins, 1990).

Pharyngeal response duration (PRD), a measure of pharyngeal physiological activity duration, measures the hyoid's movement by calculating the duration between the time the hyoid begins its maximal pharyngeal-stage excursion, and the time that the hyoid returns to its resting position at the end of the pharyngeal response (Lof & Robbins, 1990). Some researchers have begun to call the onset of this duration the "hyoid burst" (Azola et al., 2015).

The *duration of UES transit* (DUEST) is the duration between the time the head of the bolus enters the UES to the time the tail of the bolus passes through the UES (Lof & Robbins, 1990).

Duration of upper-esophageal sphincter (DUESO) is the time it takes for the UES to open and then reclose. This is found by calculating the duration between the time the UES opens and closes (Lof & Robbins, 1990; Mendell & Logemann, 2007).

There is also interest in whether the first material to enter the pharynx during swallowing is the propelled bolus or oral contents that were poorly controlled during the oral preparatory stage. This duration, the *duration of impaired oral containment* (DIOC), is a measure of the duration of time in which unorganized material being held in the oral cavity is exposed to the unprotected pharynx. This stage is calculated by subtracting the time at which the organized, propelled bolus head first crosses the radiographic shadow of the ramus of the mandible from the time any barium first crosses the ramus. We developed this duration for it was germane to the nature of potential impairments in post-SLT dysphagia.

1.3.2.2 Penetration-Aspiration Scale

Measurement of airway invasion during swallowing provides an estimate of potential exposure of the respiratory tissues to swallowed material that has entered the airway. In 1996, Rosenbek and colleagues developed the penetration-aspiration scale (PAS) to characterize the severity of airway compromise during swallowing. Penetration-aspiration scores are determined from the videofluoroscopic images. This ordinal measure helps to characterize a patient's airway protection competence using an eight-point scale that possesses some qualities of an interval scale (McCullough et al., 1998). This non-parametric measure identifies depth to which swallowed material enters and courses into the airway, specifies presence of airway residue after the swallow ends, and identifies whether there is an overt reflexive response to material entering the airway. Clinically, PAS scores are a relevant indicator of pulmonary aspiration and provide a prognostic measure of aspiration pneumonia risk. Aspiration severity and impaired swallowing physiology seem to be closely linked. Identification of the severity of the aspiration and the biomechanical causes of impaired airway protection help to pinpoint the nature of dysphagia and led to more accurate prognostic statements as well as intervention options to mitigate airway compromise during swallowing.

2.0 PROJECT GOALS AND DESIGN

2.1 SPECIFIC AIMS

This descriptive, retrospective study is novel; the swallowing characteristics of patients who have undergone single lung transplantation have not been previously reported. While a correlation between single lung transplantation and dysphagia is known, the results of this study are the first published data on the specific characteristics of the SLT swallow. We sought to determine whether clinically significant changes in swallow function after SLT might explain whether dysphagia should be proactively suspected following this procedure to reduce post-operative complications. The goals of this study are to define the characteristics of single lung transplant swallows in order to explicitly describe swallow physiology of a small group of specific patients and to compare these observations to published norms to determine whether overt differences exist, and to provide the first description of swallow physiology following SLT. These efforts will help to identify risk factors that physicians and clinicians should be aware of when treating patients with SLTs, and provide an initial descriptive database that identifies directions for future research.

2.2 HYPOTHESIS

We hypothesized that patients with single-lung transplantations will present with prolonged durational swallow physiologic measures as compared to published healthy swallow norms, and significantly higher (worse) numerical scores in a scale of airway protection during swallowing.

2.3 METHODS

2.3.1 Participants

Experimental group: previously recorded data from 10 patients who had recently undergone a single-lung transplant in the University of Pittsburgh Medical Center (UPMC) were analyzed. Patients were between 49-68 years of age (mean age: 61). Participants consented to and participated in an NIH funded investigation (IRB#: PRO12080498) comparing videofluoroscopic images of swallow function with signals concurrently recorded during swallowing using high resolution cervical auscultation using accelerometers and high resolution microphones (Dudik et al., 2015; Dudik et al., 2016).

Control group - durations: data from the 1990 Lof & Robbins study entitled "Test-retest variability in normal swallowing" was used to compare data from the present study to normative data of four durational measures (DST, PRD, PTD, and DUESO). 16 subjects divided evenly into two age groups; middle aged (mean age: 45) and old aged (mean age: 66) consented to and participated in this study. We compared our subjects' data to the old aged group since the mean ages were comparable (present study mean age: 61, Lof & Robbins study mean age: 66).

