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Utility of the 6-Minute Walk Test Following Lung Transplantation

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ABSTRACT

Background: The 6-minute walk test (6-MWT) has replaced standard cardiopulmonary exercises for the evaluation of lung disease. However, data on the utility and characteristics of the 6-MWT following lung transplant are lacking. This study aimed to determine if 6-MWT distance has a normal distribution at 6 months post-transplant and if lower 6-MWT distance was predictive of all-cause mortality.

Methods: We performed a retrospective chart review of 6-MWT data on all patients who were lung transplant recipients at Ochsner Medical Center between 2000 and 2005. Forty-nine lung transplant recipients completed a 6-MWT at 6 months following transplant. Of these 49 patients, 34 had completed both the 6-month and 12-month 6-MWT, and data from these were used to evaluate change in distance walked over time.

Results: The mean age was 46 $\pm$ 16 years, 57% were female, and 69% received a bilateral lung transplant. Normal distribution by Kolmogorov-Smirnov was demonstrated for 6-MWT distance at 6 months ($P = 0.873$). Mean distance walked improved from 348 $\pm$ 15 m to 478 $\pm$14 m at 12 months ($P = 0.0001$). The 6-MWT distance at 6 months was not a predictor of survival (OR = 1.002).

Conclusions: Distance for the 6-MWT followed a normal distribution following lung transplant, and distances walked continued to improve for a year following transplant. Although 6-MWT distances are not a predictor of survival, other components of the test may strengthen the predictive value for morbidity and mortality post-transplant.

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INTRODUCTION

The 6-minute walk test (6-MWT) has been used in pulmonary diseases such as chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, sarcoidosis, and pulmonary hypertension to assess functional status, response to therapy, and prognosis.[1-5] The procedure is simple, inexpensive, reproducible, and well received by patients and has replaced standard cardiopulmonary exercises for the evaluation of lung disease. The 6-MWT has been shown to better reflect daily life activities of the subjects than other walk tests.[6] It evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, peripheral circulation, blood, neuromuscular units, and muscle metabolism.[7] Little has been published about the utility of the 6-MWT following transplant. Riess et al[8] reported decreased 6-MWT distance in kidney transplant patients; the test also has been shown to be a safe, practical way to assess functional status following heart transplant.[9] Because lower 6-MWT distance has been shown to correlate with worse survival in patients with pulmonary hypertension, idiopathic pulmonary fibrosis, and COPD, 6-MWT has become one of the parameters used to calculate the lung allocation score for patients awaiting lung transplant.[10,11] However, data are lacking on the utility and characteristics of the 6-MWT in lung transplant recipients. We are not aware of any studies evaluating the utility of the 6-MWT as a predictor of outcomes following lung transplant or normative values for the 6-MWT for this patient population. This study was conducted to describe the results of the 6-MWT in our cohort of patients following lung transplant. The aims of the study were to (1) determine if 6-MWT distance has a normal distribution at 6 months following transplant and (2) determine if lower 6-MWT distance was predictive of all-cause mortality.

METHODS

The study was approved by the Institutional Review Board of the Ochsner Medical Center. We performed a retrospective chart review of 6-MWT

data on all patients transplanted at our institution between 2000 and 2005. Forty-nine lung transplant recipients completed a 6-MWT at 6 months following transplant, and 52 patients completed a 6-MWT 12 months following transplant. The 6 MWT was not a standard part of the assessment for all patients following transplant, which led to discordance between the number of completed tests at 6 months and 12 months. The 49 patients with 6-month 6-MWT data were used for analysis. Thirty-four lung transplant recipients completed both the 6-month and the 12-month 6-MWT, and these were used to evaluate change in distance walked over time. Retransplants and lung transplant recipients not surviving 6 months were excluded. The tests, with distances measured in meters, were performed according to the American Thoracic Society guidelines.[5]

Continuous variables were analyzed with a paired *t* test. Categorical variables were analyzed with the chi-square method. The Kolmogorov-Smirnov test was used to test for normality in the cohort regarding distance walked. Patients were assembled into quartiles by distance walked: 1st quartile = 240 to 362 m, 2nd = 362 to 423 m, 3rd = 423 to 480 m, and 4th = 480 to 711 m. Differences between demographic variables were assessed with either the unpaired *t* test or chi-square test as appropriate. The impact of distance walked on survival was assessed in 2 ways. A logistic regression model was constructed to assess the impact of 6-MWT distance on all-cause mortality, controlling for age, gender, race, bilateral vs. single transplant, body mass index, and hypertension. In addition, Kaplan Meier survival curves were constructed by quartiles and differences between groups were tested with the log rank test.

RESULTS

Patient Characteristics

Forty-nine patients took the 6-MWT 6 months following lung transplant. Demographic data are summarized in Table 1. The underlying diagnosis included COPD, pulmonary fibrosis, bronchiectasis, or pulmonary hypertension.

