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Effect of exercise and pump speed modulation on invasive hemodynamics in patients with centrifugal continuous-flow left ventricular assist devices

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KEYWORDS:
exercise;
left ventricular assist device;
pump speed;
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BACKGROUND: Continuous-flow left ventricular assist devices (CF-LVADs) improve functional capacity in patients with end-stage heart failure. Pump output can be increased by increased pump speed as well as changes in loading conditions.

METHODS: The effect of exercise on invasive hemodynamics was studied in two study protocols. The first examined exercise at fixed pump speed ($n = 8$) and the second with progressive pump speed increase ($n = 11$). Patients underwent simultaneous right-heart catheterization, mixed venous saturation, echocardiography and mean arterial pressure monitoring. Before exercise, a ramp speed study was performed in all patients. Patients then undertook symptom-limited supine bicycle exercise.

RESULTS: Upward titration of pump speed at rest (by 11.6 ± 8.6% from baseline) increased pump flow from 5.3 ± 1.0 to 6.3 ± 1.0 liters/min (18.9% increase, $p < 0.001$) and decreased pulmonary capillary wedge pressure (PCWP; 13.6 ± 5.4 to 8.9 ± 4.1 mm Hg, $p < 0.001$). Exercise increased pump flow to a similar extent as pump speed change alone (to 6.2 ± 1.0 liters/min, $p < 0.001$), but resulted in increased right- and left-heart filling pressures (right atrial pressure [RAP]: 16.6 ± 7.5 mm Hg, $p < 0.001$; PCWP 24.8 ± 6.7 mm Hg, $p < 0.001$). Concomitant pump speed increase with exercise enhanced the pump flow increase (to 7.0 ± 1.4 liters/min, $p < 0.001$) in Protocol 2, but did not alleviate the increase in pre-load (RAP: 20.5 ± 8.0 mm Hg, $p = 0.07$; PCWP: 26.8 ± 12.7 mm Hg; $p = 0.47$). Serum lactate and NT-proBNP levels increased significantly with exercise.

CONCLUSIONS: Pump flow increases with up-titration of pump speed and with exercise. Although increased pump speed decreases filling pressures at rest, the benefit is not seen with exercise despite concurrent up-titration of pump speed.

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The durability and reliability of continuous-flow left ventricular assist devices (CF-LVADs)[1–4] with restoration

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of normal organ function and improved quality of life[5,6] has resulted in rapid uptake into destination therapy as bridge to cardiac transplant[1,7] and, more recently, as bridge to recovery.[8,9] Despite constant pump speed, pump output from CF-LVADs varies according to level of activity and circadian rhythm.[10,11] Pump output can also be increased by increasing pump speed, although adjustments are not frequently required once patients are stable.

Despite the physiologic level of pump flows at rest, patients supported by CF-LVADs may still have significant exercise intolerance. We examined the hemodynamic effects of exercise at fixed rates and with graduated increases in pump speed in stable patients in two studies.

Methods

Study cohort

Patients studied were between 18 and 75 years of age and implanted with a centrifugal CF-LVAD for end-stage heart failure as bridge to cardiac transplantation. Characteristics of the patients are presented in Table 1. All patients were at INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) Levels 1 to 3 at implant. All were ambulatory outpatients and assessed at a median of 124 (range 61 to 490) days after pump implant. Patients recruited between 2009 and 2010 were implanted with the VentrAssist (Ventracor, Ltd., Chatswood Australia) CF-LVAD (Protocol 1). Subsequent patients received the HeartWare HVAD (HeartWare, Inc., Framingham, MA) CF-LVAD (Protocol 2). All patients were anti-coagulated with warfarin, aspirin and/or clopidogrel. The study was approved by the human research and ethics committee at St. Vincent's Hospital, Sydney, Australia (SVH HREC 08/197 and SVH HREC H07/025). All patients provided written, informed consent.