Subjects were part of a larger study that evaluated normal adult swallowing physiology at different age ranges. The authors' objective was to measure test-retest variability of swallowing parameters using videofluoroscopy. Nine durational measures of the swallow were evaluated and all were found to exhibit no statistically significant differences between repeated swallowing observations among healthy persons.

Control group – PAS: data from the 1999 Robbins et al. study entitled "Differentiation of Normal and Abnormal Airway Protection During Swallowing Using the Penetration-Aspiration Scale" was used to compare data from the present study to normative PAS scores. 98 healthy subjects were divided into three age groups: 21-32 (mean age: 23), 43-47 (mean age: 40), and 63-84 (mean age: 68). We compared our subjects' data to the 63-84 year old age group since the mean ages were comparable (present study mean age: 61, Robbins study mean age: 68). The objective of the 1999 Robbins et al. study was to define the distribution of the Penetration-Aspiration Scale scores in healthy normal subjects of different genders and ages, and compare them to those of patients with stroke and with head and neck cancer treatment, to determine whether the penetration-aspiration scale was sensitive to disordered swallowing. The authors identified distinctly and statistically significantly different distributions of PAS scores among all three groups and was the first to characterize "normal airway protection" in adults. Researchers obtained informed consent pursuant of the University of Wisconsin Hospital Human Subjects Committee (Robbins et al., 1999).

2.3.2 Design

This present study was approved by the University of Pittsburgh Institutional Review Board (IRB#: PRO15080051). This descriptive, retrospective, observational study with comparison to a historical control cohort is centered on analyzing and documenting the swallowing characteristics of patients with SLTs.

2.3.2.1 Data Collection

Certified Speech-Language Pathologists systematically collected all swallows at UPMC Presbyterian Hospital. All radiographic data were de-identified at the time of recording using a bypass recording system that captured images prior to their entering the hospital's recording and patient identification system. Data were then assigned a new identification number by study staff prior to the principal investigator having access to them.

2.3.2.2 Data Analysis

144 swallows within the target conditions were produced by the cohort. 2 of these swallows were excluded because the dependent variables could not be analyzed, as the recording did not show all necessary kinematic events. All 142 valid swallows, limited to thin or nectar thick liquids in small (spoon administered, approximately 3mL) and large (cup self-administered, unmeasured volumes) and neutral or chin-tuck head positions, were analyzed using software program Image J to determine durations and penetration-aspiration scores (Rashband, 2015). Since the sample was small, descriptive statistics were used to summarize the observations made in the various swallowing physiologic measures. Two-tailed, one-sample t-tests were used to compare durations (DST, PTD, PRD, DUESO) between subjects and the age-matched previously published normative duration values from the 1990 Lof & Robbins study and the age-matched PAS scores reported by Robbins et al. (1999). Since this study is a pilot investigation of the single-lung transplant swallow, and there are published data regarding kinematic swallowing changes after lung transplantation, there was no available data to indicate or predict the direction

of alteration (greater or less than expected) of each duration. Each direction (longer, shorter durations; higher or lower PAS scores) was equally probable therefore it was most appropriate to select the two-tailed test. The remaining two durations for which there are no published norms (DIOC and DUEST) were descriptively analyzed. IBM SPSS Statistics Version 23 was used for all statistical analyses.

The dependent variables in this study were the six swallow event durations described in section 1.3.2.1 and computed in section 3.1 and the PAS scores described in section 1.3.2.2 and reported in section 3.2. Eight discrete swallow events (Table 1) and PAS scores (Table 3) were identified by a single judge (SAP).

Because the number of trials and types of conditions administered to each patient was not identical, swallows were stratified by condition defined by the bolus consistency and utensil of bolus administration to indicate bolus volume (small volume, large volume). Utensil is used as an approximate for bolus volume; spoon is about 3ml, cup is at least 5ml and estimated to be no more than 20mL, cup with straw ranges from less than 1ml to about 10ml. Swallows were separated by independent variables; 2 consistencies and 3 utensils, resulting in six conditions: Thin Spoon (TS), Nectar Spoon (NS), Thin Cup (TC), Nectar Cup (NC), Thin Cup with Straw (TCWS), and Nectar Cup with Straw (NCWS). The swallows were also limited to two postures during swallowing, neutral and chin-down postures.

