Comparison of Exercise Performance in Patients With Chronic Severe Heart Failure Versus Left Ventricular Assist Devices

Donna Mancini, MD; Rochelle Goldsmith, PhD; Howard Levin, MD; Ainat Beniaminovitz, MD; Eric Rose, MD; Katharine Catanese, RN; Margaret Flannery, RN; Mehmet Oz, MD

**Background**—Left ventricular assist devices (LVADs) are frequently used as a bridge to cardiac transplantation and may be useful as long-term therapy. The purpose of this study was to compare the exercise performance of LVAD patients with that of ambulatory heart failure patients.

**Methods and Results**—Exercise testing with hemodynamic and respiratory gas measurements was performed in 65 congestive heart failure (CHF) patients (age 53±10 years) and 20 LVAD patients (age 49±8 years). Peak $\dot{V}O_2$ was significantly higher in the LVAD than the CHF patients (CHF, 12±3; LVAD, 15.9±3.8 mL·kg⁻¹·min⁻¹; $P<0.001$), as was the $\dot{V}O_2$ at the anaerobic threshold (CHF, 8.1±2.1; LVAD, 12.2±2.9 mL·kg⁻¹·min⁻¹; $P<0.001$). At rest, mean arterial blood pressure (CHF, 87±11; LVAD, 94±9 mm Hg) and cardiac output (CHF, 4±1; LVAD, 4.9±0.9 L/min) were increased, whereas mean pulmonary artery pressure (CHF, 28±11; LVAD, 18±4 mm Hg) and pulmonary artery wedge pressure (CHF, 16±10; LVAD 5±3 mm Hg) were reduced (all $P<0.001$). At peak exercise, heart rate (CHF, 125±24; LVAD, 148±24 bpm), blood pressure (CHF, 87±14; LVAD, 96±12 mm Hg), and cardiac output (CHF, 48±12; LVAD, 30±5 mm Hg) and mean pulmonary capillary wedge pressure (CHF, 31±11; LVAD, 14±6 mm Hg) were lower in the LVAD group (both $P<0.001$). In the LVAD patients, Fick cardiac output was higher than LVAD flow sensor value measurements (Fick, 11.6±2.5; LVAD, 8.1±1.2 L/min; $P<0.001$).

**Conclusions**—Hemodynamic measurements at rest and during exercise are significantly improved in patients with devices compared with those in ambulatory heart failure patients awaiting cardiac transplantation. Similarly, the exercise capacity of device patients is better than that of transplant candidates and in the majority of patients is similar to that of patients with mild CHF. *(Circulation. 1998;98:1178-1183.)*

**Key Words:** exercise ■ heart failure ■ heart assist device

Left ventricular assist devices (LVADs) are increasingly used as a bridge to cardiac transplantation and may represent a permanent alternative therapy for the management of end-stage heart failure. If chronic mechanical support is to become a therapeutic option, it is important to assess the functional capacity of device patients. Prior reports have described peak exercise performance with measurement of oxygen consumption in only small numbers of patients. Murali et al., in a preliminary report, described peak $\dot{V}O_2$ in 7 patients with the Novacor System. Peak $\dot{V}O_2$ averaged 16 mL·kg⁻¹·min⁻¹. Jaskie et al. reported on 2 patients with Thermo Cardio Systems (TCI) devices with an average peak $\dot{V}O_2$ of 15.5 mL·kg⁻¹·min⁻¹. We previously examined the submaximal and maximal exercise performance in 14 patients with TCI LVADs compared with patients with mild, moderate, and severe congestive heart failure (CHF). Peak $\dot{V}O_2$ averaged 17.0±4.5 mL·kg⁻¹·min⁻¹. Six-minute walk and peak $\dot{V}O_2$ in device patients were comparable to those in patients with mild CHF. Jaskie et al reported on exercise hemodynamic measurements in 10 TCI patients during supine bicycle exercise. $\dot{V}O_2$ during supine exercise was 8.2 mL·kg⁻¹·min⁻¹, and during upright exercise, it averaged 14.1 mL·kg⁻¹·min⁻¹.

The purpose of the present study was to compare upright exercise hemodynamic and metabolic measurements in a larger group of LVAD patients with those of ambulatory patients with chronic severe heart failure.

