Pulmonary function tests do not predict mortality in patients undergoing continuous-flow left ventricular assist device implantation

Edo K. S. Bedzra, MD, MBA,^a Todd F. Dardas, MD, MS,^b Richard K. Cheng, MD, MS,^b Jay D. Pal, MD, PhD,^a Claudius Mahr, DO,^b Jason W. Smith, MD,^a Kent Shively, BS,^a S. Carolina Masri, MD,^b Wayne C. Levy, MD,^b and Nahush A. Mokadam, MD^a

ABSTRACT

Objectives: To investigate the effect of pulmonary function testing on outcomes after continuous flow left ventricular assist device implantation.

Methods: A total of 263 and 239 patients, respectively, had tests of forced expiratory volume in 1 second and diffusing capacity of the lungs for carbon monoxide preoperatively for left ventricular assist device implantations between July 2005 and September 2015. Kaplan-Meier analysis and multivariable Cox regressions were performed to evaluate mortality. Patients were analyzed in a single cohort and across 5 groups. Postoperative intensive care unit and hospital lengths of stay were evaluated with negative binomial regressions.

Results: There is no association of forced expiratory volume in 1 second and diffusing capacity of the lungs for carbon monoxide with survival and no difference in mortality at 1 and 3 years between the groups (log rank $P = .841$ and $.713$, respectively). Greater values in either parameter were associated with decreased hospital lengths of stay. Only diffusing capacity of the lungs for carbon monoxide was associated with increased intensive care unit length of stay in the group analysis ($P = .001$). Ventilator times, postoperative pneumonia, reintubation, and tracheostomy rates were similar across the groups.

Conclusions: Forced expiratory volume in 1 second and diffusing capacity of the lungs for carbon monoxide are not associated with operative or long-term mortality in patients undergoing continuous flow left ventricular assist device implantation. These findings suggest that these abnormal pulmonary function tests alone should not preclude mechanical circulatory support candidacy. (J Thorac Cardiovasc Surg 2017;154:1959-70)

Kaplan-Meier survival estimates for patients by FEV₁ group.

Central Message

Abnormal pulmonary function tests alone should not preclude mechanical circulatory support candidacy.

Perspective

Many centers consider abnormal pulmonary function tests a barrier to mechanical circulatory support candidacy, but there is little research on their prognostic implications. In this retrospective series, there is no association of abnormal tests with increased mortality after left ventricular assist device implantation. Pulmonary function tests alone should not preclude mechanical circulatory support.

See Editorial Commentary page 1971.

See Editorial page 1957.

The prevalence of heart failure is increasing steadily in the United States.¹ Mechanical circulatory support (MCS) is a proven therapy in advanced heart failure and is shown to improve survival in selected patients.² The presence of

lung disease is associated with increased mortality in the Society of Thoracic Surgeons risk calculator.³ However, in heart failure surgery, studies of pulmonary function tests (PFTs) have found both a negative correlation with mortality and postoperative pulmonary complications as well as an absence of any relationship between the tests and outcomes.⁴⁻¹² This may be distinct from noncardiac

From the Divisions of ^aCardiothoracic Surgery and ^bCardiology, University of Washington Medical Center, Seattle, Wash.

Read at the 42nd Annual Meeting of The Western Thoracic Surgical Association, Waikoloa, Hawaii, June 22-25, 2016.

Received for publication June 8, 2016; revisions received Jan 10, 2017; accepted for publication Feb 12, 2017; available ahead of print May 16, 2017.

Address for reprints: Edo K. S. Bedzra, MD, MBA, 1959 NE Pacific St, Box 356310, Seattle, WA 98195 (E-mail: ebedzra@uw.edu).

0022-5223/\$36.00

Copyright © 2017 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2017.02.069>

Scanning this QR code will take you to a supplemental video and table for this article.

Abbreviations and Acronyms

CI	= confidence interval
DLCO	= diffusion capacity of the lungs for carbon monoxide
FEV ₁	= forced expiratory volume in 1 second
ICU	= intensive care unit
INTERMACS	= Interagency Registry For Mechanically Assisted Circulatory Support
LOS	= length of stay
LVAD	= left ventricular assist device
MCS	= mechanical circulatory support
PFT	= pulmonary function test

thoracic surgery, in which preoperative pulmonary function measures are correlated unequivocally with postoperative morbidity and mortality.¹³ Many heart failure centers evaluate PFTs when considering patients for MCS.

This study investigates the efficacy of percent predicted forced expiratory volume in 1 second (FEV₁) and diffusion capacity of the lungs for carbon monoxide (DLCO) in predicting mortality in patients with heart failure who undergo implantation of a continuous-flow left ventricular assist device (LVAD). Secondary measures such as intensive care unit (ICU) and total hospital lengths of stay (LOS) are also explored.

METHODS**Patients and Methods**

Institutional review board approval was obtained to retrospectively review the MCS quality improvement database at a single institution. A total of 310 sequential patients who underwent continuous-flow LVAD implantations for all indications between July 2005 and September 2015 were evaluated. All patients with recorded data for FEV₁ and DLCO were included in our primary analysis. All patients with DLCO testing also had FEV₁ testing, but the reverse was not true. Patients with no PFT testing were excluded from initial analyses, leaving 263 (85%) and 239 (77%) patients, respectively, for further analysis. Patients were then stratified into groups based on the respective PFTs. A cutoff value of 40% was chosen for the first group, which is a more stringent criterion for pulmonary dysfunction than previously used in the literature.^{3,4,10} The remaining patients were then stratified accounting for even distribution of patients to allow statistical comparison. For FEV₁, the groups were defined as follows: Group 1: FEV₁ <40% predicted, Group 2: FEV₁ 40% to 55% predicted, Group 3: FEV₁ 56% to 67% predicted, Group 4: FEV₁ 68% to 78% predicted, and Group 5: FEV₁ >78% predicted. DLCO groups were defined as Group 1: DLCO <40% predicted, Group 2: DLCO 40% to 46% predicted, Group 3: DLCO 47% to 53% predicted, Group 4: DLCO 54% to 61% predicted, and Group 5: DLCO >61% predicted.

Demographic, preoperative, operative, and postoperative variables such as serum creatinine, hemodynamic profile and Interagency Registry For Mechanically Assisted Circulatory Support (INTERMACS) profile, cardiopulmonary bypass time, reoperation status, additional cardiac surgical procedures at the time of implantation, ventilator time, postoperative pneumonia, reintubation status, tracheostomy, postoperative ICU and total hospital LOS, and mortality at 30 days, 1 year, and 3 years were collected.

Statistical Analysis

Univariate and multivariable analyses were performed on outcome variables, with adjustment for factors such as age, sex, INTERMACS profile, serum creatinine, reoperation status, ventilator time, postoperative pneumonia, and cardiopulmonary bypass time, which are known risk factors for poor outcomes after cardiac surgery. First, the data were analyzed with FEV₁ and DLCO treated as continuous variables. Comparisons were then made across groups using the group with highest observed values as a reference.

Overall survival analysis was conducted with the Kaplan-Meier method. Multivariable regressions were performed with the Cox proportional hazard model, which was applied to the entire cohort with the categories of FEV₁ and DLCO entered into the model. The proportional-hazard assumption was tested, on basis of Schoenfeld residuals from separate Cox proportional hazard models, treating the variables as continuous and then as categorical and was not violated ($P = \text{FEV}_1$ and DLCO .413 and .152, and .222 and .090, respectively, for continuous and categorical variables). LOS analysis was performed with negative binomial regressions to accommodate overdispersion of this outcome variable. For time-to-event analyses, patients were followed from implant until death without censoring for LVAD exchange, explant, or heart transplantation. Sensitivity analyses were performed by including patients with no PFT data in the lowest groups. Furthermore, FEV₁ and DLCO were included as linear splines to detect possible nonlinear relationship which was absent (Table E1). All statistical analyses were performed with Stata, version 14 (Stata Corporation, College Station, Tex).

