Pulmonary Function Testing Pre–heart Transplant Predicts Posttransplant Survival

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Introduction. Although pulmonary function testing (PFT) is typically performed for heart transplant evaluation, the prognostic utility of PFTs after transplantation is unknown. We evaluated whether PFT parameters were correlated with outcomes following heart transplantation. **Methods.** International Society for Heart and Lung Transplantation Thoracic Organ Transplant Registry data were utilized. Survival was assessed using Kaplan-Meier method and compared via log-rank test. Cox proportional hazard modeling was used to evaluate univariate and multivariate predictors of survival. **Results.** Eight hundred two patients pretransplant PFT data were available for evaluation. Forced expiratory volume in 1 s (FEV1) < 50% predicted ($P < 0.0001$), and forced vital capacity (FVC) < 50% predicted each had significantly higher mortality ($P = 0.001$) compared with patients with FEV1 or FVC 50%–80% or >80%. FEV1/FVC < 0.7 was not associated with increased mortality. FEV1 and FVC below 50% both predicted longer lengths of stay ($P = 0.028$ for FEV1 and $P = 0.0075$ for FVC). After adjusting for male gender, age, body mass index, smoking history, chronic obstructive pulmonary disease, creatinine, albumin, and total bilirubin, FEV1 < 50% (hazard ratio, 4.91; $P < 0.0001$; 95% confidence interval, 2.69-8.94) and FVC < 50% (hazard ratio, 2.75; $P = 0.003$; 95% confidence interval, 1.4-5.4) both remained independent predictors of mortality. **Conclusions.** Abnormal pulmonary function (FEV1 or FVC below 50% of predicted) pre–heart transplantation is associated with increased mortality and longer lengths of stay posttransplant.

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INTRODUCTION

Both restrictive and obstructive lung disease are common comorbidities in the heart failure population regardless of smoking status or history of chronic obstructive pulmonary disease (COPD).[1,2] Prior studies have demonstrated a correlation between the severity of pulmonary function testing (PFT) abnormalities and severity of heart failure, with several pathophysiological mechanisms proposed—increased airway resistance leading to compression and reduced airway compliance, alveolar damage, and direct mechanical compression from cardiomegaly.[3-7] Although PFT parameters have been shown to predict the development of systolic heart failure[8,9] and clinical outcomes,[10-12] little information is available regarding the utility of PFTs in predicting outcomes following heart transplantation (HT).

Previous studies have suggested that significant obstructive pulmonary disease is defined as a forced expiratory volume in 1 s (FEV1) of less than 1 L as an absolute contraindication for HT and a FEV1 less than 40% as a relative contraindication but without supporting data.[13] An analysis using the International Society for Heart and Lung Transplantation's (ISHLT) 2017 heart transplant registry reported that only 5.1% of patients who underwent HT between January 2009 and June 2016 had a prior history of COPD, which is an increase compared with 3.6% from 2004 to 2008.[14] This report also showed that survival following HT was worse in patients with a history of COPD compared with those without COPD.[14] Given that 45.8% of recipients during this same time period have a history of cigarette use, the likelihood of

developing clinically evident COPD following HT is not negligible and underscores the need in further establishing PFT parameters rather than clinical diagnoses to identify patients at risk of worse outcomes following HT.

Although PFTs continue to be frequently performed as part of an evaluation for heart transplant candidacy, limited data on whether PFTs predict posttransplant outcomes and what values should be used as relative contraindications to transplant. Kobashigawa et al at Cedars-Sinai have presented 2 retrospective, single-center abstracts evaluating pretransplant PFTs and outcomes following HT and identified forced expiratory volume in 1 s to forced vital capacity ratio (FEV1/FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO) as important parameters for post–orthotopic heart transplantation prognosis. (Patel) Patients with FEV1/FVC < 70% and DLCO < 60% had significantly longer intubation times and reduced survival at 3 y compared with patients with FEV1/FVC > 70% and DLCO > 60%.[15]

We aimed to evaluate the impact of common PFT measurements (FEV1, forced vital capacity [FVC], FEV1/FVC, and DLCO) captured pretransplant on survival, duration of intubation, and length of stay following HT.

