Evaluation of Myocardial Function in Patients With End-Stage Heart Failure During Support With the Jarvik 2000 Left Ventricular Assist Device

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In 2 patients with the Jarvik 2000 left ventricular assist device (LVAD), we assessed left ventricular systolic function through pressure–volume loops and E_{max} at the beginning and end of the support period to potentially predict the possibility of pump removal without transplantation. Immediately before LVAD implantation and explantation, pressure and volume measurements were made with catheters and echocardiography, respectively, the E_{max} being calculated from the slope of the pressure–volume loops, and the left ventricular ejection fraction (LVEF) being estimated by echocardiography. Transplantation was performed after 14 and 62 days, respectively, during which the LVEF increased by 75% (from 12% to 21%) in Patient 1 and remained unchanged (from 16% to 18%) in Patient 2, whereas the E_{max} increased from 0.63 and 0.42 mm Hg/ml, respectively, to 1.31 and 1.07 mm Hg/ml, reflecting a 107% and 155% improvement. In these 2 cases, the E_{max} was a more reliable indicator of intrinsic myocardial contractility than was the LVEF. J Heart Lung Transplant 2005;24:226–8. Copyright © 2005 by the International Society for Heart and Lung Transplantation.

Left ventricular assist devices (LVADs) reduce mortality and permit hospital discharge and cardiac rehabilitation for heart transplant candidates.[1] Improvements in myocyte histology and biochemistry, as well as in left ventricular (LV) anatomy, physiology and hemodynamics,[1] have been observed in patients with end-stage dilated cardiomyopathy receiving prolonged mechanical circulatory support, even to the extent that the pump could be removed and transplantation avoided.[2] The systematic use of "bridging to recovery" necessitates precise assessment of the cardiac status independent of intracardiac factors (e.g., heart rate) and extracardiac factors (e.g., central venous pressure, peripheral vascular resistance) that may transiently alter systolic function by means of the Starling mechanism without affecting myocardial contractility. The slope of the LV end-systolic pressure–volume relationship (E_{max}) is an afterload- and preload-independent index of LV contractility.[3] To calculate the E_{max}, the change in LV-generated pressure as a function of the change in LV volume is plotted at a given loading condition. The area within this so-called pressure–volume (PV) loop represents the stroke work at that particular preload–afterload combination. The loop can be made to shift toward the lower left or the upper right by respectively decreasing or increasing the preload or afterload. The E_{max} is calculated from the slope of the straight line that connects the upper left corners (end-systole) of the loops thus obtained. Because each line is created from multiple loops, each representing a different loading condition, E_{max} is inherently independent of extracardiac hemodynamics.

Intraoperatively, instantaneous LV pressures can be recorded with fluid-filled catheters, and LV volumes can be calculated simultaneously with echocardiography. However, varying the cardiac preload or afterload to produce the desired shifts in the loops would require maneuvers such as caval or aortic constriction, which would be considered risky in critically ill, anesthetized patients. A continuous-flow cardiac assist device might be suitable for this purpose, as the left ventricle could be unloaded to different degrees by varying the pump outflow. We undertook the present study to determine whether myocardial function can be evaluated with this method in recipients of the Jarvik 2000 LVAD (Jarvik Heart, Inc., New York, NY).

METHODS

Surgical Procedure

With the aid of partial cardiopulmonary bypass, the pump was implanted into the LV apex through a

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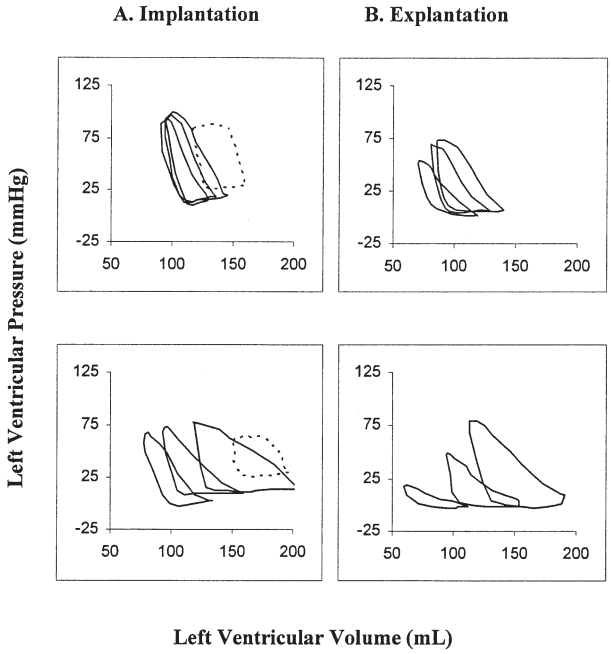