RESULTS**Baseline Characteristics**

The baseline characteristics are reported in Table 1. The average patient presented for implantation as INTERMACS 3. The average age of patients in the FEV₁ cohort was 54 years; 81.7% were male, and 60.5% of these patients were eligible for transplantation, three quarters of whom underwent eventual heart transplantation. The average time from LVAD implantation to heart transplantation was 282 days. There was no difference in rates of heart transplantation across any of the 5 FEV₁ or DLCO groups (average 45.6%, $P = .56$, and 45.2%, $P = .99$, respectively). FEV₁ ranged from 23% to 113% predicted, whereas DLCO ranged from 28% to 101% predicted. Heartmate II (St Jude, St. Paul, Minn) implantations comprised 79% of procedures in the FEV₁ group, whereas the remainder underwent HeartWare HVAD (HeartWare, Framingham, Mass) implantation. There was a similar distribution for the DLCO analysis.

Hemodynamic Profile

The average patient had a left ventricular ejection fraction of 19.7%, a cardiac index of 2.3 L/min/m², and a mean pulmonary arterial pressure of 32 mm Hg with a pulmonary capillary wedge pressure of 22 mm Hg. A total of 17.3% were supported with intra-aortic balloon pumps (Table 2). The average serum creatinine level was 1.3 mg/dL. On group level analysis, the only significant difference between groups was found in the INTERMACS profile at presentation (2.3, standard deviation [SD], 0.5, in the lowest FEV₁ group vs 3.1 [SD 1.0] in the highest group, $P = .01$). In the DLCO groups, a greater percentage of patients with lower test values

TABLE 1. Demographics and baseline characteristics

Characteristic	1	2	3	4	5	Total	P value
FEV₁ group							
n	13	57	64	67	62	263	
Age, mean (SD)	49.4 (14.2)	54.9 (13.8)	55.2 (12.1)	55.8 (13.5)	51.9 (14.3)	54.2 (13.5)	.3
Sex, male	10 (77%)	46 (81%)	57 (89%)	55 (82%)	47 (76%)	215 (81.7%)	.4
INTERMACS profile, mean (SD)	2.3 (0.5)	2.9 (1.2)	3.0 (1.1)	3.4 (1.3)	3.1 (1.0)	3.1 (1.2)	.0124
Device							
HeartWare	3 (23%)	10 (18%)	14 (22%)	12 (18%)	16 (26%)	55 (20.9%)	.79
HeartMate II	10 (77%)	47 (82%)	50 (78%)	55 (82%)	46 (74%)	208 (79.1%)	
Intent of therapy							
Bridge to transplantation	1 (8%)	21 (33%)	32 (50%)	33 (53%)	32 (53%)	119 (45.2%)	.024
Bridge to eligibility	5 (38%)	11 (17%)	11 (17%)	7 (11%)	8 (13%)	42 (16.0%)	
Destination therapy	7 (54%)	32 (50%)	21 (33%)	22 (35%)	20 (33%)	102 (38.8%)	
DLCO group							
n	41	55	51	46	46	239	
Age, mean (SD)	56.6 (14.0)	54.7 (13.5)	54.8 (11.2)	54.6 (13.9)	51.3 (14.4)	54.4 (13.4)	.45
Sex, male	38 (93%)	46 (84%)	41 (80%)	37 (80%)	34 (74%)	196 (82.0%)	.24
INTERMACS profile, mean (SD)	2.9 (1.3)	2.9 (1.1)	3.2 (1.1)	3.2 (1.3)	3.1 (1.0)	3.1 (1.2)	.57
Device							
Heartware	8 (20%)	7 (13%)	9 (18%)	11 (24%)	10 (22%)	45 (18.8%)	.66
Heartmate II	33 (80%)	48 (87%)	42 (82%)	35 (76%)	36 (78%)	194 (81.2%)	
Intent of therapy							
Bridge to transplantation	12 (29%)	26 (47%)	20 (39%)	20 (43%)	24 (52%)	119 (45.2%)	.38
Bridge to eligibility	6 (15%)	6 (11%)	11 (22%)	9 (20%)	6 (13%)	42 (16.0%)	
Destination therapy	23 (56%)	23 (42%)	20 (39%)	17 (37%)	16 (35%)	102 (38.8%)	

FEV₁, Forced expiratory volume in 1 second; SD, standard deviation; INTERMACS, Interagency Registry For Mechanically Assisted Circulatory Support; DLCO, diffusion capacity of the lungs for carbon monoxide.

were supported with an intra-aortic balloon pump at implantation (34% in the lowest DLCO group vs 7% in the highest DLCO group, P value .01), and right-sided fill pressures tended to be greater (12.2 mm Hg [SD 5.3] in the lowest FEV₁ group vs 7.8 [SD 4.8] mm Hg in the highest FEV₁ group, $P < .001$ for right atrial pressures), where as the trend was towards a greater wedge pressure in groups with lower FEV₁ (24.3 mm Hg in the lowest FEV₁ group vs 20.3 mm Hg in the highest FEV₁ group, $P = .057$). All other measures were similar across the groups.

Intraoperative Details

A total of 19.8% of patients had undergone a previous sternotomy for cardiac surgery before LVAD implantation (Table 3). A total of 31.2% of patients had additional procedures at the time of surgery, including tricuspid valve repair (25.1%) and aortic valve repair. A total of 2.7% of patients required implantation of a right ventricular assist device at the time of surgery. The average cardiopulmonary bypass time was 90.8 minutes.

Postoperative Outcomes

Postoperative outcomes for the patient population are listed in Tables 3 and 4 (additional data are available in Table E1). The average ventilator time was 51.1 hours for

the FEV₁ cohort with a median of 24 hours (interquartile range, 19-43), reflecting the outliers with very prolonged ventilator times (maximum 1222 hours). Reintubation, postoperative pneumonia, and tracheostomy rates were 10.6%, 6.8%, and 3.8%, respectively. There were no significant differences in these pulmonary function measures across the 5 FEV₁ groups ($P = .54, .12, .36$, and .61 for ventilator time, postoperative pneumonia, reintubation, and tracheostomy rates).

The median ventilator time was 25 hours (interquartile range 20-43) for the DLCO cohort. Reintubation, postoperative pneumonia, and tracheostomy rates were 9.6%, 6.7%, and 3.3%, respectively. There were no significant differences in these pulmonary function measures across the 5 DLCO groups ($P = .24, .09, .29$, and .07 for ventilator time, postoperative pneumonia, reintubation, and tracheostomy rates, respectively).

In the linear analysis, there was no association of FEV₁ or DLCO with survival (hazard ratio 0.99, confidence interval [CI] 0.84-1.18 and 0.91, CI 0.73-1.14; $P = .925$ and .435, respectively). This relationship held after adjustments in a multivariable model. However, there was a negative correlation between these PFT parameters and hospital LOS. Each 10%-point increase in FEV₁ or DLCO was associated with a 7% decrease in hospital LOS (Table 4).