MATERIALS AND METHODS:

Patient Population

This retrospective study utilized deidentified data collected in the ISHLT International Thoracic Organ Transplant (TTX) Registry, which receives data from national and multinational organ and data exchange organizations as well as individual centers. A total of 481 heart transplant centers, 260 lung transplant centers, and 184 heart-lung transplant centers have reported data to the Registry since its inception, accounting for approximately 80% of the worldwide thoracic transplant activity. The dataset included 62 237 patients who underwent HT between 2004 and June 2017. These patients were evaluated for availability of pulmonary function test results. This study utilized deidentified data from an international registry and was thus exempt from institutional board review.

Clinical Variables and Definitions

Data elements collected in the International Thoracic Organ Transplant Registry can be found in detailed spreadsheets on the Registry's website (http://ishlt.org/registries/ttx-registry). Submission of core donor, recipient, and transplant procedure variables are required at baseline and at annual follow-up. Submission of PFT data within the TTX Registry is completely voluntary and as such completeness of data that relies on voluntary submission may vary. Survival data were available for all patients included in this study. Values for FEV1 and FVC are entered as percent predicted and for FEV1/FVC as the calculated ratio of FEV1 in liters over FVC in liters. Currently, DLCO is not a submitted variable within the TTX Registry and thus not available for evaluation within this study.

For analysis, patients were divided into groups based on common cut points of grading severity as defined by the Global Initiative for Chronic Obstructive Lung Disease executive summary.[16] For FEV1 and FVC, patients were grouped as <50% predicted (severe), 50%–79% predicted (moderate), and ≥80% predicted (mild). For FEV1/FVC, patients were grouped as ≥0.7 or <0.7.

Statistical Analysis

Descriptive statistics (means, standard deviations, counts, and percentages) were used to summarize the data. The independent sample t-test was used to compare continuous measures between the 2 groups. Fisher's exact test was used to compare categorical measures between groups. Overall survival, censored at 5 y, was determined by the Kaplan-Meier method and compared using log-rank testing. Comparison of survival curves was done using the log-rank test. Cox proportional hazards regression modeling was used to assess for univariate and multivariate predictors of overall survival. Any factor on univariate analysis with a $P \leq 0.10$ was entered into the multiple regression model. The variables were entered into the baseline univariate model included the following: age, body mass index (BMI), male sex, history of smoking, history of COPD, albumin, creatinine, total bilirubin, and FEV1 and FVC < 50% predicted. These variables were selected based on the availability within the TTX Registry and previous associations with poor outcomes following HT. Based on the results of the univariate analysis, the following variables were entered into the baseline multivariate model: age, creatinine, total bilirubin, male sex, and FEV1 and FVC < 50% predicted. All analyses were done using SAS, Version 9.4 (SAS Institute, Cary, NC). A $P < 0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics and Pulmonary Function Parameters

Of the 62 327 patients available in the TTX Registry, a total of 802 patients (1.3%) were identified with paired FEV1 and FVC values available for evaluation. Of these 802 patients, only 475 patients had a FEV1/FCV value that had also been submitted and was available for inclusion. The mean age of patients was 49.3 (±14.6) y, 183 (22.8%) were female, and 30 (3.8%) had a history of COPD before transplant. Additional baseline characteristics based on data available within the TTX Registry are listed in Table 1. Given that a large number of patients in the registry had incomplete or missing PFT data, between group comparisons were made of those patients included in this study versus those excluded to ensure our patients were representative of the entire population. Although statistically significant differences were present, these differences were not clinically meaningful. Complete between group comparisons can be found in the Supplemental Materials, SDC, http://links.lww.com/TXD/A345.

