Original Article

Risk factors and impact of swallowing impairment and aspiration after lung transplantation

Kahla Graham[1]^, Taisuke Kaiho[2], Benjamin Louis Thomae[2], Yuriko Yagi[2], Emily Cerier[2], Bonnie Martin-Harris[1,3], Ankit Bharat[2,4], Chitaru Kurihara[2]

[1]Department of Communication Sciences and Disorders, Northwestern University, Evanston, IL, USA; [2]Division of Thoracic Surgery, Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [3]Department of Otolaryngology - Head & Neck Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [4]Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Contributions: (I) Conception and design: K Graham, C Kurihara, B Martin-Harris; (II) Administrative support: BL Thomae, Y Yagi, E Cerier, C Kurihara, B Martin-Harris; (III) Provision of study materials or patients: K Graham, C Kurihara, B Martin-Harris; (IV) Collection and assembly of data: K Graham, C Kurihara, B Martin-Harris; (V) Data analysis and interpretation: K Graham, T Kaiho; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Chitaru Kurihara, MD. Division of Thoracic Surgery, Department of Surgery, Northwestern University Feinberg School of Medicine, 676 N. Saint Clair St., Suite 650, Chicago, IL 60611, USA. Email: chitaru.kurihara@northwestern.edu.

Background: Oropharyngeal swallowing impairment frequently occurs following lung transplantation, placing patients at risk of aspiration-related complications and mortality. The primary objectives of this study were to characterize swallowing impairment and explore potential risk factors for aspiration after lung transplantation.

Methods: A retrospective review of lung transplant recipients treated between January 2018 and December 2022 that received an instrumental swallow study was conducted. Clinical characteristics, post-operative outcomes, and results of swallow studies were evaluated. Airway invasion was classified using the Penetration-Aspiration Scale (PAS). Swallowing physiology was characterized using the Modified Barium Swallow Impairment Profile. Chi-squared, Wilcoxon signed-rank, Kaplan-Meier, Student's *t*-tests, and regression analyses were conducted.

Results: One hundred eighteen patients underwent lung transplantation and had an instrumental swallow study. Fifty-nine percent (70/118) demonstrated airway invasion. Delayed swallow initiation occurred in all patients that had videofluoroscopy (39/118). Body mass index (BMI) and body surface area (BSA) were significantly lower in patients with airway invasion (24.7±4.5 *vs.* 26.8±4.6 kg/m^2, P=0.02; 1.8±0.2 *vs.* 1.9±0.2 m^2, P=0.02, respectively), and were associated with airway invasion [odds ratio (OR): 0.91, P=0.02; OR: 0.13, P=0.02]. Intra- and post-operative outcomes and long-term survival did not differ significantly in our cohort.

Conclusions: Oropharyngeal swallowing impairment and airway invasion occurred with high frequency, and linkages to low BMI or frailty were found. Although the true prevalence of aspiration after lung transplantation might be underestimated by referral patterns in this cohort, the negative impact of aspiration after lung transplantation may be mitigated by appropriate recognition and intervention.

Keywords: Lung transplant; swallow; dysphagia; aspiration; oropharyngeal

Submitted Apr 30, 2024. Accepted for publication Jul 26, 2024. Published online Sep 21, 2024.
doi: 10.21037/jtd-24-707
View this article at: https://dx.doi.org/10.21037/jtd-24-707

^ ORCID: 0000-0002-1693-7311.

Introduction

Lung transplantation is a life-saving procedure for patients with end-stage lung disease (ESLD). According to the Organ Procurement & Transplantation Network (OPTN; 2023), 3,026 individuals underwent lung transplantation in the United States in 2023, and that number is projected to steadily increase (1). Despite advances in the transplant procedure, aspiration, or the entry of foreign material into the trachea or lungs, is a prevalent complication following lung transplantation (2-7). Post-prandial aspiration, or aspiration of esophageal or stomach contents, has been well-studied in the lung transplant population. Prandial aspiration, or aspiration of food and liquids as a result of oropharyngeal swallowing impairment, has recently gained more attention due to its association with acute and long-term complications after lung transplant, such as increased length of stay, re-admission to the intensive care unit, and discharge to dependent care (2,4,6). Pulmonary function is also impaired by the consequences of aspiration, which is a known risk factor for developing chronic lung allograft dysfunction (CLAD), the leading cause of late mortality in lung transplant recipients (8).

