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The effects of lung volume on swallowing in chronic obstructive pulmonary disease

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The Effects of Lung Volume on Swallowing in Chronic Obstructive Pulmonary
Disease

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A dissertation submitted to the Graduate Faculty of

JAMES MADISON UNIVERSITY

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Abstract

Chronic Obstructive Pulmonary Disease (COPD), a respiratory disease that leads to reduced airflow, may result in difficulty swallowing with disease progression. The coordination between the respiratory and swallowing systems decouple and they may experience increased risk of aspiration. This study aimed to determine the effects of lung volume on swallowing in individuals with COPD compared with older healthy. Specifically, the study examined if altering lung volume at the time of the swallow changed swallowing timing, specifically pharyngeal swallow duration, and impacted the respiratory-swallow pattern in individuals with COPD. Measurement of estimated lung volume (ELV), pharyngeal swallow duration, and respiratory-swallow patterning in individuals with COPD was compared with older healthy at varying lung volume conditions. Participants completed seven 20 ml water bolus swallows by medicinal cup across 4 lung volumes: non-cued volume (NC), and in order of increasing volume, resting expiratory level (REL), tidal volume (TV), and total lung capacity (TLC) . ELV was determined using respiratory inductive plethysmography (RIP) and spirometry. Swallow timing was measured by events during the swallow with pharyngeal manometry. Individuals with COPD had lower lung volumes at the time of the swallow than older healthy individuals. A moderate to strong negative relationship between estimated lung volume at the time of the swallow and pharyngeal swallow duration was found in individuals with COPD that was not present in the healthy participants. They had a longer pharyngeal duration when swallowing at lower lung volumes. The percentage of swallows resuming on

inspiration post-swallow were significantly greater in individuals with COPD than the healthy. In the COPD group, resumption of respiration in inspiration occurred significantly less often at the higher lung volumes (TLC and TV) than the lower volume condition, REL. In conclusion lower lung volumes at the time of the swallow in individuals with COPD were associated with longer pharyngeal swallow duration and increased resumption of respiration in inspiration post-swallow.

Introduction

The American Thoracic Society (ATS), European Respiratory Society (ERS) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) define Chronic Obstructive Pulmonary Disease (COPD) as a respiratory disease characterized by reduced airflow that is not reversible by use of a bronchodilator or anti-inflammatory therapies (Celli et al, 2004). COPD is preventable and treatable. The World Health Organization predicts that COPD will be the third most prevalent disease and rank fifth in level of disability by 2020 (O’Kane & Groher, 2009). The National Heart, Lung, and Blood Institute estimated an annual cost of managing COPD at \$50 billion. COPD is the fourth leading cause of mortality in the United States and Europe (Celli et al., 2004). Dysphagia, impairment in swallowing, is present in 27% of individuals with COPD and the incidence of dysphagia increases with COPD disease progression (McKinstry, Tranter, & Sweeney, 2010). Patients with COPD demonstrate a discoordination between breathing and swallowing that may be related to increased respiratory drive. Respiratory and swallowing discoordination places patients at risk for penetration or aspiration, entrance of food or liquid into the airway, and aspiration pneumonia (Coelho, 1987; Cvejic et al., 2011). Further, adverse events such as increased hospitalizations and higher mortality rates occur in individuals with COPD and dysphagia (Cvejic et al., 2011).

Historically, individuals with COPD were labeled with a range of obstructive respiratory conditions such as emphysema or chronic bronchitis. Cross-agency

efforts were instrumental in ensuring consistent, centralized diagnosis with the umbrella term, COPD, to improve healthcare service delivery. Noxious particle or gas exposure such as cigarette smoke, chemicals, or other toxins results in chronic, abnormal inflammation of the lungs. In addition to inflammation reducing airflow, emphysema impairs the elastic integrity of the alveolar sacs within the lungs resulting in hyperinflation or air trapping (Celli et al., 2004; Hess, MacIntyre, Mishoe, Galvin & Adams, 2012). Chronic bronchitis is indicated when an individual has a productive cough lasting for three months or longer in two consecutive years which cannot be explained by another condition (Celli et al., 2004). However, Hess et al. (2012) cautions that individuals diagnosed with chronic bronchitis do not all meet the irreversible airflow obstruction criteria for the COPD diagnosis. In the past, individuals with repetitive airway inflammation presentation were labeled with chronic bronchitis; however, in recent years, practitioners have been urged to diagnose individuals with 'airway disease' (Hess et al, 2012). The preferred term, airway disease, addresses the pulmonary changes evidenced in the central and peripheral airway as opposed to the pulmonary changes only in the central airway suggested by the chronic bronchitis definition (Hess et al., 2012). While cystic fibrosis, bronchiolitis obliterans and bronchiectasis cause chronic limited airflow, these conditions are not classified within COPD (Hess et al., 2012). Additionally, individuals with asthma are rarely diagnosed with COPD (Mannino, 2002).

The gold standard for diagnosing COPD is spirometry, a "standardized and reproducible test that objectively confirms the presence of airflow obstruction" (Juvelekian & Stoller, 2010, p. 3). Spirometry is one component in pulmonary

functioning testing (PFT). With calibration, spirometry is used to measure the volume of air and rate of air movement (airflow) during an individual's inhalation and exhalation. The airflow and volume measurements are obtained by having the individual breathe into a mouthpiece while in the sitting or standing position (Hess et al., 2012). FEV₁ is the amount of air an individual can forcefully exhale in one second. Forced vital capacity (FVC) is the total air volume an individual exhales with force after a large inspiration. Diagnostic testing with spirometry can measure forced expiratory volume in one second (FEV₁) divided by forced vital capacity (FVC)¹. A ratio of ≤ 0.7 documents the required airflow limitation to meet the COPD diagnosis criteria (Celli et al., 2004).

COPD severity, determined via a classification scale such as the GOLD staging system shown in Table 1, is based on the measured amount of lung function impairment using spirometry (Mannino, 2002). The GOLD staging system is a 5-stage scale (0-IV) ranging from 'at risk' (0) to 'very severe' (IV). In addition to the use of the fixed FEV₁/FVC ratio ≤ 0.7 confirming COPD diagnosis, the percent forced expiratory volume in 1 second (FEV₁%) is utilized to stage individuals with COPD (Celli et al., 2004; Hess et al., 2012). The FEV₁% is derived by comparing an individual's expiratory volume in one second to his/her peers of a similar age, gender, height and mass. Celli et al. (2004) recognized limitations in singular use of spirometry outcomes for severity staging and suggested stronger consideration of body mass index (BMI) and dyspnea evaluation during exercise. However, the GOLD

¹ FEV₁/FVC is the amount of air that can be forcibly exhaled in one second divided the amount of air that can be forcibly exhaled after taking as deep a breath as possible.

severity staging scale, based on spirometry results, continues to be the most widely accepted rating scale.

Table 1

GOLD COPD Severity Staging

Stage	Description	Findings: Postbronchodilator
0	At risk	FEV ₁ /FVC > 0.7
I	Mild	FEV ₁ /FVC < 0.7; FEV ₁ ≥ 80%
II	Moderate	FEV ₁ /FVC < 0.7 FEV ₁ at 50 to <80%
III	Severe	FEV ₁ /FVC < 0.7 FEV ₁ at 30% to <50%
IV	Very Severe	FEV ₁ /FVC < 0.7 FEV ₁ at <30% or FEV ₁ < 50% with severe chronic symptoms

Note. FEV₁ ratios are based on a percentage of predicted normal value given age, gender, height, mass and ethnicity.

Symptoms associated with COPD are dyspnea (shortness of breath) on exertion, chronic cough, sputum expectoration and wheezing. Pursed-lip breathing with prolonged expiration, barrel chest, accessory muscles usage during respiration and cyanosis may also be present in individuals with COPD (Juvelekian & Stoller, 2010). Non-pulmonary complications may include: cardiovascular disease, peripheral edema, cachexia (wasting syndrome), skeletal muscle dysfunction, osteoporosis, and depression (Hess et al., 2012). Celli et al. (2004) identified COPD risk factors to include:

- Smoking
- Socio-economic status
- Occupation

- Environmental pollution
- Perinatal events and childhood illness
- Recurrent bronchopulmonary infections
- Diet
- Genetic predisposition
- Gender
- Airway hyperactivity and asthma

Exacerbation of COPD is defined as acute changes in: (1) dyspnea level, (2) cough, and/or (3) sputum which require adjustments in regularly prescribed medications (Celli, 2004). COPD exacerbations result in inflammation which may cause irreversible disease severity progression (Hess et al., 2012). Medical management for exacerbations may include: (1) a course of corticosteroids, (2) antibiotic therapy, (3) oxygenation therapy adjustments to maintain $\geq 90\%$ SpO₂ while minimizing CO₂ retention, and (4) intubation with ventilation (Hess et al., 2012). Individuals with an exacerbation of COPD have demonstrated a statistically significant higher respiration rate (24 breaths/minute) in comparison with healthy elderly individuals (15.6 breaths/minute) (Shaker et al., 1992).

The cause of COPD exacerbations is still a point of debate in the medical community although increased aspiration and penetration have been posited as a trigger for an exacerbation onset (Gross et al., 2009; Terada et al., 2010). Abnormal swallowing in COPD is associated with a significantly increased frequency of COPD exacerbations per year than in individuals without swallowing impairment after adjusting for other factors (Terada et al., 2010). Others posit that the respiratory

decline during a COPD exacerbation, such as increased dyspnea and tachypnea, further impair the respiratory-swallow coordination and result in greater penetration and/or aspiration. This evidence suggests a relationship between altered swallowing and increased frequency of COPD exacerbations.

Airway protection during a swallow requires a cessation of respiration, or “swallow apnea”, ranging from .75-1.5 seconds while the bolus passes through the pharynx followed by a resumption of respiration signaling the end of the swallow (Klahn & Perlman, 1999; Martin-Harris, 2008; Perlman, He, Barkmeier & Leer, 2005). This suggests a central coordination between the respiratory and swallowing central pattern generators (Broussard & Altschuler, 2000; Jean, 1984). Young healthy individuals typically couple a swallow with the expiratory phase of respiration (Cedborg et al., 2010; Martin-Harris et al., 2005; Martin-Harris, Brodsky, Price, Michel, & Walters, 2003; Shaker et al., 1992; Wheeler Hegland, Huber, Pitts, Sapienza, 2009). Specifically, they initiate the swallow and resume respiration after the swallow during the expiratory phase (E-E pattern) of the respiratory cycle (Martin-Harris et al., 2005). Resumption of respiration in the expiratory phase after the swallow is posited to reduce aspiration risk. Deviations in the respiratory-swallow patterning occur in older healthy individuals resulting in more frequent onset of the swallow during inhalation (I-E or I-I pattern) or respiratory resumption in the inspiration cycle after the swallow (E-I or I-I pattern) than in younger healthy persons (Shaker et al., 1992). Individuals with moderate to severe stable state COPD have an altered respiratory-swallow patterning; specifically, they swallow solids in inhalation and resume respiration on inhalation for semi-solid texture boluses

(Gross, Atwood Jr., Ross, Olszewski, & Eichhorn, 2009). COPD patients in the exacerbated state resume respiration post-deglutitively in the inspiratory phase more frequently than healthy older peers (Shaker et al., 1992).

