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Systemic perfusion at peak incremental exercise in left ventricular assist device recipients: Partitioning pump and native left ventricle relative contribution

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ABSTRACT

Background: In continuous-flow left ventricular assist device (LVAD) recipients, little is known about the relative pump- and left ventricle-generated blood flow (PBF and LVBF, respectively) contribution to peak systemic perfusion during incremental exercise and about how PBF/LVBF interplay and exercise capacity may be affected by pump speed increase.
Methods: Twenty-two LVAD recipients underwent ramp cardiopulmonary exercise tests at fixed and increasing pump speed (+1.5% of baseline speed/10 W workload increase), echocardiography and NT-proBNP dosage. Peak systemic perfusion was peak VO_2/estimated peak arterio-venous O_2 difference, and LVBF was systemic perfusion minus PBF provided by LVAD controller. A change of peak percentage of predicted VO_{2max} ($\Delta peak\%VO_2$) ≥3 in increasing- vs. fixed-speed test was considered significant.
Results: Tricuspid annular plane systolic excursion (TAPSE) and NT-proBNP were significantly lower and higher, respectively, in $\Delta peak\%VO_2 < 3$ than ≥3. A LVBF contribution to systemic perfusion significantly larger than that of PBF was observed in $\Delta peak\%VO_2 \geq 3$ vs. <3 in fixed-speed test, which was further amplified in increasing-speed test (2.4 ± 1.7 l/min vs. 2.0 ± 1.5 l/min and 0.8 ± 2.2 l/min vs. 1.3 ± 2.3 l/min, respectively, p for trend <0.0005). Among several clinical-instrumental parameters, logistic regression selected only TAPSE >13 mm as a predictor of $\Delta peak\%VO_2 \geq 3$.
Conclusions: A significant LVBF contribution to peak systemic perfusion and pump speed increase-induced peak VO_2 improvement was detectable only in patients with a more preserved right ventricular systolic function and stable hemodynamic picture. These findings should be taken into consideration when designing LVAD controllers aiming to increase pump speed according to increasing exercise demands.
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1. Introduction

Continuous-flow left ventricular assist devices (LVADs) are increasingly used as destination therapy in end-stage chronic heart failure (CHF), and patients can be supported by LVADs in their habitual activities even for some years [1,2]. In such a clinical setting, knowledge of exercise pathophysiology plays an important role. LVAD implantation determines a peculiar exercise hemodynamic picture, where two pumps, i.e., LVAD and native left ventricle, can act in parallel to generate systemic perfusion [3]. Even in the presence of a fixed pump speed, some increase of PBF is actually detectable during exercise testing and habitual activities [3–6], as both exercise-induced tachycardia and augmentation of telediastolic left ventricular pressure do reduce the pressure gradient across the pump [3,5]. The contribution of native left ventricle to systemic perfusion can also increase during exercise, due to augmented venous return, decrease of peripheral resistances and activation of sympathetic drive [3]. However, notwithstanding the device boost to O_2 delivery, LVAD-implanted patients often suffer from a reduced exercise capacity [3,7,8], due to the limited ability of both the LVAD and the dysfunctioning left ventricle to adapt to increasing energetic demands. In this regard, scant data are available as to the relative contribution of PBF and left ventricle-generated blood flow (LVBF) to

Abbreviations: LVAD, left ventricular assist device; PBF, pump-generated blood flow; LVBF, left ventricle-generated blood flow; TAPSE, tricuspid annular plane systolic excursion; CHF, chronic heart failure; NYHA, New York Heart Association; CaO_2, resting arterial O_2 content; Hb, hemoglobin; PASP, pulmonary arterial systolic pressure.

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peak systemic perfusion [3], nor is it known how such an interplay may be affected by pump speed increase. In addition, few studies have evaluated the effects of pump speed increase on exercise capacity in LVAD-implanted patients, showing either no change or a significant increase [9–11].

The aim of this study was to evaluate the relative contribution of PBF and LVBF to peak systemic perfusion in a group of LVAD recipients with severely reduced exercise capacity, tested at two different pump speeds during incremental exercise. In addition, we evaluated the effects of pump speed increase on peak aerobic power (peak VO_2) in this population and sought for possible clinical–instrumental predictors of peak VO_2 increase in response to changes in pump speed.

2. Methods

2.1. Study population

Twenty-two patients implanted with LVAD were studied. Inclusion criteria were: 1) clinical stability, defined as no change in NYHA class, absence of hospitalization and stable medical treatment during the month prior to evaluation; 2) LVAD implanted ≥30 days prior to evaluation; 3) cardiopulmonary exercise tests stopped for fatigue and/or dyspnea with peak respiratory exchange ratio of ≥1.05; 4) absence of angina and/or instrumentally inducible myocardial ischemia and/or evidence of complex ventricular arrhythmias. Indication for LVAD implantation was persistent hemodynamic decompensation not responsive to intensive medical therapy. No patient had undergone aortic valve suturing at LVAD implantation. The protocol was approved by the Central Ethics Committee of the S. Maugeri Foundation, IRCCS and informed written consent was obtained from all participants in the study.