Spirometry and Posttransplant Survival

Overall group survival at 1, 3, and 5 y was 82% (79%–85%), 80% (76%–82%), and 76% (72%–80%), respectively (Figure 1). Patients with an FEV1 < 50% before transplantation had significantly lower survival at 5 y compared with patients with FEV1 50%–80% or >80% ($P < 0.0001$) (Figure 2). In patients with an FEV < 50%, overall survival at 1, 3, and 5 y was 56% (43%–68%), 54% (41%–66%), and 54% (41%–66%) compared with 88% (83%–91%), 83% (78%–87%), and 80% (73%–84%) in patients with FEV1 > 80%. Similarly, patients with an FVC < 50% before transplantation had significantly worse survival at 5 y compared with patients with FVC 50%–80% or > 80% ($P = 0.001$) (Figure 3). In patients with an FVC < 50%, overall survival at 1, 3, and 5 y was 64% (49%–76%), 61% (45%–74%), and 61% (45%–74%) compared

TABLE 1.

Relevant baseline characteristics of the evaluated cohort

Variable	TTX Registry (802 patients)
Age, y (SD)	49.3 (15.6)
Female sex, N (%)	183 (22.8)
BMI, kg/m² (SD)	26 (5)
History of tobacco use, N (%)	383 (48)
COPD, N (%)	30 (3.8)
Creatinine, mg/dL (SD)	1.4 (1.4)
Albumin, g/dL (SD)	4.1 (0.8)
Total bilirubin, mg/dL (SD)	1.2 (1)
FEV1 percent predicted, % (SD)	74.5 (18.6)
FVC percent predicted, % (SD)	77.8 (19.1)
FEV1/FVC, ratio (SD)	79.3 (14.5)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; N, number; TTX, thoracic organ transplant.

with 87% (83%–90%), 83% (79%–87%), and 79% (74%–84%) in patients with FVC > 80%. There was no difference in survival in patients with an FEV1/FVC < 0.7 compared with those patients with an FEV1/FVC ≥ 0.7 (Figure 4).

Univariate and Multivariate Predictors of Mortality

On univariate analysis, FEV1 < 50% predicted, FVC < 50% predicted, male gender, BMI, pretransplant creatinine, and pretransplant bilirubin were significant predictors of posttransplant mortality (Table 2). Utilizing results from the univariate model, multivariate models were then run separately for FEV1 < 50% and FVC < 50% and were adjusted for male gender, smoking history, age, BMI, history of COPD, pretransplant creatinine, pretransplant albumin, and pretransplant total bilirubin. On multivariate analysis, both FEV1 < 50% and FVC < 50% remained independent predictors of posttransplant mortality. Other predictors of mortality were total bilirubin and male gender. Body mass index remained a significant predictor of mortality in the FEV1 model with a trend toward significance in the FVC model (Table 2).

Spirometry and Length of Stay

Reduced FEV1 and FVC below normal were significantly associated with increased lengths of stay following HT (Table 3). On univariate analysis, FEV1 and FVC were predictors of length of stay, with patients with FEV1 ≥ 50% staying 7.9 d less than patients with FEV1 < 50 ($P = 0.04$) and patients with FVC ≥ 50% staying 10 d less than patients with FVC < 50% ($P = 0.02$). Albumin was the only other significant predictor of length of stay with every 1 g/dL increase in albumin associated with 3.9 fewer days in the hospital ($P = 0.02$). On multivariate analysis, FEV1, FVC, and albumin all remained independent predictors of length of stay. After adjusting for albumin, patients with FEV1 ≥ 50% stayed 9.6 d less than patients with FEV1 < 50% ($P = 0.03$), whereas patients with FVC ≥ 50% stayed 10.1 d less than patients with FVC < 50% ($P = 0.03$).

DISCUSSION

In this retrospective analysis of pulmonary function testing before HT, we found that patients with an FEV1 or FVC < 50% predicted before transplantation had significantly increased mortality within the first 5 y posttransplantation. After correction for multiple risk factors, FEV1 and FVC < 50% predicted remained independent predictors of mortality. In this cohort, FEV1/FVC was not found to be a significant predictor of mortality. Based on results from this study and others, we recommend that all clinically stable patients undergo pulmonary function testing as part of their evaluation for HT candidacy. Our data indicate that severe airflow limitation (FEV < 50% and FVC < 50% predicted) should be considered a relative contraindication for HT. Steps to remove potential offending agents or optimizing pulmonary function before consideration for listing are necessary to help improve post-transplant outcomes.