In addition to the reduction in respiratory-swallow pattern coordination, individuals with COPD demonstrate: (1) diminished laryngeal elevation during the swallow, (2) trending towards a lower laryngeal position at rest, (3) increased pharyngeal transit duration, (4) fatigue of oral mastication with need for rest breaks, (5) lingual peristalsis, (6) cricopharyngeal dysfunction and (7) a voluntary prolongation of airway closure on certain bolus types (Coelho, 1987; Mokhlesi, Logemann, Rademaker, Stangl, & Corbridge, 2002; Chaves et al., 2014). Pharyngeal residue in individuals with stable COPD is not significantly different from their healthy older peers (Chaves et al., 2014). Severe COPD individuals also demonstrate severe cricopharyngeal dysfunction and particular difficulty with opening of the upper esophageal segment for bolus passage into the esophagus. Some have suggested that there is a correlation between cricopharyngeal dysfunction and gastroesophageal reflux (GER) (Stein, Williams, Grossman, Weinberg & Zuckerbraun, 1990). Persons with severe COPD have a higher prevalence of GER than healthy individuals. Further, GER was identified as a risk factor for exacerbations (Sakae, Pizzichini, Teixeira, da Silva, Trevisol & Pizzichini, 2013).

Mechanisms driving respiratory-swallow coordination are largely unknown. Central pattern coordination between respiration and swallowing involves neurons in the ventrolateral medulla (Broussard & Altschuler, 2000; Davenport, 2011; Jean,

1984). Sensory feedback to the respiratory and swallowing central systems prior to swallowing is important for airway protection during swallowing (Table 2).

Increases in lung volume will activate pulmonary stretch receptors and increase recoil forces in the chest wall (Gross, Steinhauer, Zajac, & Weissler, 2006; Gross et al., 2012). Pulmonary stretch receptors provide peripheral feedback to the medulla on lung volumes achieved before swallowing. Inadequate volumes are reported to alter the coupling of respiration and swallowing and result in timing variances that reduce airway safety (Gross et al., 2003).

Table 2

<i>Lung Volume Sensory Feedback for Swallowing Coordination</i>				
	Swallowing Target Involved in Healthy Subjects	Feedback mechanism	Time of Occurrence relative to swallow	Requirements to Achieve Target
Lung Volume (Wheeler Hegland et al., 2009)	43%-64% of Vital Capacity	Pulmonary stretch receptors	Before the swallow	Thoracic expansion to intake air

Given the bronchoconstriction and hyperinflation in COPD, lung volume is posited as impaired in swallowing (Table 3). Decreased airflow within the smaller airways, along with thoracic muscle wasting with disease progression and hyperinflation, reduce lung volume in individuals with COPD (Gatta, Fredi, Aliprandi, Pini, & Tantucci, 2013). Vital capacity measures of total lung volume were reduced to 2.72 L (SD=.72) in COPD from the normal expected range of 3-5 L (Yuan et al., 2014). Restricted thoracic expansion will lower inspiratory volumes limiting

pulmonary stretch receptor input and reduce thoracic recoil. Further, a decrease in expiratory airflow results in hyperinflation. An examination of the role of lung volume on swallowing control in persons with COPD is needed.

Table 3

Proposed Mechanisms Affecting Swallowing Coordination in COPD

<u>Respiratory Abnormality in COPD</u>	<u>Mechanisms affecting Swallowing in COPD</u>
Reduced Vital Capacity	Airway obstruction on Inspiration and Expiration Thoracic Muscle Wasting, Decreased Recoil
Reduced Expiration Speed	Airflow obstruction Decreased Mechanical Recoil during Passive Expiration
Reduced Inspiration Volume	Hyperinflation Thoracic Muscle Wasting Bronchoconstriction

Proposal

This research project investigated the role of lung volume in the coordinated coupling of breathing and swallowing in individuals with COPD when compared with healthy individuals. The study examined how individuals with COPD swallow at different lung volumes compared to older healthy individuals. In particular, the effects of swallowing at different lung volumes on timing measures during swallowing were investigated. Respiratory-swallow patterning in COPD is known to vary from healthy individuals with more frequent resumption of respiration in the inspiratory phase thus increasing the risk of aspiration. This study examined whether swallowing at a higher lung volume changed timing of the pharyngeal phase of swallowing and the pattern of resuming respiration on inspiration after the swallow.

Research Aim

Problem: Mechanism for dysphagia in COPD is not known.

Aim: Examination of the Relationship between Lung Volume and Swallowing

Control in COPD

The study contrasted varying lung volume during swallowing between individuals with COPD and healthy participants. Further, the effects of lung volume manipulation on temporal measures of swallowing such as pharyngeal duration were determined. Respiratory-swallow patterning in COPD participants was also compared across lung volume conditions.

Hypotheses:

- 1.** Lung volumes for swallowing would be significantly lower in COPD than in healthy participants.
- 2.** Pharyngeal swallow duration will be related to lung volume at the time of the swallow in COPD participants. Specifically, pharyngeal duration will decrease when increasing lung volume in individuals with COPD.
- 3.** Swallowing at higher lung volumes would result in less frequent resumption of respiration during inspiration than lower lung volume conditions in individuals with COPD.

Collectively, this research examined the effects of lung volume on swallowing in individuals with COPD. It was determined whether lung volume abnormalities related to difficulties in the coordination of breathing and swallowing in COPD. Also, the effects of lung volume changes were examined on pharyngeal swallowing timing in individuals with COPD.

Significance

Individuals with COPD are at increased risk for swallowing impairment resulting in aspiration and aspiration pneumonia (Terada, 2010). COPD patients demonstrating an impaired swallowing reflex also have increased COPD exacerbations (Terada, 2010). A respiratory decline is evidenced in COPD exacerbations and patients frequently require hospitalization. Researchers hypothesize that aspiration may be a risk factor for COPD exacerbations in addition to risk of aspiration pneumonia. The lack of identification of the mechanisms driving the COPD patient's swallowing impairment is a critical barrier to determining models to improve clinical outcomes in COPD. Further, investigation of the effects of changes in lung volume is pivotal for developing appropriate treatment approaches. This study will identify the mechanism driving the swallowing impairment and determine if adaptations in volume can positively influence coordination between the respiratory and swallowing systems. The study will have a broader impact by providing a theoretical framework for additional clinical investigation studies aimed at improving swallowing function in COPD and other respiratory compromised populations such as lung cancer.

Innovation

The effects of varying lung volume on swallowing in individuals with COPD have not been investigated. Individuals with COPD exhibit progressive limitations in airflow which are not completely reversible. We hypothesize that a limitation in lung volume interferes with swallowing physiology and respiratory-swallow coordination in COPD patients. Previous studies in healthy adults, found a reduction in the lung volume amount at the time of the swallow resulted in alternations in swallowing physiology such as delays in swallowing onset and increases in the pharyngeal swallow duration (Gross, 2003). Our study will examine some of these relationships in patients with COPD to better understand the mechanisms underlying this disorder. Although others have documented swallowing deficits in the COPD population, this research is the first aimed at establishing the pathophysiology of swallowing in COPD. Without understanding the mechanisms involved in swallowing difficulties in this disorder, treatment cannot be aimed at improving the deficits in COPD. Increases in duration of the swallow could increase the risk for aspiration in this respiratory compromised population. Mechanisms that may improve the coupling of respiration and swallowing in COPD are not known. Based on the first attempt to increase understanding of the pathophysiology of swallowing in COPD to be provided by this investigation, investigations altering the respiratory system by respiratory strength training could be relevant. Future investigations could focus on altering respiration for prevention of aspiration by using inspiratory and expiratory muscle strength training to change lung volume for swallowing.

Research Approach

1. Aim: Examination of the Relationship Between Lung Volume and Swallowing Control in COPD

We determined: (1) lung volumes during swallowing in individuals with COPD in comparison with healthy participants (2) the effects of manipulating lung volume at time of swallow on swallowing physiology and (3) the effects of varying lung volume on the respiratory-swallow patterning in COPD.

1.1 Background

Wheeler-Hegland et al. (2009) reported that healthy individuals (age range 19-28) swallow at 43-64% of vital capacity. Participants were observed to inspire or expire to achieve the preferred lung volume (% VC) at the time of the swallow. The vital capacity volume in individuals with COPD is reduced to 2.72 L (SD=.72) from the normal expected range of 3-5 L (Yuan et al., 2014). The lung volume levels when COPD individuals swallow is not known but is posited to be lower than healthy older volunteers. Thus, individuals with COPD may need to swallow at a higher percentage of their vital capacity to swallow safely.

One study found a reduction in lung volume at the time of swallow resulted in delays in swallow onset and longer pharyngeal phase durations in healthy participants (Gross, 2003). COPD patients had longer pharyngeal durations when compared with healthy volunteers completing bolus swallows at their typical lung volumes (Cassiani et al., 2015). Mokhlesi et al. (2002) noted prolonged airway

closure for certain bolus types in 45% of COPD participants and suggested this was a potential compensation mechanism to protect the airway.

A study examining the effects of swallowing at varying lung volumes in COPD may identify mechanisms to help these patients swallow safely.

1.2 Purpose

Determine the effects of varying lung volume on swallowing control in COPD.

1.3 Hypotheses

1. Lung volumes for swallowing will be significantly lower in COPD than in healthy participants.
2. Swallow duration will demonstrate a negative relationship with lung volume in individuals with COPD. Specifically, individuals with COPD will decrease their pharyngeal duration when swallowing at increased lung volumes.
3. Swallowing at higher lung volumes will result in less frequent resumption of respiration during inspiration than lower lung volume in individuals with COPD.

1.4 Independent Variables

- Participant group (Healthy or COPD)
- Lung volume condition (Table 4)

Table 4

Lung Volume Condition Definitions

Condition	Abbreviation	Operational Definition
Non-Cued	NC	No instruction of when to swallow
Resting Expiratory Level	REL	Bottom of tidal breath
Tidal Volume	TV	Peak of tidal breath
Total Lung Capacity	TLC	Peak of deep breath

1.5 Dependent Variables (Table 5)

Table 5

Dependent Variable Definitions and Measurement

Variable	Definition	Method of Measurement
Estimated Lung Volume (L)	Estimated volume at time of the swallow (Liters) *%VC will be reported	<ul style="list-style-type: none"> • Respiratory inductive plethysmography (RIP) • Interpolation using RIP and spirometer
Pharyngeal Swallow Duration	Onset of BOT pressure increase to upper esophageal sphincter (UES) negative pressure offset	<ul style="list-style-type: none"> • Time of BOT onset pressure increase <ul style="list-style-type: none"> ○ BOT manometer pressure sensor • Time of offset of negative UES pressure (at second peak in M wave) <ul style="list-style-type: none"> ○ UES manometer pressure sensor
Respiratory-Swallow Pattern	Expiratory-Expiratory (E-E)	Begin and end swallow in expiration phase
	Expiratory-Inspiratory (E-I)	Begin in expiration; resume in inspiration
	Inspiratory-Expiratory (I-E)	Begin in inspiration; resume in expiration
	Inspiratory-Inspiratory (I-I)	Begin and end swallow in inspiration phase

1.6 Methods

We studied the relationship between respiratory functioning and swallowing functioning in persons with COPD when compared to healthy peers.

Participants

Healthy and COPD participants were 45 years of age or older to participate.