Prior studies exploring this underrecognized complication have found that between 67–100% of patients demonstrate laryngeal penetration or aspiration due to oropharyngeal dysphagia after lung transplantation (2-7,9,10). Furthermore, airway invasion is often clinically undetectable, as it occurs silently or without physiologic response. Intubation and thoracic procedures can cause direct and indirect injury to the larynx and vagal nerve (11,12), making lung transplant patients susceptible to sensorimotor deficits and compromised airway protection post-operatively. Premorbid risk factors for dysphagia, such as frailty (13,14), disrupted respiratory swallow coordination (15,16), and decreased laryngeal sensitivity (17,18) are also common in patients with ESLD and may predispose patients to more significant swallowing complications after lung transplant. Despite this awareness, procedures for evaluating the swallowing function of lung transplant recipients vary within and between medical institutions, limiting the generalizability of findings and true estimation of dysphagia after lung transplantation (6).

The purpose of this study was to characterize the severity of airway invasion identified on instrumental swallow evaluations and explore potential risk factors associated with aspiration after lung transplantation. The nature of swallowing impairment was also described to elucidate the potential pathophysiology of airway invasion post-lung transplantation. Additionally, we aimed to evaluate the potential impact of airway invasion on short- and long-term post-operative outcomes with the underlying hypothesis that patients with unsafe swallowing would have poorer outcomes. This study may guide future investigations and aid in the development of standardized protocols for the evaluation of swallowing after lung transplantation. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-707/rc).

Highlight box

Key findings
- Airway invasion due to oropharyngeal swallowing impairment after lung transplantation may be linked to low body mass index or frailty before surgery.
- Aggressive clinical management of aspiration, when identified with instrumental swallow evaluations, may mitigate complications after lung transplantation.

What is known and what is new?
- Aspiration is known to occur with high frequency following lung transplantation.
- Swallowing impairments demonstrated in this cohort included impaired initiation of the pharyngeal swallow, laryngeal elevation, and pharyngoesophageal segment opening, which may contribute to unsafe swallowing.

What is the implication, and what should change now?
- Instrumental swallow studies should be conducted routinely after lung transplantation for identification and characterization of the specific physiologic impairments contributing to airway invasion and the selection of specific, evidenced-based interventions to improve swallowing function and mitigate the risk of aspiration-related complications after lung transplantation.

Methods

Study design

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Northwestern University (STU00207250, STU00213616, and STU00215512) and written consent was waived due to the retrospective study design. A single site, cross-sectional review was conducted for all patients over 18 years of age who had a single or bilateral lung transplantation between January 2018 and December 2022 and received a Modified Barium Swallow Study (MBSS) or Flexible Endoscopic Evaluation of Swallowing (FEES) following lung transplantation. Data were collected from the electronic medical record and a clinical lung transplant database at the Northwestern University Medical Center in Chicago, Illinois, USA.

Measures of oropharyngeal swallowing impairment and airway invasion

At the time of this study, patients that demonstrated clinical indicators of aspiration or were suspected to be at greater risk for aspiration (e.g., intubated >48 hours, underwent tracheostomy, required high flow oxygen therapy) after lung transplantation were referred for a swallow evaluation by a Speech-Language Pathologist (SLP). Swallow evaluations were not routinely conducted during the pre-operative evaluation for lung transplantation, and not all patients were referred for testing after transplantation. In our center, Northwestern Memorial Hospital, patients with connective tissue disease or severe esophageal dysmotility underwent gastro-jejunal tube placement before lung transplant and were not referred for a swallow evaluation during their immediate post-operative recovery. For patients referred for a swallow evaluation, the type of instrumental swallow study conducted was determined through careful consideration of patient-related factors (e.g., ability to transfer to radiology, pain, lines/tubes) and the clinical question. Per standard of care, MBSS were administered and analyzed using the Modified Barium Swallow Impairment Profile (MBSImP™) protocol (19) by two certified SLPs (achieved >80% inter-rater reliability). The FEES exams were also conducted and interpreted by two trained SLPs using a modified version of the Langmore protocol (20).

The maximum Penetration-Aspiration Scale (PAS) scores were reported for both MBSS and FEES. The PAS is a validated ordinal scale (1, absence of airway invasion; 8, silent aspiration) that captures the presence, degree, and response to airway invasion (Table S1) (21). Scores of 1–2 are considered within normal variation in healthy adults (22), therefore, scores were dichotomized into safe (PAS 1–2) and pathological airway invasion (PAS ≥3).

MBSImP scores were reported for MBSS only. The standardized and validated scoring metric includes 17 physiologic swallowing components rated on an ordinal scale. The highest (most severe) score contributes to the overall impression (OI) score for each component (19).

