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Exercise physiology, testing, and training in patients supported by a left ventricular assist device

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The left ventricular assist device (LVAD) is an accepted treatment alternative for the management of end-stage heart failure. As we move toward implantation of LVADs in less severe cases of HF, scrutiny of functional capacity and quality of life becomes more important. Patients demonstrate improvements in exercise capacity after LVAD implantation, but the effect is less than predicted. Exercise training produces multiple beneficial effects in heart failure patients, which would be expected to improve quality of life. In this review, we describe factors that are thought to participate in the persistent exercise impairment in LVAD-supported patients, summarize current knowledge about the effect of exercise training in LVAD-supported patients, and suggest areas for future research.
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Heart failure (HF) exerts changes in multiple organ systems, leading to profound and progressive impairments in functional capacity (FC) and quality of life (QoL). Cardiac rehabilitation (CR) and exercise training are now accepted standards of care that produce multiple benefits in patients with HF.[1–3] Mechanical circulatory support has evolved rapidly during the last decade, and the left ventricular assist device (LVAD) is now an established therapy for the management of end-stage HF.[4,5] Continuous flow (CF) LVADs improve survival, FC, and QoL,[6,7] and may become an alternative to heart transplantation (HTx).[8] Clinical trials are ongoing to determine the efficacy of LVAD implantation in higher functioning HF patients.

The increasing volume of implantations correctly forces scrutiny over the value of LVAD implantation on FC and QoL. Despite the hemodynamic support provided by LVAD, patients are unable to achieve a normal (i.e., age-predicted and sex-predicted values) aerobic capacity post-implantation. Therefore, developing a more thorough understanding of these limiting factors is a critical area for research in the field. Cardiac rehabilitation and exercise training in LVAD-supported individuals appear to be safe[9]; however, there are no specific exercise prescription guidelines for these patients. The purpose of this review is to:

1. describe changes in the physiology of exercise secondary to HF;

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2. describe factors that are thought to participate in the persistent exercise impairment in LVAD supported patients;
3. summarize current knowledge regarding the impact of exercise training in patients supported by LVAD; and
4. identify knowledge gaps and areas for future research.

This review focuses predominantly on CF-LVAD, and pulsatile flow (PF)-LVAD is used in some areas for comparison. A PubMed English literature search was performed by one author (R.L.) using the keywords "LVAD and exercise," "LVAD and rehabilitation," "LVAD and peakVo_2," and "heart failure and exercise." Relevance of original and review manuscripts was assessed for inclusion in this publication by all authors.

Physiologic responses to exercise in the presence of HF

Exercise requires the coordinated response of multiple organ systems to ensure an adequate energy supply to meet increased metabolic demands and to eliminate associated metabolic end products. In healthy individuals, the hemodynamic changes during exercise occur without significant changes in filling pressures.[10] Exercise intolerance due to dyspnea on exertion and fatigue is one of the earliest and most important HF symptoms. The adaptations to exercise and the pathophysiologic changes in the neurologic, cardiovascular, respiratory, and musculoskeletal systems that lead to exercise impairments with HF have been thoroughly described[11–17] and are summarized in Table 1.

Cardiopulmonary exercise testing (CPX) is a sophisticated yet non-invasive method to assess the physiologic response to exercise. A broad range of variables are captured, and several of them have been convincingly shown to accurately predict poor outcome in HF patients and are used to identify individuals who are in need of a HTx or LVAD implantation.[18–21] CPX is also used as a gold standard to quantify improvement in FC after HF therapies, including devices such as cardiac resynchronization therapy.[22] Another method for measurement FC is the 6-minute walk test (6MWT). Several studies have described the improvement in 6MWT distance in LVAD patients[23] and described its usefulness as a predictor of poor outcome.[24] However, the 6MWT measures submaximal exercise capacity, and although reproducible, is subjective and could be affected by other variables besides cardiovascular status.[25] The improvement in FC measured by the 6MWT was reported recently,[24,26] and in this review, we will focus on maximal exercise capacity as determined by CPX (Table 2).

Physiology of exercise with LVAD

Although the benefits of LVAD support are unquestionable, patients still exhibit significant impairment in their ability to achieve a normalized maximal exercise capacity. Given the multiorgan damage caused by HF, the limitations to exercise in LVAD patients are also complex and multifactorial. Factors such as device type, inability to increase cardiac output (CO) during exercise, right ventricular (RV) dysfunction, chronotropic incompetence, impaired pulmonary function, skeletal myopathy, endothelial dysfunction, and anemia appear to play a synergistic role in the observed exercise intolerance (Figure 1).

Type of LVAD

Currently, PF-LVADs are seldom used as durable support but offer the opportunity to analyze the physiologic response to exercise and provide comparisons with CF-LVADs. The PF-LVADs use a pneumatically/electrically driven ventricle that operates in the complete fill/empty mode. Thus, CO during exercise will increase as a function of preload and pump rate. PF-LVADs are afterload independent and produce a maximal CO (CO_{max}) of ~10 liters/min with a pump rate of 120 beats/min.[27] On the other hand, the CF-LVAD is free of valves, unloads the ventricle both in systole and diastole, and operates at a fixed speed. The 2 types of CF-LVADs are axial and centrifugal. Pump flow varies according to the differential pressure between the inflow and outflow cannulas. The sensitivity of axial and centrifugal pumps to changes in preload is similar, whereas centrifugal pumps are more sensitive to after load .[28] During exercise, pump flow increases in the CF-LVAD as a function of changes in preload and afterload.

Mancini et al[29] studied the hemodynamic responses during exercise in 20 patients supported by PF-LVADs. The CO was 4.9 ± 0.9 liters/min at rest and increased with exercise to 11.2 ± 2.6 liters/min, which was associated with a concomitant increase in pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP) from 5 ± 3 to 14 ± 6 mm Hg and from 3 ± 3 to 8 ± 4 mm Hg, respectively. Patients achieved a mean peak oxygen consumption (Vo_2) of 16 ± 3.8 ml/kg/min. Haft et al[30] compared the exercise hemodynamic responses between PF-LVAD and CF-LVAD. Resting central venous pressure, mean arterial pressure, and PCWP were similar in both groups. Peak Vo_2 was not different between groups (~15 ml/kg/min, 48% of predicted), and pump flow increased in both groups. However, the increase in pump flow was greater in the PF-LVAD than in the CF-LVAD (4 ± 0.5 vs 3.4 ± 0.4 liters/kg/m^2). The significance of this finding is unclear given the flow through for the CF-LVAD is not directly measured but estimated. A more recent report evaluated the hemodynamic response of 30 patients who received a CF-LVAD. Patients achieved a peak Vo_2 of 18 ± 6.2 ml/kg/min (55% ± 12% of predicted) and total CO_{max} of 8.5 ± 2.8 liters/min.[31] Taken together, patients appear to achieve a similar peak Vo_2 independently of the type of LVAD, and although CO_{max} increases with exercise, it does not reach levels observed in healthy individuals with normal cardiac function.

The effect of speed on LV unloading in CF-LVAD

LV unloading is important during LVAD support, and as a result, device speed is adjusted to optimize LV unloading.

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