Both chronic and decompensated heart failure are known to cause restrictive and obstructive changes in pulmonary function as well as abnormalities in gas exchange.[4-7,17] The reasons behind these changes in pulmonary function are likely multifactorial and include risk factors like obesity and history of
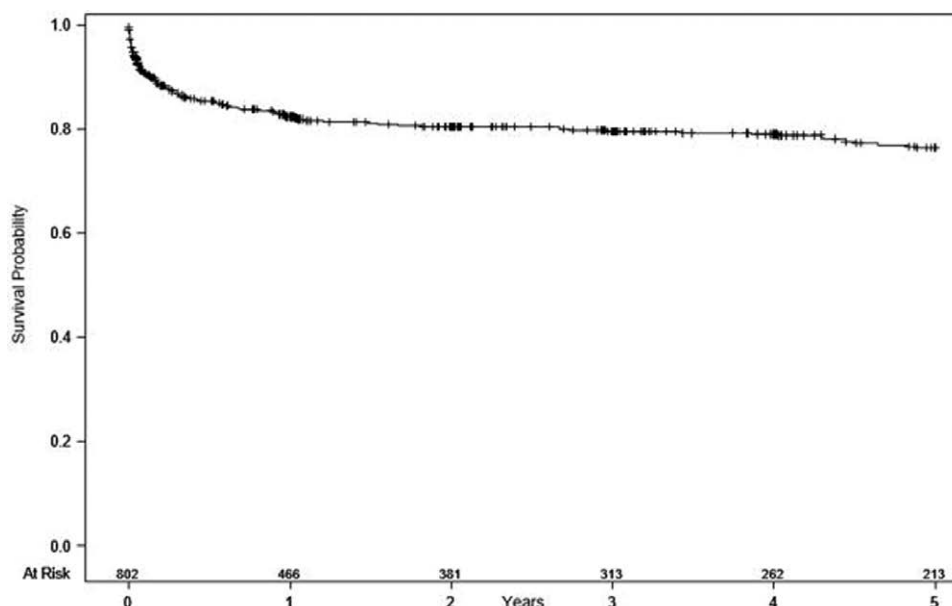

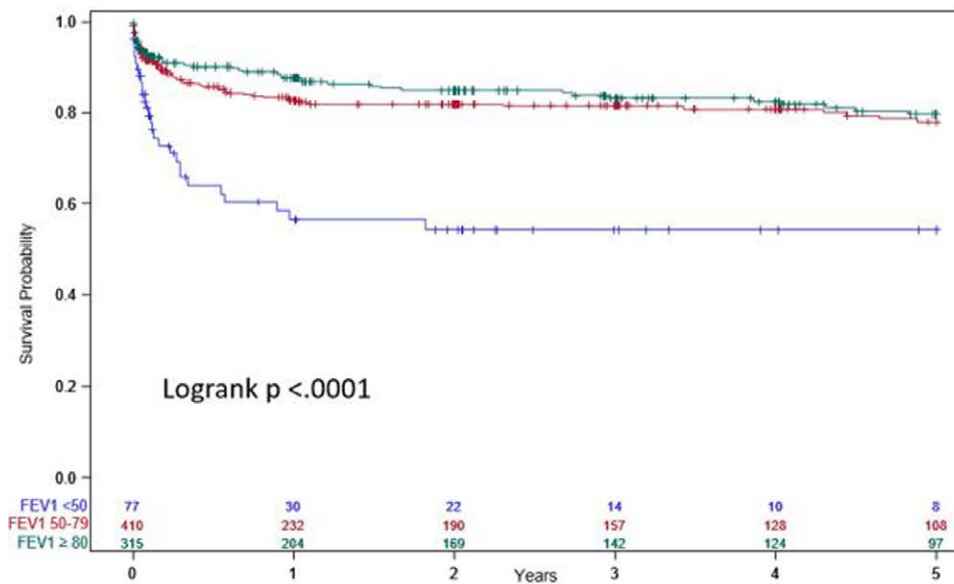**FIGURE 1.** Overall survival following heart transplantation.