Penetration-aspiration scale (PAS) scores for thin liquid swallows were also analyzed and compared to previously published norms from the 1999 Robbins et al. study using descriptive statistics on SPSS. Swallows were separated and analyzed in the same way as the six durational measures, by utensil and by consistency.

Inter- and intra-rater reliability were tested using intra-class correlation coefficient and percent exact agreement on IBM SPSS Statistics 23. Details of these analyses can be found in section 3.4.

Table 1. Discrete measures of biomechanical events used to compute durations

Swallow Event	
Oral Events	
1	First Barium Cross Ramus
2	First Bolus Cross Ramus
Pharyngeal Events	
3	First Hyoid Max
4	Hyoid to Rest
UES Events	
5	UES First Prox Open
6	Head into UES
7	Tail through UES
8	UES Closed

Table 2. Formulae for computing durations

Durations	
(2-1)	Duration of Impaired Oral Containment (DIOC)
(3-2)	Duration of Stage Transition (DST)
(7-2)	Pharyngeal Transit Duration (PTD)
(4-3)	Pharyngeal Response Duration (PRD)
(8-5)	Upper-Esophageal Sphincter Opening Duration (DUESO)
(7-6)	Duration of Upper-Esophageal Sphincter Transit (DUEST)

Table 3. Penetration-aspiration scale as defined in Rosenbek et al., 1996

PAS Definitions	
Score	Definition
1	Material does not enter the airway
2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4	Material enters the airway, contacts the vocal folds, and is ejected from the airway
5	Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6	Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
7	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8	Material enters the airway, passes below the vocal folds, and no effort is made to eject

3.0 RESULTS

3.1 DESCRIPTIVE STATISTICS – DURATIONS

10 patients produced 142 swallows (Table 4). These swallows were divided into 6 categories defined by bolus consistency and utensil. 6 durations comprised of 8 swallow events were analyzed for each category. Descriptive statistics were found for all durations/conditions (Table 5).

Table 4. Total number of swallows by condition

TOTAL # OF SWALLOWS BY CONDITION	
THIN SPOON (TS)	27
NECTAR SPOON (TS)	17
THIN CUP (TC)	33
NECTAR CUP (NC)	8
THIN CUP WITH STRAW (TCWS)	32
NECTAR CUP WITH STRAW (NCWS)	25
TOTAL	142

Table 5. Descriptive summary of durations in seconds

		N	MEAN	ST. DEV	CONTROL N	CONTROL MEAN
DIOC	TS	27	0.4063	0.54643		
	NS	17	0.1571	0.27004		
	TC	33	0.4978	1.08005		
	NC	8	0.1450	0.26981		
	TCWS	32	0.4734	0.91850		
	NCWS	25	0.2464	0.48881		
DST	TS	27	-0.0459	0.09170	24	-0.22
	NS	17	-0.0092	0.08261		
	TC	32	-0.0225	0.09528		
	NC	8	-0.0725	0.05203		
	TCWS	32	-0.0447	0.08692		
	NCWS	25	0.0020	0.11347		
PTD	TS	27	0.5293	0.10539	24	0.51
	NS	16	0.5494	0.09546		
	TC	33	0.5836	0.11497		
	NC	7	0.5729	0.06775		
	TCWS	32	0.5919	0.20041		
	NCWS	25	0.5560	0.15500		
PRD	TS	27	0.8044	0.19809	24	1.14
	NS	16	0.7231	0.13390		
	TC	32	0.8416	0.20959		
	NC	7	0.7857	0.09846		
	TCWS	32	0.8384	0.20089		
	NCWS	25	0.7948	0.21129		
DUESO	TS	27	0.5293	0.10539	24	0.45
	NS	16	0.5488	0.09542		

	TC	33	0.5836	0.11497		
	NC	7	0.5729	0.06775		
	TCWS	32	0.5919	0.20041		
	NCWS	25	0.5560	0.15500		
DUEST	TS	27	0.3622	0.12125		
	NS	16	0.3538	0.14742		
	TC	33	0.4303	0.12267		
	NC	7	0.3914	0.09317		
	TCWS	32	0.3825	0.13122		
	NCWS	25	0.3016	0.13921		

3.2 PENETRATION-ASPIRATION SCALE SCORES

All 142 swallows were also analyzed for penetration-aspiration scores (PAS). Descriptive statistics were computed for the PAS for each category (Table 6). Age-matched, normative scores from the 1999 Robbins et al study were compared to the SLT population's scores for thin condition penetration aspiration scores. Post-hoc analysis was conducted to investigate the relationship between PAS and volume (Table 7). Overall distribution of PAS scores for all swallows are summarized in Figure 1 and for thin-liquid swallows only in Figure 2.