The 6-Minute Walk Test

No complications were reported for any of the patients undergoing the 6-MWT. The mean (±SD) distance walked at 6 months was 426 ± 84.5 m (range, 240-711 m). The 6-MWT distance per quartile is described in Table 2. A normal distribution by Kolmogorov-Smirnov was demonstrated for 6-MWT distance at 6 months ($P = .873$) following transplant (Figure 1). When one compares just the 34 patients that completed both the 6-month and 12-month 6-MWT, there was a significant improvement in 6-MWT distance at 12 months compared to 6 months. The mean distance walked improved from 348 ± 15 m to 478 ± 14 m at 12 months ($P = .0001$). The demographics are reported in Table 3. Twenty-six (77%) of lung transplant recipients improved their 6-MWT distance from 6 to 12 months, 3 (9%) remained

Table 1. Demographics of the 49 Patients Taking the 6-Month 6-Minute Walk Test

Age, y (mean ± SD)	46 ± 16
Gender: Female	57%
Body mass index (mean ± SD)	22 ± 5
Height, inches (mean ± SD)	66 ± 4
RVEF (MUGA) (mean ± SD)	44 ±12
Bilateral lung transplant	69%
Creatinine clearance (mL/min)	103

RVEF (MUGA), right ventricular ejection fraction (multigated acquisition)

Table 2. Distance by Quartile of Distance Walked at 6 Months

Quartile (meters)	Distance (meters), (mean ± SD)
1 (240-362)	329 ± 33
2 (362-423)	390 ± 19
3 (423-480)	457 ± 17
4 (480-711)	538 ± 70

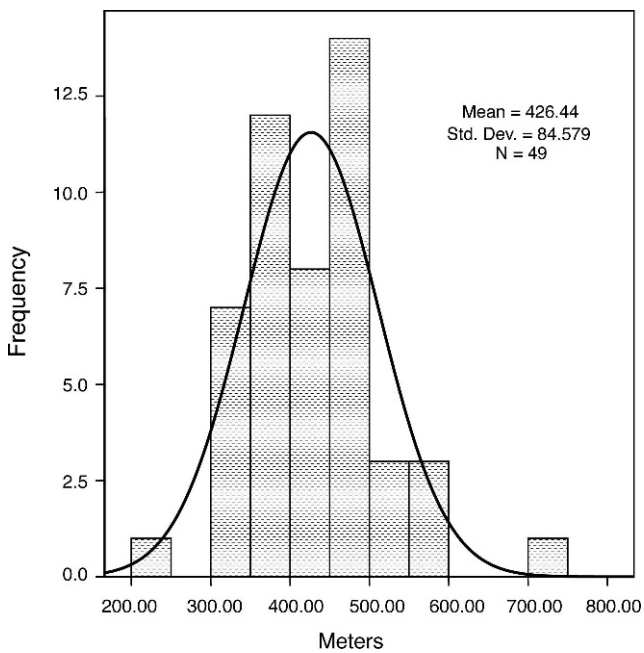

Figure 1. Normal distribution by Kolmogorov-Smirnov for 6-minute walk test distance at 6 months ($P = .873$) following lung transplant.

Table 3. Demographics of Cohort Completing 6-month and 12-month 6-Minute Walk Test (n=34)

Age (mean ± SD)	47 ± 16	
Gender (Female %)	41%	
Bilateral lung transplant	71%	
Diagnosis (%)	IPF 26%	COPD 41%
	CF 30%	BAC 3%

IPF=idiopathic pulmonary fibrosis, COPD=chronic obstructive pulmonary disease, CF = cystic fibrosis, BAC=bronchoalveolar cell carcinoma

the same, and 5 (14%) walked a shorter distance at 12 months.

Predictors of Survival

Kaplan Meier curves showed that the 6-MWT distance at 6 months following lung transplant was not predictive of survival when analyzed by quartiles (Figure 2) or when analyzed with respect to the median distance walked (Figure 3). Using a logistic regression model, adjusted for confounding variables, only bilateral lung transplant was an independent predictor of improved survival with an odds ratio of 0.106. The 6-MWT distance at 6 months was not a predictor of survival (OR = 1.002). Reason for lung transplant was not predictive of survival (Figure 4).