Definition of complication

Primary graft dysfunction (PGD)

The definition of PGD is based on the 2016 International Society for Heart and Lung Transplantation (ISHLT) guideline (23). Patients with no evidence of pulmonary edema on chest X-ray (CXR) are classified as grade 0. The lack of mechanical ventilation was quantified according to the ratio of PaO_2 to FiO_2. In the absence of PaO_2 data, an oxygen saturation/FiO_2 ratio was employed for the calculation of the PaO_2/FiO_2 ratio. Grade 1: PaO_2/FiO_2 ratio >300; Grade 2: PaO_2/FiO_2 ratio =200–300; Grade 3: PaO_2/FiO_2 ratio <200. The lowest PaO_2/FiO_2 ratio observed within 72 hours after lung transplantation was utilized. The application of extracorporeal membrane oxygenation (ECMO) for bilateral pulmonary edema as depicted on CXR images was classified as grade 3, while the continuous use of ECMO in the absence of pulmonary edema on CXR imaging was excluded.

CLAD

In accordance with the 2019 ISHLT consensus document on the nomenclature of CLAD and its clinical phenotypes (8), CLAD was identified as a persistent decline (≥20%) in the measured forced expiratory volume in 1 second (FEV_1) from the post-transplantation baseline. Patients with fewer than three total FEV_1 measurements were excluded from analysis, as this was insufficient to diagnose CLAD.

Acute kidney injury (AKI)

The definition of AKI was based on the risk, failure, loss of kidney function, and end-stage kidney disease classification (24).

Statistical analysis

A comparison was made between patients with safe swallowing and those with airway invasion (PAS ≥3) on MBSS and FEES, with regard to recipient and donor characteristics, preoperative laboratory values, and intra- and post-operative outcomes. The Chi-squared test was employed to assess the statistical significance of categorical variables, which were presented as numerical values and percentages. Univariate logistic regression analyses were utilized to assess the ability of recipient characteristics to predict airway invasion. Subsequently, a multivariate logistic regression analysis was conducted utilizing variables from the univariate logistic regression analyses with a P value

Table 1 PAS scores

Dichotomization	Category	PAS score	Frequency (n=118), n [%]
Safe	Normal	1	28 [24]
		2	20 [17]
Airway invasion	Penetration	3	21 [18]
		4	0
		5	11 [9]
	Aspiration	6	6 [5]
		7	6 [5]
		8	26 [22]

PAS, Penetration-Aspiration Scale.

Table 2 Physiologic swallowing impairment using MBSImP OI scores

MBSImP swallowing components	N=39, n [%]
C1—lip closure[a]	15 [38]
C2—bolus hold	21 [54]
C3—bolus preparation/mastication[b]	21 [66]
C4—lingual transport	18 [46]
C5—oral residue[a]	30 [77]
C6—Initiation of pharyngeal swallow	39 [100]
C7—soft palate elevation	3 [8]
C8—laryngeal elevation	30 [77]
C9—anterior hyoid excursion	28 [72]
C10—epiglottic movement	23 [59]
C11—laryngeal vestibular closure	27 [69]
C12—pharyngeal stripping wave	19 [49]
C13—pharyngeal contraction	NA
C14—pharyngoesophageal segment opening	27 [69]
C15—tongue base retraction[a]	20 [51]
C16—pharyngeal residue[a]	24 [62]
C17—esophageal clearance	NA

OI >0 is considered impaired for all components except for those demarcated by [a] (for these components, OI >1 is considered impaired and included in frequency); [b], a score for this component was missing for seven participants due to reasons unrelated to oral impairment. OI scores not obtained for C13 and C17 because of positioning constraints. MBSImP, modified barium swallow impairment profile; OI, overall impression; C, component; NA, not applicable.

<0.2. Odds ratio (OR) and 95% confidence interval (CI) were reported. The Kaplan-Meier method was used to estimate survival, and the log-rank test was performed to compare survival between the groups. Statistical significance was set at P<0.05. Receiver operating characteristic (ROC) curves were plotted using variables identified as predictors of airway invasion. The performance of the two models were compared using the DeLong test (25). The EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), was utilized to conduct all the analyses (26).

Results

Oropharyngeal swallowing

Of the 251 patients that underwent a single or bilateral lung transplant during the study period, 118 received an instrumental swallow study (79 FEES, 39 MBSS) post-operatively and were included in this study. Airway invasion (PAS ≥3) was observed in 59% (70/118) of patients (*Table 1*). Of the patients with airway invasion, 46% (32/70) demonstrated laryngeal penetration (PAS 3–5) and 54% (38/70) aspirated. Silent aspiration (PAS 8) occurred in 68% (26/38) of aspiration events.