Figure 1. Left ventricular PV loops before device implantation (**A**) and explantation (**B**). Top: Patient 1 (13-day support); bottom: Patient 2 (64-day support).

thoracotomy, and the outflow graft was anastomosed to the ascending or descending thoracic aorta as described elsewhere.[1]

Measurement of Left Ventricular Pressures and Volumes

Data were acquired with a WINDAQ computer data acquisition system (DATAQ Instruments, Akron, OH) connected to pressure-processor amplifiers (Gould Instrument Systems, Valley View, OH) and fluid-filled, disposable pressure transducers and tubes (Edwards Lifesciences, Irvine, CA), which were themselves connected to the left ventricle via a 19-gauge angiocatheter. Pressure data were collected continuously at 200 Hz in synchrony with LV volume measurements by multiplane transesophageal echocardiography, immediately before LVAD implantation and just before device removal for cardiac transplantation.

Derived Parameters and Calculations

Left ventricular volumes were calculated with the modified Simpson rule in 4- and 2-chamber views over 10 consecutive heart beats and at 32 points in the cardiac cycle for each loop. Linear approximation of the end-systolic PV relationships and the Pearson product moment correlation coefficient, *r,* were performed using Microsoft EXCEL, by fitting the data to generate the lines of the general equation $LVP = E_{max} * LVV + V_0$, where LVP and LVV are the instantaneous LV pressure and volume, respectively, and the intercept V_0 is the theoretical, residual volume at LVP = 0. Left ventricular contractility (E_{max}) was estimated from the slope of the relationship. The conventional parameters of stroke work index (SWI) and LV ejection fraction (LVEF) were estimated from the area enclosed by the PV loops normalized by the body surface area and echocardiographic images obtained in the long and short axes, respectively.

RESULTS

Patients

Both study patients signed an institutional review board (IRB)-approved informed consent form. A 52-year-old woman (body surface area [BSA] 1.68 m^2, LVEF <10%, LV diastolic dimension 5.3 cm, cardiac index 2.0 liters/min·m^2, pulmonary capillary wedge pressure [PCWP]

Table 1. Left Ventricular Geometry and Function at Implantation and Explantation of the Jarvik 2000 Left Ventricular Assist Device

Variable	Pump speed (rpm)	Patient 1*		Patient 2†	
		Implantation	Explantation	Implantation	Explantation
LVEDV (%)	Off	160	—	203	—
	10,000	136	130	159	154
	12,000	130	119	133	112
LVESV (%)	Off	116	—	160	—
	10,000	94	81	93	94
	12,000	90	80	77	60
LVEF (%)	Off	12	21	16	18
	10,000	31	38	42	39
	12,000	31	41	42	46
SWI (%)	Off	9.9	—	6.6	—
	10,000	8.4	7.7	7.6	6.6
	12,000	6.5	5.4	5.9	3.0
E_{max} (mm Hg/ml)	—	0.63	1.31	0.42	1.07

E_{max}, slope of the left ventricular end-systolic pressure–volume relationship; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; SWI, stroke work index.

*A 52-year-old woman with 13-day support.

†A 58-year-old man with 64-day support.

Table 2. Linear Approximation of End-Systolic Pressure–Volume Relationships

	Equation	Pearson correlation coefficient (r^2)
Patient 1		
Implantation	LVP = 0.6328 LVV + 31.8240	0.73
Explantation	LVP = 1.3098 LVV − 40.3670	0.99
Patient 2		
Implantation	LVP = 0.4189 LVV + 27.0000	0.95
Explantation	LVP = 1.0674 LVV − 47.4770	0.98

LVP, left ventricular pressure; LVV, left ventricular volume.