Inclusion criteria for COPD participants were: (a) a respiratory function screening ratio result of 30% to < 70% (Ratio of forced expiratory volume in 1 second to forced vital capacity via spirometry) (Celli et al., 2004), (b) COPD diagnosed by a physician, (c) no exacerbation of COPD within last month, (d) no use of continuous oxygen (O₂) and (e) not diagnosed with bullous emphysema. COPD group respiratory function screening ratio was $M=51.67\%$ ($SD=8.31$). The percent predicted FEV₁, determining COPD severity, ranged 34% to 80%. Applying the GOLD COPD severity rating scale (Table 1), COPD participants' severities were: one mild, three moderate, and five severe COPD. One COPD participant was prescribed supplemental oxygen at a rate of 2L O₂ by nasal cannula at night and as needed during exertional activities. This participant did not use oxygen during the study. Healthy participants demonstrated a respiratory function screening ratio of >70% FEV₁/FVC for inclusion in the healthy group, $M=82.2\%$ ($SD=7.4$). Healthy participants scored 8 or less (normal) on the Dysphagia Handicap Index (DHI) which is a 100 point scale based on patient reports of swallowing difficulty (Silbergleit, Schultz, Jacobson, Beardsley & Johnson, 2012). COPD participants completed the DHI although no minimum or maximum scores were required for

participation (see additional discussion of DHI in Other Screening Tools, p.31).

Three COPD participants exceeded the normal range on the DHI, 2 mild and 1 moderate. The moderate scoring participant was previously evaluated by a speech-language pathologist and diagnosed with dysphagia, but had not yet received treatment. Healthy and COPD prospective participants also met a minimum score of 21 points on Mini Mental State Evaluation (MMSE) (21-24 points=mild, 25-30 points=normal cognition) (Folstein, Folstein & McHugh, 1975) and had a Reflux Symptom Index (RSI) score <15. Additional exclusion criteria for COPD or healthy participants were:

- Direct dysphagia treatment within the last 3 months
- History of brain injury or stroke
- Diagnosed with progressive neurodegenerative disorders such as Parkinson's Disease, multiple sclerosis, peripheral neuropathy, and amyotrophic lateral sclerosis
- Previous neck injury requiring physician intervention
- History of psychiatric disorder other than medically managed depression
- Have a speech disorder with reduced ability to be understood by others
- History of epileptic seizures
- Inability to speak or understand English.

Healthy participants were recruited through James Madison University (JMU) bulk emails and handouts or flyers at JMU. COPD volunteers were recruited through Sentara Rockingham Memorial Hospital (SRMH) physician practices and related

clinics such as pulmonology, cardiopulmonary rehabilitation clinic, or other surrounding area healthcare providers within a one hour radius of the research site. Community flyers and word of mouth recruitment methods were also employed in recruitment of healthy and COPD volunteers. Telephone screens for inclusion eligibility were conducted for each prospective participant. Informed consent and the experimental study were conducted at the Voice and Swallowing Services clinic in the Outpatient Treatment Center at Sentara RMH. Prospective participants completed screening tasks for inclusion on the date of their scheduled visit after completing informed consent. The study took 3 hours to complete including informed consent, screening, and the experimental tasks. A copy of the signed consent form was distributed to participants to take home.

Instruments

Instruments for measurement included: respiratory inductive plethysmography, oral pressure, 3-sensor manometry, and spirometry. The spirometer was utilized in the calibration tasks but was not used during the experimental swallow tasks. Instruments used for identifying events included a single axis accelerometer, synchronized video recording and a button-push pulse generator.

Estimated lung volume was measured with respiratory inductive plethysmography (RIP) (Respirtrace®, Ambulatory Monitoring, Ardsley, NY) using two elastic inductobands around the rib cage (RC) and abdominal (AB) cavities measuring change in thoracic circumference in volts with synchronous spirometry.

The Resptrace® recorded chest wall and abdominal movement. Although swallow apnea, the period of respiratory cessation (respiratory offset to respiratory resumption onset), has been reported in the literature as a method to determine pharyngeal phase timing (Martin, Logemann, Shaker, Dodd, 1994), respiratory onset or offset in the sum signal for RC and AB were not selected as temporal markers in this study because liquid swallows by cup have shown variable apnea onset signals (Martin-Harris, Brodsky, Price, Michel & Walters (2003). The RIP signal was used to determine inclusion or exclusion of a trial in a lung volume condition based on lung volume at time of swallow in real-time and off-line data analysis. Oral and pharyngeal pressure signals were used instead to mark durations in swallowing.

Measurement of Respiratory Volume

The RC inductoband was positioned at the axilla with the connector pins down and the AB band was placed below the last rib at the umbilicus with the connector pins up. The signals from the AB and RC respiratory bands were input into the oscillator module and RIP amplifier set on DC signal amplification with a 1:1 amplification for RC and AB signals. The RC, AB and Sum signals were input into a 16 channel PowerLab (ADInstruments, Dunedin, New Zealand). A sampling rate of 1K/s was applied in LabChart (ADInstruments, Dunedin, New Zealand) for signal analysis. The bands were placed on the participant over tight fitting clothing for accurate measurement of ribcage and abdomen movement. A mesh retainer was positioned on the participant after placement of the inductobands to reduce displacement during the study.

A Universal Ventilation Meter (UVM) spirometer (Vacu-Med®, Ventura, CA) was used during the calibration tasks. The bidirectional flow meter has a turbine transducer. The inhalation and exhalation signals are combined into a sine-wave signal by signal summation. Signal input into the PowerLab included the inspiratory, expiratory and sum signals, each with a sampling rate of 1K/s. A new filter mouthpiece was attached to the spirometer head prior to use for each participant.

Measurement of Pharyngeal Pressure

A 3-sensor manometer, CTO-3(Gaeltec®, Hackensack, NJ), was placed transnasally into the pharynx to measure pressure changes during the swallow. The flexible strain-gauge manometric probe was passed nasally and positioned in the upper airway with pressure sensors inferiorly to superiorly as follows: (1) top of the upper esophageal sphincter (UES) opening, (2) in the hypopharynx, and (3) at the base of the tongue. The changes in pressure were used to mark temporal events occurring in the sequence of the swallow. This study obtained two event markers from the manometry signal: (1) the onset of increase in base of tongue pressure served as the onset of the pharyngeal phase of the swallow and (2) the offset of upper esophageal sphincter negative pressure signaled UES closure after the swallow and the offset of the pharyngeal phase of the swallow (Figure 1).

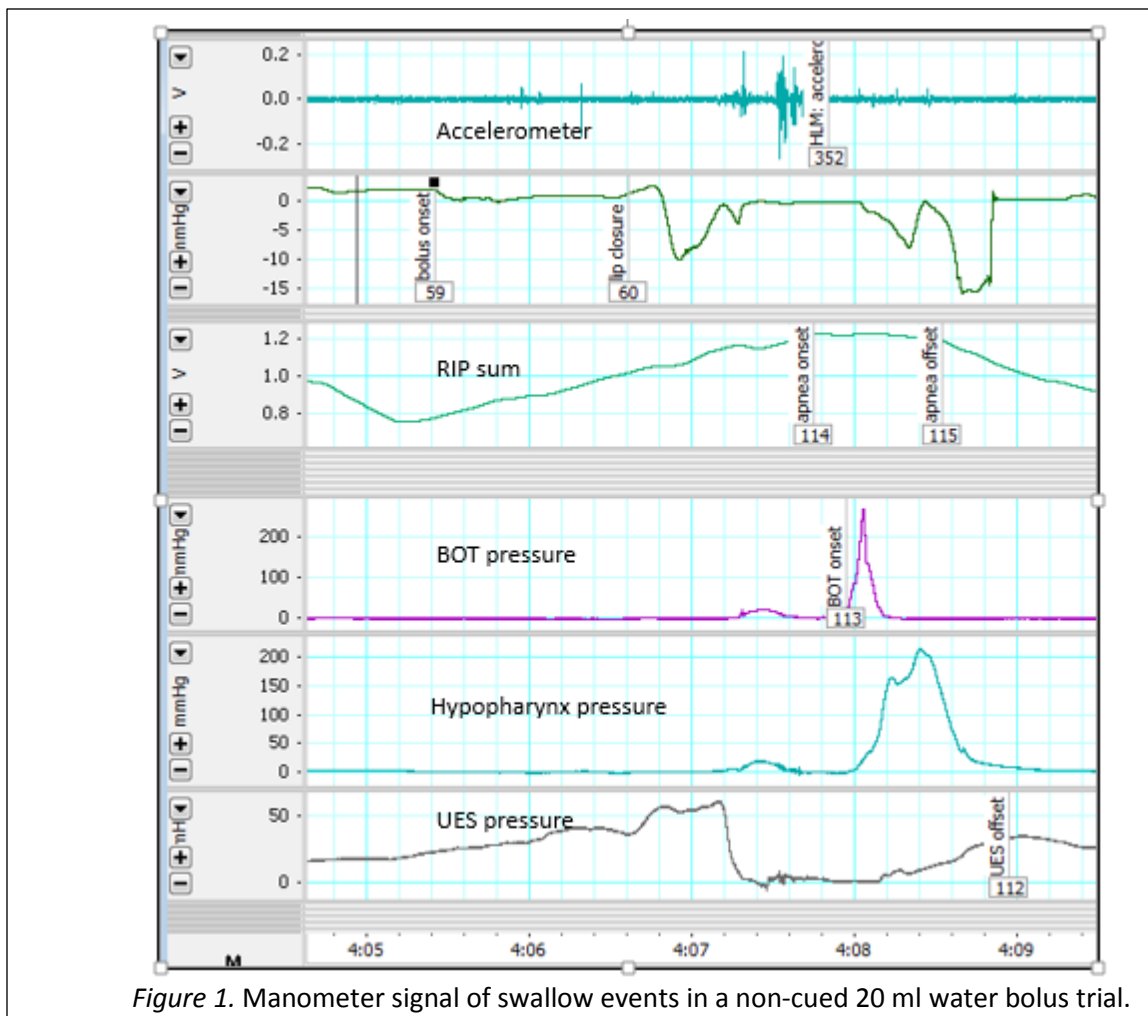


Figure 1. Manometer signal of swallow events in a non-cued 20 ml water bolus trial.

Placement of the Manometer

The manometer was placed in a warm water bath before insertion to acclimate the catheter to body temperature versus room temperature. Prior to manometer catheter insertion, participants were administered two puffs of Afrin into each nostril. The lubricated catheter was inserted into the predetermined left or right naris, passed over the soft palate and through the pharynx. The Gaeltec CTO-3 diameter is 2.7 mm and 100 cm in length with numeric markings at 10 cm increments to guide placement. Participants were instructed to swallow water

boluses to assist with manometer entry into the upper esophageal sphincter (UES) when directed by the speech-language pathologist. Accurate positioning of the pressure transducer was determined by utilizing the pull-through placement method (Witte, Huckabee, Doeltgen, Gumbley & Robb, 2008). The catheter was swallowed into the upper esophagus with a typical reading of approximately 20 cm at the nares. The catheter was correctly positioned when a M-wave pattern was observed in the UES digitized data signal when asking the participant to swallow. The pressure transducer was repositioned by incrementally retracting 1 cm on the catheter until the peak-trough-peak signal was noted for the UES sensor signal and a single pressure peak was observed for the base of tongue and hypopharyngeal sensors in the LabChart signal. The manometry catheter was secured with Medipore tape at the nares and forehead after a stable signal was maintained. A strain-relief loop was adhered at the participant's shoulder to prevent dislodging the catheter. The Gaeltec CTO- 3 pressure transducer was connected to a quad bridge amplifier (AD Instruments, Dunedin, New Zealand) with a Gaeltec connector, meeting ADInstruments specifications. This connector allowed for 3 channel input to the bridge amp and LabChart. A sampling rate of 10K for each channel was applied during digitization.