All patients that had a MBSS (39/118 patients with instrumental exam) had delayed initiation of the pharyngeal swallow (component 6) (*Table 2*). Many patients who underwent a MBSS also demonstrated oral residue (30/39; component 5), partial laryngeal elevation (30/39; component 8), incomplete laryngeal vestibular closure (27/39; component 11), and incomplete pharyngoesophageal segment opening (27/39; component 14), all of which can contribute to laryngeal penetration or aspiration.

Patients

Patient characteristics are summarized in *Table 3* (lab values obtained before transplantation are summarized in Table S2). Body mass index (BMI) and body surface area (BSA) were collected at the time of listing for lung transplantation. Patients with airway invasion had significantly lower BMI (24.7±4.5 *vs.* 26.8±4.6 kg/m^2,

Table 3 Patient characteristics

Variables	Safe swallow (N=48)	Airway invasion (N=70)	P value
Recipient factors			
Age (years)	53.8±13.3	57.2±13.3	0.17
Male	26 (54.2)	43 (61.4)	0.55
BMI (kg/m^2)	26.8±4.6	24.7±4.5	0.02
BSA (m^2)	1.9±0.2	1.8±0.2	0.02
Smoking history	19 (39.6)	36 (51.4)	0.28
Hypertension	15 (31.3)	37 (52.9)	0.03
Diabetes	16 (33.3)	19 (27.1)	0.60
CKD	1 (2.1)	7 (10.0)	0.19
Dialysis	5 (10.4)	13 (18.6)	0.3
GERD	21 (43.8)	35 (50.0)	0.63
OSA	10 (20.8)	12 (17.1)	0.79
Pre-ECMO use	12 (25.0)	14 (20.0)	0.68
Bilateral	37 (77.1)	50 (71.4)	0.64
LAS	62.1±22.1	59.3±19.4	0.47
Etiology			
COPD	10 (20.8)	13 (18.6)	0.95
ILD	8 (16.7)	22 (31.4)	0.11
ARDS (COVID-19)	17 (35.4)	18 (25.7)	0.35
PAH	5 (10.4)	6 (8.6)	0.99
Others	8 (16.7)	11 (15.7)	>0.99

Data are presented as mean ± standard deviation or n (%). BMI, body mass index; BSA, body surface area; CKD, chronic kidney disease; GERD, gastroesophageal reflux disease; OSA, obstructive sleep apnea; ECMO, extracorporeal membrane oxygenation; LAS, lung allocation score; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; PAH, pulmonary arterial hypertension.

P=0.02), lower BSA (1.8±0.2 *vs.* 1.9±0.2 m^2, P=0.02), and a greater frequency of preoperative hypertension (52.9% *vs.* 31.3%, P=0.03). No other significant differences were identified between patients with safe swallowing and those with airway invasion.

Intra- and post-operative outcomes

Intra- and post-operative outcomes were similar between patients with safe swallowing and patients with airway invasion (*Table 4*). The median follow-up for this cohort is 431 (Q1–Q3, 194–705) days. The survival curves are shown in *Figure 1*. There were no significant differences between the two curves using the Wilcoxon signed-rank test (P=0.69).

Risk factors associated with airway invasion

Univariate logistic regression analysis revealed that BMI (OR 0.91, 95% CI: 0.83–0.99, P=0.02), BSA (OR 0.13, 95% CI: 0.02–0.76, P=0.02), and hypertension (OR 2.47, 95% CI: 1.14–5.33, P=0.02) before transplantation were predictors of airway invasion after lung transplantation (Table S3). In subsequent multivariate logistic regression analysis, hypertension (OR 2.62, 95% CI: 1.09–6.29, P=0.03) was an independent predictor of airway invasion (*Table 5*).

Table 4 Intra- and post-operative outcomes

Variables	Safe swallow (N=48)	Airway invasion (N=70)	P value
Intra-operative outcome			
Operative time (h)	7.2±2.1	7.0±2.2	0.57
Ischemic time (h)	5.6±1.7	5.2±1.9	0.10
VA ECMO use	33 (68.8)	47 (67.1)	0.86
VA ECMO time (h)	3.2±0.8	3.3±1.7	0.91
Post-operative outcomes			
Post op ECMO use	8 (16.7)	15 (21.4)	0.69
PGD (all grades)	24 (50.0)	38 (54.3)	0.79
PGD (grade 3)	4 (8.3)	11 (15.7)	0.37
AKI	23 (47.9)	36 (51.4)	0.85
Dialysis	5 (10.4)	13 (18.6)	0.34
Stroke	0	3 (4.3)	0.39
PE	3 (6.3)	1 (1.4)	0.37
Digital ischemia	0	1 (1.4)	>0.99
Post-transplant ventilator (days)	2 [1–6]	3 [1–9]	0.60
Post-transplant swallow study (days)	4 [1–9]	6 [2–13]	0.07
ICU stay (days)	15 [6–25]	14 [8–25]	0.80
Hospital stay (days)	24 [16–34]	27 [17–39]	0.25