FIGURE 2. Patients with FEV1<50% predicted before transplantation have an increased risk of mortality posttransplant. FEV1, forced expiratory volume in 1 s.

tobacco use. Cardiac-specific mechanisms also play a significant role. Cardiomegaly can significantly reduce intrathoracic space and decreases the ability of the lungs to fill sufficiently, leading to reduced exhalatory recoil and reduced maximal expiratory flows.[6,7] Elevation in the pulmonary capillary wedge pressure or pulmonary edema can alter distal airway spaces and injure the alveolar-capillary membrane, reducing DLCO.[5] A reduction in static lung compliance has also been observed in chronic heart failure and can result in alterations of pulmonary function, as measured by total lung capacity.[4]

The present data suggest an increased risk of mortality within the first 5 y following HT in patients with abnormal pretransplant PFTs. Previous studies in heart failure have shown conflicting results regarding the ability of pulmonary function testing in predicting morbidity and mortality, and it is unclear which PFT parameters (FEV1, FVC, FEV1/FVC,

DLCO, etc.) are most clinically relevant. Small, single-center studies have previously shown that reduced FEV1[10-12] as well as reduced FVC and DLCO are associated with increased mortality in a range of heart failure patients.[10] However, another single-center study evaluating the utility of PFTs in predicting outcomes in stage D heart failure patients did not find that FEV1 or FVC were predictors of death, left ventricular assist device implantation, or urgent transplantation.[18]

The only data analyzing pretransplant pulmonary function testing and their impact on posttransplant outcomes are single-center studies primarily published in abstract form. Kobashigawa et al have previously shown that both FEV1/FVC<70% and DLCO<60% pretransplant were associated with decreased survival, but FEV1<50% predicted had no impact on survival.[15,19] Daimee et al published their single-center experience and reported that lower (absolute
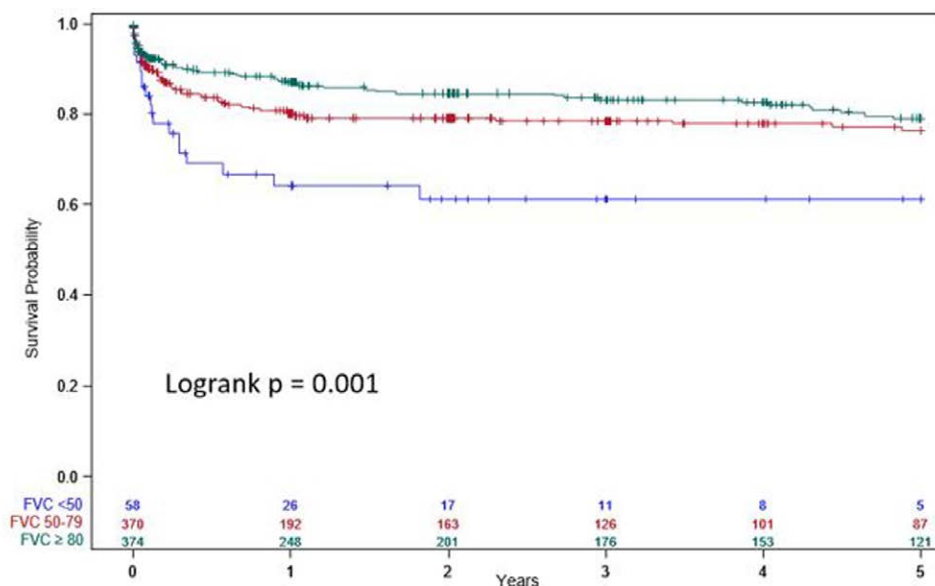