Table 6. PAS scores

	N	MEAN	ST. DEV	RANGE	CONTROL N	CONTROL MEAN
TS	27	2.2963	1.51441	1-6	153	1.2679
NS	16	2.5625	1.67207	1-5*		
TC	32	1.9630	0.75862	1-4*		
NC	7	1.8571	0.37796	1-2*		
TCWS	33	2.3030	1.40278	1-8*		
NCWS	26	2.3077	1.01071	1-5*		

* Conditions for which comparative/control data does not exist.

Table 7. Paired sample t-test TS vs. TC

PAIRED SAMPLE T-TEST TS vs. TC		
t	df	Sig. (2-tailed)
1.071	26	0.294

Figure 1. Overall distribution of PAS scores for all swallows

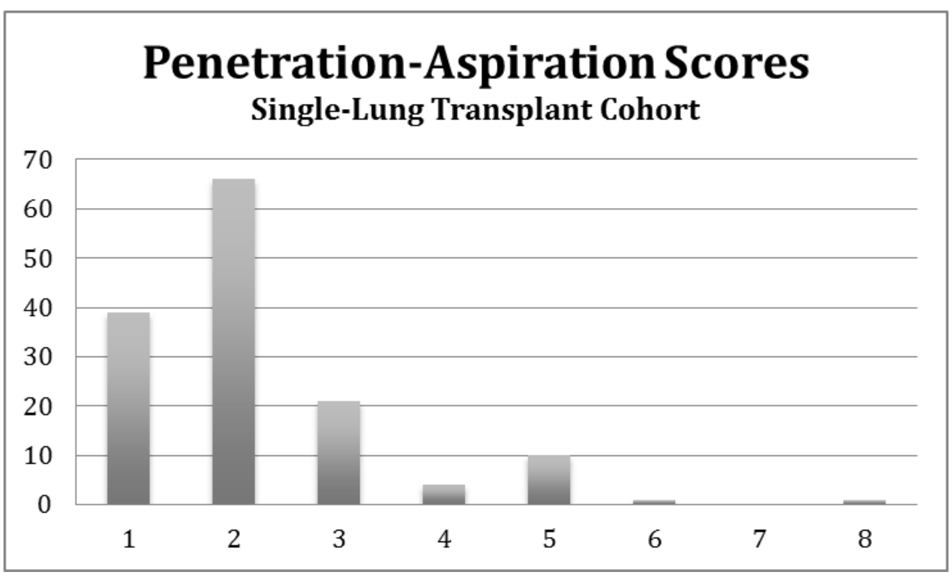
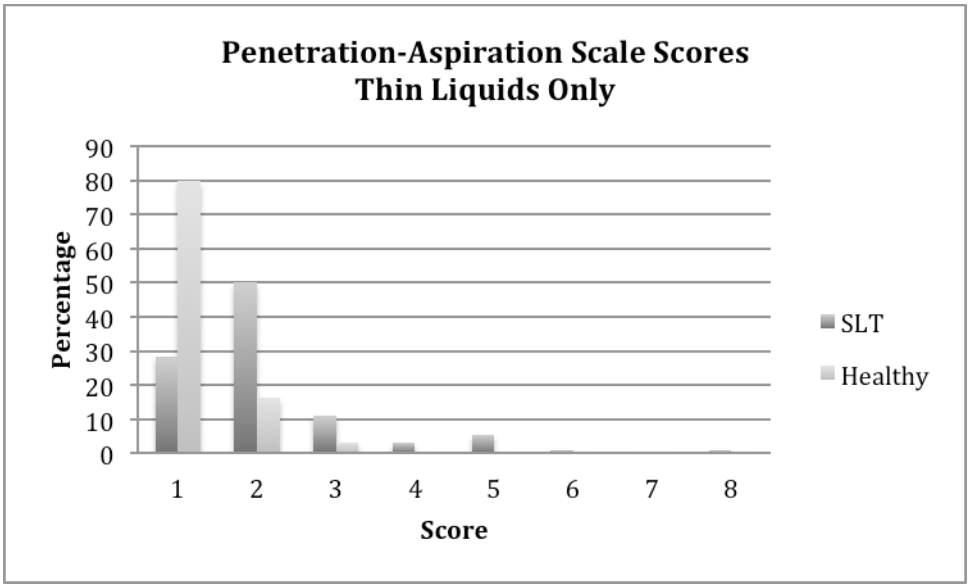