A Glottal Enterprises (GE) PTL-1 oral pressure transducer and MS-110 data amplifier (Glottal Enterprises, Syracuse, NY) transduced intraoral air pressure changes during the swallow. The pressure transducer was connected to a 15 cm length Tygon® tubing (Model R-3603, Saint Gobain, Valley Forge, PA) with an adaptor, allowing insertion of an individually fit 3-4 cm length Tygon® tubing in the

mouth. The inner tubing diameter was 3 mm, outer diameter was 5 mm and the wall was 1 mm. The new, oral tubing was individually fit to rest on the anterior tongue tip. The tubing was adhered to the cheek and the GE oral pressure transducer was strain-relieved to the face (see Figure 4). The oral pressure transducer was input to the GE MS-110® amplifier before entering the A-D converter, Power-Lab®. An event comment was entered into the oral pressure channel signal off-line based on the frame-by-frame synchronized video capture determination of bolus onset.

For each participant, a single axis piezoelectric accelerometer (Kistler Instrument Co., Amherst, NY) taped with 3M transpore tape® to the skin and placed midline on the neck between the thyroid notch and the bottom of the thyroid cartilage was used to detect laryngeal elevation onset. The signal was input into the Kistler Piezotron power supply coupler (Type 5118B2, Kistler, Amherst, NY). A gain of 100 dB with a HP filter=.03 was applied at the power supply coupler. Off-line data analysis was conducted using a 30 Hz high pass filter with signal rectification. Digital video capture (Logitech mountable with USB connection) of the oral and neck regions was temporally synchronized with the LabChart signal. Video recording was at 30 frames/second.

Calibration

Respiratory Inductive Plethysmography Calibration into Liters

Prior to the participant's arrival, both the RC and AB signals were zeroed by pressing the Calibrate button and RC button to obtain a reading from the Resptrace™ amplifier. If the reading was other than zero, then the RC zero knob was

adjusted until a 0 was shown on the digital display. This process was repeated for the AB by leaving the Calibrate button pushed and depressing the AB button. The sum button was depressed to ensure that the display still read zero and adjustments completed as needed with the AB zero knob. The Resptrace™ amplifier gain for both the RC and AB were set to 1. Calibrate and reference buttons were pressed along with the RC. If the reading was other than 1, then the RC gain knob was adjusted until the digital display reads 1. This process was repeated with AB after pressing the AB button. Finally, the sum digital display read a gain of 2 to complete the Resptrace™ instrument calibration.

Spirometer Calibration

The UVM spirometer was calibrated by delivering a known volume across a known time to the spirometer head. The spirometer turbine was placed on the GE calibrator unit (Glottal Enterprises, Syracuse, NY) using an adaptor and calibration filter. The flow setting on the GE calibrator was set for 1 L/sec and 2 L volume. Digitization in LabChart of the calibration flow cycle was initiated. Expiration and inspiration values (in volts) were highlighted and entered into the DataPad in LabChart for the second positive and zero segments. The 2 calibration points (in volts) for the known 1 L/s and 0 L/s flow for expiration and inhalation respectively were added to the DataPad and manually entered into LabChart as conversion units.

Manometer Calibration-Oral Pressure

Prior to the participant's arrival, oral pressure offset was zeroed while digitizing in LabChart by adjusting the knob on the MC-110 amplifier. Resting

reading from the oral pressure transducer (PTL-1, Glottal Enterprises, Syracuse, NY) in a room was set to 0 volts as the atmospheric pressure. The GE calibrator unit was used to input a known pressure into the pressure transducer to complete a 2 point calibration process in LabChart. The stopper was inserted in the top flow port (used for pressure calibration tasks) on the GE calibrator unit and the pressure transducer was inserted into the pressure port. The setting on the GE calibrator was toggled to pressure. Digitizing in LabChart was initiated and the following pressures were applied: 0 mmHg, 3 mmHg, 5 mmHg, 7 mmHg, 10 mmHg, 15 mmHg. The pressure values (in volts) for the 5 mmHg and 15mmHg known pressure values were added to the DataPad and manually entered into the unit conversion. The millimeters of mercury (mm Hg) measurement was used in this study.



Figure 2. Manometer calibration. Catheter is inserted into pressure chamber of the Delta-Cal digital pressure calibrator.

Manometer Calibration-Pharyngeal Pressure

Prior to the participant's arrival, the CTO-3 Gaeltec manometer calibration was a 2 part process. The manometer catheter was connected to the bridge amplifier. The three pressure sensors, base of tongue, hypopharyngeal and UES, were zeroed by selecting the zero function under the bridge amp tab in the channel menu. Each channel was zeroed separately. The digitizing display window demonstrated the pre-zeroed pressure reading graphically drop to zero. If zero, then the researcher pressed 'okay' to accept. The second step was to determine 2 calibration points for unit conversion from volts into mmHg pressure. Prior to beginning the calibration process, a battery tester was used to ensure adequate charge for the digital manometer calibrator. The CTO-3 manometer was placed into a flexible tubing chamber attached to the Delta-Cal® digital pressure calibrator (Utah Medical, Midvale, UT) (Figure 2). The collet was tightened after the 3 sensors were placed deep in the chamber without risk of being damaged. Digitizing in LabChart was initiated while incremental known pressures were applied within the sealed tubing chamber connected to the Delta-Cal. The pressures applied included: 0 mmHg (atmospheric pressure), 5 mmHg, 25 mmHg, 50 mmHg, 75 mmHg, 100 mmHg, 125 mmHg, 0 mmHg, -25 mmHg, and -50 mmHg. Based on the experimental tasks, signal recording values (in volts) were added to the DataPad for 50 mmHg and 125 mmHg from each of the 3 channels. The conversion values from DataPad (in volts) are added to LabChart. A linear interpolation in excel of the CTO-3

manometer sensors using conversion values of ranging -50 mmHg to 125 mmHg revealed a $R^2=0.999$ (Figures 3-5).

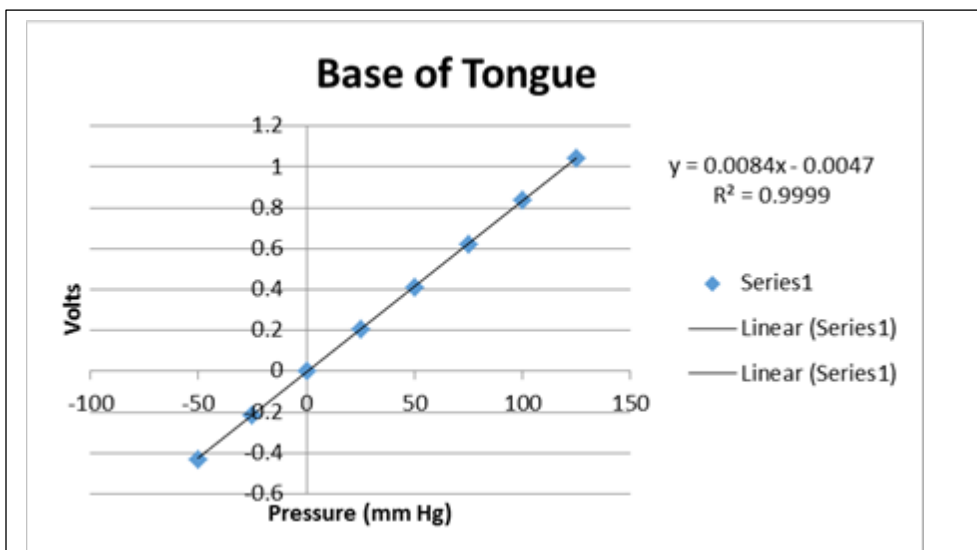


Figure 3. Linear relationship during manometer calibration for base of tongue (BOT). A linear relationship was determined when applying a known pressure (mmHg) from the pressure calibrator to the BOT sensor in the manometer transducer.

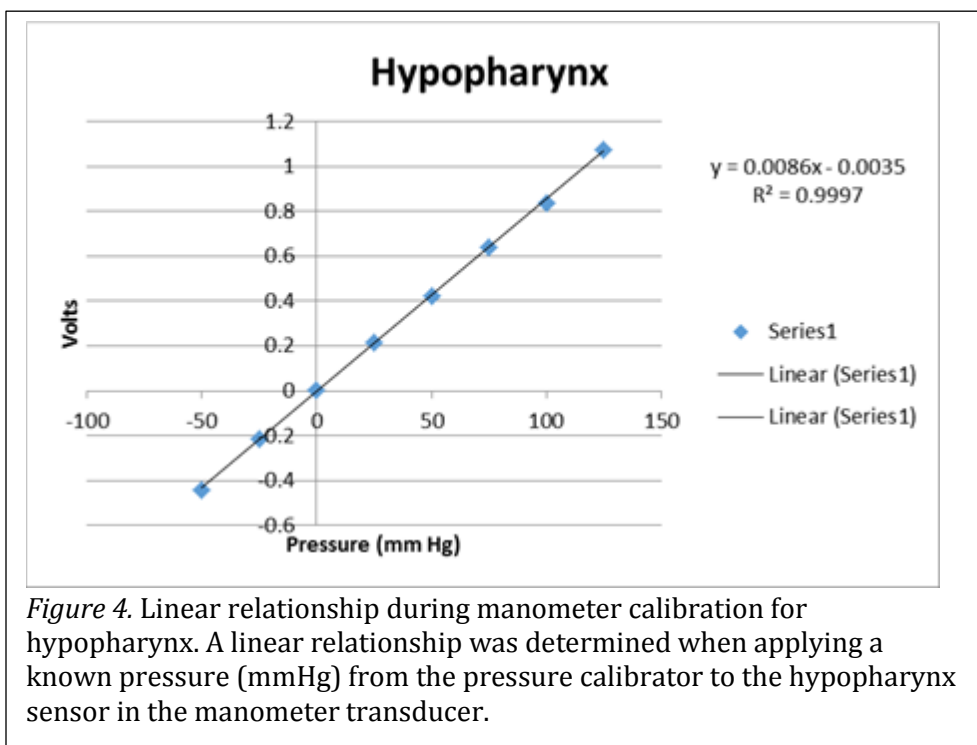
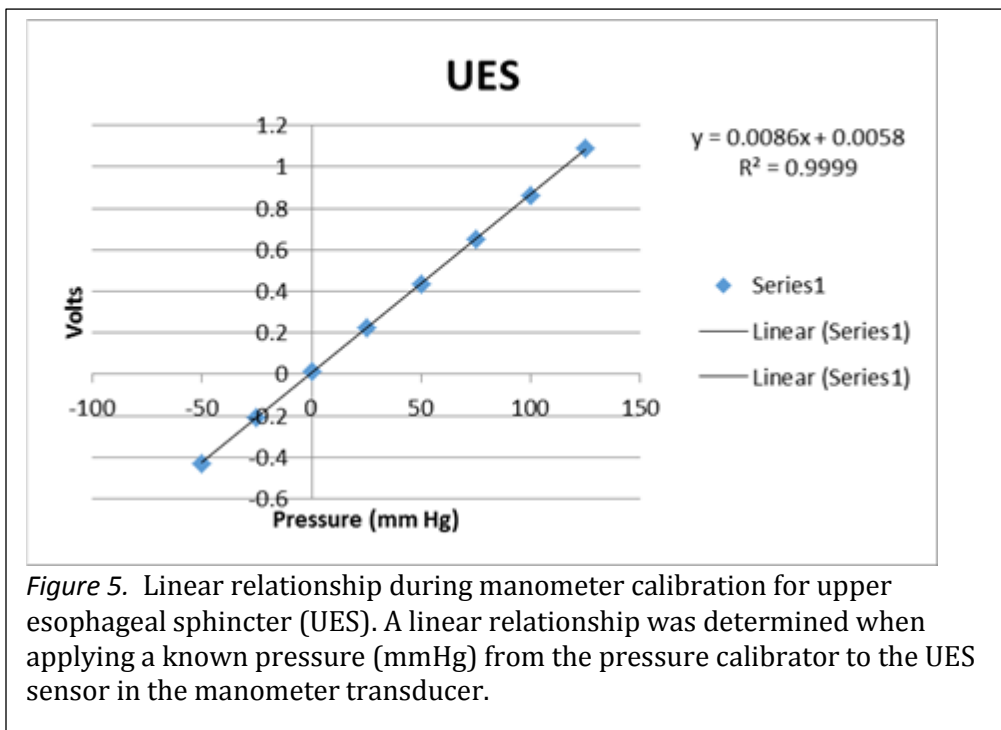


Figure 4. Linear relationship during manometer calibration for hypopharynx. A linear relationship was determined when applying a known pressure (mmHg) from the pressure calibrator to the hypopharynx sensor in the manometer transducer.



