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Changes in Cardiopulmonary Exercise Testing Parameters Following Continuous Flow Left Ventricular Assist Device Implantation and Heart Transplantation

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Abstract

Background—Reduced exercise tolerance from impaired cardiac output is an important criterion for left ventricular assist device (LVAD) implantation. However, little is known about how exercise capacity changes following LVAD, and how changes compare with patients undergoing heart transplant.

Methods and Results—We compared changes in cardiopulmonary exercise testing performed pre- and post-operatively in patients who underwent HeartMate II LVAD implantation (n=25) and heart transplantation (n=74) at the Mayo Clinic in Rochester, Minnesota from 2007–2012. Pre-operatively, patients undergoing LVAD and transplant had markedly reduced exercise time (mean 5.1 minutes [45% predicted] and 5.0 minutes [44% predicted], respectively), low peak VO₂ (mean 11.5 mL/kg/min [43% predicted] and 11.9 mL/kg/min [38% predicted]), and abnormal ventilatory gas exchange (VE/VCO₂ nadir 39.4 and 37.4). Following LVAD and transplant, there were similar improvements in exercise time (mean +1.2 vs. 1.7 minutes, respectively, p=0.27) and VE/VCO₂ nadir (mean –3.7 vs. –4.2, p=0.74). However, peak VO₂ increased post-transplant but did not change post-LVAD (mean +5.4 vs. +0.9 mL/kg/min, respectively, p<0.001). Most patients (72%) had a peak VO₂<14 mL/kg/min post-LVAD.

Conclusions—While improvements in exercise capacity and gas exchange are seen following LVAD and heart transplant, peak VO₂ doesn't improve post-LVAD and remains markedly abnormal in most patients.

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DISCLOSURES. None.

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Keywords

exercise capacity; left ventricular assist device; heart transplantation

INTRODUCTION

A limitation in exercise capacity is one of the hallmark features of patients with advanced heart failure (HF). Cardiopulmonary exercise testing (CPET) is a mainstay in the objective assessment of exercise capacity in patients with advanced HF. A marked reduction in peak oxygen consumption (VO_2) is a widely established marker of adverse prognosis^{1,2}, and an important criterion in determining candidacy for heart transplantation³. However, the limited supply of donor organs and prolonged wait list times have prompted the development of alternative cardiac replacement strategies such as left ventricular assist devices (LVAD). With advances in technology and mechanical circulatory support, LVADs are increasingly being used in patients with advanced HF as a bridge to transplant (BTT) or as destination therapy (DT). Early on, patients were implanted with LVADs that provided pulsatile flow, but in the current era, patients primarily receive LVADs that deliver continuous flow. While pulsatile LVADs more closely mimicked normal physiologic conditions, continuous flow devices are smaller, more durable, and associated with better outcomes⁴.

However, information on exercise capacity changes after implantation of a continuous flow LVAD is limited, and how this may compare to patients treated with heart transplantation has not been comprehensively explored. Earlier reports have suggested that exercise performance remains suboptimal in some post-LVAD patients⁵⁻⁷, however, these studies are limited as CPET was not performed pre-LVAD for comparison and hence the effect of this intervention on exercise parameters is unknown. There have also been disparate reports regarding whether exercise capacity is comparable in patients who have had LVAD as compared to heart transplantation⁵⁻⁷, which is important given that LVADs are being considered as an alternative to heart transplantation in some patients. In addition, it is unknown how exercise capacity may change in women, older patients, and especially those treated with LVAD as DT rather than BTT, as these populations have not been represented in prior studies.

Therefore, we undertook the present study to investigate how CPET parameters change following continuous flow LVAD when implanted as DT and BTT, and how these changes compare to patients treated with heart transplantation.