TABLE 2. Hemodynamic profile and laboratory values

Characteristic	1	2	3	4	5	Total	P value
FEV₁ group							
n	13	57	64	67	62	263	
Creatinine, mg/dL	1.3 (0.4)	1.3 (0.4)	1.4 (0.4)	1.2 (0.4)	1.2 (0.4)	1.3 (0.4)	.14
Intra-aortic balloon pump, n (%)	6 (55)	17 (31)	8 (14)	7 (11)	5 (8)	43 (17.3)	<.001
Right atrial pressure, mm Hg	12.2 (5.3)	11.3 (5.3)	11.6 (6.7)	8.6 (4.2)	7.8 (4.8)	9.9 (5.5)	<.001
Right ventricular systolic pressure, mm Hg	49.5 (9.6)	47.9 (12.0)	49.7 (13.2)	46.9 (14.5)	44.1 (15.9)	47.3 (13.9)	.25
Right ventricular diastolic pressure, mm Hg	13.3 (5.2)	11.6 (5.6)	11.2 (6.3)	9.3 (5.6)	8.7 (5.4)	10.3 (5.8)	.01
Mean pulmonary arterial pressure, mm Hg	36.4 (6.4)	33.1 (7.3)	34.0 (8.4)	30.8 (9.8)	29.9 (10.0)	32.1 (9.0)	.03
Pulmonary capillary wedge pressure, mm Hg	24.3 (5.8)	24.1 (7.4)	22.7 (7.2)	21.7 (8.8)	20.0 (7.9)	22.2 (7.9)	.06
Cardiac output by thermodilution, L/min	4.5 (1.0)	4.7 (1.3)	5.1 (3.1)	4.6 (1.4)	4.5 (1.2)	4.7 (1.9)	.48
Cardiac index by thermodilution, L/min/m ²	2.4 (0.4)	2.2 (0.6)	2.3 (0.7)	2.3 (0.7)	2.3 (0.6)	2.3 (0.6)	.94
Left ventricular ejection fraction, %	18.9 (9.4)	19.0 (7.3)	19.9 (7.1)	19.5 (6.3)	20.6 (6.3)	19.7 (6.9)	.74
DLCO group							
n	41	55	51	46	46	239	
Creatinine, mg/dL	1.3 (0.4)	1.4 (0.5)	1.3 (0.4)	1.2 (0.3)	1.3 (0.4)	1.3 (0.4)	.12
Intra-aortic balloon pump, n (%)	13 (34)	11 (20)	8 (17)	5 (11)	3 (7)	40 (17.5)	.01
Right atrial pressure, mm Hg	9.3 (6.0)	10.3 (5.1)	10.9 (6.3)	9.4 (5.2)	10.0 (5.1)	10.0 (5.5)	.67
Right ventricular systolic pressure, mm Hg	46.9 (12.5)	47.8 (14.4)	50.3 (13.4)	46.4 (14.8)	46.6 (13.7)	47.6 (13.8)	.65
Right ventricular diastolic pressure, mm Hg	9.9 (6.2)	10.5 (5.4)	10.3 (5.7)	10.5 (5.9)	10.8 (6.1)	10.4 (5.8)	.97
Mean pulmonary arterial pressure, mm Hg	31.5 (8.2)	32.7 (9.2)	33.4 (8.2)	31.5 (10.3)	32.0 (8.3)	32.3 (8.9)	.83
Pulmonary capillary wedge pressure, mm Hg	21.1 (8.2)	22.5 (7.0)	22.7 (8.0)	22.2 (9.0)	23.5 (7.0)	22.4 (7.8)	.71
Cardiac output by thermodilution, L/min	4.8 (1.3)	5.0 (3.2)	4.7 (1.1)	4.5 (1.4)	4.8 (1.5)	4.8 (1.9)	.75
Cardiac index by thermodilution, L/min/m ²	2.4 (0.6)	2.3 (0.7)	2.3 (0.6)	2.2 (0.6)	2.3 (0.7)	2.3 (0.6)	.52
Left ventricular ejection fraction, %	21.3 (8.5)	19.7 (7.8)	19.1 (6.8)	19.0 (5.3)	20.7 (6.1)	19.9 (7.0)	.48

FEV₁, Forced expiratory volume in 1 second; DLCO, diffusion capacity of the lungs for carbon monoxide.

No linear effect was shown for ICU LOS, although analysis of the groups showed a correlation of increased ICU LOS with decreased DLCO for values greater than 46% predicted.

In the multivariable regression, age >60 years, postoperative pneumonia, and increasing cardiopulmonary bypass and ventilator times were associated with increasing risks of mortality. Female patients with postoperative pneumonia and longer ventilator times experienced longer ICU and hospital LOS.

FEV₁ as Predictor of Outcomes

Patients with FEV₁ less than 40% predicted (n = 13) had no operative deaths in this study. Mortality and 95% CIs at 1 and 3 years were 0.09 (0.01-0.60) and 0.11 (0.04-0.34) deaths per person year, respectively. This did not differ significantly from patients with normal FEV₁ values. In line with this, Kaplan-Meier analysis showed no difference in survival across groups (Figure 1, log rank *P* = .841). Hospital LOS was significantly greater for patients with lower FEV₁. Patients with FEV₁ less

TABLE 3. Perioperative details

Characteristic	1	2	3	4	5	Total	P value
FEV ₁ group							
n	13	57	64	67	62	263	
Intraoperative							
Reoperation	2 (15%)	12 (21%)	12 (19%)	20 (30%)	6 (10%)	52 (19.8%)	.074
Tricuspid valve	5 (38%)	16 (28%)	22 (34%)	11 (16%)	12 (19%)	66 (25.1%)	.084
Aortic valve	0 (0%)	2 (4%)	3 (5%)	2 (3%)	2 (3%)	9 (3.4%)	.94
Right ventricular assist device	1 (8%)	0 (0%)	1 (2%)	3 (5%)	2 (3%)	7 (2.7%)	.4
Cardiopulmonary bypass time, mean (SD)	110.5 (42.3)	94.3 (34.7)	94.3 (41.4)	86.6 (52.6)	84.5 (44.6)	90.8 (44.2)	.27
Postoperative							
Ventilator time in hours, median (IQR)	24 (17-51)	25 (20-45)	24 (19-40)	24 (22-41)	23 (17-38)	24 (19-43)	.47
Reintubation	1 (8%)	6 (9%)	5 (8%)	11 (18%)	5 (8%)	28 (10.6%)	.36
Pneumonia	3 (23%)	3 (5%)	5 (8%)	2 (3%)	5 (8%)	18 (6.8%)	.12
Tracheostomy	0 (0%)	3 (5%)	2 (3%)	4 (6%)	1 (2%)	10 (3.8%)	.61
DLCO group							
n	41	55	51	46	46	239	
Intraoperative							
Reoperation	15 (37%)	16 (29%)	7 (14%)	7 (15%)	5 (11%)	50 (20.9%)	.009
Tricuspid valve	11 (27%)	11 (20%)	14 (27%)	14 (30%)	14 (30%)	64 (26.8%)	.75
Aortic valve	1 (2%)	1 (2%)	1 (2%)	2 (4%)	4 (9%)	9 (3.8%)	.36
Right ventricular assist device	1 (2%)	1 (2%)	1 (2%)	0 (0%)	4 (9%)	7 (3.0%)	.12
Cardiopulmonary bypass time, mean (SD)	97.2 (43.1)	97.0 (44.7)	88.1 (37.0)	87.8 (35.1)	96.4 (60.2)	93.3 (44.6)	.68
Postoperative							
Ventilator time in hours, median (IQR)	24 (20-37)	25 (20-49)	27 (22-44)	24 (17-43)	24 (20-32)	25 (20-43)	.5
Reintubation	3 (7%)	5 (9%)	5 (10%)	8 (17%)	2 (4%)	23 (9.6%)	.29
Pneumonia	3 (7%)	1 (2%)	3 (6%)	7 (15%)	2 (4%)	16 (6.7%)	.094
Tracheostomy	1 (2%)	0 (0%)	3 (6%)	4 (9%)	0 (0%)	8 (3.3%)	.07