Determination of Rib Cage and Abdominal Ratios

Before converting the RIP signal into volumes, the amplification ratios of the RC and AB contributions to lung volume was set for each individual in the seated position (Konno & Mead, 1967). The RC and AB contributing factors were solved for in the following equation: estimated lung volume (ELV): spirometer = $RC(x) + AB(y)$. The AB signal factor, “y”, was equal to 1 based on the study population and experimental tasks. Therefore, the equation was $spirometer = RC(x) + AB(1)$ to compute the least errored solution for “x”. The three tasks completed to determine

the calibration factor included tidal volume breathing, swallow-like breathing and vital capacity. Tidal volume breathing and swallow-like breathing trial files were exported off-line into a .RespCal MatLab program provided by Dr. Jessica Huber, Purdue University. The MatLab script applied a pseudoinverse function to compute a least errored solution for “x”, the RC contribution ratio.

Tasks

Pulmonary Function Testing

The pulmonary function test is the standard for confirming diagnosis of COPD and staging of severity based on the forced expiratory volume results (Celli, 2004; Mannino, 2002). A bedside spirometer calculated the forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) ratio. Participants took a deep breath while keeping a lip seal on a new, unused Moe filter (nSpire Health, Inc.; Longmont, CO) and blew out hard and fast until they had no additional air to expire. The screening task was completed with three trials in a seated position to match the experimental task positioning. The Koko Legend (nSpire Health, Inc.; Longmont, CO) bedside spirometer unit is regularly used in the clinical respiratory environment. The spirometer computed the FEV₁/FVC ratio accounting for participant age, gender, height, and weight in determining expected values. These values were entered using the touchscreen before beginning the screening task with the participant. The KoKo Legend provided printable graphic and table-type output. Healthy participants exceeded 70% and COPD participants performed at 70% or below.

Calibration of the spirometer was completed prior to participant arrival using an nSpire 3 liter (L) canister. The calibration sequence prompts were provided on the touchscreen. The Koko Legend's spirometer head zeros while held steady in the room without airflow. The 3 L canister was securely fit to an nSpire Moe filter attached to the spirometer head. The canister plunger was pulled and plunged based on the time sensitive device prompts. Graph and table calibration output was printed, reviewed, and included in the participant's research file.

Other Screening Tasks

Participants completed the Dysphagia Handicap Index (DHI), a valid and reliable measure of the physical, emotional, and functional impact of swallowing difficulties on individuals (Silbergleit, Schultz, Jacobson, Beardsley, & Johnson, 2012). Responses to 25 statements were recorded as either always (4 points), sometimes (2 points) or never (0 points) resulting in a maximum potential score of 100. The nine physical statements related to tangible symptoms such as coughing, weight loss or utilization of strategies to swallow better. Participant responses to nine functional statements focused on alterations in lifestyle such as alternative nutrition, taking longer to eat or altering their diet. The seven emotional statements addressed the participant's perception of their response to difficulty swallowing such as being more fearful, experiencing avoidance, or being embarrassed. DHI respondents also provided a self-perceived, overall severity of swallowing difficulty. Overall severity rating ranged 1 (normal) to 7 (severe problem) on an equal interval scale but was not included in the total score (Silbergleit et al., 2012). A maximum

score of 8 on the 25 statements is within normal limits (Silbergleit et al., 2012). The cut-off score on the DHI for healthy participant inclusion was 8. COPD participants completed the DHI but a requisite score for inclusion was not applied to allow symptomatic and asymptomatic individuals with COPD to participate.

The MMSE, a widely administered cognitive screening tool, with a max score of 30, was administered to all participants. A score of 21 points or greater was required for inclusion in both the healthy and COPD groups. A score between 25 and 30 was normal; the score of 21-24 suggested mild cognitive impairment. This inclusion level was determined based on the cognitive load necessary to complete the experimental tasks. Prospective participants completed the Reflux Symptom Index to determine the symptom severity of reflux. The RSI, a valid and reliable rating tool, contains 9 self-scored symptom statement items with ordinal ratings ranging 0 (no problem) to 5 (severe problem). A score >13 is considered abnormal (Belafsky, Postma, & Koufman, 2002). Reflux may alter the sensory input response for swallowing. Healthy and COPD participants scored ≤ 15 for inclusion in this study. The higher cut-off score on the RSI for inclusion was set to avoid false positives of reflux symptoms in the COPD group. Specifically, RSI statements requiring COPD participants to rate symptoms of excess throat mucous, cough, or breathing difficulties may relate to their respiratory disease and not be indicative of reflux symptoms.

Experimental tasks

Prior to beginning the experimental swallow task, COPD and healthy participants completed three tasks for individual participant calibration to determine lung volume when swallowing. These tasks included: two 45 second tidal volume breathing segments, 5 swallow-like breathing trials, and 5 vital capacity maneuvers. The participant calibration tasks were completed using respiratory inductive plethysmography and concurrent spirometry. A nose clip was secured on the nasal ala, preventing nasal airflow during these tasks. The participant completed the calibration and experimental tasks in an upright, seated position in a dental chair. Participants were instructed to “breathe naturally” for the tidal volume task. Swallow-like breathing instructions were to “imagine you are taking a drink of water per exhalation but do not swallow” (Hegland, Huber, Pitts, & Sapienza, 2009). Instructions for the vital capacity maneuver were to “take a deep breath and blow out hard as much as possible”.

Participants swallowed 20 ml water boluses via medicinal cup across lung volume conditions for the experimental task. Seven swallow trials at each lung volume condition were completed. Additional water bolus trials were completed if real-time signal analysis review verified a trial was not completed at the target lung volume or insufficient rest breaths occurred before or after the swallow. All participants completed non-cued, natural swallow trials as the first experimental task condition to control for carry-over between tasks. The non-cued swallow condition determined the participant’s usual lung volume for swallowing and

provided a baseline recording of respiratory-swallow patterning. Three additional lung volume conditions were completed in a counterbalanced order across participants: (1) tidal volume (TV, volume at top of quiet inhalation), (2) total lung capacity (TLC, maximum volume after forced inhalation) and (3) resting expiratory level (REL, volume at end of quiet exhalation). Participants were instructed to achieve their target lung volume, insert the bolus into the mouth, and swallow. Each participant received instruction for the 3 cued lung volume conditions and demonstrated competence on each condition before beginning experiment task trials. Competence at lung volume conditions was determined by real-time signal analysis in LabChart (AD Instruments). Additional instruction on lung volume conditions was provided when participants were unable to reach a targeted lung volume condition. Additional bolus trials were added to compensate for discarded trials.

Participants rated their sensation of shortness of breath on the Modified Borg Dyspnea Scale before and after lung volume condition tasks using a visual scale. The Modified Borg Dyspnea Scale is a valid and reliable perceptual rating scale for disordered populations with COPD and asthma (Kendrick, Baxi, & Smith, 2000). Participants answered the question "How much difficulty is your breathing causing you now?" Ordinal scale responses ranged zero to ten with 0=nothing at all to 10=maximal. Individuals responding in the 3 (moderate) to 10 (maximal) scale range were provided a rest break and rescored. Participants responding with a score of <3 advanced to the next task. Two COPD participants reported changes on the Modified Borg Dyspnea Scale at a scale score of 3 (moderate) and one reported a

4 (somewhat severe). All three participant's dyspnea resolved within one minute to lower scores of <3 and each received a 3-5 minute break or rested until they indicated their verbal consent to continue. Participant's oxygenation levels were assessed during each event with a score >3 and found within the expected range.

Participants completed baseline and interval blood oxygenation (SpO₂%) screens using a clinical bedside pulse oximeter, the NellCor™ N-20 (Medtronic, Minneapolis, MN USA). A finger-tip probe was placed on the index finger to determine the arterial oxygenation saturation percentage, the percent of red blood cells carrying oxygen. Values of 90-100% SpO₂ are considered within acceptable range; healthy individuals are typically 94-100%. Participants with COPD can have resting oxygenation levels in the lower 90% range. Rest breaks after exertion typically return individuals back to their baseline oxygenation levels. One COPD participant experienced a singular instance of desaturation to <90% SpO₂ but immediately returned to >90% when given a short 3-5 minute rest break. Dyspnea level rating via the Modified Borg Dyspnea Scale remained <3 participant response rating during the desaturation.

A 10-point visual analogue scale for fatigue was administered at baseline and between lung volume condition tasks. A score of zero indicated energetic with no fatigue. A score of five specified moderate fatigue and a score of 10 was the worst possible fatigue. A score of three (mild-moderate fatigue) was the threshold to implement a rest break. Two COPD participants provided a score of 5. Both

participants were provided a 3-5 minute rest break, reassessed, and able to proceed with tasks without incident.

Off-Line Computation Methods

Swallows that were not at the intended lung volume condition were excluded from analysis. Estimation of lung volume was calculated by taking an average of the end expiratory level (EEL) on a minimum of 3 tidal volume breaths preceding the experimental swallow trials. The RC and AB values at the time of BOT pressure increase onset, the marker of pharyngeal swallow onset in the study, were added to DataPad. A mean of end expiratory level (EEL) in quiet breaths before each swallow trial was computed and subtracted from each RC and AB value to account for signal drift. The estimated lung volume (ELV) was calculated for each swallow trial using the formula: $ELV = RC(x) + AB(1)$. Mean vital capacity was determined from peak to trough difference in the spirometer signal from the participant's vital capacity trials. The ELV was reported in liters while the percent vital capacity (%VC) was computed by $(ELV/VC) * 100$. The expiratory reserve volume (ERV) was computed and included in the equation $ELV = RC(x) + AB(1) + ERV$. End expiratory levels in tidal breathing prior to each vital capacity (VC) trial were averaged. The difference from EEL to vital capacity trough was determined using the spirometer signal.