METHODS**Patient Population**

This was an observational retrospective cohort study including patients that underwent heart transplantation or LVAD implantation at the Mayo Clinic from 2007–2012. We included all patients who underwent LVAD implantation who had cardiopulmonary exercise testing (CPET) performed both pre- and post-LVAD. As we were interested in comparing changes in CPET parameters post-LVAD to post-transplant, we also included patients undergoing

cardiac transplantation from 2007–2012 who had CPET performed pre- and post-transplant. We excluded patients who underwent transplantation of multiple organs. Given the age distribution in the LVAD population (youngest patient 37 years old), we excluded transplant patients who were <30 years old at the time of transplant. This study was approved by the Mayo Clinic Institutional Review Board.

Cardiopulmonary Exercise Testing

Symptom-limited treadmill exercise testing with respiratory gas exchange analysis was performed using a modified Naughton protocol (2-min workloads, 2 METs/min increments in work) as previously described⁸. Electrocardiograms were continuously monitored and blood pressure was assessed the last 30 s of each 2-min workload. Patients were encouraged to exercise to exhaustion. Exercise duration was expressed in minutes and in percent of age- and gender-predicted value⁹. Predicted exercise time was calculated according to the following formula: $17.1 - 0.13 \times \text{age}$ (in men) and $14.3 - 0.10 \times \text{age}$ (in women). The ratio of minute ventilation to carbon dioxide production (VE/VCO_2), a measure of the efficiency of respiratory gas exchange, and peak oxygen consumption (peak VO_2) were measured using a Medical Graphics metabolic cart (St. Paul, Minnesota). Calibration used gravimetric quality gases before each test and physiologic calibration for weekly quality control. VE/VCO_2 nadir was taken as the lowest 30 second average during exercise. Peak VO_2 was the highest averaged 30-s VO_2 during exercise and was expressed as absolute peak- VO_2 or normalized peak VO_2 (percent of age, gender, and weight predicted). Quality of exercise effort was assessed by respiratory exchange ratio (RER) and the Borg Rating of Perceived Exertion Scale. This scale measures patient-perceived exertion with numeric values ranging from 0 to 20; values of 17 and above are indicative of very hard, extremely hard, and maximal exertion. Abnormal heart rate (HR) recovery was defined as a decline in HR of ≥ 12 bpm at one-minute after maximal exercise. CPET is routinely done as a part of the pre-transplant evaluation (unless the patient is too unstable to complete) and annually post-transplant. CPET is not a requirement at our institution pre-LVAD, as patients are often too unstable to complete the testing. Since 2010, the performance of CPET at one-year post LVAD has been encouraged. When two or more CPET were performed pre-LVAD or transplant, we used the one closest to the date of surgery. When two or more CPET were performed post-LVAD or transplant, we used the test performed closest to one year post-LVAD or transplant. All LVAD patients were on full LVAD support at the time of CPET.

Clinical Characteristics

Diabetes was defined by physician's diagnosis or use of medications to treat diabetes at the time of LVAD implantation or heart transplant. Peripheral vascular disease was defined by physician's diagnosis or the presence of $>50\%$ stenosis in a carotid artery on duplex ultrasound routinely performed pre-LVAD and heart transplant. Chronic obstructive pulmonary disease (COPD) was defined by physician's diagnosis or the presence of moderate or severe obstruction on pulmonary function testing performed pre-LVAD and heart transplant. Body mass index (BMI) was calculated based on the height and weight at the time of LVAD implantation or heart transplantation. Left ventricular ejection fraction (EF) was recorded from transthoracic echocardiograms performed during routine clinical practice as previously described¹⁰.

Sensitivity Analysis

On average, the patients undergoing LVAD implantation were older than patients undergoing heart transplantation. To address the issue of whether differences in age may have impacted results observed, we performed a sensitivity analysis where we matched LVAD patients and heart transplant patients by age (± 3 years) and sex. To maximize the number of patients included, we matched up to 4 heart transplant patients per LVAD patient. As the overall findings were similar compared with the primary analysis, the results of the sensitivity analysis are presented in the Supplementary Materials.