FEV₁, Forced expiratory volume in 1 second; SD, standard deviation; IQR, interquartile range; DLCO, diffusion capacity of the lungs for carbon monoxide.

than 40% predicted stayed 10 days longer in the hospital on average than patients with FEV₁ greater than 78% predicted (ratio 1.43, 95% CI 1.03-2.0, $P = .04$). Patients with FEV₁ 68% to 78% predicted showed no significantly greater LOS than the normal group (Supplementary material). ICU LOS varied from 7.2 to 8.7 days in the different FEV₁ groups, but no significant statistical difference existed between groups.

DLCO as Predictor of Outcomes

In the group of patients with DLCO less than 40% predicted ($n = 41$), operative and medium term mortality rates and 95% CIs at 1 and 3 years were 0, 0.14 (0.06-0.33), and 0.11 (0.06-0.22) deaths per person-year. This was statistically similar to observed rates in the other groups and is reflected in the Kaplan-Meier analysis (Figure 2, log rank test P value = .713). Hospital LOS was significantly longer in the groups with lower DLCO (Figure 3). Patients with DLCO less than 40% predicted stayed 7 days longer on average than those with DLCO >61% predicted (ratio 1.44, 95% CI 1.16-1.78,

$P < .001$). However, patients with DLCO between 40% and 46% predicted ($n = 55$) had no different LOS than patients with DLCO greater than 61% predicted ($n = 40$).

ICU LOS was significantly greater in Group 3, representing DLCO of 47% to 53% predicted compared with the group with DLCO >61% predicted (ratio 1.78, 95% CI 1.3-2.4, $P < .001$). However, patients with the lowest DLCO values in this study did not show increased ICU LOS compared with the reference group (Table E1).

Sensitivity Analysis Results

A total of 47 patients had no testing for FEV₁, whereas 71 had none for DLCO. These patients were on average 4 years younger than patients who underwent testing ($P = .042$), more likely to have worsening cardiac and renal function on inotropes (INTERMACS profile 2), and more likely to be supported with an intra-aortic balloon pump at implantation (P value < .001). In a Kaplan-Meier survival analysis, patients with no FEV₁ testing had worse survival than the cohort of patients who were tested before implantation (log rank test $P = .046$). When the former were included

TABLE 4. Correlation of postoperative outcomes with pulmonary function tests as continuous variables

Outcome	FEV ₁		DLCO	
	Ratio	P value	Ratio	P value
N	263		239	
Mortality (hazard ratio per 10% change)*				
Unadjusted	0.99 (0.84-1.18)	.925	0.91 (0.73-1.14)	.435
Adjusted	1.08 (0.90-1.30)	.433	0.98 (0.77-1.24)	.838
Hospital length of stay (ratio of means per 10% change)†				
Unadjusted	0.93 (0.90-0.97)	.001	0.93 (0.88-0.98)	.008
Adjusted	0.94 (0.91-0.98)	.002	0.93 (0.88-0.97)	.004
ICU length of stay (ratio of means per 10% change)†				
Unadjusted	1.00 (0.94-1.06)	.936	0.96 (0.88-1.04)	.286
Adjusted	1.00 (0.95-1.04)	.772	0.94 (0.88-1.00)	.055

Regressions adjusted for age, sex, INTERMACS profile, serum creatinine, reoperation status, ventilator time, postoperative pneumonia, and cardiopulmonary bypass time. FEV₁, Forced expiratory volume in 1 second; DLCO, diffusion capacity of the lungs for carbon monoxide; ICU, intensive care unit. *3-year mortality, Cox regression. †Negative binomial regression.

entirely in the lowest FEV₁ group (FEV₁ <40% predicted), there were no observed changes in the relationships between groups. There was no observed difference in survival (ratio 1.68, 95% CI 0.80-3.53, log rank test $P = .462$) between the group inclusive of patients with no testing and the reference group (FEV₁ > 78% predicted). The ratio of ICU LOS of patients with FEV₁ less than 40% predicted to the reference increased from 1.08 (.7-1.7) to 1.53 (1.11-2.11) with inclusion of patients with no FEV₁ testing, but this remained statistically insignificant ($P = .062$). Hospital LOS difference remained statistically significant (ratio 1.53, 95% CI 1.22-1.92 from 1.43 (1.0-2.0), $P = .03$ and $P < .001$). Patients without DLCO testing had similar survival to the cohort of patients who were tested (log rank test, P value .706).

DISCUSSION

Patient selection for advanced heart failure therapy, and more specifically, MCS, has been a focus of clinicians as devices have improved in reliability and durability. As a community, we generally have been successful in identifying patients who were ill enough to benefit from therapy. This has led to improved outcomes with 2-year survival in excess of 70%.^{14,15} However, our judgment has been challenged repeatedly in the assessment of those too ill to benefit from this therapy. This is because one of our major risk indicators, noncardiac frailty, cannot be expected to improve with improved hemodynamics, and the greater the noncardiac frailty, the less the potential benefit.¹⁶ Noncardiac frailty can take many forms, including physical debilitation, cachexia, and end-organ dysfunction. Although there are well-studied physical debilitation measures such as handgrip strength, gait speed, and unintentional weight loss, the prognostic value of end organ damage is still under investigation. There have been attempts at assessment of liver disease, which have suggested acceptable outcomes with liver dysfunction.^{17,18} Although continuous-flow LVAD implantation results in improved postoperative renal function,¹⁹ patients with preoperative renal dysfunction have been shown to have worse survival with MCS.^{20,21} However, lung disease has not been well investigated in the MCS population and to date, there has been no concerted effort to evaluate the efficacy of PFTs as predictors of mortality in this patient population. Ghotra and colleagues²² presented preliminary data suggesting a significant association between DLCO less than 50% predicted and increased mortality in their patients undergoing MCS at a single center.

In this study, patients with very low PFTs were implanted with ventricular assist devices. A significant percentage of patients underwent redo sternotomy, and a third had additional

FIGURE 1. Kaplan-Meier survival estimates for patients by FEV₁ groups (Group 1: <40%, Group 2: 40%-55%, Group 3: 56%-67%, Group 4: 68%-78%, Group 5: >78%). FEV₁, Forced expiratory volume in 1 second.

FIGURE 2. Kaplan-Meier survival estimates for patients by DLCO groups (Group 1: <40%, Group 2: 40%-46%, Group 3: 47%-53%, Group 4: 54%-61%, Group 5: >61). *DLCO*, Diffusion capacity of the lungs for carbon monoxide.

procedures during device implantation. However, we found no association between either DLCO or FEV₁ with mortality. These findings may be anticipated; by modifying patients’ heart failure with treatment, the natural history of their PFTs could be altered. For example, it is known that DLCO and FEV₁ worsen with heart failure as the heart dilates and left ventricular end-diastolic pressure increases, leading to pulmonary interstitial edema and hydrostatic alveolar injury,²³ but data exist on the improvement of these tests with treatment of heart failure and particularly after heart transplantation.²⁴

Therefore, we would expect that with MCS and particularly subsequent transplant (for those transplant-eligible), the pulmonary morbidity would be improved. This would lead to better outcomes in these patients than in patients who undergo nonheart failure surgery where the expected postoperative improvement in pulmonary function may be more limited.