Figure 2. Distribution of PAS scores for thin liquid swallows – SLT vs. Healthy



3.3 SWALLOW DURATIONS

Four of the six durations that we computed were compared to the age-matched normative data set published by Lof & Robbins (1990) using a one-sample t-test, and are summarized in Table 8. The participants in the Lof & Robbins study received 2ml of radiopaque material (barium) via spoon during a MBSS.

Significant differences between the test value (control group neutral position only) and SLT (neutral, chin-down position) were observed for DST, PRD, and DUESO in both the neutral and chin-down positions (Table 8). No significant differences were observed for PTD in either position.

Table 8. Summary of one-sample t-test results (participant group stratified by head position vs. published norms indicated by "test value")

	Head Position	t	df	Sig. (2-tailed)	Mean Difference
DST TS Test value = -0.22	Neutral	8.785	23	0.000	0.17458
	Chin Down	17.000	2	0.003	0.17000
PTD TS Test value = 0.51	Neutral	0.627	23	0.537	0.01417
	Chin Down	3.464	2	0.074	0.06000
PRD TS Test value = 1.14	Neutral	-7.793	23	0.000	-0.33458
	Chin Down	-16.933	2	0.003	-0.34333
DUESO TS Test value = 0.45	Neutral	3.285	23	0.003	0.07417
	Chin Down	6.928	2	0.020	0.12000

3.4 RELIABILITY

3.4.1 Inter-Rater

Inter-rater reliability was established a-priori following training in the swallowing research lab, on practice data from previously recorded and de-identified videofluoroscopic images. The principal investigator (SAP) scored 100 swallows on all eight-swallow kinematic events and PAS scores. Rater 2, the principal investigator's research mentor and an expert judge (JLC), then scored a randomly selected 10% of the 100 swallows. Inter-rater agreement was assessed by means of intra-class correlation coefficient (ICC) and percent exact agreement on IBM SPSS

Statistics 23. Tolerance for agreement of kinematic measures was 0.1 second (Lof & Robbins, 1990). Six of the eight swallow events and PAS scores had 80% or higher exact agreement for frame selection (both JLC and SAP scores within 0.1 second of each other for all swallows of each event). The other two measures were resolved by consensus while maintaining the tolerance level. 20 of the 100 swallows did not include all eight swallow events; the recording either started late or was ended early. These swallows were eliminated from the reliability test and were deemed invalid. SAP then re-rated the swallows and ran an ICC on all 80 valid swallows. The intra-class correlation coefficient, using an absolute agreement definition, found that the 80 valid cases were highly reliable with an Intraclass correlation coefficient of 1.000 ($p<.001$, 95% CI = 0.999-1.000).

3.4.2 Intra-Rater

Intra-rater reliability was established on the data from previously recorded and de-identified videofluoroscopic images. SAP scored a random 10% of the 100 practice swallows. Intra-rater agreement was assessed by means of intra-class correlation coefficient and percent exact agreement on SPSS statistical software. SAP was allowed a three-frame tolerance (or 0.10 second) between scores. All eight swallow events had a greater than or equal to 80% exact percent agreement. An intra-class correlation coefficient, using an absolute agreement definition, found that the 10 valid cases were highly reliable at 1.000 ($p<.001$, 95% CI = 0.999-1.000).

SAP also retested a random 10% of the test data and ran an ICC using the same absolute agreement definition. The results of the 15 valid cases showed that the data was reliability measured at 1.000 ($p<.001$, 95% CI = 0.999-1.000).

4.0 DISCUSSION

This study showed significant durational differences between the SLT population and the normal population. Our first specific aim was to describe the swallow characteristics of the SLT population. This was accomplished by collecting and analyzing descriptive data for all six durations and PAS scores. Our second specific aim was to compare the SLT swallow cohort to data from a normal, healthy population. The 1990 Lof & Robbins study was used for comparison of the durations while the 1999 Robbins et al. study was used to compare the PAS scores.