**Methods**

**Subjects**

Sixty-five patients referred for cardiac transplantation participated in the exercise study (Table 1). Forty-seven patients were male and 19 female. The mean±SD age was 53±10 years. Twenty-nine percent of patients had NYHA class II, 65% had class III, and 6% had class IV heart failure symptomatology. The pathogenesis of heart failure...
was coronary artery disease in 29% of patients, dilated cardiomyopathy in 63%, and end-stage valvular disease in the remaining 8%. Left ventricular ejection fraction averaged 22±9%. Peak exercise oxygen consumption averaged 12.1±3.0 mL kg⁻¹ min⁻¹. All patients were receiving treatment with digoxin, diuretics, and vasodilators. Patients who were limited by angina or claudication were not eligible for study. All patients had had a prior exercise test as part of their transplantation evaluation. Eighty-two percent of the CHF patients had a prior exercise test as evaluation for cardiac transplantation. Eighty-two percent of the CHF patients had an electrical device and 9 a pneumatic device. Only 6 of these patients had coronary artery disease and 13 had cardiomyopathy. Eleven patients had coronary artery disease and 13 had cardiomyopathy. Eleven patients had an electrical device and 9 a pneumatic device. Only 6 of these patients had a prior exercise test as part of their transplantation evaluation. Eighty-two percent of the CHF patients were accepted as transplant candidates, with only 6% being considered too well (n=4) for transplantation.

Twenty LVAD patients (TCH HeartMate, Thermo Cardiosystems, Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%. Inc) were studied. The mean age of the 18 men and 2 women was 53±10 years. Ejection fraction averaged 22±9%.
Thus, the heart failure patients were at peak exercise when the device patients were just becoming anaerobic. Respiratory quotient at peak exercise was similar between the 2 groups, indicating similar efforts (CHF, 1.12 ± 0.0; LVAD, 1.14 ± 0.1).

The anaerobic threshold occurred at 67% of peak \( V \dot{O}_2 \) in the CHF and 76% of peak \( V \dot{O}_2 \) in the LVAD patients. Resting and peak lactate levels were similar between the 2 groups (Table 2).

### Hemodynamic Measurements

Resting heart rates were comparable for the 2 groups (Table 2). At peak exercise, maximum heart rate was significantly higher in the LVAD group (CHF, 125 bpm; LVAD, 148 bpm; \( P < 0.001 \)). This may reflect the greater amount of work performed by LVAD patients versus an improvement in baroreceptor function during exercise. Resting and peak mean arterial blood pressures were significantly higher in the LVAD patients, averaging 94 and 96 mm Hg at rest and peak exercise, respectively, versus 87 at rest and peak exercise in patients with CHF.

Mean right atrial pressure tended to be lower in the LVAD patients at rest and during exercise, but this did not reach statistical significance. At peak exercise, mean right atrial pressure was 11 mm Hg in the CHF patients and 8 mm Hg in the LVAD patients.

In both the CHF and LVAD patient groups, pulmonary pressures rose significantly with exercise (\( P < 0.05 \) for all). However, patients with severe CHF developed marked pulmonary hypertension during exercise. In patients with CHF, mean pulmonary artery pressure at rest averaged 28 mm Hg, ranging from 11 to 51 mm Hg. At peak exercise, pulmonary artery pressure averaged 48 mm Hg, ranging from 21 to 70 mm Hg. Mean pulmonary artery pressure was dramatically lower at rest and throughout exercise in the LVAD patients (Figure 2). Indeed, the peak mean pulmonary artery pressure of the LVAD patients at 30 mm Hg approximated the resting value in CHF patients. Similarly, resting and peak pulmonary capillary wedge pressures were significantly lower in the LVAD patients. In CHF, pulmonary capillary wedge pressures rose from 16 to 31 mm Hg. In the LVAD patients, in contrast, pulmonary capillary wedge pressures rose from 5 to 14 mm Hg. Figure 2 shows the mean pulmonary capillary wedge pressures at rest and throughout exercise for the heart failure and device patients.

Cardiac output and cardiac index at rest and peak exercise were significantly greater in the LVAD patients than the heart failure patients. Cardiac index in the CHF patients rose from 2.1 to 3.8 \( L \cdot \text{min}^{-1} \cdot \text{m}^{-2} \). In the LVAD patients, in contrast, cardiac index rose from 2.6 to 5.8 \( L \cdot \text{min}^{-1} \cdot \text{m}^{-2} \). The cardiac output response to exercise for the heart failure and LVAD patients is depicted in Figure 3.

### Table 2. Rest and Exercise Metabolic and Hemodynamic Measurements in the CHF and LVAD Patients

<table>
<thead>
<tr>
<th></th>
<th>CHF</th>
<th>LVAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>( V \dot{O}_2 ), mL \cdot kg^{-1} \cdot min^{-1}</td>
<td>3.9 ± 0.7</td>
<td>12.1 ± 3.0</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>86 ± 16</td>
<td>125 ± 24</td>
</tr>
<tr>
<td>Mean arterial BP, mm Hg</td>
<td>87 ± 11</td>
<td>87 ± 14</td>
</tr>
<tr>
<td>Right atrial, mm Hg</td>
<td>4 ± 5</td>
<td>11 ± 8</td>
</tr>
<tr>
<td>Pulmonary artery, mm Hg</td>
<td>28 ± 11</td>
<td>48 ± 12</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>16 ± 10</td>
<td>31 ± 11</td>
</tr>
<tr>
<td>Pulmonary artery saturation, %</td>
<td>53 ± 8</td>
<td>27 ± 9</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>4.04 ± 1.02</td>
<td>7.58 ± 2.15</td>
</tr>
<tr>
<td>Cardiac index, L \cdot \text{min}^{-1} \cdot \text{m}^{-2}</td>
<td>2.06 ± 0.47</td>
<td>3.80 ± 1.31</td>
</tr>
<tr>
<td>Lactate, mmol/L</td>
<td>1.0 ± 0.5</td>
<td>5.2 ± 1.7</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; PCWP, pulmonary capillary wedge pressure.