Data are presented as mean ± standard deviation, median and interquartile range [Q1–Q3], or n (%). VA ECMO, venoarterial extracorporeal membrane oxygenation; PGD, primary graft dysfunction; AKI, acute kidney injury; PE, pulmonary embolism; ICU, intensive care unit.

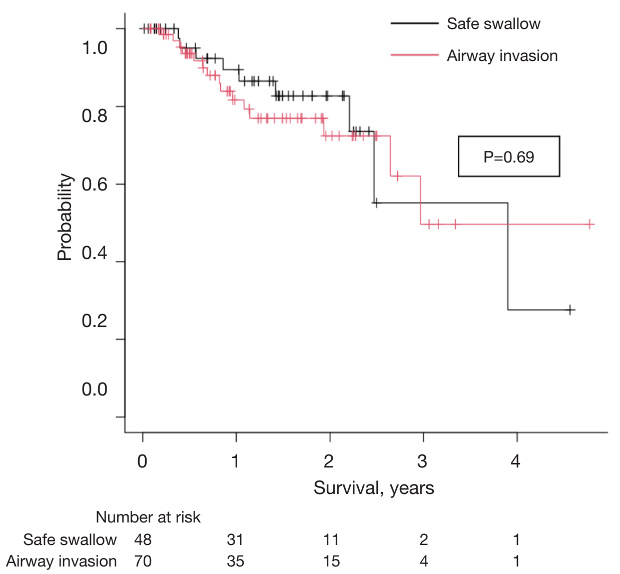

Figure 1 Survival curves of patients with safe swallowing *vs.* airway invasion. The survival curves for patients with safe swallowing and those with airway invasion demonstrated no significant differences between the two curves (P=0.69).

Table 5 Multivariate logistic regression for risk factors associated with airway invasion (PAS ≥3)

Variables	Multivariate		P value
	OR	95% CI	
Recipient factors			
Age (years)	0.96	0.96–1.03	0.78
BMI (kg/m^2)	0.95	0.84–1.07	0.39
BSA (m^2)	0.20	0.02–2.38	0.20
Hypertension	2.62	1.09–6.29	0.03
CKD	5.03	0.52–48.6	0.16
Etiology			
ILD	2.63	0.91–7.59	0.07
Post-operative outcomes			
CLAD	0.11	0.01–2.02	0.14

PAS, Penetration-Aspiration Scale; OR, odds ratio; CI, confidence interval; BMI, body mass index; BSA, body surface area; CKD, chronic kidney disease; ILD, interstitial lung disease; CLAD, chronic allograft dysfunction.

ROC analysis to identify the cutoff value

A *post-hoc* ROC analysis was performed to identify and evaluate the cut off value of BMI and BSA to predict airway invasion. Sensitivity, specificity, and predictive values are demonstrated in Figure S1A,S1B. BMI gave an AUC of 0.63 (95% CI: 0.52–0.73) with cut off 23.9 kg/m^2, and BSA gave an AUC of 0.64 (95% CI: 0.53–0.74) with cut off 1.74 m^2 for predicting airway invasion. There was no significant difference between the two ROC curves (P=0.93) (Figure S1C).

Discussion

Swallowing impairment resulting in laryngeal penetration and aspiration occurred with high frequency (59% of patients) in this cohort of patients following lung transplantation. Iatrogenic injury to the recurrent laryngeal nerve and superior laryngeal nerve, which provide motor and sensory innervation to the larynx, can occur from trauma during intubation, intubation with large (>8 mm) or double lumen endotracheal tubes, or traction injury during surgery. Such injuries may disrupt sensorimotor function of the larynx and increase risk of silent aspiration after cardiothoracic procedures (12,27,28). Our results reflect the presence of sensorimotor disruption, as we found that 68% of aspirators had no cough in response to aspiration (PAS 8), consistent with the high rates of silent aspiration reported in other studies. It is plausible that aspiration may have gone undetected in patients without clinical indicators of aspiration who were not referred for an instrumental swallow evaluation and, therefore, not included in our study, and the prevalence of airway invasion may in fact be higher.