FIGURE 3. Patients with FVC<50% predicted before transplantation have an increased risk of mortality posttransplant. FVC, forced vital capacity.
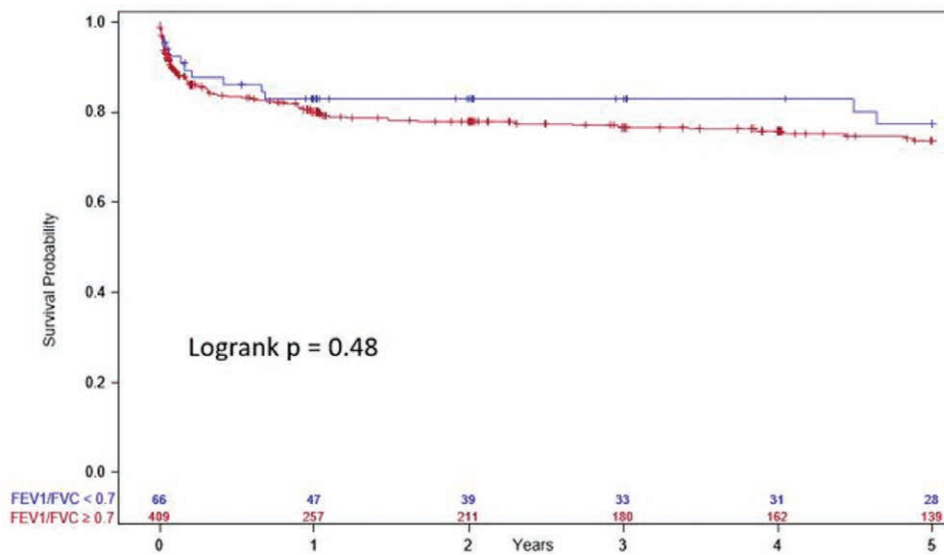
FIGURE 4. Pretransplant FEV1/FVC does not predict mortality following heart transplantation. FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

and percent predicted) FEV1 and FVC were associated with increased hospital and intensive care unit lengths of stay and increased number of ventilator days.[20] No correlation was present between FEV1 or FVC and postoperative mortality.[20] In our study, we also observed that patients with decreased FEV1 and FVC have longer lengths of stay posttransplantation. More importantly, patients with FEV1 or FVC < 50% predicted had a significantly increased risk of mortality within the first 5 y posttransplantation.

In our study, history of tobacco use and COPD were not associated with increased risk of mortality following HT in the evaluated cohort. This is in contrast to the 2019 ISHLT TTX Registry, which shows decreased survival in heart transplant patients who previously smoked, but a similar evaluation in COPD patients has not been performed.[21] Previous studies, primarily in coronary artery bypass grafting, have generally shown decreased survival in patients with COPD.[22,23] However, these studies relied on historical and self-reported diagnoses of COPD, which are likely suboptimal compared with PFT-derived definitions of airflow obstruction. Adabag et al reported that by utilizing PFTs before cardiac surgery, they identified 178 patients with a historical diagnosis of COPD that did not have airflow limitation on PFT, whereas 186 patients without a COPD diagnosis had evidence of airflow limitation.[24] This study and others have shown that when utilizing PFTs to define COPD (generally FEV1 < 80% and FEV1/FVC < 0.7), patients with evidence of airway obstruction on PFTs had increased short- and long-term mortality.[24,25]

TABLE 2.

Univariate and multivariate analysis of variables predicting increased mortality following heart transplantation