Statistical Analysis

Baseline patient characteristics are presented as mean $\pm$ standard deviation, median (interquartile range) or number (%) as appropriate. Differences in baseline characteristics between LVAD and heart transplant patients were compared using t-tests for normally-distributed continuous variables, Wilcoxon rank sum test for non-normally distributed continuous variables, and χ^2 or Fisher's exact test for binary variables. To determine whether changes in CPET parameters occurred following LVAD and heart transplant, pre- and postoperative values were compared using paired t-tests. To detect whether changes occurring post-LVAD differed from changes post-transplant, we compared paired differences between groups using t-tests. Least-squares regression analysis modeling was used to estimate the relative contributions of the clinical variables to the change in normalized peak VO_2 following LVAD implantation or heart transplantation. Variables with a significance level of $p < 0.1$ were included in the multivariable model. Data were analyzed using Stata/SE 13.0. A p value of < 0.05 was used as the level of significance in all analyses.

RESULTS

Study Population

From 2007–2012, there were 198 patients who had LVAD implantation, 181 of whom received the HeartMate II device, a continuous axial flow pump. In total, 25 patients who underwent LVAD (all HeartMate II) had CPET performed both pre- and post-operatively, and are included in this analysis. In the same time frame, there were 116 patients ≥ 30 years old that had a heart transplant, of whom 74 completed CPET both pre- and post-transplant and are included in this analysis. Patients undergoing LVAD implantation were older than transplant patients (mean 63 vs. 54 years, Table 1), though other baseline characteristics were similar. Baseline CPET was performed on average 10.9 ± 8.1 months prior to heart transplant and 3.0 ± 4.5 months prior to LVAD. The type of beta blocker prescribed at the time of CPET (69% carvedilol, 21% metoprolol succinate, 9% metoprolol tartrate) and total daily dose (median carvedilol dose 25 mg total daily, median metoprolol succinate/tartrate dose 50 mg daily) did not differ in patients pre-LVAD compared with pre-transplant. At CPET, the resting HR, blood pressure, exercise time, and peak VO_2 were similar pre-LVAD and pre-transplant.

Changes in Cardiopulmonary Exercise Testing After LVAD

Pre-LVAD, patients had markedly reduced exercise time (5.1 ± 1.4 minutes, $45\% \pm 15\%$ predicted) and peak VO_2 (11.5 ± 2.5 mL/kg/min, normalized peak VO_2 $43\% \pm 10\%$, Table 2, Figure 1). They often had impaired gas exchange with exercise as noted by an elevated VE/VCO_2 nadir (39.4 ± 5.2). Nearly all patients (96%) had abnormal HR recovery. Post-LVAD, patients underwent CPET testing a median (25th, 75th percentile) of 12 months (4, 25 months) after LVAD implantation. Nine patients (36%) were in atrial fibrillation at the time of CPET; baseline HR was similar to patients who were not in atrial fibrillation. It was not feasible to obtain blood pressure during exercise in most patients post-LVAD. Post-LVAD patients were able to exercise an average of 1.2 minutes longer than pre-LVAD, with substantial improvements in gas exchange during exercise (mean VE/VCO_2 nadir -3.7). While abnormal HR recovery persisted in most patients (72%), the magnitude of HR recovery improved post-LVAD (mean 1-minute decline 4.7 bpm pre-LVAD compared with 11.6 bpm post-LVAD, $p=0.008$). However, the modest increases seen in peak VO_2 (mean $+0.9$ mL/kg/min) were not statistically significant, and peak VO_2 remained markedly abnormal in most patients (normalized peak VO_2 $48\% \pm 12\%$, Figure 1). Notably, 18 patients (72%) had a peak VO_2 of <14 mL/kg/min post-LVAD. There were no differences in the change in exercise capacity or peak VO_2 in patients who had LVAD implanted as DT vs. BTT, in patients with ischemic cardiomyopathy vs. non-ischemic cardiomyopathy, or by age at implant. However, women had greater improvements in exercise time (mean $+3.1$ vs. $+0.6$ minutes, $p=0.033$) and had a trend toward more frequent improvement of their normalized peak VO_2 (100% vs. 63%, $p=0.10$) compared with men following LVAD. There was no relationship between the timing of CPET post-LVAD and peak VO_2 ($r=0.014$, $p=0.95$) and change in VO_2 ($r=-0.18$, $p=0.39$) compared with pre-LVAD. There was no relationship between EF at the time of CPET post-LVAD and peak VO_2 . Quality of exercise effort (as measured by the RER and Borg Rating of Perceived Exertion scale) was similar on CPET pre- and post-LVAD.