The MBSS reveal possible physiologic mechanisms of airway invasion after lung transplantation, including delayed initiation of the pharyngeal swallow, reduced hyolaryngeal excursion, and incomplete distention of the pharyngoesophageal segment. Reedy *et al.* [2023] found similar swallowing impairments in a cohort of patients after lung transplantation, reporting that most patients initiated the pharyngeal swallow when the bolus head reached the pyriform sinuses (MBSImP component 6, score of 3), and demonstrated partial laryngeal elevation (MBSImP component 8, score 1) and incomplete laryngeal vestibular closure (MBSImP component 11, score 1) (7). The identification of the specific swallowing impairments contributing to aspiration are critical for selection of appropriate interventions to rehabilitate swallowing and minimize aspiration. As suggested in previous literature, one potential etiology of these specific impairments is the injury to the vagal nerve due to manipulation of the aerodigestive tract and surgical procedures (2-7). However, it has recently been hypothesized that atypical respiratory-swallow coordination may also play a role in swallowing impairment after lung transplant (7,10). Respiration and swallowing are two tightly coupled, critical functions of the body that likely have bidirectional interactions. In healthy adults, swallowing occurs during the expiratory phase of the respiratory cycle at mid-to-low tidal lung volumes, and expiration resumes after a brief respiratory cessation that occurs during the swallow (29,30). This respiratory-swallow pattern, expiration-swallow-expiration, provides a biomechanical advantage for swallowing, facilitating swallowing safety and bolus clearance (31). Given the significant changes in respiratory mechanics that occur as a result of ESLD and lung transplant surgery and the specific swallowing impairments exhibited in this cohort, alterations in respiratory-swallow coordination may be another potential contributor to swallowing impairment and aspiration after lung transplantation.

Patients undergoing lung transplantation are a heterogenous group, and there are likely several patient and clinical factors that influence post-operative swallowing safety. Our results suggested statistically significant associations between BMI, BSA, and hypertension and airway invasion, however, their clinical significance requires further exploration. Malnutrition occurs in patients with ESLD and can manifest as sarcopenia and reduced exercise endurance as pulmonary severity increases (32). In studies of dysphagic adults, low BMI, malnutrition, and frailty have been linked to swallowing impairment (33). As swallowing consists of highly synchronized skeletal and smooth muscular activity, changes in muscle composition and physical endurance may influence swallowing kinematics and timing and ultimately make patients with lower BMI more susceptible to airway invasion upon further deconditioning after lung transplantation. Although several studies have identified hypertension as a common comorbidity in dysphagic adults, the underpinnings of the linkage between swallowing and hypertension are not clear. One potential mechanism may be the use of calcium channel blockers as a treatment for hypertension. Calcium channel blockers have been shown to reduce lower esophageal sphincter pressure, increase esophageal acid exposure, and induce hypomotility in patients without history of esophageal dysfunction (34). As there is a functional interrelationship between oropharyngeal and esophageal swallowing, it is possible that the use of calcium channel blockers may result in disruptions along the entire swallowing continuum (35). Further investigation is needed to better understand how anti-hypertension medications may impact oropharyngeal swallowing. Although not statistically significant, the risk of airway invasion was roughly 2.6 times greater in patients with a history of interstitial lung disease (ILD), signaling that the type of lung disease necessitating lung transplantation may influence swallowing impairment. Other factors that have been found to be associated with airway invasion in previous investigations of swallowing after lung transplantation include preoperative gastroesophageal reflux, longer intubation durations, reintubation after surgery, tracheostomy, and the intraoperative use of venovenous (VV)-ECMO (6,9). Our study did not confirm these associations; however, sampling method and the small sample size may have contributed to the discrepancy.

Our results indicate that post-operative outcomes and survival rates were similar among patients with safe swallowing and those with airway invasion detected upon instrumental swallow assessment. Patients with airway invasion (PAS 3–8) were treated conservatively and risk stratification with the transplant surgeon, pulmonologist, and SLP helped to determine whether an oral diet would be initiated. This process took into consideration the patient's cognitive status, physical conditioning, and respiratory status (e.g., values on incentive spirometry, supplemental oxygen needs, airway clearance). Many patients with aspiration were kept *nil per os* (NPO), received enteral nutrition, underwent pulmonary toileting, and were closely monitored to protect lung function and promote recovery after lung transplantation. Diet advancement occurred when there was evidence of improvement in airway protection and overall conditioning. It is possible that this collaborative approach to clinical management in patients with airway invasion may have minimized the negative consequences of aspiration, thus resulting in similar post-operative outcomes between the two groups.

