

# Cardiac Rehabilitation in Patients with Left Ventricular Assistive Device (LVAD)

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## Abstract

For severe heart failure patients who are refractory to medical treatments or who are unable to receive heart transplantation because of a shortage of donor organs, left ventricular assist device (LVAD) therapy could be a valuable option as not only bridge to transplantation but also destination therapy. The LVAD can substitute the circulatory function of one or both sides of the heart via several pump drive mechanisms. The native left ventricle–LVAD complex responds physiologically and demonstrates a significant circulatory reserve consistent with the capability to meet demands of daily activities. Although several studies have suggested that LVAD patients showed a significant improvement in physical function, exercise capacity and quality of life, early initiation of cardiac rehabilitation should be needed to facilitate improvements in functional independence and survival rate in LVAD patients. To date, unfortunately, exercise training in LVAD patients is in its infancy, and evidence on content, setting, duration of the sessions and safety are inconclusive. Therefore, the further development of various cardiac rehabilitation programs for LVAD patients through ongoing controlled exercise training trials would be warranted. (*J Med Life Sci* 2015;12(2):44–51)

**Key Words :** Left ventricular assist device, Heart failure, Rehabilitation

## Introduction

For severe heart failure (namely, end-stage congestive heart failure (CHF)) patients who are refractory to maximized inotropic medical therapy, intra-aortic balloon pump therapy, or percutaneous cardiopulmonary support, heart transplantation (HT) has been widely accepted as the most effective surgical treatment<sup>1</sup>. However, heart transplantation is rationed by the availability of suitable donor hearts and there has been a steady decline in donor hearts over time<sup>2</sup>.

National Institutes of Health support for cardiac assistive devices led to the formation of research groups involved in the development of the left ventricular assist device (LVAD), a new level of cardiac assistance, in the late 1970s and early 1980s<sup>3, 4</sup>. Ventricular assist devices (VADs) were first used to support 20 transplant candidates with rapidly failing circulation who were considered unlikely to survive until a suitable organ could be found. Of these 20 LVAD recipients,

10 patients were successfully bridged to transplantation, with end-organ dysfunction restored before HT<sup>5</sup>. This situation is described as bridge to transplantation.

Over the years LVADs have become more durable and reliable, smaller, simpler, easier to implant and more comfortable<sup>6,7</sup>. Along with improvements in technology, an extensive experience has now been accumulated with use of LVADs showing that they led to successful hospital discharge and outpatient management for periods of months to years, and significant improvement of functional status. The current approach is to delay delisting of patients for HT until they have recovered physical condition and are stable<sup>8</sup>. In addition, available evidence over the past 10 years have proved to be both an effective bridge to transplantation and, possibly, a realistic alternative to transplantation as a long-term mechanical circulatory support for the vast majority of end-stage CHF patients, ineligible for transplantation due to co-morbidities<sup>7,9,10</sup>. This situation is described as destination therapy.

Given the increasing use of this device in expanding heart failure population, at present, it seems realistic that LVADs will become an alternative to heart transplantation, but one of the prerequisites for long-term LVAD use is that exercise

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performance should be adequate for activities of daily living. Thus, a critical therapeutic goals of cardiac rehabilitation in LVAD patients are to increase functional capacity, to relieve symptoms related with heart failure, to improve psychosocial well-being, and eventually to enhance quality of life(QoL) in LVAD patients. For successful cardiac rehabilitation in LVAD patients, a basic understanding of exercise physiology, exercise testing, and exercise training is essential.

## Exercise hemodynamics

### Structure and function of the LVAD

For LVAD patients, apart from their disease severity, the design itself of the device is also important. There are several versions of LVADs. The principal issue in the selection of a LVAD device are associated with variations in the pump drive(pneumatic-driven versus electrically-driven). In the pneumatic LVAD, a line exiting the patient's abdomen and extending to an external drive console is necessary to provide the pulses of pressurized air that drive the pump. The data console is 8 inches in height and approximately 21 inches in both width and depth. When mounted on the mobile cart, the unit is 42 inches high, about the size of a portable electrocardiogram cart(73 pounds), thus significantly limiting the patients' daily activities. They seem to be preferred for patients who have been on cardiopulmonary bypass support, and those who require biventricular support<sup>11-13</sup>. While electronically powered, the battery permits considerable mobility within the hospital and serves as an emergency backup in the event of a power failure. Although ambulation and upper extremity exercises are feasible, the abdominal location of the externalized driven line makes cycling and various other lower extremity functional activities, such as stair climbing, somewhat problematic. The alternative device is an exclusively battery-dependent device that requires no external drive console; rather, the batteries are contained in a shoulder harness, delivering electrical impulses to drive the pump. Currently, the electric intracorporeal LVAD devices are the preferred device for function of the LVAD, quality of life, and success in bridging to transplantation or recovery. Electric units have used either a single or double pusher plate system to expel blood from the unit. The pusher plates are driven by either a rotary electric motor or an electromechanical activation. Regardless of the drive system, the inflow and outflow of blood is similar for all implantable systems<sup>13-17</sup>.