2.2. Echocardiographic evaluation

Within 7 days prior to ergometric evaluation, all participants underwent an echocardiogram according to reported standards in patients with LVAD [12]. Left ventricular cavity areas at end-diastole and end-systole from the apical 4- and 2-chamber views were obtained. The modified Simpson's rule was used to obtain biplane left ventricular volumes, and left ventricular ejection fraction was derived from the standard equation. Tricuspid annular plane systolic excursion (TAPSE) was used as a descriptor of right ventricular systolic function. To obtain TAPSE, the apical 4-chamber view was used, and an M-mode cursor was placed through the lateral tricuspid annulus in real time. Offline, the brightness was adjusted to maximize the contrast between the M-mode signal arising from the tricuspid annulus and the background. TAPSE was measured as the peak excursion of the tricuspid annulus (mm) from the end of diastole to the end of systole, with values representing TAPSE being averaged over 3 to 5 beats. Right ventricular systolic pressure was determined from the tricuspid regurgitation jet velocity using the simplified Bernoulli equation, and this value combined with an estimate of the right atrial pressure by the diameter and collapsibility of the inferior vena cava to yield pulmonary arterial systolic pressure (PASP).

2.3. Ergometric evaluation

All tests were performed on an electromagnetic bicycle ergometer (Ergo-metrics 800S; Sensormedics; Yorba Linda, CA, USA). Each patient underwent two ramp cardiopulmonary exercise tests, one with fixed LVAD speed (as set soon after implantation by the cardiac surgery team to allow maximum hemodynamic support at rest while avoiding suction events) and one with increasing LVAD speed. The two tests were separated by 48 h and their sequence was randomized. Brassard et al. [9] recently used a 400 rpm/30 W increase of pump speed during incremental exercise, equal to an average percent increase of 1.5%/10 W with respect to baseline. The latter figure was used as the criterion for pump speed increase in the present study, given the presence of 3 types of LVAD (Table 1) with different baseline pump speeds (HeartWare, range 2400–2800 rpm; HeartMate II, range 8600–9400 rpm; Incor, range 6850–7500 rpm). Heart rate and 12-lead ECG were monitored continuously during the test (CASE; GE Healthcare; Fairfield, CT, USA). After a 1-min 20 W warm-up period, a ramp protocol of 5, 7, or 10 W/min at a pedaling rate of 60 rev/min was started, and respiratory gas exchange measurements were obtained breath-by-breath (Vmax29; SensorMedics; Yorba Linda, CA, USA). Peak VO_2 was the mean VO_2 value observed during the last 30 s of the exercise period.

Table 1
Demographic and clinical characteristics.

	Total group ($n = 22$)	$\Delta peak\%VO_2 \geq 3$ ($n = 13$)	$\Delta peak\%VO_2 < 3$ ($n = 9$)
Age (years)	57 ± 9	56 ± 8	57 ± 10
Male gender (n, %)	21 (95)	13 (100)	8 (89)
BMI (kg/m^2)	24.99 ± 3.71	25.74 ± 3.27	23.90 ± 4.22
LVAD type (n, %)	HM 9 (41)	HM 6 (46)	HM 3 (33)
	HW 8 (36)	HW 3 (23)	HW 5 (55)
	INC 5 (23)	INC 4 (31)	INC 1 (12)
Indication for LVAD implantation (n, %)	BR 15 (68)	BR 11 (85)	BR 5 (55)
	DT 6 (32)	DT 2 (15)	DT 4 (45)
Time since implantation (days)	156 ± 186	168 ± 171	138 ± 215
Etiology	I 14 (64)	I 8 (61)	I 6 (66)
	D 8 (36)	D 5 (39)	D 3 (34)
β-Blockers (n, %)	21 (95)	12 (92)	9 (100)
LVEF (%)	26 ± 8	26 ± 3	25 ± 12
TAPSE (mm)	12.3 ± 2.7	13.4 ± 2.3	10.7 ± 2.3[a]
PASP (mm Hg)	32 ± 8	28 ± 4	38 ± 9[a]
Hematocrit (%)	36 ± 3	37 ± 4	34 ± 2
NT-proBNP (pg/ml)	2825 ± 2907	1961 ± 1889	4073 ± 3724[b]

Values are n (%) or mean ± standard deviation.
$\Delta peak\%VO_2 \geq 3$ = increase of peak % predicted VO_{2max} between fixed and increasing pump speed tests ≥3; $\Delta peak\%VO_2 < 3$ = increase of peak % predicted VO_{2max} between fixed and increasing pump speed tests <3; BMI = body mass index; LVAD = left ventricular assist device; HM = HeartMate II; HW = HeartWare; INC = Incor; BR = bridge to transplantation/decision/recovery; DT = destination therapy; I = ischemic cardiomyopathy; D = dilative cardiomyopathy; LVEF = left ventricular ejection fraction; TAPSE = tricuspid annular plane systolic excursion; PASP = pulmonary arterial systolic pressure.
[a] $P < 0.05$ vs. $\Delta peak\%VO_2 \geq 3$.
[b] $P < 0.08$ vs. $\Delta peak\%VO_2 \geq 3$.

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