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Impact of Oropharyngeal Dysphagia on Long-Term Outcomes of Lung Transplantation

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Background. Lung transplantation, definitive therapy for end-stage lung disease, is limited long-term by allograft dysfunction including bronchiolitis obliterans syndrome (BOS). Few modifiable risk factors for pulmonary transplant-related mortality are recognized. However, oropharyngeal dysphagia frequently occurs after thoracic surgical procedures, including lung transplantation, and increases morbidity. We evaluated the impact of oropharyngeal dysphagia on survival and BOS after lung transplantation.

Methods. A total of 263 consecutive lung transplant patients were reviewed. Each underwent clinical swallowing evaluation early after surgery; 149 patients underwent additional fiberoptic or videofluoroscopic swallowing evaluation (SE). Results of SE were correlated with BOS, defined by accepted criteria, and mortality using Kaplan-Meier survival curves. Cox proportional hazard modeling assessed preoperative and postoperative variables associated with development of BOS and mortality.

Results. Mean follow-up was 920 ± 560 days. The SE identified tracheal aspiration and (or) laryngeal penetra-

tion in 70.5%. Preoperative tobacco abuse, gastroesophageal reflux, and cardiopulmonary bypass independently predicted oropharyngeal dysphagia. Peak FEV₁ (forced expiratory volume in the first second of expiration) alone independently predicted BOS (hazard ratio 0.98; confidence interval 0.975 to 0.992, $p < 0.0001$); oropharyngeal dysphagia was not associated with BOS. Independent predictors of mortality by multivariable analysis were ventilator dependence ($p = 0.038$) and peak FEV₁ ($p < 0.0001$); normal SE was associated with improved survival (hazard ratio 0.13; confidence interval 0.03 to 0.54, $p = 0.03$).

Conclusions. Oropharyngeal dysphagia, often overlooked on clinical examination, is common after lung transplantation. Normal deglutition may improve survival after lung transplantation, but oropharyngeal dysphagia does not independently affect BOS. Institution of protocols aimed at identifying previously unrecognized dysphagia may improve results of pulmonary transplantation.

(Ann Thorac Surg 2010;90:1622-9)

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Pulmonary transplantation is now considered the definitive treatment for end-stage lung disease of various etiologies in appropriate patients. Better surgical techniques, donor organ management protocols, improved immunosuppressive regimens, and other advances have significantly improved early and late survival after lung transplantation (LT) recently [1-3]. Despite these successes, long-term allograft function remains affected by chronic graft dysfunction, often termed bronchiolitis obliterans and considered a form of chronic rejection [1, 4]. Histologically characterized by airway scarring and fibrosis, bronchiolitis is recognized clinically by the obstructive pattern seen on pulmonary

function testing [4, 5]. An accepted surrogate marker for bronchiolitis is based on reduced forced expiratory volume in 1 second (FEV₁) and is termed the bronchiolitis obliterans syndrome (BOS) [6].

Several factors impact 1-year and 5-year survival after LT, but few modifiable risk factors for mortality or for BOS development have been identified [1]. Gastroesophageal reflux is recognized as an important contributor to BOS development [7-9], and surgical treatment of reflux with fundoplication has been shown to reduce BOS and chronic allograft dysfunction [7, 9, 10]. Similarly, it is increasingly recognized that new-onset oropharyngeal dysphagia (OPD) is common after various thoracic surgical procedures, including LT [11-17]. In these contexts, OPD is associated with increased postoperative complications including pneumonia, which has been associated with increased operative mortality [13, 18]. We have previously shown that OPD is surprisingly common after

Accepted for publication June 18, 2010.

Presented at the Poster Session of the Forty-sixth Annual Meeting of The Society of Thoracic Surgeons, Fort Lauderdale, FL, Jan 25-27, 2010.

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Abbreviations and Acronyms

BOS	= bronchiolitis obliterans syndrome
FEES	= fiberoptic endoscopic evaluation of swallowing
FEV ₁	= forced expiratory volume in 1 second
LT	= lung transplantation
OPD	= oropharyngeal dysphagia
SE	= swallowing evaluation
VCP	= vocal cord paralysis
VFSS	= videofluoroscopic swallowing study

LT and associated with increased perioperative morbidity [11]. In addition, we have developed a protocol used to assess and manage OPD after LT. Similar practice applications have reduced complications in patients at high risk for tracheal aspiration and attendant complications [17, 19].