	Univariate		FEV 1 multivariate model		FVC multivariate model	
	Hazard ratio	P (95% CI)	Hazard ratio	P (95% CI)	Hazard ratio	P (95% CI)
FEV 1 < 50% predicted	2.96	<0.0001 (1.97-4.46)	4.91	<0.0001 (2.69-8.94)		
FVC < 50% predicted	2.24	0.001 (1.38-3.64)			2.75	0.003 (1.4-5.4)
Smoking history	0.85	0.32 (0.61-1.17)	0.89	0.64 (0.53-1.47)	0.89	0.65 (0.53-1.48)
Male sex	1.75	0.014 (1.12-2.74)	2.74	0.006 (1.33-5.66)	2.13	0.03 (1.07-4.26)
Age	1.01	0.14 (0.99-1.02)	1.0	0.38 (0.99-1.03)	1	0.46 (1-1.03)
BMI	1.04	0.32 (0.61-1.17)	1.06	0.04 (1.0-1.12)	1.05	0.06 (1-1.11)
COPD	1.18	0.7 (1.0-1.07)	1.6	0.39 (0.55-4.62)	1.85	0.25 (0.64-5.32)
Creatinine	1.09	0.01 (1.02-1.16)	1.03	0.51 (0.94-1.13)	1.03	0.54 (0.94-1.12)
Albumin	0.81	0.15 (0.61-1.08)	0.93	0.71 (0.65-1.34)	0.91	0.61 (0.64-1.3)
Total bilirubin	1.25	0.0008 (1.1-1.42)	1.27	0.04 (1.01-1.59)	1.34	0.008 (1.08-1.66)

BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV, forced expiratory volume in 1 s; FVC, forced vital capacity.

TABLE 3.

Hospital length of stay depending on pretransplant FEV1 or FVC

Clinical variable	FEV1			P	FVC			P
	FEV1 < 50%	50%–80%	FEV1 > 80%		FVC < 50%	50%–80%	FVC > 80%	
Mean length of stay, d (SD)	34.4 (37.3)	28.2 (30.1)	24.2 (25.8)	0.028	37 (33.7)	28.8 (32.2)	24.3 (25.1)	0.0075

FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Limitations

Our study has several limitations. This study utilizes data from an international registry wherein pulmonary function data are not submitted by US centers and is optional for international centers, thus leading to substantial missing data. Whereas a large number of patients within the registry had missing or incomplete PFT data, we feel that our included study population is well representative of the entire population. Statistical comparisons were completed and did not reveal any clinically significant differences (eg, creatinine 1.4 mg/dL in the study group and 1.3 mg/dL in the excluded group [$P = 0.001$] or total bilirubin 1.4 mg/dL in the study group versus 1.2 mg/dL in the excluded group [$P < 0.0001$]) that would likely lead to any change in pretransplant clinical management. The statistically significant differences between groups are primarily because of the large sample size within the excluded group.

Also, the TTX Registry does not include DLCO. We recognize DLCO may have the highest predictive value in this population based on previous publications. Unfortunately, we were not able to assess the impact of DLCO in this study because of the lack of data capture in the TTX Registry. Finally, the TTX Registry does not capture an exhaustive list of comorbidities and laboratory data, therefore limiting the depth of our multivariate model. Although previous single-center reports have shown that reduced FEV1/FVC pretransplant predicts worse posttransplant survival, we did not see this in our cohort. We recommend the completion of a multi-institutional study assessing the prognostic impact of complete pulmonary function testing before HT on predicting clinical outcomes following transplantation.

CONCLUSION

In conclusion, patients with a FEV1 or FVC < 50% predicted before HT have an increased risk of mortality following HT. FEV1/FVC was not a predictor of mortality in our study. FEV1 and FVC < 50% were associated with longer lengths of stay following transplantation. Further research is needed to fully assess the importance of individual pulmonary function parameter and the cutoff values that predict worse outcomes in patients undergoing HT.