\( * P < 0.01 \) LVAD vs CHF.
Echocardiography reveals that the aortic valve is usually closed at rest during device support. With exercise, however, opening of this valve can be seen. Fick cardiac output measures total cardiac output, whereas the LVAD sensor measurement monitors flow through the device. Fick and LVAD sensor measurements for each device patient at peak exercise are shown in Figure 4. In the LVAD patients, peak Fick cardiac output averaged 11.6 L/min and was significantly greater than the sensor measurement of 8.1 L/min. Moreover, the difference between the Fick cardiac output and LVAD sensor output was incremental with exercise workload. The differences were 1.8±1.3, 2.0±1.1, 2.5±1.5, and 3.6±1.9 at 0, 25, 50, and 75 W, respectively (P<0.002). These findings suggest some contribution from the native heart.

Ventilatory Measurements
Patients with CHF have an excessive ventilatory response to exercise that may be due to increased physiological dead space ventilation, early lactic acidosis, or reduced lung perfusion. Despite the improved hemodynamic measurements, minute ventilation (Ve) was the same at rest and throughout exercise in the CHF and LVAD patients (Figure 5). Ve/VCO2, the ventilatory equivalent for CO2 production at the anaerobic threshold, can also be used to assess the ventilatory response to exercise normalized for CO2 production. The Ve/VCO2 was the same for both groups, averaging 39 (normal, ~27).

The symptoms limiting exercise were comparable between the 2 groups of patients (Table 3). Thirty-five percent of patients with LVAD and 23% of patients with CHF were limited by dyspnea; 55% of patients with LVAD and 71% of patients with CHF were limited by fatigue. Ratings of perceived dyspnea and fatigue in the CHF and LVAD patients are shown in Table 4. At submaximal and peak workloads, ratings of fatigue were lower in the LVAD patients. However, perceived dyspnea was similar between the two groups at submaximal and peak exercise.

Discussion
This study demonstrates that the exercise capacity of ambulatory device patients as measured by peak VO2 is significantly greater than that of ambulatory patients with severe heart failure. Additional findings included a higher VO2 at anaerobic threshold in the device patients, improved hemodynamic measurements at rest and throughout exercise, and a similar ventilatory response to exercise in the two groups.

Peak Exercise Performance
The peak VO2 of the device patients was similar to that in previous reports of patients with the TCI or Novacor systems. However, this is the first large comparison study of maximal upright exercise in patients with mechanical assist devices versus patients with severe heart failure. Peak exercise performance of the LVAD patients was significantly greater than that of the patients with severe CHF. Medical treatment of the device patients was minimal, with only 15% of patients receiving ACE inhibitors; therefore, their level of exercise performance was achieved almost exclusively from device therapy. Whether additional medical therapy could further improve the exercise performance of the device patients is unclear; however, it is likely, particularly in patients with significant right ventricular dysfunction.

Before implantation of the device, all the device patients were bedridden on multiple positive inotropic agents or temporary mechanical support. The preimplant VO2 of these

**TABLE 3. Symptoms Limiting Exercise Performance**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>CHF, n</th>
<th>LVAD, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>46</td>
<td>11</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Both</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
The measured peak \( V_{\text{O}_2} \) in the LVAD patients, although significantly better than that in the heart failure patients, is lower than predicted on the basis of maximum device output. For example, in a man weighing 70 kg, peak \( V_{\text{O}_2} \) should approach 25 \( \text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \), given a maximum device output of 10 L/min. Inability to achieve maximal performance may be the result of peripheral abnormalities and/or right ventricular dysfunction, which is not treated with LVAD support. Some of the abnormalities in the vasculature and/or skeletal muscle described in patients with heart failure may be irreversible. Katz et al.\(^\text{10}\) demonstrated an improvement in the vasodilatory capacity of the LVAD patients but not a total normalization of the peak hyperemic response. Several studies have focused on acute right heart function after LVAD insertion, but none have described the effect of extended LVAD support on right ventricular function. Unfortunately, we do not have measurement of right ventricular function in our LVAD patients. Future studies on the contribution of right ventricular function to peak exercise capacity in these patients is also warranted.