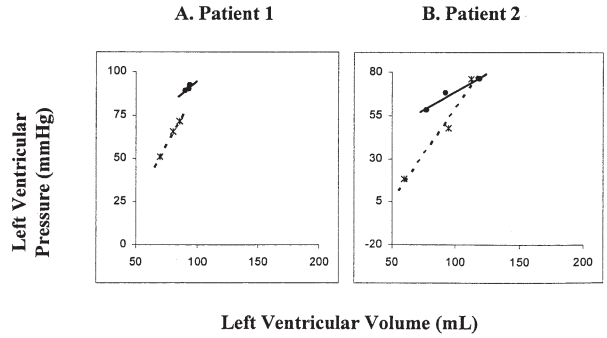


Figure 2. E_{max} calculated from the slope of end-systolic PV relationships before device implantation (solid line) and explantation (dotted line).

18 mm Hg), with dilated cardiomyopathy, in New York Heart Association (NYHA) Class IV, and refractory to milrinone lactate and dopamine, underwent Jarvik 2000 LVAD implantation. After 13 days of LVAD support, she underwent successful transplantation without significant complications. After 27 months of follow-up, she is in NYHA Class I with no clinical problems.

A 58-year-old man (BSA 1.72 m^2, LVEF 15%, cardiac index 1.63 liters/min·m^2, PCWP 20 mm Hg) with ischemic cardiomyopathy refractory to maximal medical therapy received the Jarvik 2000 and underwent transplantation after 64 days of support. Sixteen months later, he is in NYHA Class I.

Derivation of Pressure–Volume Loops

In both patients, as a result of LV unloading by the pump, PV loops slanted to the left during simultaneous closure of the aortic and mitral valves (Figure 1), and LV end-systolic and end-diastolic dimensions were reduced by 9% to 22% (Table 1). Table 2 shows the results of the linear approximation equations for end-systolic PV relationships at implantation and explantation. In Patient 1, during the 13-day support period, the E_{max} (mm Hg/ml) increased by 107% (from 0.63 at device implantation to 1.31 at explantation) (Figure 2). Compared with the respective values at implantation, the resting LVEF increased by 11% to 75%, and the SWI decreased by 7% to 17%. In Patient 2, during the 64-day support period, E_{max} increased by 155% (from 0.42 to 1.07 mm Hg/ml) (Figure 2). The resting LVEF changed by −2% to 13%, and the SWI decreased by 3% to 45% (Table 1).

CONCLUSIONS

In humans, the E_{max} varies from 1.1 ± 0.6 (LVEF <0.40) to more than 2.6 ± 0.5 mm Hg/ml (LVEF >0.60). In both cases presented herein, the initial depression in E_{max}, LVEF, and SWI was consistent with profound cardiac failure at admission. With support, the cardiothoracic ratio was markedly reduced, clinical status improved, and cardiomyocyte histomorphology enhanced. The resting LVEF and SWI, conventional measures of global LV function, not only failed to reflect this improvement but also depended on the load (i.e., pump speed). Clearly, the E_{max} was the only index that reflected intrinsic myocardial contractility independently of the volume status or LV loading conditions.

Our method accurately reflected the non-pulsatile, continuous-flow characteristics of the Jarvik 2000 LVAD. In its present form, however, the method was susceptible to observer-dependent measurement errors, with the echo-dense body of the pump presenting technical problems. Also, volume calculations with echocardiography were labor-intensive, limiting the number of measurements and thus negatively affecting the power of the linear approximation. Moreover, invasion of the chest cavity was required, which is unacceptable for routine measurement of cardiac contractility during pump support. Therefore, we are developing a simpler, less invasive variant involving simultaneous recording of the arterial pressure and intraventricular volume during the aortic notch (i.e., end-systole) only, for various pump speeds (i.e., preloads). This simple, minimally invasive method allows multiple end-systolic PV coordinates, points on the upper left shoulder of the PV loops. The E_{max} is indicated by the slope of the line that connects these points. Clinical application of this less invasive method is currently in progress to determine the predictive power of the E_{max} for bridging device recipients to myocardial recovery and pump explantation without transplantation.

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