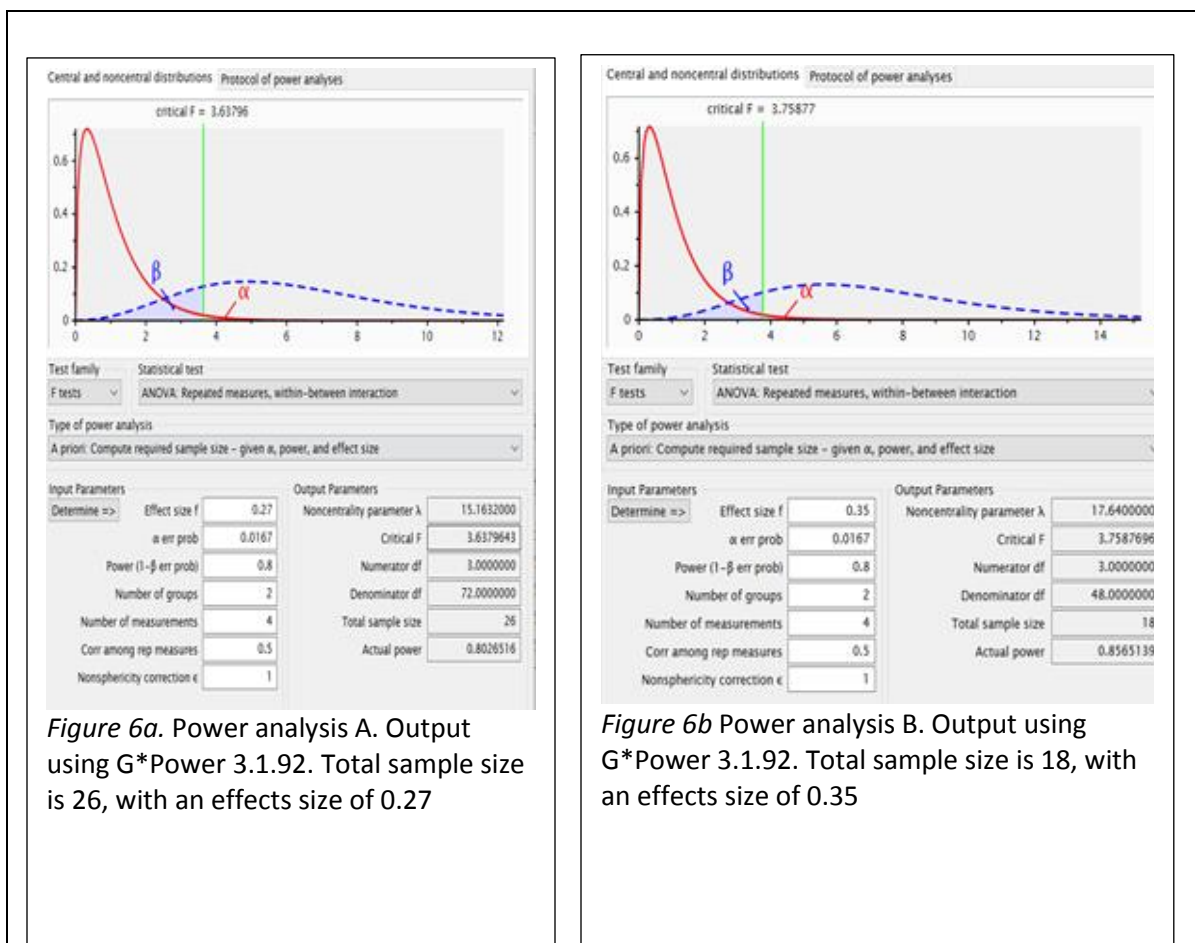
1.7 Results

Power

Pilot data (n=4) of pharyngeal swallowing durations were utilized to determine effect size based on means and standard deviations (SD). Pilot data sampling

included 3 healthy participants and 1 COPD. Effect size computation was .27 using G*Power 3.1.9.2. An ANOVA repeated measures, within-between subject interactions were run with a Bonferroni correction to $\alpha=0.017$ to account for 3 dependent variable measures. Power was set at .8 yielding a requisite sample size of 26 total participants, 13 in each group (Figure 6a).

Recruitment was slower than expected and the study only resulted in 10 healthy older adults (7 female, $M_{age}=59.4$) and 9 individuals with COPD (3 female, $M_{age}=71.9$) who completed the study. If the effect size was higher, at 0.35, then the power would remain the same at 0.80 with 9 subjects in each group (Figure 6b).



Statistical analyses were completed with IBM® SPSS® Statistics 24.

Statistical analysis methods were determined by a statistical consultant. Participant group characteristics are provided in Table 6.

Table 6

<i>Characteristics of COPD and Healthy Participants</i>		
	COPD (n=9)	Healthy (n=10)
Criteria		
Age	<i>M</i> =71.99 years Range=61-83 years	<i>M</i> =59.40years Range=50-77 years
Gender	3 Female; 6 Male	7 Female; 3 Male
Respiratory Function Screening Ratio (FEV ₁ /FVC)	<i>M</i> =51.67% (<i>SD</i> =8.31)	<i>M</i> =82.2% (<i>SD</i> =7.4)
FEV ₁ % Predicted	<i>M</i> =52.33% (<i>SD</i> =16.95) Range= 34%-80%	<i>M</i> =101.6% (<i>SD</i> =13.89) Range=72%-120%
Dysphagia Handicap Index (DHI)	<i>M</i> =10.44 (<i>SD</i> =7.99) Mild(n=2); Moderate (n=1); Normal(n=6)	<i>M</i> =1.80 (<i>SD</i> =2.39) Normal (n=10)
Reflux Symptom Index	<i>M</i> =7.44 (<i>SD</i> =3.75)	<i>M</i> =2.50 (<i>SD</i> =2.37)
Mini Mental State Examination (MMSE)	<i>M</i> =27.89(<i>SD</i> =1.45)	<i>M</i> =29.70 (<i>SD</i> =0.48)

Note. FEV₁ % predicted is derived from the participant's forced expiratory volume in one second divided by the average FEV₁% in the population based on comparable age, gender, height, and mass. FEV₁% predicted values determine COPD severity in conjunction with a requisite FEV₁/FVC <0.7.

Lung volume estimations

A mixed model ANOVA analysis determined the effects of group (healthy or COPD) and within subject repeated lung volume conditions (NC, TV, TLC, and REL). The estimated lung volumes (in liters) during swallowing were significantly lower in individuals with COPD compared with older healthy, $F(1,17)=8.119$, $p=.011$ (Table 7, Figure 7). A statistically significant main effect was found of lung volume condition on estimated lung volume, $F(3,51)=64.82$, $p<.001$ (Table 9). Pairwise comparisons of lung volume conditions demonstrated significant differences between all lung volume conditions ($p<.001$) except the NC and TV volume conditions, $p=.249$. Non-cued lung volume condition means, regardless of group, were lower than TV condition means (Table 7). The interaction between group and lung volume condition was not statistically significant, $F(3,51)=.871$, $p=.462$.

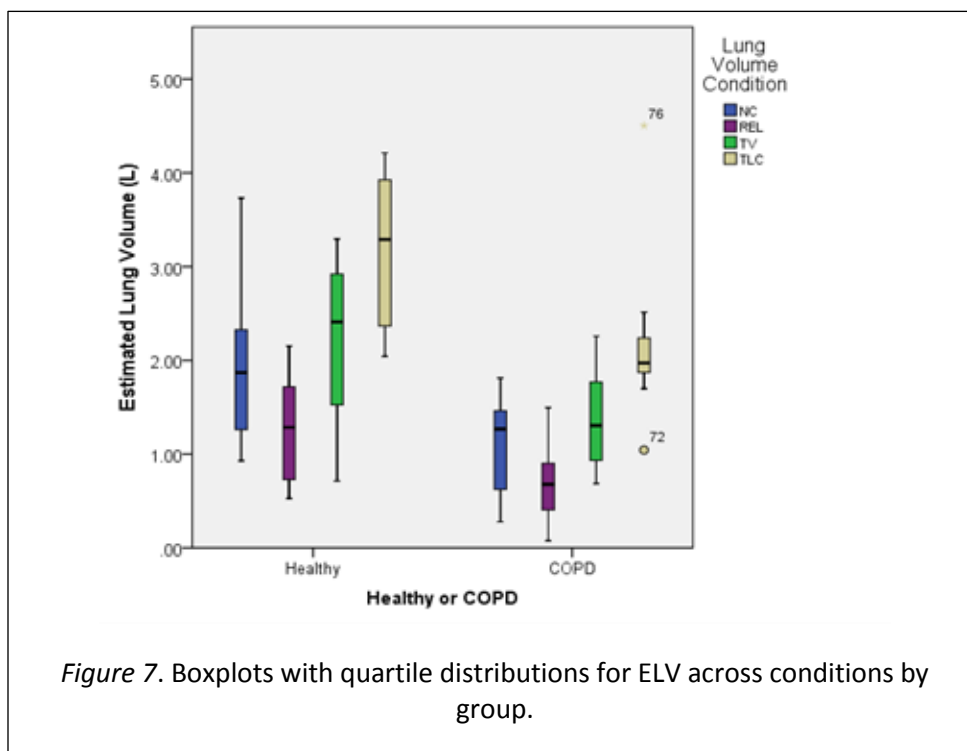


Table 7

Estimated Lung Volume and Percent Vital Capacity Means with Standard Deviations

Condition	COPD (n=9)		Healthy (n=10)	
	Mean (SD)	%VC(SD)	Mean(SD)	% VC(SD)
NC	1.12(.55)	37.49(13.36)	1.98 (.87)	47.82(17.42)
TV	1.38(.55)	47.74(11.39)	2.25(.83)	54.84(17.62)
TLC	2.22(.95)	76.09(16.75)	3.24(.83)	80.15(16.98)
REL	.687(.41)	23.10(10.68)	.1.30(.58)	32.17(13.89)

Note. Mean is in liters. % Vital Capacity (%VC) is derived from estimated lung volume mean divided by vital capacity.

Estimated lung volumes were also analyzed as a percent of vital capacity (%VC), calculated by $ELV/VC \times 100$. Mean vital capacity for individuals with COPD in this study was 2.81L (SD=.93) and healthy averaged 4.08L (SD=.921). Percent vital capacities for each group were similar across the 4 lung volume tasks (Table 7).

Pharyngeal Durations

The pharyngeal durations were very similar in the two groups (Table 8). Pharyngeal swallow durations were analyzed by mixed method ANOVA to determine group differences across volume conditions. Main effects for group ($F(1,17)=.903$, $p=.355$) and by ELV condition ($F(3,51)=.311$, $p=.817$) were not significant. An interaction between individuals with COPD and healthy across volume conditions was also not significant, $F(3,51)=1.70$, $p=.178$. Descriptive means suggest that the pharyngeal swallow durations in the NC condition tended to be longer in individuals with COPD than the healthy controls ($M=.977s$, $SD=.31$).