Placement of the device is within the abdominal cavity, with the inflow cannula and graft traversing either an

opening in the diaphragm or within a pocket below the rectus muscle or posterior to rectus fascia. The inflow cannula is inserted into the left ventricular apex, which uses a pusher-plate mechanism to drive blood flow, and an outflow circuit is anastomosed to the ascending aorta<sup>18</sup>. The chamber capacity of both devices(pneumatic-driven & electrically-driven) is approximately 83 mL, with a rate that increases to a maximum of 140 strokes/min in the pneumatic device and 120 strokes/min in the electric device, providing a mechanical cardiac output of more than 10 L/min, as needed<sup>13</sup>. Implantable LVADs operate in either an automated or manual mode. Although the automated mode is preferred given the increasing number of patients resuming normal daily activity, manual adjustment might be necessary depending on the patient's symptomatic response or in the event the internal sensor fails. In the automated mode, the LVAD senses changes in left ventricular preload or left atrial pressure and makes the corresponding change in rate to keep pace with the increase or decrease in blood flow from the left ventricle. Essentially, all LVADs operate in a fill to empty mode in a "fixed rate", "fill-rate trigger", or "electrocardiogram trigger". Each of these can be set to perform in a synchronous or asynchronous fashion with left ventricular contraction. Synchronous contraction on "fill-rate trigger" allows for maximal unloading of the left ventricle, and pump action is immediately after ventricular systole. This mode allows for control of the pump via native heart function and maximized output. Adequate right-sided cardiac function is essential for optimal LVAD function<sup>19</sup>.

### Exercise physiology

To understand the physiology of exercise in the presence of an LVAD, it is important to consider the function of the native left ventricle; that is, the native left ventricle continues to contract during LVAD operation, and the native heart-LVAD complex responds physiologically and demonstrates a significant circulatory reserve consistent with the capability to meet demands of daily activities. Although the LVAD is essentially placed in parallel, it effectively functions in series with the left ventricle<sup>13</sup>. At rest, Jaski et al<sup>20</sup>, and Branch et al<sup>21</sup>, have demonstrated that during Fick measurement of cardiac output, the LVAD contributes virtually the total cardiac output. However, during exercise, the native left ventricle contributes a varying amount of the total cardiac output. Thus, although the maximal LVAD output can be calculated based on rate and chamber capacity parameters, total cardiac output can be higher, theoretically increasing the central contribution to oxygen

consumption. An analysis of Jaski's<sup>20</sup> and Branch's<sup>21</sup> patient data suggests that peak LVAD output is closer to 9 to 10 L/min for most patients and that in maximal exercise studies that contribution of the LVAD ranges from 66% to 93% of the total cardiac output, with the remainder met by increased native left ventricular ejection. The highest Fick value obtained in their subjects was 12.9L/min, with the LVAD accounting for 9.4L/min, or 73% of total cardiac output. The degree to which the native left ventricle contributes to total cardiac output likely is dependent on the degree of left ventricular dysfunction. Interestingly, this degree of dysfunction may be dynamic in the sense that over time, with some natural recovery via rest, ventricular remodeling, and exercise training, the native left ventricle might well contribute significantly more to systemic cardiac output during exercise. This has not been demonstrated to date, but improvement in resting native heart function has been reported by Frazier et al<sup>22</sup>.

Native heart rates and LVAD rates are not simultaneous, as the drive mechanisms of native heart rate and LVAD rate differ. As noted, in the automatic mode, the LVAD operates on a fill-to-empty basis, with a subsequent rate that is essentially independent of native sympathetic drive. Nonetheless, both rates increase in a linear fashion with exercise. It is important to note, however, that the rates are in fact different and that assessment of the native heart rate response to exercise must be done via conventional methods and not inferred from the LVAD console, which reflects the LVAD rate<sup>13</sup>. Blood pressure response to exercise is somewhat variable at the outset of training in these patients, which is likely secondary to adjustment of fluid volume, but after several weeks, pressor response to exercise is essentially normalized<sup>13</sup>. Although published data regarding perceived exertion is lacking, it appears that is is unaffected by LVAD implantation, as observed by Morrone et al<sup>23</sup>. More research would be needed to verify both objective and subjective responses to exercise therapy in LVAD patients.