Review of the patients with the lowest FEV₁ values shows that pulmonary optimization such as drainage of pleural effusions and oxygen wean contributed at least partially to

FIGURE 3. Lengths of stay of different patient groups. FEV₁ Groups (Group 1: <40%, Group 2: 40%-55%, Group 3: 56%-67%, Group 4: 68%-78%, Group 5: >78%). DLCO Groups (Group 1: <40%, Group 2: 40%-46%, Group 3: 47%-53%, Group 4: 54%-61%, Group 5: >61). *FEV₁*, Forced expiratory volume in 1 second; *DLCO*, diffusion capacity of the lungs for carbon monoxide.

VIDEO 1. Minimally invasive, off-pump implantation of a HeartWare HVAD (HeartWare, Inc., Framingham, Mass). The patient is a 31-year-old man with nonischemic cardiomyopathy and a dilated left ventricle. Right ventricular function was reasonable for isolated LVAD implantation. The ventricular apex was marked with a transthoracic echocardiogram. An 8-cm incision was made in the left sixth interspace, the seventh rib was divided, a soft-tissue retractor was placed, and a pericardial well created. Simultaneously, a right third interspace incision was made and the rib was divided. The mammary vessels were ligated. A soft-tissue retractor was placed and a pericardial well was created. An umbilical tape was passed between the incisions for later use as a guide for the outflow graft. The apex was elevated into the field by placing a sponge behind the heart. Radial 2-0 braided sutures with pledgets were placed through the sewing cuff and then tied down (note: the anchoring screw should be loosened but not removed at this point). A pacing wire was placed for rapid ventricular pacing (optional). The pump was primed and prepared on the back table. Sizing of the incision was confirmed with the pump, and the patient was heparinized with a goal activated clotting time of 300 seconds. A cruciate incision was made in the apex under rapid ventricular pacing. The coring tool was inserted atraumatically (note: once the coring tool is flush with the sewing cuff, it is generally hemostatic). Coring was then completed and the LVAD inserted with the outflow graft unclamped for deairing (note: during this process, approximately 100 mL of blood can be lost). The umbilical tape was tied to the outflow graft and tunneled to the right thoracotomy incision. The driveline was tunneled out the abdominal wall leaving the velour buried, looped in the pericardium, and then attached to the controller. A side-biting clamp was placed on the aorta, and the outflow graft anastomosis was performed with a 5-0 monofilament suture. A de-airing needle was placed in the outflow graft. The LVAD was then started and slowly increased to nominal speed of 2400 rpm. The apex was covered with a Gore-Tex (Gore, Newark, De) pericardial membrane and the right thoracotomy pericardial incision was closed primarily. A paracostal suture was placed over the apex and the wound closed in layers. The right third rib was reapproximated and the wound closed in layers. Transesophageal echocardiography confirmed excellent inflow orientation; a topogram demonstrates the overall lay of the pump. The patient made an excellent recovery and awaits heart transplant. *LVAD*, Left ventricular assist device. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)30675-X/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)30675-X/fulltext).

increased LOS in one half of the patients with prolonged hospital stays. However, other significant factors like severe right ventricular failure, renal dysfunction, and exercise deconditioning were other etiologies that contributed. Again, there was no observed difference in postoperative pulmonary morbidity as characterized by reintubation rates, ventilator time, tracheostomy rates, and pneumonia. This finding further supports the principle that measured preoperative PFTs may be indicators of cardiac, more so, than pulmonary disease in this patient population.

These findings may help explain the observations in our group analysis, where we found that while generally showing increased ICU LOS with worsening DLCO, patients in the lowest DLCO group showed no significantly longer ICU LOS than those in the normal group, although they did not have increased early mortality. The major contributor to these patients' preoperative performance may be their severe cardiac dysfunction that is then rapidly improved postoperatively, allowing more rapid transit through the ICU.

The economic impact of longer LOS with poor PFTs cannot be ignored. LVAD surgery is expensive, as demonstrated in a Columbia University study, which reported an initial hospitalization cost of \$169,535 for a 37-day stay.²⁵ Thus, although the overall survival was the same in our analysis, the increase of 10 days in overall hospital LOS for patients with the worst FEV₁ values can have a meaningful impact on hospital and personnel resource use. Perhaps future studies can clarify what interventions, if any, when applied to patients with the worst PFT values can decrease the LOS differences observed. Since this study, our practice has evolved in the use of PFTs as part of preoperative evaluation of patients undergoing LVAD implantation. When patients have concerning PFT values, we work collaboratively with our pulmonary medicine colleagues, obtain cross-sectional imaging for evaluation of pulmonary parenchymal disease, determine obvious clinical morbidity such as oxygen dependence, and perform functional tests such as the 6-minute walk test and cardiopulmonary exercise testing as tolerated. The integration of this assessment ultimately guides patient selection with respect to pulmonary comorbidity.

Limitations

This study was retrospective and nonrandomized and thus limited by the usual confinements of such studies. The data obtained were abstracted from a quality improvement database, which had limited fields of data. Importantly, it is likely that some patients with very low PFTs and other comorbidities were evaluated but not offered MCS during the period under review and thus not analyzed. The small number of patients in the lowest FEV₁ group may not be sufficient to demonstrate small survival differences. Patients did not routinely undergo postimplant PFTs, and, therefore, we are unable to evaluate changes in these measures over time. Furthermore, not all patients underwent pulmonary function testing before LVAD implantation.

CONCLUSIONS

This study finds no association between abnormal PFTs and increased mortality after continuous flow LVAD implantation. Our program performs a multidisciplinary evaluation that takes patient comorbidities into consideration. Our experience suggests that carefully selected patients, including those with PFT abnormalities, can

undergo MCS with excellent survival. Therefore, PFTs alone should not preclude advanced heart failure therapies to such patients.

Conflict of Interest Statement

Dr Mahr is a consultant to St Jude, HeartWare, and Abiomed. Dr Mokadam is a consultant to St Jude, HeartWare, and Syncardia Systems Inc. Dr Smith reports a relationship with HeartWare and Transmedics. Drs Pal and Levy report research grants from HeartWare. Dr Dardas reports research support from International Society of Heart Lung Transplant/HeartWare. All other authors have nothing to disclose with regard to commercial support.

We thank Orvalho Augusto for assistance with statistical analysis.