4.1 DURATIONS

Descriptive statistics were found for all six durations. Four of the six durations were compared to age-matched normative data from the 1990 Lof & Robbins study. Contrast consistency and volume impacted the durations. Clinically significant information was found from these analyses.

4.1.1 Descriptive Data

Descriptive data was collected and analyzed for all six durations.

Duration of stage transition (DST) is the time the propelled bolus is in the pharynx before the swallow begins (Coyle, 2008). The durations were highly variable for each condition and did not follow any specific pattern in terms of bolus consistency and bolus volume. This shows that consistency and volume do not significantly impact DST in following SLT. In the normal population, larger boluses produce a shorter DST, and thicker material exits the oral cavity sooner than thin (Saitoh et al., 2007).

Pharyngeal response duration (PRD) is the duration of pharyngeal motor activity indicated by hyoid onset of maximal motion to hyoid returns to rest. PRD is significantly shorter for nectar thick liquids (average: 0.7679 seconds) than thin liquids (average 0.8281 seconds) for all volumes (a 0.06 second difference). This indicates that PRD is affected by consistency. Thicker liquids of all volumes lead to a shorter PRD.

Pharyngeal transit duration (PTD) is the duration of bolus transit from entering pharynx to exiting pharynx. PTD was shorter for thin liquids than nectar thick liquids in for contrast administered via spoon. PTD was longer for thin liquids than nectar thick liquids in boluses administered via cup or cup with straw. This shows that PTD is influenced by bolus volume and bolus consistency. Small, thin liquid boluses lead to shorter PTD than larger boluses of both thin liquid and nectar thick consistencies. How these findings may relate to swallowing interventions in patients with SLT warrants further investigation.

Duration of UES opening (DUESO) is the duration between the onset of the opening of the UES to onset of closure of the UES. DUESO durations varied for both consistencies and volumes. According to the 1990 Lof & Robbins study, DUESO tends to be the most variable duration across normal patients. Therefore, it logically follows that the SLT population would produce similarly varied results.

Duration of UES transit (DUEST) is the duration of contrast flow through the upper esophageal sphincter (Coyle, 2008). Durations for all conditions fell within 0.30-0.43 second and are well within one standard deviation of the mean. Bolus volume may impact the length of the duration of contrast flow through the UES. The contrast administered via spoon (smallest volume) presented with shorter durations as compared to cup (largest volume).

DIOC is a duration that the research advisor, JLC, developed to characterize the duration that contrast is in the pharynx before the bolus has been volitionally propelled into the pharynx. The average duration of exposure of the as-yet inactive pharynx to the contrast solution was on average 0.4592 seconds for thin conditions and 0.1828 seconds for nectar conditions. These findings indicate that there is a degree of poor bolus organization during the oral preparatory stage and that posterior oral containment may explain the airway penetration or aspiration scores observed. Shorter DIOC for thicker liquids may reflect their adherence to the oral mucosa and less gravity dependence toward their flow than thin liquids. Observationally, thin liquid boluses are less organized than nectar thick boluses of the same volume for all utensils of administration for patients with SLT. Significant differences were seen between the thin liquid boluses and the nectar thick boluses, justifying the use of thick liquids in cases where prolonged impairment of oral containment leads to aspiration. All conditions were within about one standard deviation of the mean. Bolus volume also impacted DIOC with larger volumes administered from a cup leading to longer durations of impaired oral containment. This may justify the use of smaller bolus volumes to improve oral containment. Although the conditions were not stratified by head position for data analysis, swallows that utilized the chin-down position during both thin liquid and nectar thick liquid swallow resulted in a shorter DIOC. This suggests that chin-down posture is effective in improving oral containment and previous research has supported that this position is more acceptable to patients who tend to prefer thin liquids (Robbins et al., 2008).

4.1.2 Comparison of SLT Swallows to Published Norms

Four durations (DST, PRD, DUESO, and PTD) have normative data for the thin spoon (TS) condition and three of these durations (DST, PRD, and DUESO) demonstrated significant differences when compared to the normal cohort data from the 1990 Lof & Robbins study.