Changes in Cardiopulmonary Exercise Testing After Heart Transplant

Pre-transplant, both exercise time (5.0 ± 1.5 minutes, $44\% \pm 15\%$ predicted) and peak VO_2 (11.9 ± 3.4 mL/kg/min, normalized peak VO_2 $38\% \pm 11\%$) were markedly reduced, with impairment in VE/VCO_2 nadir (Table 2, Figure 1). Post-transplant, patients underwent CPET a median (25th, 75th percentile) of 12 months (12, 13 months) after heart transplantation. Post-transplant, both exercise duration (mean $+1.7$ minutes) and peak VO_2 (mean $+5.4$ mL/kg/min) significantly increased. Consistent with cardiac denervation post-transplant, the baseline and peak HR was higher post-transplant, and HR recovery was markedly abnormal. There was no relationship between the timing of CPET post-transplant and peak VO_2 ($r=-0.038$, $p=0.75$) and change in VO_2 ($r=-0.13$, $p=0.26$) compared with pre-transplant.

Comparing Changes in Cardiopulmonary Exercise Testing Post-LVAD and Post-Transplant

Patients who underwent heart transplantation had greater improvements in peak VO_2 compared with patients who underwent LVAD implantation (Table 2, Figure 1B and 2). On multivariable analysis, normalized peak VO_2 pre-LVAD or pre-transplant, BMI, and LVAD

implant (compared with heart transplant) were independent predictors of the change in normalized peak VO_2 following LVAD or heart transplant (Table 3). Patients receiving a heart transplant had 11.6% greater improvement in their normalized peak VO_2 compared with patients who underwent LVAD ($p=0.001$). In contrast, improvements in VE/VCO_2 nadir were similar post-LVAD and transplant. Comparing changes in exercise time following heart transplant and LVAD, the absolute difference in exercise time (mean increase 1.7 vs. 1.2 minutes, respectively, $p=0.27$) and the proportion of patients who improved their exercise time (92% vs. 80%, $p=0.13$) were similar. However, the change in age and sex-predicted exercise time was greater post-transplant compared with post-LVAD (mean increase 22% vs. 12%, respectively, $p=0.010$). Less patients were taking beta blockers post-transplant compared with post-LVAD (7% vs. 76%, $p<0.001$), though heart rate reserve during CPET was similar ($p=0.13$). There were two LVAD patients (both men) who had CPET performed at baseline, with an LVAD, and after heart transplant. Both had improvements in their exercise time and peak VO_2 after heart transplant compared to LVAD.

DISCUSSION

This study provides important information comparing changes in CPET parameters pre- and post-LVAD and orthotopic heart transplant. First, while improvements in exercise duration and gas exchange were seen following LVAD, peak VO_2 did not change, and most patients continued to have markedly impaired exercise capacity. Results were similar in patients who had LVAD as DT vs. BTT, though women had greater improvements in exercise time compared with men. Patients who underwent heart transplantation had improvements in peak VO_2 in addition to exercise duration and gas exchange.

There are limited data informing us on how exercise capacity and CPET parameters change following LVAD. Previous studies have reported the average peak VO_2 after LVAD implant to range from 14.5 to 24.2 mL/kg/min^{5-7, 11-13}. By comparison, the peak VO_2 post-LVAD was only 12.4 ± 2.8 mL/kg/min in this study, though this may reflect that our population was much older (mean age 63 years) than patients included in prior studies, who were primarily in their 30s and 40s. When compared with normal age- and sex-predicted values, similar to prior reports, we found that exercise capacity and peak VO_2 were still low. Both Kugler and deJonge reported that workload and peak VO_2 were 50–60% of age and sex-predicted after LVAD^{5, 7}, which is similar to our population.