DISCUSSION

The 6-MWT is a safe, quick, and inexpensive measure of functional status that is routinely used in pulmonary diseases. The 6-MWT following lung transplantation is feasible and follows a normal distribution at 6 months. The distance walked

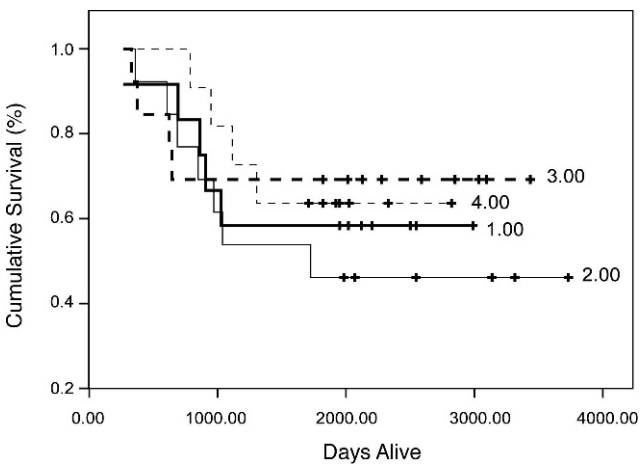

Figure 2. Survival curves based on 6-minute walk test distance at 6 months following lung transplant analyzed by quartiles. 1=below 1st quartile; 2=between 1st and 2nd quartile; 3=between 2nd and 3rd quartile; 4=above 3rd quartile.

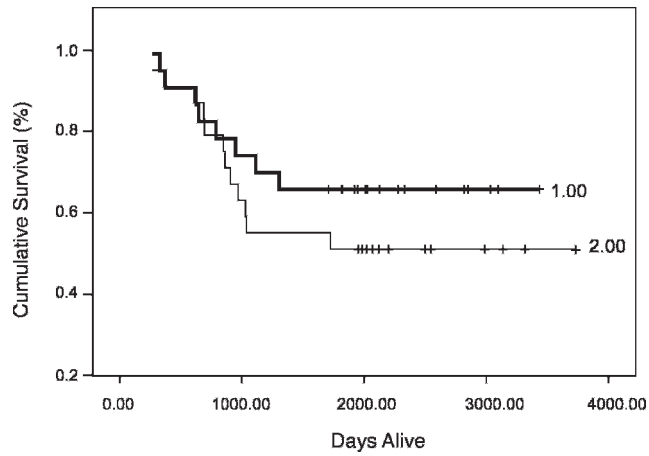

Figure 3. Survival curves based on 6-minute walk test distance at 6 months following lung transplant analyzed by median distance walked. 1=below median; 2= above median.

continues to improve during the first year in patients who have undergone lung transplant.

Bilateral lung transplant was consistently the best predictor of survival in our analysis. Lower distance walked during 6-MWT at 6 months following lung transplant was not predictive of all-cause mortality in our cohort of lung transplant recipients. However, there was a trend to worse outcomes in the cohort that had lower 6-month 6-MWT distances than the median when compared with the cohort that walked longer distances than the median. This trend was not always consistent when comparing different quartiles because of the small sample sizes. Although we did not find that 6-MWT distance predicted outcomes, further studies are warranted to assess if a larger sample size or other features of the 6-MWT beyond distance walked have prognostic significance. For example, assessing 6-MWT distance prior

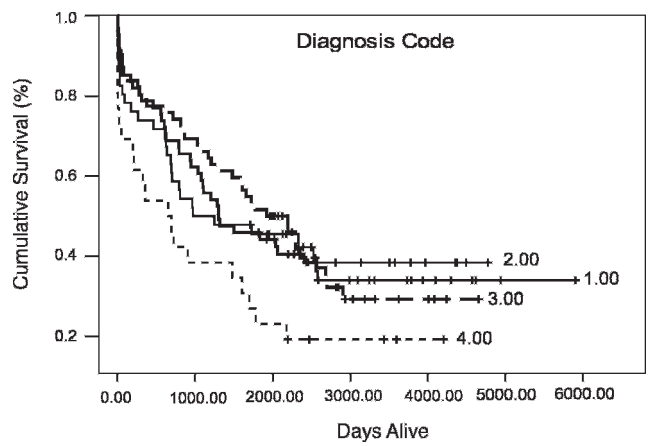

Figure 4. Survival curves for patients with the 4 diagnostic categories. 1=cystic fibrosis/bronchiectasis; 2=pulmonary fibrosis; 3=chronic obstructive pulmonary disease; 4=other.

to 6 months, change in distance over time, or desaturation during the test may be predictive of outcomes. The 6-MWT distance may also have some predictive value if used in combination with other predictive measures. In addition, the 6-MWT may have some predictive value for patients who develop bronchiolitis obliterans syndrome. Further study is required to delineate which factors affect 6-MWT distance following lung transplant, but understanding normative values for 6-MWT distance following transplant and expected improvement over time is an important step to exploring the utility of the 6-MWT in this situation.

The present study has several limitations. First, it is a retrospective study with a relatively small sample size of mostly Caucasian patients. Although we have some understanding of the factors that affect 6-MWT distance in the normal population (ie, height, body mass index, age, and gender), we do not know which factors may influence the distance walked by patients following transplant.[12]

In summary, the 6-MWT distance follows a normal distribution when administered after lung transplant, and distances walked continue to improve for a year postoperatively. Although the 6-MWT distance was not a predictor of survival, other components of the test may strengthen the predictive value for morbidity and mortality following transplant.

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