Duration of Stage Transition (DST) is the duration that the propelled bolus is in the pharynx, before the pharyngeal swallow begins (Coyle, 2008). The normal comparison group produced an average DST of about -0.22s indicating that the onset of pharyngeal swallowing began an average of 0.22 seconds *before* the bolus entered the pharynx. The SLT subjects had an average DST of about -0.04s, a 0.17s difference indicating that DST is more than 5 times *longer* for patients following SLT than healthy people of the same age. This indicates that the bolus crosses the ramus shortly before the start of hyoid elevation. The results indicate that DST in the SLT cohort is more similar to that of a much older, healthy population (Lof & Robbins, 1990). Prolonged DST indicates that the airway is left unprotected and exposed to potential penetration and aspiration for a longer period of time. A prolonged transition between the end of the oral stage and the beginning of the pharyngeal stage, or the initiation of the pharyngeal swallow has been linked to aspiration (Kim et al., 2005). While other factors may contribute to aspiration pneumonia, delayed in the onset of airway closure, which is a sentinel component of the pharyngeal stage, may in part, explain some of the increased prevalence of post-SLT pulmonary infection. Furthermore, these DST results may account for increased PAS (Shanahan et al., 1993). These findings support the present study's first hypothesis: the SLT cohort will present with prolonged durational measures as compared to the healthy population.

Duration of Pharyngeal Response (PRD) is the duration of pharyngeal motor activity indicated by hyoid onset of maximal motion to hyoid returns to rest. The SLT population's duration was significantly shorter than the normal subjects. It is possible that a shorter PRD leads to impaired airway protection as a swallow that begins late and ends early may lead to airway penetration before (late response) and after (early end of PRD) the swallow (Kim et al., 2005). Additionally, the patients with SLTs may have reduced distance of hyolaryngeal excursion (HLE) which we did not measure in this study; a duration that often coincides with a shorter PRD (Bisch et al., 1994).

Duration of Upper Esophageal Sphincter Opening (DUESO) is the duration between onset of opening of the upper esophageal sphincter to onset of closure of the UES. Normal subjects presented with a mean of 0.45s while patients with SLTs presented with a mean of 0.53s. The mean difference was 0.079s. This difference shows that the esophagus remains open significantly longer for the SLT population. The UES compliments protection of the pharynx and the airway by preventing escape of swallowed material and gastric contents into the supraesophageal space. This can be viewed as either an advantage or a disadvantage. Prolonged UES opening may compensate for the reduction in the pharyngeal response duration that we observed, that may improve bolus clearance. However with prolonged UES opening, the patient is at an increased risk for retrograde flow of the swallowed material, potentially leading to retrograde aspiration (Jadcherla, 2010). This finding also supports the present study's first hypothesis.

Pharyngeal Transit Duration (PTD) is the duration of bolus transit from entering pharynx to exiting pharynx. The normative value for this duration is 0.51s while the SLT sample's duration was about 0.53s. The healthy population and the SLT population presented with similar durations, indicating that SLT did not seem to affect transit of swallowed material. Although the durations were different, the difference in transfer time is non-significant. This indicates that changes in the timing of the sequence of swallow events (when they begin and end) and not the duration of bolus clearance seems to define swallowing changes following SLT.

The data was also stratified by head position and analyzed using one-sample t-tests and compared to the same published norms of neutral position TS swallows. Since the chin-down position delivered statistically significant differences from the comparison data set in the neutral position, the chin-down position did not produce significantly different DST, PRD, or DUESO than the neutral position though the degree of significance between chin-down and control TS swallows were smaller than neutral position controls. This separate analysis indicates that the head posture did not significantly impact the results. Additionally, the sample size was very small; therefore little can be inferred from the results of the chin down position presented in Table 8.

4.2 PAS

Patients with SLT were highly variable in their PAS scores. The average PAS score ranged from 1.86-2.56. Individual ranges for each condition were also identified (Table 6). PAS thin scores were compared to age-matched normative data from the 1999 Robbins et al. study. Their study found that healthy persons of the same age as our participants rarely exhibited more than transient, shallow laryngeal penetration. Additionally, the healthy population ejects 97% of shallow penetrations while the SLT population ejects only 78% of shallow penetrations. This leaves residue in the airway above the glottis, increasing the risk of aspiration of residual contrast on the successive swallow. Quantitatively this indicates that patients with a SLT are at risk for deeper and more clinically significant airway penetration. Furthermore, 12% of the SLT swallows would be classified as “unsafe” (Robbins et al., 1999). Swallows with scores this high (PAS 4-8) occur a mere 0.6% of the time in healthy people of this age; indicating an increased risk of aspiration for the SLT population. These findings support the present study’s second hypothesis: the SLT cohort will present with higher (worse) PAS scores than the healthy population.