References

- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6-245.
- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 ACCF/AHA Guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:e240-327.
- Shih T, Paone G, Theurer PF, McDonald D, Shahian DM, Prager RL. The Society of Thoracic Surgeons adult cardiac surgery database version 2.73: more is better. *Ann Thorac Surg*. 2015;100:516-21.
- Iversen KK, Kjaergaard J, Akkan D, Kober L, Torp-Pedersen C, Hassager C, et al. The prognostic importance of lung function in patients admitted with heart failure. *Eur J Heart Fail*. 2010;12:685-91.
- Olson T, Denzer D, Sinnett W, Wilson T, Johnson B. Prognostic value of resting pulmonary function in heart failure. *Clin Med Insights Circ Respir Pulm Med*. 2013;7:35-43.
- de Oliveira EK, da Silva VZM, Turquette ALR. Relationship of postoperative walk test and lung function with the length of heart surgery hospital stay. *Rev Bras Cir Cardiovasc*. 2009;24:478-84.
- Henn MC, Zajarias A, Lindman BR, Greenberg JW, Melby SJ, Quader N, et al. Preoperative pulmonary function tests predict mortality after surgical or transcatheter aortic valve replacement. *J Thorac Cardiovasc Surg*. 2016;151:578-86.e2.
- Zibrak JD, O'Donnell CR, Marton K. Indications for pulmonary function testing. *Ann Intern Med*. 1990;112:763-71.
- Hawkins NM, Petrie MC, Jhund PS, Chalmers GW, Dunn FG, McMurray JJV. Heart failure and chronic obstructive pulmonary disease: diagnostic pitfalls and epidemiology. *Eur J Heart Fail*. 2009;11:130-9.
- Ivanov A, Yossef J, Tailon J, Worku BM, Gulkarov I, Tortolani AJ, et al. Do pulmonary function tests improve risk stratification before cardiothoracic surgery? *J Thorac Cardiovasc Surg*. 2016;151:1183-9.e3.
- Cohen A, Katz M, Katz R, Hauptman E, Schachner A. Chronic obstructive pulmonary disease in patients undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 1995;109:574-81.
- Bevelacqua F, Garritan S, Haas F, Salazar-Schicchi J, Axen K, Reggiani J-L. Complications after cardiac operations in patients with severe pulmonary impairment. *Ann Thorac Surg*. 1990;50:602-6.
- Berry MF, Jeffrey Yang C-F, Hartwig MG, Tong BC, Harpole DH, D'Amico TA, et al. Impact of pulmonary function measurements on long-term survival after lobectomy for stage I non-small cell lung cancer. *Ann Thorac Surg*. 2015;100:271-6.
- Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, et al. Sixth INTERMACS annual report: a 10,000-patient database. *J Heart Lung Transplant*. 2014;33:555-64.
- Lietz K, Miller LW. Improved survival of patients with end-stage heart failure listed for heart transplantation. *J Am Coll Cardiol*. 2007;50:1282-90.
- Flint KM, Matlock DD, Lindenfeld J, Allen LA. Frailty and the selection of patients for destination therapy left ventricular assist device. *Circ Heart Fail*. 2012;5:286-93.
- Demirozu ZT, Hernandez R, Mallidi HR, Singh SK, Radovancevic R, Segura AM, et al. HeartMate II left ventricular assist device implantation in patients with advanced hepatic dysfunction. *J Card Surg*. 2014;29:419-23.
- Sargent JE, Dardas TF, Smith JW, Pal JD, Cheng RK, Masri SC, et al. Periportal fibrosis without cirrhosis does not affect outcomes after continuous flow ventricular assist device implantation. *J Thorac Cardiovasc Surg*. 2016;151:230-5.
- Sandner SE, Zimpfer D, Zrunek P, Rajek A, Schima H, Dunkler D, et al. Renal function and outcome after continuous flow left ventricular assist device implantation. *Ann Thorac Surg*. 2009;87:1072-8.
- Coffin ST, Waguespack DR, Haglund NA, Maltais S, Dwyer JP, Keebler ME. Kidney dysfunction and left ventricular assist device support: a comprehensive perioperative review. *Cardiorenal Med*. 2015;5:48-60.
- Yoshioka D, Sakaguchi T, Saito S, Miyagawa S, Nishi H, Yoshikawa Y, et al. Predictor of Early mortality for severe heart failure patients with left ventricular assist device implantation. *Circ J*. 2012;76:1631-8.
- Ghotra AS, Hussain Z, Bhatia N, Perez R, Cheng A, Slaughter MS, et al. Impact of pulmonary function tests on outcomes in patients after left ventricular assist device implantation. *J Card Fail*. 2015;21:S93.
- Apostolo A, Giusti G, Gargiulo P, Bussotti M, Agostoni P. Lungs in heart failure. *Pulm Med*. 2012;2012:1-9.
- Mettauer B, Lampert E, Charloux A, Zhao QM, Epailly E, Oswald M, et al. Lung membrane diffusing capacity, heart failure, and heart transplantation. *Am J Cardiol*. 1999;83:62-7.
- Miller LW, Guglin M, Rogers J. Cost of ventricular assist devices: can we afford the progress? *Circulation*. 2013;127:743-8.

Key Words: heart failure, mechanical circulatory support, heart transplantation, pulmonary function tests

Discussion

Discussant 1: Dr Sagar Damle

Discussant 2

Discussant 3: Dr Dan Miller

Moderator: Dr Craig Sussman

Presenter: Dr Edo Bedzra

Dr Craig Sussman. Our next speaker is from the University of Washington, presenting “Pulmonary Function Tests Do Not Predict Mortality in Patients Undergoing Continuous Flow LVAD Implantation,” Dr Edo Bedzra.

Dr Edo Bedzra. Good morning. I thank the Western Thoracic Surgical Association for the privilege of presenting our research into the prognostic efficacy of PFTs in patients undergoing continuous-flow LVAD implantation. These are our disclosures. PFTs are known to portend an increased risk of mortality in general cardiac surgery, as shown by this evaluation of the Society of Thoracic Surgeons risk calculator. Specifically, patients with FEV₁ less than 50% had 1.77 times the operative mortality of patients with FEV₁ greater than 75%. The presence of pulmonary disease also is known to increase risk of mortality in heart failure. In this 2010 analysis, 532 patients with medically managed heart failure were evaluated. In the multivariable analysis, each 10% decrease in FEV₁ was associated with a 14% increase in risk of mortality. Now, this may be

because of the known consequences of heart failure such as a restrictive effect of cardiomegaly and the adverse interstitial and hydrostatic alveolar injury caused by an elevated left ventricle and diastolic pressure. However, it also is known that treatment of heart failure leads to improvement in observed PFTs.

Keeping this in mind, we set out to examine our experience in mechanical circulatory support surgery. Our aim was to explore the effects different preoperative PFTs had on postoperative outcomes after continuous-flow LVAD implantation. We obtained institutional review board approval from the University of Washington, Human Subjects Division, to retrospectively review our mechanical circulatory support quality improvement database. A total of 310 sequential patients who underwent LVAD implantations for all indications between 2005 and 2015 were evaluated. Patients with no preoperative testing were analyzed separately. A total of 263 patients underwent spirometry, and a subset of these also underwent DLCO testing. We divided our patients into 5 groups. We arbitrarily chose the sickest cohort to represent patients with percent predicted values of less than 40%. The rest of the patients were then evenly distributed over the remaining 4 groups to allow for statistical comparison. Kaplan-Meier survival analysis was used for evaluation of overall survival.

Overall survival analysis was conducted using the Kaplan-Meier method, cumulative mortality with the Cox proportional hazard model and Length of stay using negative binomial regressions. Corrections were made for age, sex, INTERMACS profile, serum creatinine, reoperative status, and cardiopulmonary bypass time in the multivariable model. For the sake of simplicity, we will focus our discussion on the FEV₁ analysis, recognizing that the DLCO analysis was nearly identical. The average patient was a 54-year-old man who presented to implantation stable on inotropes. There was a 4:1 ratio of Heartmate II to HVAD implantations, with nearly half of this as bridged to transplantation. A total of 17.3% of patients were supported with an intra-aortic balloon pump at implantation. The average patient presented with some element of renal dysfunction and depressed left ventricular end diastolic pressure ejection fraction of 19.7%, resulting in an increased left ventricle and diastolic pressure, manifested by the pulmonary capillary wedge pressure of 22.2. A total of 19.8% of patients underwent a previous sternotomy before LVAD implantation; 31.2% of patients had an additional procedure, including the 25% who underwent tricuspid valve repair; and 2.7% of patients required a right ventricular device implantation at the time of surgery.