Table 8

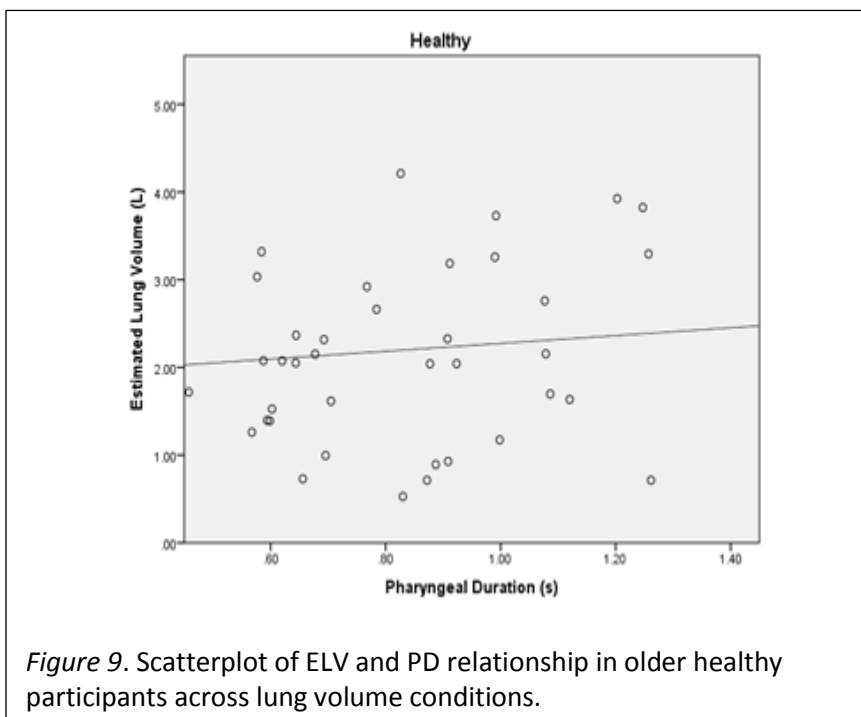
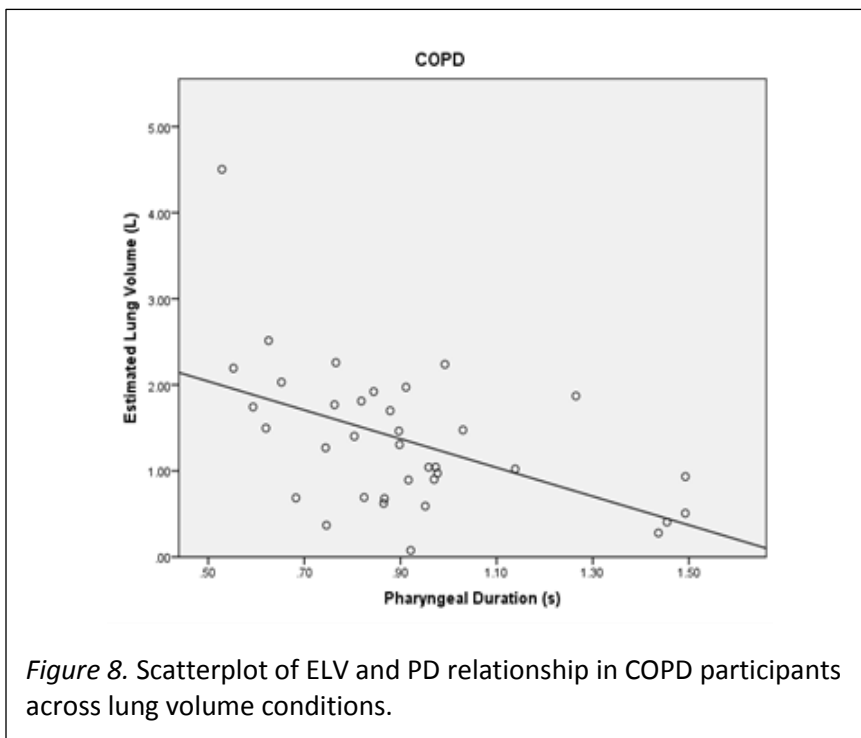
Pharyngeal Swallow Durations

Condition	COPD (n=9)	Healthy (n=10)
NC	.977(.31)	.787(.20)
REL	.926(.23)	.807(.26)
TV	.907(.25)	.823(.24)
TLC	.841(.24)	.841(.27)

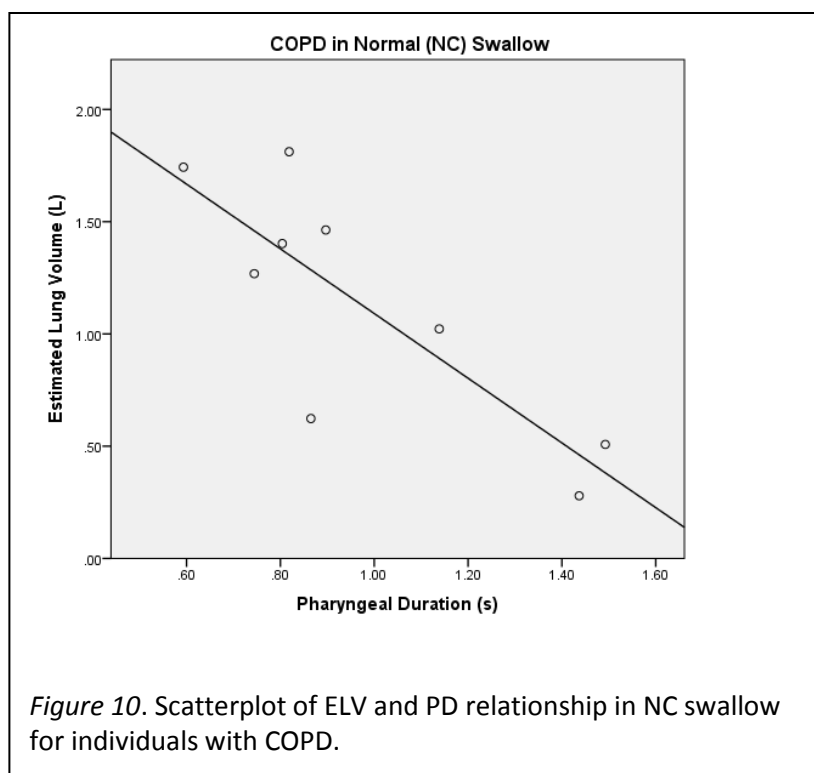
Note. Mean is in seconds. Parentheses values represent the standard deviations.

Relationships Between Pharyngeal Durations and Estimated Lung Volume

The relationship between lung volume and pharyngeal swallow duration was analyzed by Pearson's correlation analysis. In individuals with COPD, there was a significant inverse correlation between lung volume and the duration of the pharyngeal swallow, $r(34)=-0.506$, $p=.002$ (Figure 8). The estimated lung volume at the time of the swallow explained 26% of the variation in pharyngeal swallow duration. In the older healthy participants, no relationships were found between estimated lung volume and pharyngeal swallow duration $r(38)=.099$, $p=.542$ (Figure 9).



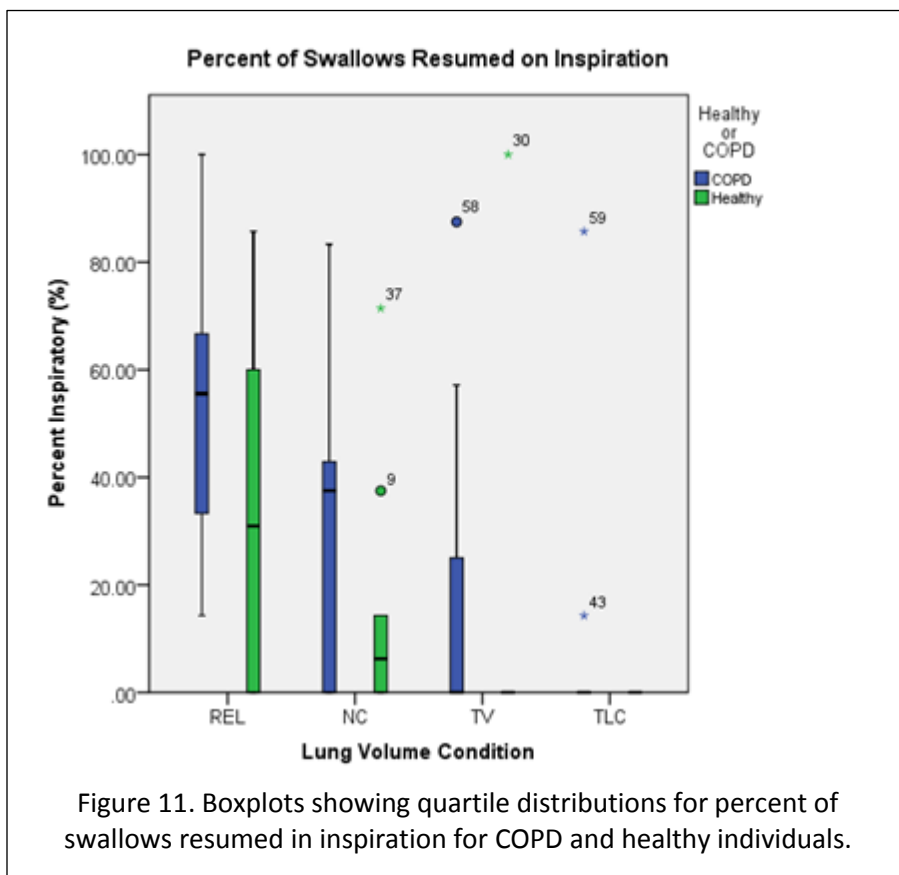
In individuals with COPD, correlation analyses *within* each lung volume condition were also computed. In the normal swallows (NC) condition, there was a significant inverse relationship between ELV and pharyngeal swallow duration, $r(1)=-0.817, p=.007$ (Figure 10). Individuals with COPD also tended to have an inverse relationship with pharyngeal swallow duration in the TLC volume condition, $r(1)=-0.606, p=.085$.



In the healthy adults, no relationship between ELV and PD was found within any of the lung volume conditions for older healthy participants.

Respiratory-Swallow Patterning

To compute the percent of respiratory cycles that resumed swallowing in the inspiratory phase, we combined the percent of cycles with an expiratory onset to an inspiratory swallowing offset with the percent of cycles that had inspiratory onset to inspiratory off set. Box plots of the percentages in each group of swallowing offsets in the inspiratory cycle showed that the healthy participant group had some resumption of swallowing on inspiration in the REL condition.



Within each lung volume condition, we conducted a t-test between groups with a directional hypothesis that the COPD participants would have a higher percentage of swallows resume on inspiration than the healthy participants. The

results are presented in Table 9. In the NC condition, the COPD participants had a greater percentage of swallows resuming on inspiration than the healthy participants, $t(11)=-1.978, p=0.037$.

Table 9

Percent of Swallow Resuming on Inspiration

Condition	COPD (S.D.)	Healthy (S.D.)	T- test (p value)
REL	54.71 (30.7)	32.43 (32.15)	-1.54 (0.071)
NC	31.35 (28.87)	10.54 (13.46)	-1.978 (0.037)
TV	18.851 (32.31)	10.00 (31.623)	-0.602 (0.278)

A one-way repeated measures ANOVA was conducted to determine whether individuals with COPD had statistically significant differences in resumption of respiration in inspiration across lung volume conditions. Analyses revealed that lung volume condition at the time of the swallow results in significant changes in percent of swallows resumed in inspiration ($F(3,24)=7.803, p=.001, \text{partial } \eta^2=.494$). The percent occurrence for COPD participants resuming respiration on inspiration after the swallow decreased as lung volumes increased (Figure 11). Post hoc analysis with a Bonferroni adjustment revealed that the percent of respiration resumption in inspiration was statistically significantly decreased in TLC compared with REL (43.59(95% CI, 14.82 to 72.36) %, $p=.005$) and in TV compared with REL (35.85(95% CI, 14.37 to 57.34) %, $p=.002$). Other post hoc comparison groups including NC swallows with cued swallow lung volume conditions were not significantly different.

Discussion

Lung volume at the time of the swallow has been posited to play an important role in the coordination of breathing and swallowing by altering sensory feedback from respiration. Pulmonary stretch receptors provide sensory input to the central pattern generators for respiration which may assist in regulation of the requisite, coordinated patterning between swallowing and respiration. The pattern ensures the cessation of respiration during the swallow followed by a resetting in the preferred expiration phase (Martin-Harris et al., 2003; Martin-Harris, 2008; Shaker, 1992). This study investigated the effects of lung volume on swallow timing and respiration resetting patterning in individuals with COPD, in comparison with healthy participants.