Study protocol

Patients were studied supine with hemodynamic measurements obtained using a 7.5Fr continuous cardiac output (CCO) Swan–Ganz catheter (CCOmbo; Edwards LifeSciences, Irvine, CA). After calibration with pulmonary venous blood, mixed venous saturation (SVO_2) was calculated continuously (Vigilance II Monitor; Edwards LifeSciences). Mean resting cardiac output by CCO thermodilution was 5.54 ± 1.75 liters/min and by LVAD flow estimate 5.22 ± 1.01 liters/min ($p = 0.53$). Corresponding cardiac output with exercise at baseline speed (available from both cohorts) was 6.17 ± 1.80 liters/min and 6.21 ± 1.02 liters/min ($p = 0.95$).

Non-invasive mean arterial pressure (MAP) was measured using arterial Doppler-guided sphygmomanometry. Arterial

Table 1 Patients' Characteristics

Patient ID	Baseline pump speed (rpm)	Implant duration (days)	Age (years)	Etiology of cardio-myopathy	Gender	BSA (m^2)	MAP (mm Hg)	AV status	LVEDD (mm)	LVEF (%)	RV function or impairment	Medications[a]
Series 1												
VA01	2,000	490	44	IHD	M	2.19	90	c	81.0	16	Mild	W, A, S
VA02	2,100	274	46	IHD	M	1.80	100	c	53.0	20	Normal	W, A, S, Amiod, I
VA04	2,000	313	19	DCM	F	1.60	70	c	51.0	21	Mild	W, A, L, Amiod, PPI
VA07	2,100	140	50	IHD	M	1.96	95	c	71.0	25	Mild	W, A, C, L, AA
VA08	2,200	157	46	IHD	M	2.20	86	c	66.0	23		W, C, S, ACE, Mg
VA10	2,100	101	43	DCM	M	1.84	120	c	69.0	10	Moderate	W, A, B, ACE, L
VA11	2,100	222	29	DCM	M	2.10	65	c	71.0	13	Moderate	W, A, ACEI, AA, L
VA12	2,000	120	37	DCM	M	2.14	90	c	63.0	20	Normal	W, A, C, AA, B, PPI
Series 2												
HW1	2,800	166	51	HCM	M	1.53	84	c	38.0	64	Normal	W, A, C, B, D
HW2	2,600	365	40	DCM	F	1.57	74	c	49.0	35	Normal	W, A, C, AA, L
HW3	2,800	449	57	IHD	M		92	c	86.0	20	Moderate	W, A, C, AA, D, L, S
HW4	2,800	95	51	IHD	M	2.1	68	i	87.0	30	Mild	W, A, C, B, AA, L
HW5	2,700	110	43	IHD	M	1.59	70	c	49.0	25	Mild	W, A, C, ACEI, AA, D, S
HW6	2,500	81	22	DCM	F	1.61	68	c	55.0	15	Mild	W, A, C, A2RA, B, D, L
HW7	2,600	61	48	IHD	M	2.39	90	NA	NA	35	Normal	W, A, C, A2RA, AA, Amiod, L, PPI
HW8	2,700	89	42	DCM	F	1.61	83	NA	NA	20	Mild	W, A, C, ACEI, AA, D, L, PPI
HW9	2,800	75	40	HCM	M	2.39	98	o	59.0	20	Mild	W, C, A, AA, B, PPI
HW10	2,700	103	57	DCM	M	1.96	68	i	54.0	20	Normal	W, C, A, AA, L, PPI
HW11	2,700	124	56	IHD	M	1.96	72	c	43.0	35	Normal	W, C, A, B, Amiod, A2RB, AA, PPI, S

AV, aortic valve; BSA, body surface area; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; IHD, ischemic heart disease; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; rpm, revolutions per minute; RV, right ventricular.

[a]AV status: c, closed; i, intermittently open; o, open; NA, not available. Medications: W, warfarin; A, aspirin; B, beta-blockers; C, clopidogrel; D, digoxin; S, statins; AA, aldosterone antagonists; Amiod, amiodorone; ACEI/A2RA, angiotensin-converting enzyme inhibitor/angiotensin II receptor antagonist, renin-angiotensin-aldosterone system blockade; L, loop diuretics; PPI, proton pump inhibitor; I, insulin.