REFERENCES

1. Wright RS, Levine MS, Bellamy PE, et al. Ventilatory and diffusion abnormalities in potential heart transplant recipients. *Chest.* 1990;98:816–820.
2. Naum CC, Sciurba FC, Rogers RM. Pulmonary function abnormalities in chronic severe cardiomyopathy preceding cardiac transplantation. *Am Rev Respir Dis.* 1992;145:1334–1338.
3. Dimopoulou I, Daganou M, Tsintzas OK, et al. Effects of severity of long-standing congestive heart failure on pulmonary function. *Respir Med.* 1998;92:1321–1325.
4. Evans SA, Watson L, Cowley AJ, et al. Static lung compliance in chronic heart failure: relation with dyspnoea and exercise capacity. *Thorax.* 1995;50:245–248.
5. Guazzi M. Alveolar-capillary membrane dysfunction in heart failure: evidence of a pathophysiologic role. *Chest.* 2003;124:1090–1102.
6. Olson TP, Beck KC, Johnson BD. Pulmonary function changes associated with cardiomegaly in chronic heart failure. *J Card Fail.* 2007;13:100–107.
7. Agostoni P, Cattadori G, Guazzi M, et al. Cardiomegaly as a possible cause of lung dysfunction in patients with heart failure. *Am Heart J.* 2000;140:e24.
8. Gottdiener JS, Arnold AM, Aurigemma GP, et al. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. *J Am Coll Cardiol.* 2000;35:1628–1637.
9. Kannel WB, D'Agostino RB, Silbershatz H, et al. Profile for estimating risk of heart failure. *Arch Intern Med.* 1999;159:1197–1204.
10. Olson TP, Denzer DL, Sinnett WL, et al. Prognostic value of resting pulmonary function in heart failure. *Clin Med Insights Circ Respir Pulm Med.* 2013;7:35–43.
11. Iversen KK, Kjaergaard J, Akkan D, et al; ECHOS Lung Function Study Group. The prognostic importance of lung function in patients admitted with heart failure. *Eur J Heart Fail.* 2010;12:685–691.
12. Miniati M, Monti S, Bottai M, et al. Forced expiratory volume in one second: prognostic value in systolic heart failure. *Int J Cardiol.* 2013;168:1573–1574.
13. Mancini D, Lietz K. Selection of cardiac transplantation candidates in 2010. *Circulation.* 2010;122:173–183.
14. Lund LH, Khush KK, Cherikh WS, et al; International Society for Heart and Lung Transplantation. The Registry of the International Society for Heart and Lung Transplantation: thirty-fourth adult heart transplantation report—2017; focus theme: allograft ischemic time. *J Heart Lung Transplant.* 2017;36:1037–1046.
15. Patel J, Shao E, Patel J, et al. 570: pre-transplant FEV1/FVC but not FEV1 alone by pulmonary function testing predicts poor outcome after heart transplantation: the bane of COPD. *J Heart Lung Transplant.* 2009;28:S264.
16. Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2013;187:347–365.
17. Petermann W, Barth J, Entzian P. Heart failure and airway obstruction. *Int J Cardiol.* 1987;17:207–209.
18. Georgiopoulou VV, Deka A, Li S, et al. Pulmonary function testing and outcomes in subjects with heart failure listed for heart transplantation. *Respir Care.* 2015;60:731–739.
19. Kafi A, Patel J, Kittleson M, et al. Abnormal pulmonary function tests contraindicate heart transplant. *J Heart Lung Transplant.* 2014;33:S141–S142.
20. Daimee U, McGrane-Minton H, Massey T, et al. Pre-operative pulmonary function tests and outcomes after heart transplantation. *J Card Fail.* 2015;21:S117.
21. Khush KK, Cherikh WS, Chambers DC, et al; International Society for Heart and Lung Transplantation. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-sixth adult heart transplantation report—2019; focus theme: donor and recipient size match. *J Heart Lung Transplant.* 2019;38:1056–1066.
22. Leavitt BJ, Ross CS, Spence B, et al; Northern New England Cardiovascular Disease Study Group. Long-term survival of patients with chronic obstructive pulmonary disease undergoing coronary artery bypass surgery. *Circulation.* 2006;114:I430–I434.
23. Angouras DC, Anagnostopoulos CE, Chamogeorgakis TP, et al. Postoperative and long-term outcome of patients with chronic obstructive pulmonary disease undergoing coronary artery bypass grafting. *Ann Thorac Surg.* 2010;89:1112–1118.
24. Adabag AS, Wassif HS, Rice K, et al. Preoperative pulmonary function and mortality after cardiac surgery. *Am Heart J.* 2010;159:691–697.
25. Ried M, Unger P, Puehler T, et al. Mild-to-moderate COPD as a risk factor for increased 30-day mortality in cardiac surgery. *Thorac Cardiovasc Surg.* 2010;58:387–391.