Preoperative Performance Status Impacts Perioperative Morbidity and Mortality After Lung Transplantation

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Background. **The aim of this study was to determine which factors predict poor postoperative performance and to evaluate the impact of these variables on 1-year mortality.**

Methods. **The United Network for Organ Sharing database was queried for adult patients undergoing lung transplantation (LTx) from 2007 to 2011. Patients were divided based on their preoperative Karnofsky Performance Status score (KPS) into 3 groups. Regression analysis was conducted to determine which factors predicted poor postoperative performance. Cox modeling was utilized to identify which of these factors was associated with an increased risk of mortality after LTx.**

Results. **Of the 7,832 patients included in this study, 30.1% required complete assistance, 57.7% required partial assistance, and 12.3% needed no assistance preoperatively. Postoperative KPS was assessed at a mean of 2.6 ± 1.5 years after transplant. A number of factors, including primary graft failure, redo and single LTx, and intensive care unit status prior to LTx independently predicted poor performance; whereas a body mass index 18.5 kg/m^2 or greater and some degree of preoperative functional independence were protective. Age greater than 60 years, donor tobacco use, and intensive care unit status, extracorporeal membrane oxygenation support, and mechanical ventilation prior to LTx were associated with an increased risk 1-year mortality, while preoperative functional independence and a body mass index 18.5 to 30 kg/m^2 were protective.**

Conclusions. **This is the largest known study to examine the issue of disability in LTx and its relationship to mortality. Preoperative performance status significantly impacts post-LTx mortality. Patient optimization may improve outcomes and should alter decisions regarding graft selection and allocation.**

(Ann Thorac Surg 2015;99:482–9)

Lung transplantation (LTx) offers patients with end-stage pulmonary disease, and limited alternative therapeutic options, a means for improving quality of life [1, 2]. Early studies utilized various quality of life metrics as surrogates for posttransplant function; however, these demonstrated an inability to predict postoperative outcomes [3, 4]. The Karnofsky Performance Status (KPS) scale, initially developed to quantify the functional status of cancer patients after an intervention, is a proven predictor of response to therapy and survival [5]. Extensive use of KPS in abdominal solid-organ transplantation occurs, and recent studies have validated KPS as an accurate predictor of outcomes after redo LTx [6]. The true clinical applicability of the KPS in the modern era of LTx remains unknown as large studies do not exist in the literature.

Accordingly, we utilized the United Network for Organ Sharing (UNOS) database to evaluate whether preoperative performance status influenced patient outcomes after LTx. Additionally, we sought to not only determine which donor and recipient-specific factors predicted poor postoperative performance but to also assess the impact of these variables on 1-year mortality.

Material and Methods

Population

Patients aged 18 years or older who underwent LTx between 2007 and 2011 were identified in the UNOS database. Initial stratification into 3 cohorts by the KPS score as entered at the time of LTx was performed as follows: (1) those needing complete assistance; (2) partial assistance; or (3) no assistance; which correlated to scores of 10 to 40, 50 to 70, and 80 to 100, respectively (Table 1). Patients undergoing simultaneous heart-lung transplants and those without documented preoperative and postoperative Karnofsky scores were excluded from

Accepted for publication Sept 12, 2014.

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0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.09.038

Abbreviations and Acronyms

BMI = body mass index
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
KPS = Karnofsky performance status
LAS = lung allocation score
LTx = lung transplantation
PGF = primary graft failure
UNOS = United Network for Organ Sharing

analysis. The current study was approved by The Johns Hopkins Institutional Review Board.

Data and Analysis

Baseline donor and recipient characteristics as well as transplant-related outcomes were compared between the 3 performance status cohorts. Recipient-specific variables included age, lung allocation score (LAS), sex, race, body mass index, single or bilateral LTx, serum bilirubin, etiology of end-stage lung disease, diabetes, mechanical ventilation and extra-corporeal membrane oxygenation (ECMO) prior to transplant, and intensive care unit (ICU) status at the time of transplant. Donor-related variables included age, body mass index, tobacco use, race, and sex. Transplant outcomes included new onset hemodialysis, postoperative stroke, primary graft failure (PGF), KPS score 40 or less, and 30-day and 1-year mortality. Continuous variables (mean $\pm$ standard deviation) were compared using a one-way analysis of variance. Categoric variables (number and percentage) were analyzed using Pearson χ^2 analysis. Significance was established at a p value of less than 0.05.

Primary outcomes studied were post-LTx survival and postoperative functional status as measured by the KPS. Postoperative KPS scores are entered at the time of most recent follow-up. One-year overall survival was evaluated by the Kaplan-Meier method, with comparison between performance status cohorts provided by the log-rank test.

Univariate logistic regression analysis was performed to determine the influence of each donor, recipient, and transplant-related variable on postoperative performance. This sub-analysis was restricted to patients who were alive at most-recent follow-up. Covariates associated with poor postoperative performance ($p < 0.2$) were then analyzed in multivariable logistic regression modeling. Conversely, an additional model was constructed, with identical limitations for covariate inclusion, in order to identify factors that resulted in an improvement in the functional status of those with the lowest preoperative KPS scores (0 to 40). These separate models were built in a forward and backward fashion using the Akaike information criterion, likelihood ratio test, and Homer-Lemeshow goodness-of-fit test.

Univariate Cox proportions hazards regression modeling was performed to determine the association of each of the aforementioned variables on 1-year mortality. Covariates were then included in a similar fashion into a multivariable Cox proportional hazard regression model. Stata 12.1 (StataCorp, College Station, TX) was utilized for statistical analysis.

Results

Demographics and Recipient-Specific Factors

A total of 7,941 adult patients underwent LTx during the study period; 109 patients were excluded due to missing preoperative KPS scores. Thus, 7,832 were ultimately included for analysis. Stratifying for preoperative functional status, 12% of patients needed no assistance, 58% needed partial assistance, and 30% of patients needed complete assistance. Those needing partial assistance were older than both of the other cohorts ($p < 0.001$). The LAS at the time of match was higher ($p < 0.001$) and the incidence of redo-LTx greater ($p < 0.001$) in those with the worst functional status at transplant. Similarly, this

Table 1. Karnofsky Performance Scale Scores and Their Clinical Equivalents

Variable	Score	Clinical Presentation
Those needing no assistance	100	Normal to no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Those needing partial assistance	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his/her personal needs.
	50	Requires considerable assistance and frequent medical care.
Those needing complete assistance	40	Disabled, requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick, hospital admission necessary, active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead.

Modified from: (1) Crooks V, Waller S, Smith T, Hahn TJ. The use of the Karnofsky Performance Scale in determining outcomes and risk in geriatric outpatients. J Gerontol 1991;46:M139–144. (2) Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. J Clin Oncol 1984;2:187-93.