Comparing pre-LVAD exercise parameters to post-LVAD values in each patient allowed us to assess the improvement in exercise capacity conferred by the LVAD, a comparison that was lacking in most prior studies. A single previous study assessed peak VO_2 in 9 patients both pre and 3–6 months post-LVAD, and reported improvement in 8 of 9 patients¹⁴. However, quantification was limited by sample size, and this was primarily a younger population with LVAD implanted as BTT. Other prior reports have solely reported on CPET post-LVAD. Interestingly, we found that patients had a greater improvement in exercise duration than peak VO_2 following implantation of a continuous flow LVAD. Exercise time is affected by many factors and is generally considered at best only a fair surrogate for cardiac output. Physiologically, the suboptimal oxygen consumption post-LVAD may be in

part due to the fact that continuous flow devices have limited ability to modulate cardiac output during exercise. Unlike pulsatile flow LVADs, continuous flow devices are set at a fixed speed. The speed is chosen with a goal of effectively offloading the left ventricle while avoiding excessive emptying (i.e. “suck down”). While cardiac output will increase with increasing venous return, even at fixed pump speed¹⁵, this response may be limited. As such, one might hypothesize that an individual’s ability to augment their cardiac output with exercise may be partially reliant on their native cardiac function. Accordingly, a previous report suggested that LVAD patients with lower EF (18% vs. 24%) had lower peak VO₂ and their exercise capacity was more sensitive to changes in pump speed¹³. However, we saw no relationship between EF at the time of exercise testing after LVAD and peak VO₂. In addition, a separate report found only a moderate correlation ($r=0.53$) between measured cardiac output and peak VO₂ during treadmill testing of patients with LVADs¹¹.

In contrast with an LVAD, patients who have received a heart transplant may have a greater ability to increase their cardiac output in response to exercise, as they don’t have to rely on a device with a fixed pump speed. Certainly these physiologic differences may help to explain the differential improvement in peak oxygen consumption we observed in patients treated with heart transplant vs. LVAD. However, while improvements were greater in heart transplant recipients, they still remained well below age- and sex-predicted normal values. This suboptimal improvement in exercise capacity and VO₂ has been previously reported after orthotopic heart transplant^{16, 17}. Potential contributing factors are numerous and may include chronotropic incompetence due to cardiac denervation¹⁶, effects of chronic corticosteroid use¹⁸, elevated body mass index of the recipient¹⁷, allograft hypertrophy¹⁹, and advanced age of the donor¹⁸. Chronic and likely minimally reversible changes at the level of the skeletal muscle resulting in inefficiency in extracting oxygen²⁰ may contribute to persistently low oxygen consumption in both LVAD and transplant recipients.

While peak VO₂ did not improve following LVAD, we did see improvements in both exercise time and ventilatory gas exchange. Continuous flow LVADs maintained at adequate pump speed are extremely efficacious at offloading the left ventricle. Morgan et al recently reported their experience of 130 patients who had right heart catheterization performed one month after continuous flow LVAD insertion²¹. They found marked improvements in the pulmonary capillary wedge pressure, which decreased from an average of 23.0 mmHg (markedly elevated) to 12.9 mmHg (normal). This marked reduction in left ventricular filling pressure as a consequence of LVAD therapy could account for the improvement in VE/VCO₂ seen herein. As patients are experiencing less dyspnea with exercise due to their improved gas exchange, they are likely to feel better and become more active, leading to improved muscular strength and stamina resulting in the ability to exercise longer. Similarly, it has been previously reported that most patients demonstrate an improvement in 6 minute walk distance following LVAD^{22, 23}.