A paired sample t-test was done to compare TS swallows to TC swallows. Typically, better (lower) scores are seen with smaller bolus sizes rather than the results our SLT cohort produced; larger bolus size correlated with better (lower) PAS scores. Although small, the improved PAS scores for the larger thin liquid bolus compared to the smaller bolus, may reflect either the effects of the bolus command condition which was employed with the TS condition compared to a natural swallowing condition used with TC swallows, or a volume effect. Although the results of the paired sample t-test (Table 7) showed the difference was not statistically significant, the inherent difference may warrant further clinical investigation.

4.3 LIMITATIONS OF THE CURRENT STUDY

The current study has several limitations. First, the sample size was very small. A larger sample would produce more generalizable results. A prospective study would be a natural extension of our research and our data may facilitate an estimation of the number of subjects needed to produce adequate statistical power to determine if these findings are generalizable. Second, due to the study design, the PI did not have access to the patient's medical records. This limited the PI's ability to measure the effects of comorbid conditions and significant components of the medical histories that may have been associated with patient's swallowing ability. Third, the bolus volume and consistency was not strictly controlled. Because the MBSS were performed in the manner determined by the examining SLP for the purposes of the parent investigation, each patient received different consistencies and volumes and each patient swallowed a different number of times. Additionally, some swallows were multiple swallows (multiple attempts to clear a single bolus) or sequential swallows (multiple boluses in quick succession). However such factors more closely represent the manner in which people eat and drink during meals, and may, or may not, be a limitation since the study goal was to describe SLT swallowing.

4.4 DIRECTIONS FOR FUTURE RESEARCH

Some modifications to the statistical analyses may be appropriate. The direction of each duration was established and it would now be fitting for future studies to utilize a one-tailed t-test for more precise results.

Future research may aim to prospectively control for several of the potentially confounding variables of this present study. Researchers could collect data from both healthy and SLT age-matched patients, standardize data collection by consistent bolus administration, bolus volume, bolus consistency, number of trials, command swallows, head positions, etc. Furthermore, a pre-test/ post-test comparison of SLT patients may strengthen the significance of the post-operative evaluation, especially if it is not feasible to include healthy participants. This would help to quantify the nature and extent of the changes as a consequence of the transplantation.

Future projects may want to consider the difference between right and left lung transplantations as well as the impact of double lung transplantations. Because the position of significant nerves innervating the pharynx and larynx are anatomically different on right and left sides of the thoracic cavity, the specific lung that was transplanted may be of clinical significance. Additionally, co-morbid conditions may be factored in the analysis to see if initial diagnosis impacts durational measures and ordinal scores. Evaluation of pre-operative information may help to parse out some characteristic confounding variables.

Future studies may also aim to find and analyze normative data for conditions such as DIOC and DUEST for which the SLT data may be compared to. The hope is that data from this study will serve as an initial descriptive database against which future research may be compared. Clinicians may use the information presented here to consider the patient with SLT to possess a higher risk of dysphagia and consider this, along with their immunocompromised state, as compelling reasons to proactively screen and assess patients with SLT before resuming ordinary oral intake, and to create intervention strategies to improve the swallowing of patients with single-lung transplants. This area of research within speech-language pathology has tremendous room for growth and continued investigation into the consequences of post-operative dysphagia may lead to better treatment options and intervention strategies, prolonging the functional lifespan of the transplant organ and thusly the lifespan of the transplant recipient.

4.5 CONCLUSION

This study described the swallow physiology of a small sample of convenience, of patients with single-lung transplantation through analysis of durations and penetration-aspiration scores in order to identify possible clinically significant risk factors for physicians and other clinicians to be aware of when managing such patients. Although the sample size was small, the results showed that patients with SLTs have significantly longer stage transition durations (DST), prolonged UES opening durations (DUESO), and reduced pharyngeal response durations (PRD) as compared to their healthy age-matched peers. Patients with SLT also showed an increased risk for airway penetration and a reduced ability to eject the residual contrast material. These results underscore that patients with single-lung transplants are at risk for dysphagia that may compromise their allograft function and long-term prognosis.

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