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Exercise in heart failure patients supported with a left ventricular assist device

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After implantation of a continuous-flow left ventricular assist device (CF-LVAD), exercise capacity in heart failure patients remains reduced with peak oxygen uptake (peak VO_2) values averaging from 11 to 20 ml/kg/min. Total cardiac output in CF-LVAD patients during exercise is predominantly determined by pump speed, the pressure difference across the pump, and in some cases ejection through the aortic valve. Fixed pump speed utilized in CF-LVADs may provide insufficient support, resulting in a moderate cardiac output increase during increased physical strain. Ongoing studies are evaluating whether pump speed changes in response to varied loading conditions may enable LVADs to provide sufficient support even during strenuous exercise. In the currently used devices, evidence suggests that focus on optimizing non-cardiac peripheral parameters is vital. Extra-cardiac potentially reversible factors are anemia with low oxygen-carrying capacity, obesity and general deconditioning with low muscle mass. In addition, exercise training in CF-LVAD patients can improve peak VO_2. To design interventions to improve functional capacity in patients treated with modern durable LVADs, a detailed understanding of exercise physiology in a continuous-flow circulatory system is necessary. In this review we address the different components of exercise physiology in LVAD patients and point out potential solutions or areas of future research.

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Implantation of a continuous-flow left ventricular assist device (CF-LVAD) in advanced heart failure (HF) patients is associated with increased survival and improved quality of life.[1–8] In the majority of patients, functional capacity, as measured by New York Heart Association (NYHA) functional classification, improves significantly post-implant.[9,10] Yet, improvements in maximal cardiac work are marginal. Due to the ongoing lack of donor organs, mechanical circulatory support is being increasingly used as destination therapy (DT).[7] This increased use of CF-LVADs as final therapy for HF calls for greater focus on methods to improve exercise tolerance. Detailed understanding of exercise physiology in a continuous-flow circulatory system is necessary to design interventions aimed to improve functional capacity in patients treated with modern durable LVADs. The purpose of this study is to provide a systematic description of the different components of exercise physiology in adult LVAD patients and to point out potential solutions and areas of future research.

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Review strategy

A systematic literature search in PubMed was conducted by identifying studies on exercise capacity in LVAD patients using the search terms “exercise capacity,” “oxygen uptake,” “peak oxygen consumption,” “LVAD,” “CF-LVAD,” “exercise training” and “submaximal exercise.” In the relevant studies, baseline characteristics in the form of

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age, gender, device type, pump settings, indication, support duration, etiology and echocardiographic measurements were systematically collected. Parameters of functional capacity were reviewed, including the 6-minute walk test (6MWT), NYHA functional classification, peak oxygen uptake (peak VO_2), percent of predicted peak VO_2 (% peak VO_2), anaerobic threshold (AT), ventilatory equivalent ratio for carbon dioxide (VE/VCO_2) and respiratory exchange ratio (RER).

LVAD and exercise hemodynamics

Pulsatile- vs continuous-flow LVADs

The currently used second- and third-generation CF-LVADs operate with a pulseless flow, either axial or centrifugal.[7] HeartMate II (HMII; Thoratec Corporation, Pleasanton, CA) and HeartWare (HVAD; HeartWare International, Inc., Framingham, MA) devices are the most commonly used second- and third-generation pumps, respectively. These non-pulsatile devices are set at a fixed pump speed regardless of patient activity. The HMII can be regulated from 6,000 to 15,000 revolutions per minute (rpm), whereas the HVAD operates in the range of 2,400 to 3,200 rpm. Within these pump speeds, both devices are able to deliver flows of up to 10 liters/min, depending on pre- and after-load.[11,12] To date, the Jarvik 2000 has been the only device in which the patient could manually adjust the pump speed.[13] Contrary to CF-LVADs, the formerly used first-generation pulsatile devices adjusted pump rate directly in relation to changes in pre-load as they operated in a full-to-empty fashion,[9,14] increasing cardiac output (CO) during exercise. However, pulsatile devices had the disadvantage of being larger, less durable and associated with worse outcome.[15,16] It is unclear the extent to which lack of or low pulsatility of CF-LVADs contributes to poor exercise capacity. Theoretically, exercise-induced peripheral vasodilation may be enhanced by pulsatile flow. In addition, left ventricle (LV) and right ventricular (RV) output may be improved by pulsatility if pulsatile function of the LVAD increases the contribution of the septum to RV function. However, it has been demonstrated that exercise capacity 3 months post-implant is comparable in pulsatile- and continuous-flow device patients.[14]