The primary limitations of this study were the retrospective study design and patient selection methods. Although all patients that received an instrumental swallow evaluation were included, not all patients who underwent lung transplantation were referred for swallow assessment. During the study period, only patients with clinical signs of swallowing impairment or aspiration were referred for MBSS or FEES. It can be argued that selective referral for instrumental assessment after this complex procedure likely underestimates the true prevalence of airway invasion after lung transplantation (2,3,6,10). Future investigations should include prospective evaluation of swallowing with consideration of baseline swallowing function, swallowing pathophysiology, and respiratory-swallow coordination in order to optimize oropharyngeal swallowing function before and after lung transplantation.

Conclusions

A high prevalence of silent aspiration was observed after lung transplantation. Although associations between BMI and hypertension and airway invasion were statistically significant, additional work is needed to better understand these relationships and their clinical significance. Post-operative outcomes were found to be similar between patients with safe swallowing and those with airway invasion. This is thought to be due to aggressive clinical management following identification of aspiration, which may have mitigated the impact of airway invasion on post-operative recovery. The high frequency of airway invasion in this study and the likelihood of undetected aspiration in the patients that were not referred for swallow assessment influenced a change in clinical practice at our institution. Instrumental swallow studies are now routinely conducted for all patients after lung transplantation, which allows for characterization of the specific physiologic impairments contributing to airway invasion and the selection of specific, evidenced-based interventions to improve swallowing function and reduce risk of aspiration-related complications.

Acknowledgments

Funding: This work was supported by the National Institute on Deafness and Other Communication Disorders at the National Institutes of Health (NIH/NIDCD 2K24DC012801-0).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-707/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-707/dss

Peer Review File: Available at https://jtd.amegroups.com/

article/view/10.21037/jtd-24-707/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-707/coif). B.M.H. receives grant funding from the National Institutes of Health (2K24DC012801-07, 1R01CA262502- 01, 1R01DK122975-01) and Bracco Diagnostics Inc., royalties from Northern Speech Services and the Medical University of South Carolina Foundation for Research Development, and consulting fees from Bracco Diagnostics Inc. She holds a US Provisional Patent for wearable sensor technology (US 62/710,324). A.B. is supported by the National Institutes of Health, HL145478, HL147290, and HL147575. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Northwestern University (STU00207250, STU00213616, and STU00215512) and written consent was waived due to the retrospective study design.

References

1. Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN/SRTR 2022 Annual Data Report. U.S. Department of Health and Human Services, Health Resources and Services Administration; 2024.
2. Atkins BZ, Trachtenberg MS, Prince-Petersen R, et al. Assessing oropharyngeal dysphagia after lung transplantation: altered swallowing mechanisms and increased morbidity. J Heart Lung Transplant 2007;26:1144-8.
3. Baumann B, Byers S, Wasserman-Wincko T, et al. Postoperative Swallowing Assessment After Lung Transplantation. Ann Thorac Surg 2017;104:308-12.
4. Black RJ, Bogaardt H, McCabe P, et al. Clinical predictors for oropharyngeal dysphagia and laryngeal dysfunction after lung and heart transplantation. Int J Lang Commun Disord 2019;54:894-901.
5. Miles A, Barua S, McLellan N, et al. Dysphagia and medicine regimes in patients following lung transplant surgery: A retrospective review. Int J Speech Lang Pathol 2021;23:339-48.
6. Dallal-York J, Segalewitz T, Croft K, et al. Incidence, risk factors, and sequelae of dysphagia mediated aspiration following lung transplantation. J Heart Lung Transplant 2022;41:1095-103.
7. Reedy EL, Simpson AN, O'Rourke AK, et al. Characterizing Swallowing Impairment in a Post-Lung Transplant Population. Am J Speech Lang Pathol 2023;32:1236-51.
8. Verleden GM, Glanville AR, Lease ED, et al. Chronic lung allograft dysfunction: Definition, diagnostic criteria, and approaches to treatment-A consensus report from the Pulmonary Council of the ISHLT. J Heart Lung Transplant 2019;38:493-503.
9. Atkins BZ, Petersen RP, Daneshmand MA, et al. Impact of oropharyngeal dysphagia on long-term outcomes of lung transplantation. Ann Thorac Surg 2010;90:1622-8.
10. Dallal-York J, Croft K, Anderson A, et al. A prospective examination of swallow and cough dysfunction after lung transplantation. Neurogastroenterol Motil 2023;35:e14458.
11. Black RJ, Novakovic D, Plit M, et al. Swallowing and laryngeal complications in lung and heart transplantation: Etiologies and diagnosis. J Heart Lung Transplant 2021;40:1483-94.
12. Plowman EK, Anderson A, York JD, et al. Dysphagia after cardiac surgery: Prevalence, risk factors, and associated outcomes. J Thorac Cardiovasc Surg 2023;165:737-746.e3.
13. Garand KL, Strange C, Paoletti L, et al. Oropharyngeal swallow physiology and swallowing-related quality of life in underweight patients with concomitant advanced chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2018;13:2663-71.
14. Schaenman JM, Diamond JM, Greenland JR, et al. Frailty and aging-associated syndromes in lung transplant candidates and recipients. Am J Transplant 2021;21:2018-24.