In summary, exercise is complex, composite integration between the physiologic systems and the device function in LVAD patients. Exercise is the result of various adaptive mechanisms that involve the native left ventricle, the right ventricle, the pulmonary hemodynamics, the overall and muscle conditioning, and the device. In addition, several non-hemodynamic-factors or device-related factors, such as duration of heart failure symptoms, preoperative length of hospital and intensive care unit stay, preoperative serum prealbumin, duration of postoperative recovery, and medical

therapy, may all affect exercise physiology as well. Of note, dissimilarities in LVAD designs seem to play a marginal role<sup>13,20,24</sup>.

## Exercise performance

### Improvement of physical function

LVAD patients demonstrate improvement in exercise tolerance and non-cardiac organ function as well as improvements in metabolic and neurohormonal levels<sup>11,25,26</sup>. The acute effects of LVAD implantation include a decrease in resting left and right atrial pressures as well as increased cardiac index, mean arterial pressure, vascular conductance, and blood flow<sup>25,27,28</sup>. Improvement in exercise tolerance after LVAD implantation is attributed to an increase in heart rate, cardiac output, and peak oxygen consumption(peak VO<sub>2</sub>). Signs of hepatic recovery also have been found, with most patients showing decreases in blood urea nitrogen and creatinine levels after LVAD implantation<sup>29</sup>. The LVAD therapy may have positive effects on levels of neurohormones including aldosterone, renin, and norepinephrine<sup>30</sup>. The positive effects of LVAD implantation on left ventricular function include marked reduction in left ventricular systolic and diastolic pressures leading to reverse left ventricular remodeling, a normalized pressure-volume relation, and myocyte recovery (improved contractile function)<sup>25</sup>. It appears the most of these positive changes occur immediately after implantation (in less than 2 days), and not during chronic support<sup>25</sup>.

### Improvement of exercise capacity

In general, LVAD therapy improves not only left ventricular function including resting cardiac measures but also exercise capacity. Humphrey<sup>13</sup> suggested that the most important physiologic contribution of the LVAD to increased exercise capacity is an increase in cardiac output. Further exercise capacity remains influenced by the degree of systolic dysfunction in the native heart despite maximal LVAD contribution. Implantation of an LVAD may have a significant effect NYHA class status, peak aerobic capacity and submaximal exercise tolerance<sup>23,31-34</sup>. In one study<sup>31</sup> in 103 LVAD patients, mean distance at the 6-minute walk(6MWD) test was 393±290m, approximately the lower range for patients without cardiovascular disease(400m), performing significantly better than dobutamine-dependent patients. Both Morrone et al<sup>23</sup>. and Levin et al<sup>26</sup>. found a significant improvement in NYHA class status. A substantial increase in peak oxygen consumption(peak VO<sub>2</sub>) has been reported within

5 months after LVAD implantation<sup>33,35,36</sup>. A range of peak  $\text{VO}_2$  from 14 to 24 mL/kg/min has been described; however, work load of most of LVAD patients remains sub-optimal<sup>13</sup>.

One study<sup>36</sup> regarding comparison of exercise capacity between LVAD patients, severe CHF patients demonstrated that peak  $\text{VO}_2$  of LVAD patients was significantly greater than that of severe CHF patients, with a mean peak  $\text{VO}_2$  of  $12 \pm 3.0$  mL/kg/min. Importantly, although LVAD patients showed a significantly greater cardiac output at rest and peak exercise, pulmonary pressures rose significantly with exercise both in CHF patients and LVAD patients. However, even though mean pulmonary artery pressure and pulmonary capillary wedge pressure were significantly lower in the LVAD patients at peak exercise, the slope of minute ventilation vs. carbon dioxide production ( $\text{VE}/\text{CO}_2$  slope) was similar between the two groups, suggesting that the relief of pulmonary hypertension achieved with LVAD therapy had no impact on the ventilator response to exercise.

Jaski et al<sup>37</sup>., citing their experience with LVAD with exercise (EVADE) trial, and the de Jonge et al<sup>35</sup>. reported exercise capacity values for patients approximately 8 to 12 weeks after LVAD implantation, and then again approximately 8 to 12 weeks after a HT, The EVADE trial<sup>37</sup> determined that peak  $\text{VO}_2$  and exercise duration were significantly lower in LVAD patients than in patients with HT. In contrast, de Jonge et al<sup>35</sup>. showed that peak  $\text{VO}_2$  12 weeks after LVAD implantation did not differ significantly from peak  $\text{VO}_2$  12 weeks after HT ( $22.8 \pm 5.3$  mL/kg/min vs  $24.6 \pm 3.3$  mL/kg/min). Kugler et al<sup>33</sup>. showed that exercise tolerance increased in both the HT and LVAD groups, however, both groups had sub-optimal exercise capacity despite optimal treatment. After adjusting for age, gender and BMI, the LVAD group had a lower exercise tolerance compared to the HT group.