The average cardiopulmonary bypass time was 19.8 minutes. Kaplan-Meier survival analysis of patients who underwent FEV₁ testing showed no difference in survival across the 5 groups. The overall survival at 3 years for

this group was 78%. Similarly, in the DLCO analysis, no difference in mortality was found between the 5 groups. The log rank $P = .713$ for this group, and the overall 3-year survival was 76.2. Analysis of the entire 310 patient cohort revealed a survival at 3 years of 75.5%. In the univariable and multivariable analysis, neither decreased DLCO nor FEV₁ was associated with an increased risk of mortality; however, increasingly normal tests were associated with significantly shorter LOS. It is worth noting here that each 10% increase in FEV₁ or DLCO was associated with a 7% decrease in the hospital LOS. I apologize that this slide is busy. Please permit me then to highlight the significant findings in our multivariable analysis. Age greater than 60 years, female sex, and increased cardiopulmonary bypass time were associated with significantly increased risk of mortality.

Younger patients had shorter ICU LOS; however, this did not translate into shorter overall hospital LOS. Female patients with increased cardiopulmonary bypass time had significantly longer LOS. A total of 47 patients had no FEV₁ testing preoperatively, and 71 patients had no DLCO testing. These patients were, on average, 4 years younger than patients who underwent testing. They were more likely to present with cardiac and renal dysfunction on inotropic support and more likely to be supported with an intra-aortic balloon pump. In our program, the policy is to obtain preoperative testing on all patients. Therefore, the absence of PFTs indicates an inability to obtain them prior to implant further confirming a sicker patient cohort. However, when these patients were included in the sickest group, patients with FEV₁ less than 40%, there was no change in the significance of observed results. LOS was prolonged, as previously observed. This study is non-randomized and retrospective and thus limited by the usual confinement of such studies. Data were abstracted from an administrative database but limited field.

Importantly, it is likely that some patients with very low FEV₁ and other comorbidities were evaluated but not offered MCS. As well, not all patients underwent preoperative testing. It is also important to note that we did not evaluate pulmonary morbidity such as ventilator time and pneumonia, because these data were not available. However, our sensitivity analysis has shown robust results, and therefore we think our results are generalizable to patients undergoing LVAD implantation. In summary, in our population, abnormal PFTs did not seem to confer an increased risk of mortality; however, PFTs may be useful predictors of postoperative LOS. In our experience, patients including those with abnormal PFTs can undergo mechanical circulatory support with acceptable outcomes, including acceptable mortality. Therefore, PFTs alone should not preclude the offer of advanced heart failure therapy to carefully selected patients. I would like to thank Orvalho Augusto for his help in the statistical analysis, and I'd personally

like to acknowledge Dr Mokadam for his mentorship through this process. Thank you and now onto your questions.

Dr Sussman. The discussion will be opened up by Dr Sagar Damle.

Dr Sagar Damle. First, I'd like to thank the association for giving me the opportunity to discuss this paper, and I'd like to congratulate the authors on a well-written, provocative manuscript and a well-prepared presentation. In the interest of time, I won't rehash all of your findings. I will comment that after reading the manuscript, I had several questions. Let me start with my first question, and it relates to your separation into quintiles. In routine practice, we generally accept FEV₁ and DLCO values greater than 40% as acceptable for really any kind of cardiac surgical procedure. Did you perform a comparison of the "Quintile 1 less than 40%" versus all others and would you suspect that that might change your significance in terms of differences?

Dr Bedzra. Thank you for the question. We did not actually examine quintile 1 less than 40% compared with the rest of the groups. Now, having said that, the univariate and multivariable analysis was performed in a linear manner, and this did not show any significant differences, so I do not expect that there would be any difference if we had examined it that way.

Dr Damle. PFTs and specifically FEV₁ and DLCO can be somewhat crude measures and incomplete measures of a patient's true pulmonary frailty or pulmonary risk. In addition, as you mentioned both in your talk and in the manuscript, both of those values can be greatly affected by a patient's volume status and degree of heart failure. You mentioned that the average wedge pressure was 22 in this group. So, my first question related to this topic is when were the PFTs measured in relationship to when VAD was implanted?

Dr Bedzra. Thank you. Again, it's our policy that we obtain routine preoperative testing for patients as recent as less than 1 year before implantation.

Dr Damle. The reason why I bring that up is that, you know, you had a significant percentage of the patients had balloon pumps before implant, and even in the group that did not have PFTs, there was a greater percentage of patients who had balloon pumps, clearly demonstrating a sicker population. PFTs that are measured a year before implant may or may not be relevant in terms of what their true value is. The second question then is did you have an opportunity to reexamine these patients after LVAD implant to see whether their PFTs improved, especially in the quintile one patients?

Dr Bedzra. That's an excellent question. We do not routinely obtain postoperative PFTs in these patients. Some have been obtained, however, we have not been able to examine that data yet.

Dr Damle. I'm sure your group, just like ours, gets a full set of PFTs with arterial blood gases. Did you, by any chance, measure any of the other markers from your PFT examinations, such as room air O₂ level, room air CO₂ level, or their degree of pulmonary hypertension, specifically in the quintile 1 group versus the others?

Dr Bedzra. We did not. However, one could look at the left ventricular end diastolic pressure as well as the right ventricular pressures as proxy for pulmonary hypertension. We do have hemodynamic data reflecting this and that's provided in our manuscript as well. These were mildly elevated, as suspected in this population.

Dr Damle. PFTs are a common preoperative test. The vast majority is performed on pretty ill patients with an LVAD. In your series, 85% of these patients have preoperative PFTs, but as we all know, PFTs are really just one of the plethora of factors that are used in the decision process for LVAD implantation. I'd like to emphasize one key limitation, which you also mentioned in your paper. That is, we don't know anything about the patients who are not offered LVADs. Specifically, we don't know what percentage of those patients were denied LVAD specifically on the basis of poor pulmonary function. I suspect your group of the low PFTs, that quintile 1 group, really represents a very select group of patients. Can you comment on the specific interquartile differences with regard to other comorbidities, not just their age or their INTERMACS score, but what were the other differences between the quartiles recognized that they may not be statistically significant, I'm sure you were able to identify trends between the quartiles. Can you comment on maybe some of the differences between the low FEV₁ patients versus the others?

Dr Bedzra. Thank you. That's an excellent question. We do have data on the demographic profile of these patients in the different quintiles. As you alluded to, there weren't any significant differences in between these. Looking at the data, the most significant difference existed in the patients supported with intra-aortic balloon pumps, however, even this varied from about 19% supported to about 25%, which was not very significant clinically. The only other significant difference was in age, and there was about a 5-year difference across the 5 groups. This was not statistically significant.

Dr Damle. Right and again, I agree with you. It's not statistically significant but the numbers were relatively small. Sometimes it's hard to reach statistical significance. It is something that I think you should include in your manuscript to let the reader decide how important that is to know.

Dr Bedzra. We will do that. Thank you.

Dr Damle. Ultimately, I agree with your conclusion that an isolated test such as an FEV₁ or a DLCO should not in and by itself be a decision maker for LVAD implant. I believe what your paper really highlights is that when

appropriately selected patients undergo VAD implantation, at an experienced center such as yours, even patients with seemingly poor pulmonary function can have excellent results. I congratulate you on your work.