Limitation, Strengths, and Clinical Implications

There are limitations that should be acknowledged to aid in interpretation of these data. First, CPET was performed as a part of routine clinical practice rather than a study protocol, so timing of CPET post-LVAD and transplant varied. However, no relationship between the

duration of time after LVAD and exercise duration or peak VO_2 was observed in this or other recent studies¹⁴. Furthermore, the 25 patients with LVAD included in this analysis represent only a subset of those who underwent LVAD implantation at our institution, as most LVAD patients did not have CPET performed both pre- and post-LVAD, and patients who were not well enough to undergo CPET would not have been included. Second, we did not control for the number of CPETs a patient might have performed prior to their index pre-LVAD or transplant CPET, meaning some patients may have experienced a test-retest improvement in their exercise time on their post-procedure CPET based on increased test familiarity. Third, our small sample size limits our ability to draw definitive conclusions based on these data, which would benefit from replication in other populations. However, there are several important strengths. First, we were able to rigorously perform CPET in a group of patients both pre- and post-LVAD and compare these findings with changes following heart transplantation. As our program implants a large number of LVADs as DT, we were uniquely positioned to examine changes in CPET in this growing population. Knowing what the destination exercise performance might be after LVAD implantation will help to provide realistic expectations regarding improvement in exercise capacity post-LVAD. A patient with a peak VO_2 that is too high and/or VE/VCO_2 nadir that reflects normal ventilatory gas exchange prior to implantation may not derive improvement in exercise capacity with left ventricular offloading.

Conclusions

While LVAD therapy results in improvement in exercise duration and gas exchange, most patients still exhibit substantial limitations in exercise capacity with use of continuous flow devices. As device technology continues to rapidly advance and evolve, improvements may be seen.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1A

Figure 1B.

Figure 1. Distribution of Exercise Time and Peak VO₂ Before and After LVAD and Heart Transplant

The distribution of exercise time (Panel A) and peak VO₂ (panel B) before and after LVAD (blue) and heart transplant (red) are shown

Figure 2. Improvement in Cardiopulmonary Exercise Testing Following LVAD and Heart Transplant

The proportion of patients with improvement in exercise time, peak VO and VE/VCO₂ post-LVAD (blue) and post-heart transplant (red) are shown

Table 1**Baseline Patient Characteristics**

	LVAD Patients (n=25)	Heart Transplant Patients (n=74)	P value
Demographics, Comorbidities, and Medications			
Age at transplant/LVAD, years	63.4 (9.9)	53.7 (10.5)	<0.001
Female, N(%)	6 (24.0)	17 (23.0)	0.92
Ischemic etiology, N(%)	10 (40.0)	27 (36.5)	0.75
Diabetes, N(%)	7 (28.0)	13 (17.6)	0.26
Peripheral vascular disease, N(%)	2 (8.0)	4 (5.4)	0.99
COPD, N(%)	3 (12.0)	8 (10.8)	0.99
Body mass index, kg/m ²	28.6 (4.5)	28.2 (5.4)	0.69
* Atrial fibrillation, N(%)	4 (16.0)	16 (21.6)	0.59
Left ventricular ejection fraction, %	22.0 (10.3)	25.8(13.4)	0.21
Taking beta blocker, N(%)	22 (88.0)	67 (90.5)	0.72
LVAD parameters			
Destination therapy, N(%)	21 (84.0)	--	
Pump speed at CPET (median, IQR)	9400 (9200, 9600)	--	
Preoperative CPET parameters			
Resting HR, bpm	75.6 (11.9)	73.2 (12.5)	0.42
Resting blood pressure, mmHg			
Systolic	102.3 (16.6)	97.1 (15.0)	0.14
Diastolic	63.0 (9.0)	63.4 (11.8)	0.88
Exercise time, minutes	5.1 (1.4)	5.0 (1.5)	0.73
Peak VO ₂ , mL/kg/min	11.5 (2.5)	11.9 (3.4)	0.54
VE/VCO ₂ nadir	39.4 (5.2)	37.4 (7.3)	0.21

All values shown are mean (standard deviation) unless otherwise noted.

* Proportion of patients in atrial fibrillation at time of pre-operative CPET.