In conclusion, exercise capacity in LVAD patients is considerably improved compared with the pre-implantation condition. Exercise capacity and daily routine activities are expected to be comparable to those of HT patients, and superior to those of severe CHF ones. However, the exercise performance remains sub-optimal. This suggests a need not only for long-time exercise rehabilitation with targeted interventions on physical and psychosocial functioning, but also a modification of focus from survival to improved coping with illness-related requirements.

#### Improvement of quality of life

Non-physiologic indices, including quality of life for both physical and emotional well-being, seem to be positively

affected by LVAD implantation. One study<sup>33</sup> reporting health-related quality of life (HRQoL) and exercise tolerance in HT and LVAD groups showed that HRQoL showed improvements for both the SF-36 physical and psychosocial component scores in the LVAD group over the time-course of the study. Another study<sup>31</sup> reported an early and sustained clinically meaningful improvement in QoL, and that the mean Minnesota Living with Heart Failure Questionnaire score was  $35 \pm 31$ , which correlates with NYHA class I to II.

LVAD patients can return to outpatient activities including self-care (eg, activities of daily living, sexual activity, vehicle driving), leisure activities (eg, dancing, tennis, movies, yard work), and productivity (eg, return to work)<sup>38</sup>. In addition, end-stage CHF patients who have an LVAD are aware that with proper care, their chances of surviving to transplantation are improved.

## Cardiac rehabilitation

### Exercise testing

The abdominal location of the externalized drive lines make cycling and stair climbing somewhat problematic. Thus, treadmill exercise is a preferred mode for exercise testing and is well tolerated. Given the limitations in cardiac output, 1MET increases in exercise intensity or a gradual ramping or Naughton protocol is preferred to more aggressive protocols<sup>37,39</sup>. As mentioned earlier, in the automatic mode, the LVAD operates with a rate that is independent of native sympathetic drive, so that native heart rate and the LVAD rates will differ. As such, pulse or EKG assessment of the native heart rate response to exercise must be done and not inferred from the LVAD console, which reflects the LVAD rate<sup>13</sup>.

### Exercise indications and contraindications

In the initial postoperative stage, management of acute care factors including surgical wound, skin integrity maintenance, pulmonary hygiene, range of motion, cardiovascular, and muscle strength maintenance should be addressed. Overall medical condition and hemodynamic stability, complications such as infections, right ventricular failure, bleeding, ventricular arrhythmia, anorexia and neurological impairments can delay initiation and progression of exercise.

The most important indication for initiation of cardiac rehabilitation is independent ambulation. Contraindications to cardiac rehabilitation include onset of angina, drop in systolic blood pressure (SBP) below resting SBP or exceedingly high SBP (>200), electrocardiogram changes including ST shifts

exceeding 1mm, and O<sub>2</sub> saturation less than 85%, hypotension associated with fainting, dizziness, or diaphoresis, supine resting heart rate >100 beats per minute, >1.8 kg increase in body mass over previous 1 to 3 days, complex ventricular arrhythmia at rest or appearing with exertion. Subjective contraindications necessitating a discontinuation of exercise include a severe, intolerable dyspnea, extreme fatigue or claudication, a rating of perceived exertion exceeding 13 at submaximal workloads, severe, significant chest pain or discomfort. A drop in LVAD flows (<3 L/min) may indicate pump failure and should be treated as the most significant contraindication to exercise or mobilization<sup>40, 41</sup>.

### Exercise prescription

Early initiation of exercise therapy has been reported to be associated with improvements in exercise capacity and survival rate<sup>23</sup>. Thus, LVAD patients should initiate an exercise program as soon as possible. The ultimate goals of early mobilization are to prevent postoperative complications due to prolonged bed rest, minimize loss of mobility, maximize independence, and facilitate weaning from the ventilator<sup>23,42</sup>.

A formal exercise training should be started after hemodynamic stability is achieved. Exercise should consist mainly of passive and active range of motion combined with incentive spirometry to facilitate pulmonary toilet. Once out of bed in a chair, leg raising and hip girdle exercises are useful as a preparation to transfer weight from sitting to standing. Once the patient is able to stand, ambulation should be initiated, initially in the patient's room, progressing later to the ward. Later on, a set routine consisting of treadmill, upper and lower body ergometries and free weights can be carried out safely in the intensive rehabilitation setting. The frequency of sessions is once a day, 6–7 days per week, with a duration varying from 15 minutes to 1 hour, as tolerated<sup>41</sup>.