Lung Volume for Swallowing

Based on the study findings, individuals with COPD swallow had significantly lower lung volumes than their older, healthy peers. Given the COPD disease characteristics of bronchoconstriction, decreased airflow within the smaller airways, and thoracic muscle wasting with disease progression (Gatta, Fredi, Aliprandi, Pini, & Tantucci, 2013), swallowing at a lower lung volume was expected. Despite the significantly lower lung volume in COPD compared with healthy individuals, the COPD had similar percent vital capacity values to the healthy participants. The similarity suggest that both groups used similar proportions of their vital capacity when breathing even though the COPD participants were

reduced in their vital capacity compared with the healthy participants, similar to a previous study (Yuan et al., 2014).

Wheeler-Hegland et al. (2009) posited that there is a lung volume range that evokes a safe and effective swallow. They found that young healthy swallow at respiratory volumes between 43% and 64% of their vital capacity. The current study found that natural, non-cued swallows in older healthy participants and individuals with COPD swallow occurred at 47.82% and 37.49% of vital capacity, respectively. The swallows of our older healthy participants were consistent with the range of normal swallows of between 43%-64% VC of Wheeler-Hegland et al. (2009), even though our healthy participants (aged 50 to 83) were older than those of Wheeler-Hegland et al. (2009) (aged 19-28). This age difference may account for the lower %VC findings in this study. Aging is associated with decreases in vital capacity due to changes in musculoskeletal function (Lalley, 2013). This raises the question whether the target %VC for a safe, effective swallow changes with age, which should be explored further.

On the other hand, individuals with COPD tended to swallow at a slightly lower %VC than their older healthy peers and potentially may have been further away from the ideal target %VC. Hyperinflation of the lungs occurs with progressive severity of COPD and may have played a role in the lower estimated lung volumes found in the COPD participants this study. Air volume residuals in the lungs after forceful exhalation in a vital capacity maneuver were not measured in this study. Possibly, larger lung volume residuals in individuals with COPD leave less

volume capacity for performing everyday tasks, such as swallowing. The lower estimated lung volume in swallowing may further support the hypothesis that persons with COPD may not adequately activate pulmonary stretch receptors or subglottal pressure receptors for adequate feedback to the respiratory central pattern generator for coordinating respiration with swallowing.

Swallow Timing and Lung Volume

Lung volume plays a significant role in altering the central neural control coordination between respiration and swallowing. However, subglottal pressure is increased when the vocal folds adduct during a swallow. The amount of increase in subglottal pressure is driven by lung volume paired with expiratory recoil forces (Gross, Carrau, Slivka, Gasser, Smith,..Sciurba, 2012). Although we did not measure subglottal pressure in this study, it may have been reduced by reduced changes in volume for swallowing in the COPD subjects. Afferent pulmonary stretch receptors may also have inputs to the central pattern generator for swallowing control to modulate the swallow motor sequence (Jean, 2001). Possibly, a reduction in subglottal pressure change due to reduced change in pulmonary volume may have played a role in the pathophysiology of swallowing control in the COPD participants in this study and should be explored further. Swallowing at a low volume near residuals in healthy participants yielded a significantly slower swallow pattern than swallowing at the top of inspiratory reserve volume (Gross et al., 2003).

Cassiani et al., (2015) found pharyngeal swallow durations of COPD patients were longer than those of healthy participants. Increased duration in pharyngeal

swallow has been posited as a compensatory mechanism to allow longer time periods for bolus movement through the pharynx (Mokhlesi et al., 2002; Chaves et al., 2014). We did not find increased pharyngeal durations in COPD in this study, however, we did find a strong inverse relationship between pharyngeal duration and estimated lung volume in individuals with COPD. The COPD participants had longer pharyngeal durations at lower lung volumes. This relationship was strongest in the non-cued swallowing condition in the COPD participants when they had pharyngeal durations of .98s and were using 1.12L or 37.49% VC, which is below the requisite volume for swallowing established in previous research. Others have found longer swallow durations result in increased respiratory rates in individuals with COPD (Shaker et al., 1992). It is unclear whether the prolonged pharyngeal durations at low lung volumes for swallowing in the COPD participants were the result of either a compensatory strategy developed by the patients when at low lung volumes or a reflexive response to increase respiratory rate due to air hunger. If it were a reflexive response then prolonged pharyngeal durations would result in an increase in respiratory rate, which was not evaluated here. However, the increased incidence of resuming respiration on inspiration after a swallow in the COPD participants in the low volume conditions suggest that increased respiratory rate due to air hunger may have played a role.

Respiratory-Swallow Patterning

This study also examined the respiratory-swallow patterning across lung volume conditions in COPD. Studies demonstrate that healthy individuals typically

swallow in an expiratory-swallow-expiratory pattern (Cedborg et al., 2010; Martin-Harris et al., 2005; Martin-Harris et al., 2003; Shaker et al., 1992; Wheeler Hegland, et al., 2009). Alterations in the respiratory-swallow pattern can result in increased risk of aspiration. Multiple studies determined that COPD respiratory-swallow patterning deviates from the preferred initiation and resumption of respiration in expiration (Cedborg et al., 2010; Martin-Harris et al., 2005; Martin-Harris et al., 2003; Shaker et al., 1992; Wheeler Hegland et al., 2009). Similar to previous studies, individuals with COPD in this study tended to resume respiration in inspiration more than their older healthy peers. Importantly, COPD restarted respiration after a swallow less often in inspiration at the higher lung volumes, TLC and TV. COPD participants swallowing at REL were significantly more likely to resume respiration on inhalation than when they were swallowing in the TLC or TV.

Summary

The study provided new evidence that individuals with COPD swallow at lower lung volumes than their healthy, older peers. Further, individuals with COPD demonstrated an inverse relationship between pharyngeal swallow duration and the lung volume at the time of the swallow which was not evidenced in the older healthy participants. Pharyngeal swallow duration was longer at the lower lung volumes in individuals with COPD. This relationship should be investigated further to determine whether longer or shorter pharyngeal swallow duration impacts the safety of the swallow in COPD.

This study found that individuals with COPD resume respiration in inspiration significantly more often in their natural swallowing in the non-cued condition, placing them potentially at greater risk for aspiration, compared with their older healthy peers. This finding supports previous studies (Cedborg et al., 2010; Martin-Harris et al., 2005; Martin-Harris et al., 2003; Shaker et al., 1992; Wheeler Hegland, et al., 2009). Importantly, we determined that increasing lung volume at the time of the swallow can alter the respiratory-swallow pattern into resumption of breathing in exhalation at the time of the swallow in individuals with COPD. Future research would be beneficial in determining if swallowing at a higher lung volume also reduces incidence of aspiration and could be used as an intervention in patients with COPD.

Future studies with a focus on improving respiratory function such as airflow exchange and recoil forces should determine if altering respiratory function results in improved swallowing outcomes, reduces incidents of COPD exacerbations, and improves quality of life for individuals with COPD. Studies should examine whether respiratory muscle strength training can improve swallowing in COPD. Resistive respiratory training exercises, such as Inspiratory Muscle Strength Training (IMST), improve inspiratory muscle strength in individuals with COPD (Geddes et al., 2008; Geddes et al., 2005) and could increase inspiratory volume prior to the swallow. Expiratory Muscle Strength Training (EMST) improves hyolaryngeal timing and movement for swallowing in patients with Parkinson Disease (Troche et al., 2010). EMST also improves expiratory force for a productive cough through active expiration in disordered populations such as COPD (Laciuga, Rosenbeck, Davenport,

& Sapienza, 2014). The effects of IMST and EMST in individuals with COPD to improve lung volume at the time of the swallow may offer benefits for improving swallow physiology, increasing airway safety and enhancing their quality of life.

Potential Limitations

Small sample size limits ability to generalize the findings and may have impacted the statistical analyses. In the pilot testing, we found that the effect size was 0.27, and the power analysis indicated that 26 participants would be needed in each group. We were only able to recruit 10 in the healthy group and 9 in the COPD group. The effect sizes that the results yielded, however, were higher in this study. For estimated lung volume, the mean of the Cohen's *d* effect sizes across the four lung volume conditions based on the data in Table 7, averaged 1.07, while the mean Cohen's *d* effect sizes for the 3 conditions in percent swallows finishing on inspiration in Table 9 averaged 0.83. Thus, both were strong effect sizes much higher than the pilot testing results. The power of the study based on these effect sizes was ≥ 0.99 .

Recruitment of participants in this study exceeded one year and may be attributed to conducting the study in a rural hospital. The limited sampling pool impacted abilities to effectively stratify participants for the study. This resulted in gender inequality between groups. The COPD group gender composition of men (n=6) compared with women (n=3) may be skewed based on recent trends of more women than men being diagnosed (American Lung Association, 2013). Additional participant sampling should be completed to address the sample inequalities.

COPD participant exclusion criteria excluded individuals with the most severe COPD, $FEV_1 < 30\%$, and individuals on continuous oxygen from participating

in the study. Study participants were predominately in the moderate (n=3) to severe (n=5) COPD severity stage. This study did not include equal representation from the mild severity (n=1) nor the most severe. Importantly, the most severe COPD are the individuals most commonly referred for swallowing assessment. Disease progression and increased frequency of exacerbations is related to increased aspiration risk (Terada, 2011). Conversely, mild COPD and the emergence of dysphagia symptoms is less understood. Additional larger studies need to be completed to include the range of COPD severity in sampling to elucidate the emergence and progression of dysphagia in individuals with COPD.

COPD participants were included in the study regardless of reported symptoms of swallowing impairment to ensure inclusion of subclinical dysphagia in COPD participants. Three participants scored outside the normal range on the DHI. Only one of the participants who scored a moderate severity on the DHI, was diagnosed with dysphagia. Two other COPD participants scored in the mild severity range on the DHI. The remaining 6 COPD participants reported no handicapping effects on their swallowing.

This study did not include videofluoroscopic assessment of swallowing to correlate the timing and volume measures with swallow physiology. Future studies should include a greater spread of individuals with COPD expressing self-perceived swallow symptoms and inclusion of videofluoroscopy. In clinical practice, individuals with COPD often underreport symptoms of dysphagia that are later confirmed in videofluoroscopy swallow examinations. This is hypothesized to result

from COPD attributing their swallowing symptoms, such as cough, throat clearing, or increased secretions, to their respiratory disorder.

This study examined individuals in the stable state of the disease process. Exacerbations of COPD result in reduced pulmonary function and increased risk of aspiration. Abnormal swallowing examination results occur in increased frequencies during COPD exacerbations as there is a strong relationship between swallowing dysfunction and exacerbations in COPD (Terada et al., 2010). Exacerbation symptoms such as increased phlegm production, significant shortness of breath, and increased respiratory drive are posited to result in increased discoordination between respiration and swallowing. However, research has largely examined individuals with COPD in the stable state. Future research should focus on determining effects of exacerbated state on swallow function and safety in individuals with COPD.

Conclusions

Lung volumes in individuals with COPD were reduced during the swallow and may contribute to other swallow physiology dysfunction. Individuals with COPD demonstrate higher pharyngeal swallow durations when swallowing at lower lung volumes. This relationship between estimated lung volume and pharyngeal swallow duration was not present in the older healthy. COPD individuals were found to resume respiration in inspiration post-swallow significantly more often than healthy. Further, increasing lung volume at the time of the swallow in individuals with COPD resulted in a significant reduction of respiration resumption in the inspiratory phase post-swallow. Resuming respiration in the expiratory phase may decrease risk of aspiration. Additional research investigating lung volume effects on swallow physiology and functional outcomes is needed to develop efficacious treatments for dysphagia in individuals with COPD.

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