Therefore, the present study was performed to determine the impact of previously unrecognized OPD on development of BOS and mortality after LT. We hypothesized that OPD is associated with BOS, and that this association would be further manifest by increased long-term mortality after LT.

Material and Methods

After Institutional Review Board approval, which waived requirements for individual patient consent, records of 263 consecutive lung transplantation recipients were reviewed. Patients underwent LT at Duke University Medical Center between January 2001 and July 2005 using standard surgical techniques. No LT recipients from this time period were excluded from the review. Preoperative demographic data and perioperative and postoperative details were recorded for each patient. Outcomes data were supplemented by accessing the Social Security Master Death Database. Follow-up was 100% complete.

Swallowing Evaluation and Management Protocol

The protocol used for assessing swallowing abnormalities after LT has been described previously [11]. All patients underwent speech pathology consultation early in the postoperative course. Initial examination, typically performed within 48 hours of endotracheal extubation, consisted of a clinical bedside assessment of swallowing, with the speech pathologist evaluating the patients' ability to manage various food boluses. Early in our experience, swallowing evaluation (SE) was undertaken when findings suggestive of OPD (poorly coordinated processes of deglutition, stimulation of cough upon swallowing, ineffectual cough, etc) were noted on clinical examination. In these cases, SE may have been delayed until gross deficiencies were resolved.

As experience with the protocol increased and as recognition of subtle abnormalities of deglutition increased, the overwhelming majority of patients underwent provocative SE by either endoscopy FEES (fiberoptic endo-

scopic evaluation of swallowing) or cineradiography (VFSS; videofluoroscopic swallowing study) [11]. Most patients (87.9%) were assessed using FEES based on several benefits compared with VFSS including portability, cost-effectiveness, and absence of radiation, while remaining equally sensitive to swallowing abnormalities and preventing complications associated with dysphagia [20, 21]. Initial SE was performed at a mean of 19 ± 20 days after LT (range, 1 to 138 days); 47.1% of the total cohort (n = 124) underwent SE within 30 days of LT, as previously reported [11].

By protocol, results of SE guided dietary advancement postoperatively. When initial SE was positive, typically by tracheal aspiration or laryngeal penetration, oral intake was restricted, aspiration precautions were enforced, and aggressive pulmonary toilet maneuvers were emphasized. Because both aspiration and penetration have been associated with increased rates of pneumonia compared with patients with normal swallowing [22], we did not distinguish between these two findings for the purpose of patient care or subsequent data analysis. Serial SE procedures were performed until the identified deficit resolved. As previously reported, those with identified OPD underwent a mean of 2.2 examinations to resolution of OPD, which occurred at a mean of 92 days (median 29.5 days) [11]. In select cases, rehabilitative speech therapy was employed, and otolaryngology consultation was necessary in 31 cases due to recurrent laryngeal nerve injury with vocal cord paralysis (VCP). Twenty-two patients with VCP underwent vocal cord medialization.

When the SE was negative, implying normal swallowing mechanisms, the appropriate form of dietary intake was prescribed and aggressive pulmonary toilet measures were followed, as per standard postoperative LT care. Therefore, the developed protocol allowed customization of postoperative details including dietary advancement and airway protective measures, which were felt to impact the risk of airway and allograft exposure to aspirated material.

Assessment of BOS

Based on locally developed protocols, each patient underwent routine FEV₁ measurement at each clinic visitation or with deteriorating respiratory status. Each FEV₁ measurement was compared with the maximal FEV₁ achieved after LT. By convention, BOS was defined as 20% or greater decrease in FEV₁ relative to the maximal FEV₁ achieved postoperatively [6]. Bronchiolitis obliterans syndrome was considered a binary variable for statistical purposes.

Data Analysis

Baseline characteristics and event rates were reported as means \pm standard deviation and data ranges for continuous variables and frequencies with proportions for categorical variables (Table 1). Descriptive data were compared using the Kruskal-Wallis or Wilcoxon rank sum test for continuous and ordinal variables. Survival analysis was performed using standard Kaplan-Meier techniques on an intention-to-treat basis. Kaplan-Meier sur-

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