15. Drulia TC, Kamarunas E, O'Donoghue C, et al. An Exploration of Lung Volume Effects on Swallowing in Chronic Obstructive Pulmonary Disease. Am J Speech Lang Pathol 2021;30:2155-68.
16. Gross RD, Atwood CW Jr, Ross SB, et al. The coordination of breathing and swallowing in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2009;179:559-65.
17. Clayton NA, Carnaby GD, Peters MJ, et al. Impaired laryngopharyngeal sensitivity in patients with COPD: the association with swallow function. Int J Speech Lang Pathol 2014;16:615-23.
18. Mokhlesi B. Clinical implications of gastroesophageal reflux disease and swallowing dysfunction in COPD. Am J Respir Med 2003;2:117-21.
19. Martin-Harris B, Brodsky MB, Michel Y, et al. MBS measurement tool for swallow impairment--MBSImp: establishing a standard. Dysphagia 2008;23:392-405.
20. Langmore SE. Endoscopic evaluation of oral and pharyngeal phases of swallowing. GI Motility online 2006. doi: 10.1038/gimo28.
21. Rosenbek JC, Robbins JA, Roecker EB, et al. A penetration-aspiration scale. Dysphagia 1996;11:93-8.
22. Robbins J, Coyle J, Rosenbek J, et al. Differentiation of normal and abnormal airway protection during swallowing using the penetration-aspiration scale. Dysphagia 1999;14:228-32.
23. Snell GI, Yusen RD, Weill D, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction, part I: Definition and grading-A 2016 Consensus Group statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2017;36:1097-103.
24. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8:R204-12.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837-45.
26. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452-8.
27. Miles A, McLellan N, Machan R, et al. Dysphagia and laryngeal pathology in post-surgical cardiothoracic patients. J Crit Care 2018;45:121-7.
28. Krisciunas GP, Langmore SE, Gomez-Taborda S, et al. The Association Between Endotracheal Tube Size and Aspiration (During Flexible Endoscopic Evaluation of Swallowing) in Acute Respiratory Failure Survivors. Crit Care Med 2020;48:1604-11.
29. Martin BJ, Logemann JA, Shaker R, et al. Coordination between respiration and swallowing: respiratory phase relationships and temporal integration. J Appl Physiol (1985) 1994;76:714-23.
30. Martin-Harris B. Clinical implications of respiratory-swallowing interactions. Curr Opin Otolaryngol Head Neck Surg 2008;16:194-9.
31. Martin-Harris B, Kantarcigil C, Reedy EL, et al. Cross-System Integration of Respiration and Deglutition: Function, Treatment, and Future Directions. Dysphagia 2023;38:1049-58.
32. Mete B, Pehlivan E, Gülbaş G, et al. Prevalence of malnutrition in COPD and its relationship with the parameters related to disease severity. Int J Chron Obstruct Pulmon Dis 2018;13:3307-12.
33. Leira J, Maseda A, Lorenzo-López L, et al. Dysphagia and its association with other health-related risk factors in institutionalized older people: A systematic review. Arch Gerontol Geriatr 2023;110:104991.
34. Yoshida K, Furuta K, Adachi K, et al. Effects of anti-hypertensive drugs on esophageal body contraction. World J Gastroenterol 2010;16:987-91.
35. Gullung JL, Hill EG, Castell DO, et al. Oropharyngeal and esophageal swallowing impairments: their association and the predictive value of the modified barium swallow impairment profile and combined multichannel intraluminal impedance-esophageal manometry. Ann Otol Rhinol Laryngol 2012;121:738-45.

Cite this article as: Graham K, Kaiho T, Thomae BL, Yagi Y, Cerier E, Martin-Harris B, Bharat A, Kurihara C. Risk factors and impact of swallowing impairment and aspiration after lung transplantation. J Thorac Dis 2024;16(9):5755-5764. doi: 10.21037/jtd-24-707