In the LVAD patients, the Fick cardiac output was significantly greater than sensor measurements. Echocardiographic studies demonstrate that the aortic valve is usually closed at rest. With stress, there is an increased opening of the aortic valve and thus a contribution from the native heart.\(^\text{4}\) The increase in Fick cardiac output over the device measurement may be a useful parameter to evaluate myocardial recovery. The increment in Fick cardiac output over device output ranged from none to 10.3 L/min. Two patients with dilated cardiomyopathy in whom the Fick cardiac output exceeded device output by 7.4 and 6.4 L/min, respectively, were subsequently successfully explanted, ie, the device was removed without transplantation. In 1 patient in whom Fick cardiac output was >10 L/min higher than that with the LVAD sensor, myocardial recovery at the time of transplantation could not be evaluated because of surgical difficulties. Conversely, a reduction in the Fick cardiac output versus the LVAD sensor may also provide useful clinical information regarding either device malfunction or native aortic insufficiency. In 2 patients, Fick cardiac output was less than that with the device. One of these patients had moderate to severe aortic insufficiency that necessitated reoperation.

### TABLE 4. Ratings of Perceived Fatigue and Dyspnea During and at Peak Exercise in the CHF and LVAD Patients

<table>
<thead>
<tr>
<th>Workload, W</th>
<th>Ratings of Perceived Fatigue (Borg Scale) CHF</th>
<th>Ratings of Perceived Dyspnea (Borg Scale) CHF</th>
<th>Ratings of Perceived Fatigue (Borg Scale) LVAD</th>
<th>Ratings of Perceived Dyspnea (Borg Scale) LVAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.7±1.3</td>
<td>0.2±0.4*</td>
<td>1.4±1.1</td>
<td>1.5±1.4</td>
</tr>
<tr>
<td>25</td>
<td>3.5±1.8</td>
<td>1.2±1.5*</td>
<td>3.0±1.4</td>
<td>2.2±1.8</td>
</tr>
<tr>
<td>50</td>
<td>5.5±2.1</td>
<td>2.8±1.7*</td>
<td>4.5±1.7</td>
<td>3.9±2.7</td>
</tr>
<tr>
<td>75</td>
<td>7.0±2.0</td>
<td>3.9±2.5*</td>
<td>5.4±1.8</td>
<td>3.4±2.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>7.3±2</td>
<td>5.9±2.6*</td>
<td>5.7±1.9</td>
<td>4.8±2.5</td>
</tr>
</tbody>
</table>

*\( P<0.01 \) CHF vs LVAD. †\( P<0.05 \) CHF vs LVAD.
Exercise Hemodynamic and Ventilatory Measurements

During exercise, patients with heart failure develop substantial pulmonary hypertension. The marked pulmonary hypertension observed in heart failure patients during exercise was not observed in the device patients. Indeed, the pulmonary pressures of the device patients at peak exercise were similar to those of the heart failure patients at rest.

During exercise, patients with heart failure have an excessive ventilatory response, possibly due to early onset of lactic acidosis, ventilation-perfusion mismatch from hypoperfusion leading to an increase in dead space ventilation, or respiratory muscle dysfunction. Surprisingly, the ventilatory response to exercise was similar between the 2 groups. Relief of pulmonary hypertension achieved with LVAD therapy had no impact on the chronic ventilatory response to exercise. This finding is consistent with prior reports that acute vasodilation does not affect the ventilatory response in patients with chronic heart failure.

The improvement in cardiac output provided by the device could alleviate dyspnea by mechanisms involving both the peripheral skeletal muscle and lung perfusion. Despite the improved hemodynamics at rest and throughout exercise provided by the LVAD, levels of perceived dyspnea during submaximal workloads only tended to be less in LVAD patients. The absence of any significant improvement in the level of dyspnea or ventilation in the LVAD patients suggests that these abnormal responses may be due to chronic changes in the lungs or the periphery.

Study Limitations

This study is limited in that consecutive LVAD and transplant candidates did not undergo study. Many LVAD patients refused Swan-Ganz catheterization. Many LVAD patients received transplants before the exercise study was scheduled. Patients with CHF on inotropic support were not studied, and CHF patients who were considered too well for transplantation on the basis of NYHA class, exercise performance, ejection fraction, and/or suboptimal medical regimens did not undergo right heart catheterizations. The random sampling of both groups may have skewed the results.

Conclusions

Exercise performance of ambulatory LVAD patients ≈3 months after device insertion is significantly better than that of ambulatory transplant candidates. Exercise performance in the majority of LVAD patients is comparable to that of patients with mild CHF. The increase in VO₂ is comparable to that afforded by cardiac transplantation and better than any single medical therapy. LVAD therapy may provide not only an effective temporary bridge to transplantation but also appropriate chronic therapy.

References

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