BPM= beats per minute, COPD= chronic obstructive pulmonary disease, CPET= cardiopulmonary exercise testing, HR= heart rate, IQR= interquartile range, LVAD= left ventricular assist device, VO₂ = peak oxygen consumption, Ve/VCO₂ = ratio of minute ventilation to carbon dioxide production

Table 2
Cardiopulmonary Exercise Test Parameters Before and After LVAD and Heart Transplant

Parameter	Pre-LVAD	Post-LVAD	* P value Change LVAD	Pre-Transplant	Post-Transplant	† P value Change Transplant	‡ P Value LVAD vs. Transplant
Vital Signs							
Baseline heart rate, bpm	75.6 (11.9)	80.7 (8.8)	0.16	73.2 (12.5)	97.3 (12.2)	<0.001	---
Peak heart rate, bpm	103.0 (17.5)	109.5 (18.6)	0.25	106.3 (21.3)	132.0 (19.2)	<0.001	---
Heart rate reserve, bpm	27.5 (14.2)	28.8 (17.9)	0.73	33.1 (20.5)	34.8 (16.7)	0.23	---
HR recovery, beats	4.7 (5.1)	11.6 (13.2)	0.008	6.9 (11.2)	-3.0 (5.7)	<0.001	---
Abnormal HR recovery, N(%)	24 (96.0)	18 (72.0)	0.11	61 (82.4)	72 (97.3)	0.51	---
Exercise Parameters							
Exercise time (minutes)	5.1 (1.4)	6.3 (1.9)	0.023	5.0 (1.5)	6.7 (1.6)	<0.001	0.27
% Predicted exercise time	45% (15%)	57% (18%)	<0.001	44% (15%)	65% (18%)	<0.001	0.010
METS	3.3 (0.7)	3.5 (0.8)	0.17	3.4 (1.0)	4.9 (1.3)	<0.001	<0.001
Peak VO2 (mL/kg/min)	11.5 (2.5)	12.4 (2.8)	0.17	11.9 (3.4)	17.3 (4.4)	<0.001	<0.001
Normalized peak VO2	43% (10%)	48% (12%)	0.051	38% (11%)	56% (19%)	<0.001	<0.001
AT as % peak VO2	78% (9%)	77% (8%)	0.69	78% (10%)	74% (9%)	0.019	0.45
VE/VCO ₂ nadir	39.4 (5.2)	35.7 (7.1)	0.017	37.4 (7.3)	33.2 (4.5)	<0.001	0.74
RER	1.14 (0.2)	1.16 (0.12)	0.47	1.16 (0.13)	1.22 (0.12)	<0.001	0.31
‡Rating of Perceived Exertion Very Hard/Maximal, N(%)	24 (96.0)	23 (92.0)	0.63	64 (88.9)	70 (95.9)	0.09	0.20

AT= anaerobic threshold, HR= heart rate, All values shown are mean (standard deviation) unless otherwise noted.

* P value compares pre- and post-exercise parameters for patients undergoing LVAD

† P value compares pre- and post-exercise parameters for patients undergoing cardiac transplantation

‡ P value compares the change in CPET measurements for patients undergoing LVAD vs. cardiac transplantation

§ Borg Rating of Perceived Exertion at Peak Exercise 17. Data missing on 2 patients pre-transplant and 1 patient post-transplant

Table 3
Associations of Clinical Variables with Change in Normalized Peak VO₂ after LVAD and Heart Transplant

Variable	Univariate analysis		Multivariate Analysis	
	Estimate	P Value	Estimate	P Value
Normalized Peak VO ₂ Pre-LVAD/Heart Transplant	-0.34	0.002	-0.32	0.027
Age at LVAD or Transplant	0.034	0.82	---	---
Male sex	-2.7	0.49	---	---
Body mass index (kg/m ²)	-0.66	0.058	-0.84	0.010
LVAD implant (compared with heart transplant)	-12.9	<0.001	-11.6	0.001
Effort quality (RER post LVAD or transplant)	19.1	0.17	---	---

LVAD= left ventricular assist device; RER= respiratory exchange ratio