### Benefits of exercise training

Actually, no standard exercise program in terms of quantitative training load has been set for LVAD patients. Various institutions have designed their own exercise programs and have reported beneficial results, mainly as care reports or care series.

Humphrey et al<sup>43</sup> reported that although measured peak oxygen consumption was not dramatically increased after exercise training, submaximal responses were substantially improved. Morrone et al<sup>23</sup> have published the largest

submaximal exercise experience to date in LVAD patients. The author reported that 20 of 34 patients initiated ambulation at 7 to 10 days with independent ambulation by 14 days in 55% of patients, and treadmill exercise was tolerated by 82% of patients, with an improvement in submaximal training workloads over 6 to 8 weeks, at which time patients were able to achieve a mean workload of 3.2 metabolic equivalent for 20 to 30 minutes. This research highlighted an importance of early progressive mobilization in LVAD patients. Mettauer et al<sup>44</sup> performed an exercise training in a single patient, 3 weeks after LVAD implantation. Exercise program consisted of 20–30 min of constant rate stationary bicycle exercise daily, with the work rate set to obtain 50 % of the maximal heart rate increase determined during the incremental exercise test. Peak VO<sub>2</sub> increased by 64% and by 56% at the anaerobic threshold after 6 weeks' exercise training, while the left ventricle filling pressure decreased with the exercise training, which result may show that exercise improves hemodynamic and exercise capacity in LVAD patients. Makita et al<sup>45</sup> measured the anaerobic threshold levels during cardiopulmonary exercise test in 9 LVAD patients when they were able to walk in the ward. Exercise training program of 10–30min of bicycle exercise at the anaerobic threshold level 2–3 times a week plus walking in the ward on other days led to a significant increase in peak work rate. This result demonstrates an increase in exercise efficacy by improving peripheral circulation. Laoutaris et al<sup>46</sup> recently conducted a randomized, controlled trial regarding the benefits of cardiac rehabilitation on exercise capacity, inspiratory muscle function, and QoL in LVAD patients about 6 months after implantation. Exercise training group underwent moderate intensity aerobic exercise using bicycle or treadmill for 45 min, three to five times a week, combined with high-intensity inspiratory muscle training, two to three times a week for 10 weeks. After training, exercise training group showed significantly improved Peak VO<sub>2</sub>, VO<sub>2</sub> at ventilator threshold, increased 6MWD, and improved inspiratory lung capacity, along with improved QoL scores. These findings suggest that exercise training may improve the functional status of LVAD patients even at a later period after implantation and thus, might have additional importance in cases of destination therapy.

In conclusion, exercise training in LVAD patients is in its infancy, and evidence on content, setting, duration of the sessions and safety are inconclusive. Although data regarding various exercise training regimens in LVAD patients are rapidly accumulating, it is still unclear how progressive long-term exercise programs should be set up. Therefore, to



improve the quality of life of LVAD patients, the time of initiation and the method of exercise therapy should be established through ongoing controlled exercise training trials.

#### Consideration during cardiac rehabilitation

Risk management in LVAD patients during the course of cardiac rehabilitation should be conducted carefully. Morrone et al<sup>(23)</sup>, reported that the limiting factors for exercise were a decrease in pump flow, infection including VAD-related endocarditis, right heart failure, hemorrhage, and ventricular arrhythmia. The most common causes of death in LVAD patients are sepsis and device failure. Device failure and problems of the coagulation system including perioperative bleeding, cerebrovascular events such as infarction and hemorrhage, and pulmonary embolism, have reported as causes of death associated with LVADs. Therefore, before beginning cardiac rehabilitation in LVAD patients, it is important to confirm the patient's general condition, including blood pressure and the state of anticoagulant therapy<sup>(47)</sup>.

### Conclusions and future directions

The incidence of heart failure continues to increase. The lack of donor hearts and the increasing wait time until HT make long-term mechanical cardiac assistance an important alternative<sup>(48)</sup>. LVAD therapy offers end-stage CHF patients improved survival and quality of life. In addition, the reduced size and the better durability of the LVADs improve independence and length of time that a patient may be implanted (up to 20 months)<sup>(49)</sup>, providing increased opportunities for cardiac rehabilitation. Evidence to date suggests that early mobilization and progressive exercise training in this population is safe and improves the transplantation experience. Therefore, the further development of various cardiac rehabilitation programs in patients with LVADs through ongoing controlled exercise training trials will be needed.

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