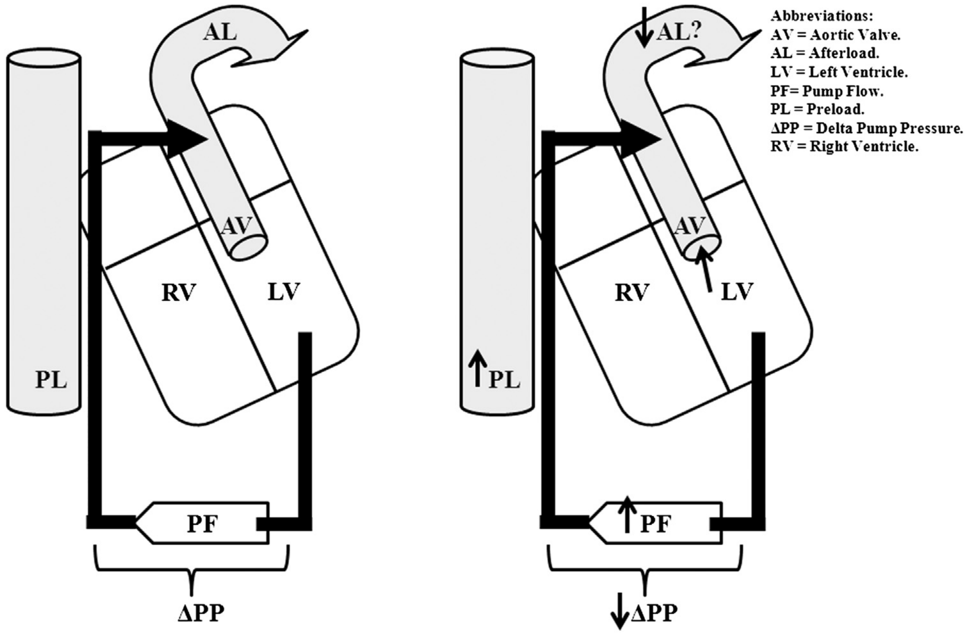
Exercise hemodynamics in CF-LVAD patients

Total cardiac output (TCO) in CF-LVAD patients during exercise is determined by: (a) flow through the pump; and (b) in some cases, ejection through the aortic valve (AV) (Figure 1).

Flow through the pump largely depends on pump speed and pressure difference across the pump (ΔPP). Increasing CF-LVAD pump speed leads to enhanced output from the device. The selected pump speed setting is adjusted by echocardiographic guidance to ensure sufficient circulatory support at rest while allowing intermittent AV opening and maintaining normal LV dimensions.[17]

In turn, ΔPP will impact pump flow in an inversely related manner. Increased pre-load during exercise will contribute to decreased ΔPP at the onset of exercise and thus increased pump flow.[15,18–20]

Changes in after-load during exercise in CF-LVAD patients are a debated topic and without any clear evidence in the literature. However, due to the fact that current LVAD mechanics are highly after-load sensitive—higher than in the human heart—it is an important area to explore.[21] Martina et al found that systemic vascular resistance (SVR) decreased significantly during exercise in HMII patients, which was attributed to exercise-induced peripheral vasodilation.[18]



A. CF-LVAD hemodynamics at rest.

B. Changes in CF-LVAD hemodynamics during exercise.

Figure 1 Hemodynamics of CF-LVAD function at rest and during exercise.