Timing and Frequency of Unplanned Readmissions After Lung Transplantation Impact Long-Term Survival

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Background. Adverse events that require hospital readmission frequently occur long after lung transplantation (LT) that has been successfully performed. We sought to identify the causes and rate of unplanned readmissions after LT and to determine whether unplanned readmissions have a significant impact on post-LT survival.

Methods. We retrospectively reviewed the outcomes in 174 LT recipients who underwent LT at our center from June 2005 to May 2014. The median follow-up period was 38 months (range, 17 to 72 months).

Results. One hundred sixty (92%) of the 174 recipients were readmitted 854 times (5.3 times per patient). The median time to first readmission was 71 days (interquartile range [IQR], 28 to 240 days), and the median hospital length of stay at readmission was 3 days (IQR, 2 to 6 days). Freedom from first readmission was observed for 65% of patients at 1 month, 48% at 3 months, 43% at 6 months, and 26% at 12 months. Gender, lung allocation score, body surface area, year of transplantation, air leak longer than 5 days after operation, and allograft function were risk factors for readmission. The causes of readmission included infections (33%), respiratory adverse events (18%), rejection (15%), gastrointestinal events (15%), renal dysfunction (5%), and cardiac events (4%). Patients who died were found to have had early readmissions ($p = 0.04$) and more frequent readmissions ($p = 0.001$).

Conclusions. The first year after LT remains a high-risk period for unplanned readmissions regardless of pretransplantation diagnosis. Readmissions soon after discharge at index hospitalization and multiple readmissions are associated with an increased risk of mortality.

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Lung transplantation (LT) has emerged as a widely accepted therapy that can improve survival rates and quality of life for patients with end-stage pulmonary diseases. Advances in surgical techniques, lung preservation strategies, induction and maintenance immunosuppression, and prevention and management of infections have decreased short-term and long-term mortality over the past decades such that statistical data from the International Society for Heart and Lung Transplantation (ISHLT) show a 53% 5-year survival rate and a 32% 10-year survival rate for LT recipients [1]. However, LT recipients remain at risk for the development of numerous post-LT adverse events resulting from sustained exposure to intense immunosuppressive regimens and other morbidities such as serious infections, and the rates of adverse events increase significantly over time [1–4]. These adverse events could result in unplanned hospital readmissions, which reduce quality of life for LT recipients and present a significant financial burden for both patients and the health care system. Additionally, LT recipients frequently have significant pretransplantation comorbidities that may become problematic after LT and require unplanned hospital readmission.

The purpose of our study was to investigate the incidence and causes of all unplanned hospital readmissions after LT at our institution, to evaluate the factors associated with readmission, and to determine whether such unplanned readmissions are associated with a reduction in recipients' survival. We also sought to assess the relative cost of readmissions and to correlate cost with

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causes of hospitalization. We suggest that a better understanding of the causes of readmissions may facilitate the identification of specific targets for quality improvement after LT, and unplanned readmission rates may prove useful as a metric that reflects quality of care after primary LT.

Patients and Methods

A total of 327 patients received lung transplants between June 2005 and May 2014 at the University of Wisconsin Hospital and Clinics (UWHC). Ten patients who died during their index hospitalization and 143 veterans who underwent transplantation at UWHC but were followed up by the Veterans Administration System were excluded from the analysis. The median follow-up period was 38 months. This study was approved by our institutional review board (IRB), and data were prospectively acquired and maintained in our IRB-approved database. Readmissions were evaluated through July 2015. Factors associated with readmissions and related costs were examined. Primary graft dysfunction (PGD) was defined and graded according to the ISHLT definition [5]. The severity of PGD was graded according to the ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2). Grade 3 PGD was defined as a PaO_2/FiO_2 ratio below 200 mm Hg.

Overall survival time was calculated from the date of transplantation to the date of last follow-up visit or death. Cumulative event rates were calculated by the method of Kaplan and Meier [6]. Conditional survival (CS) is the probability of surviving an additional y years, given that the person has already survived x years, or CS(y/x). When S(t) is the traditional actuarial life-table survival at time t, CS can be expressed as: $CS(y/x) = S(x+y)/S(x)$. For example, to compute the 5-year CS for a patient who has already survived 1 year from diagnosis, the survival at 5 + 1 years, S(6), is divided by the survival at 1 years, S(1) [7–10].

Costs were defined as direct in-patient hospital charges (costs associated with providing direct patient care, including professional charges) to most accurately reflect the direct patient care costs. Costs not associated with patient care departments (eg, environmental services, fiscal, reprocessing) were excluded. The administrative database used by the hospital to calculate costs for patients is Med Assets Alliance for Decision Support. The major goal of this analysis was to compare the direct patient care–associated costs for each cause of post-LT readmission.

Statistical Analysis

Continuous variables are represented as mean ± standard deviation, and categoric variables are represented as number and percentage. Continuous variables were compared with the t test. Categoric variables were compared with the χ^2 test.

The Kaplan-Meier survival method was used to assess post-LT survival and readmission. Log-rank tests were used to assess statistical significance in survival

differences between the groups. Cox regression was used to assess factors (age, gender, body mass index, pretransplantation diagnosis, operation type, hospital length of stay [LOS], and intensive care unit [ICU] LOS) potentially associated with readmission. Cox regression was further used to determine whether readmission within 60 days or readmission frequency within the first year had an effect on patient survival. Two-sided p values less than 0.05 were considered statistically significant. All analyses were performed with the IBM SPSS statistical software program (IBM SPSS Statistics for Windows, version 21.0, IBM Corp, Armonk, NY).

Results

The mean age of our study population was 51 ± 14 years, and 55% of them were men (Table 1). The indications for transplantation included interstitial lung disease/pulmonary fibrosis (47%), chronic obstructive pulmonary disease (13%), emphysema (12%), bronchiectasis (11%), cystic fibrosis (10%), and other (7%) (Table 1). Half of the transplants were bilateral. By the end of the follow-up period, 160 (92%) of the 174 recipients in our study population had been readmitted 854 times (5.3 times per patient) for a total of 4,773 hospital days. The median follow-up period was 38 (interquartile range [IQR], 17 to 72) months. The median time from discharge at index hospitalization to first readmission was 71 (IQR, 28 to 240) days. The median hospital LOS at readmission was 3 (IQR, 2 to 6) days. Freedom from first readmission was observed for 65% of patients at 1 month, 48% at 3 months,

Table 1. Patient Characteristics

Characteristic	Value
No. of patients	174
Age (years)	51 ± 14
Gender	
Female	79 (45%)
Male	95 (55%)
BMI	24 ± 5
Pretransplantation diagnosis	
ILD/PF	82 (47%)
COPD	22 (13%)
Emphysema	21 (12%)
Bronchiectasis	19 (11%)
CF	17 (10%)
Other	13 (7%)
Operation	
Single	87 (50%)
Bilateral	87 (50%)
Hospital LOS at transplantation (days)	13 (10, 17)
ICU LOS at transplantation (days)	2 (1, 4)

Data are presented as mean ± standard deviation or number (%) or median (interquartile range).

BMI = body mass index;   CF = cystic fibrosis;   COPD = chronic obstructive pulmonary disease;   ICU = intensive care unit;   ILD/PF = interstitial lung disease/pulmonary fibrosis;   LOS = length of stay.