Dr Bedzra. Thank you.

Discussant 2. I'd like to ask a question. We know Dr Modudan will dress a cadaver so that he can operate on them, so my question is when do you not operate on a patient? I mean, if somebody in a wheelchair comes in on 6 liters of oxygen, they have a DLCO of 25, are you still operating on these patients?

Dr Bedzra. That is an excellent question. Thank you. As Dr Damle alluded to, I think the crux of this paper is that one test does not determine the performance of the patient postoperatively.

Discussant 2. So why do you do the test? You said it's your protocol that you do preoperative PFTs, so why are you getting the test?

Dr Bedzra. Yes, so we use the test in conjunction with other measures of pulmonary morbidity, such as the presentation of the patient. Is he in a wheelchair, is he using oxygen, what are the computed tomography scan findings, and whether there is any morbidity or ambiguity. We do evaluate these patients using a cardiopulmonary exercise test to look at their cardiopulmonary exercise conditioning.

Discussant 2. But they have heart failure. They're all going to have a low cardiopulmonary exercise test score. If you're doing a VAD on somebody with a VO_2 of 18, then you probably shouldn't be doing it. How low is low? We want a number. The people in this audience want a number. When will the University of Washington not do an LVAD on a patient?

Dr Bedzra. Yeah, that's an excellent question. I can tell you that ... I can tell you that in our database, our FEV_1 values go as low as 23%; however, as has been previously mentioned, we did not evaluate patients with numbers less than this and, in fact, we have had patients with lower numbers that we had to turn down because of LVAD comorbidities, so I cannot give you an absolute number, especially since we didn't do statistical analysis looking at inflection points on this database, but I can assure you that we take all the comorbidities and tests into consideration when deciding on whom to operate.

Discussant 2. Thank you.

Dr Bedzra. Thank you.

Dr Sussman. Dan Miller.

Dr Dan Miller. Great presentation. When you include PFTs for evaluation, I think it's very important especially in these patients, you've got to look at their smoking status, their pack years, and also their oxygen supplementation before. If they're on 1 liter, if they're on 6 liters, you know, they're in a wheelchair, you know, whatever, but you've got to include O_2 supplementation and smoking in this to get a better idea because there are going to be some patients, 120 pack-year smokers, on 6 to 8 liters. A patient shouldn't be done, but you have to clarify that group. You have that information, you just need to pull that out.

Dr Bedzra. Thank you. The database we have currently does not capture that; however, a reasonable proxy for that is the FEV_1 to FVC ratio or the FVF 25% to 70%. Although that data is not presented here, we have analyzed that and the findings are entirely similar to what we've presented.

Dr Sussman. Thank you.

Readers who found these articles interesting may also like to read the following papers found in recent and future issues of our sister publications, *Seminars in Thoracic and Cardiovascular Surgery* and *Operative Techniques in Thoracic and Cardiovascular Surgery*!

Acquired: Mechanical Circulatory Support

ORIGINAL SUBMISSION: Central Cannulation as a Viable Alternative to Peripheral Cannulation in Extracorporeal Membrane Oxygenation David N. Ranney. *Semin Thoracic Surg* 2017: 188-195.

Editorial Commentary: Primum Nil Nocere, Second be Cautious and Third Try to Use the Right Extracorporeal Membrane Oxygenator Modality D Berdajs. *Semin Thoracic Surg* 2017: 196-197.

ORIGINAL SUBMISSION: Minimally Invasive Implantation: The Procedure of Choice! Jan D. Schmitt. *Oper Tech Thorac Cardiovasc* 2016: 60-73.

TABLE E1. Correlation of postoperative outcomes with pulmonary function test categories

Characteristic	1	2	3	4	5	P value
FEV₁ group						
n	13	64	64	62	60	
Mortality						
Unadjusted, HR (95% CI)	1.11 (0.3–4.0)	1.03 (0.5–2.4)	0.95 (0.4–2.2)	1.05 (0.5–2.4)	1	.999
Adjusted, HR (95% CI)	0.83 (0.2–3.2)	0.75 (0.3–1.7)	0.71 (0.3–1.7)	0.90 (0.4–2.1)	1	.934
Spline analysis, HR (95% CI)	1.02 (0.8–1.3)	0.96 (0.9–1.0)	1.05 (1.0–1.1)	1.01 (0.96–1.05)	1	.713
Hospital length of stay, d, mean (SD)	28.2 (17.4)	23.7 (15.2)	22.6 (12.6)	21.2 (14.3)	18.0 (11.8)	
Unadjusted ratio (95% CI)	1.55 (1.1–2.1)	1.32 (1.1–1.6)	1.25 (1.0–1.5)	1.10 (1.0–1.5)	1	.012
Adjusted ratio (95% CI)	1.43 (1.0–2.0)	1.27 (1.1–1.5)	1.22 (1.0–1.5)	1.07 (0.9–1.3)	1	.04
ICU length of stay, mean (SD)	8.5 (4.1)	7.5 (6.7)	8.7 (9.8)	8.7 (11.4)	7.1 (8.1)	
Unadjusted ratio (95% CI)	1.18 (0.7–1.9)	1.09 (0.8–1.4)	1.20 (0.9–1.6)	1.15 (0.9–1.5)	1	.719
Adjusted ratio (95% CI)	1.08 (0.7–1.7)	1.05 (0.8–1.4)	1.13 (0.9–1.5)	1.03 (0.8–1.4)	1	.915
DLCO group						
n	41	55	55	48	40	
Mortality						
Unadjusted, HR (95% CI)	1.20 (0.5–3.1)	1.00 (0.4–2.6)	1.55 (0.6–3.7)	1.69 (0.6–4.4)	1	.837
Adjusted, HR (95% CI)	0.95 (0.4–2.6)	0.83 (0.3–2.2)	1.46 (0.6–3.6)	1.13 (0.4–3.0)	1	.754
Spline analysis, HR (95% CI)	0.90 (0.8–1.0)	1.2 (1.0–1.4)	0.89 (0.7–1.1)	1.0 (0.9–1.1)	1	.395
Hospital length of stay, d, mean (SD)	23.9 (13.1)	19.4 (10.0)	24.4 (16.9)	21.6 (13.3)	17.0 (11.0)	
Unadjusted ratio (95% CI)	1.41 (1.1–1.8)	1.14 (0.9–1.4)	1.44 (1.2–1.8)	1.27 (1.0–1.6)	1	.005
Adjusted ratio (95% CI)	1.44 (1.2–1.8)	1.16 (0.9–1.4)	1.46 (1.2–1.8)	1.33 (1.1–1.6)	1	<.001
ICU length of stay, mean (SD)	6.8 (3.5)	6.8 (4.2)	11.1 (15.7)	8.5 (8.3)	5.8 (4.8)	
Unadjusted ratio (95% CI)	1.16 (0.8–1.6)	1.17 (0.9–1.6)	1.89 (1.4–2.5)	1.46 (1.1–2.0)	1	<.001
Adjusted ratio (95% CI)	1.19 (0.9–1.6)	1.16 (0.9–1.5)	1.78 (1.3–2.4)	1.46 (1.1–2.0)	1	<.001

FEV₁, Forced expiratory volume in 1 second; HR, hazard ratio; CI, confidence interval; SD, standard deviation; ICU, intensive care unit; DLCO, diffusion capacity of the lungs for carbon monoxide.