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Continuous-flow left ventricular assist devices induce left ventricular reverse remodeling

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Left ventricular assist device (LVAD)-induced reverse remodeling was originally studied in hearts of patients supported with pulsatile devices.[1] The mechanical unloading of the failing left ventricle (LV) with the use of LVADs has resulted in reverse remodeling, although not true normalization, of ventricular and myocardial structure and function.[2,3] Currently, the vast majority of patients are supported with continuous-flow devices. In addition, one newer device has been specifically designed to provide partial support.[4] The degree to which continuous-flow devices induce reverse *structural* remodeling is unknown. We hypothesized that the degree of reverse structural remodeling would be related to the degree of mechanical unloading by the LVAD.

Hearts were obtained at the time of transplantation from patients with chronic heart failure (CHF) who did not receive LVAD support ($n = 7$), patients bridged to transplant with a full-support continuous-flow LVAD (HeartMate II; Thoratec Corp., Pleasanton, CA; $n = 15$), and patients bridged to transplant with a partial-support continuous-flow micro-pump (Synergy; Surgical System, CircuLite, Inc., Saddle Brook, NJ; $n = 5$). The choice of support device was based on clinical criteria and was not related to this study. For the mechanical support groups, hearts were included for study only if they were supported for ≥ 45 days. Explanted hearts were studied as described previously.[1] Hearts were studied within 1 hour of explant. A balloon made from an inverted surgical glove with ligated fingers was connected to an infusion cannula and pressure sensor. The passive pressure–volume relationship (PVR) of the balloon and balloon wall volume was measured prior to use.

The balloon was then inserted in the LV through the mitral valve and held in place by a purse-string suture. Pressure was then measured at incremental saline infusions. A passive PVR was constructed for each heart. Ventricular volume was corrected for the volume of the balloon wall and ventricular pressure was corrected for the passive PVR of the balloon. Ventricular size was indexed by V_{30}, the volume at which pressure was 30 mm Hg. Continuous variables are expressed as mean ± standard deviation and significance of differences between groups assessed with Student's *t*-test. Comparison between PVRs was performed with analysis of covariance applied to PVRs linearized by logarithmic transformation and with group and patient identification numbers coded as categorical variables. In all cases, $p < 0.05$ was considered significant.

Basic characteristics for each group before transplantation are summarized in Table 1. Patients in the partial-support group had significantly shorter durations of support. Patients not requiring support were more likely to have idiopathic dilated cardiomyopathy than ischemic cardiomyopathy. Blood levels of BNP were significantly reduced in the full-support group compared with controls, with partial-support patients falling in between. Group-averaged PVRs of the explanted hearts are shown in Figure 1A and V_{30} values are summarized in Figure 1B. Patients without mechanical support had the largest hearts (V_{30}: 217.5 ± 61.7 ml). Patients bridged with a full-support device had a significantly leftward-shifted PVR (V_{30}: 141.6 ± 59.0 ml;

Table 1 Patient Demographics and Treatments Prior to Heart Transplant

	Type of support prior to transplant		
	No support	Full support	Partial support
Age (y)	50.1 ± 13.6	46.6 ± 12.0	53.8 ± 10.8
Duration of support	NA	315.4 ± 148.1	99.6 ± 69.8[a]
BSA (m^2)	2.0 ± 0.2	1.9 ± 0.2	1.8 ± 0.2
BMI	27.3 ± 4.6	26 ± 4.1	24 ± 1.6
Male	6 (85.7)	12 (75.0)	3 (60.0)
Ischemic etiology of CHF	2 (28.6)	11 (68.8)[b]	4 (80.0)[c]
NT-proBNP (ng/liter)	3,875 ± 3,248	1,425 ± 1,030[b]	2,201 ± 1,470
Medications			
β-blocker	7 (100.0)	8 (53.3)	4 (80.0)
ACE inhibitor	2 (28.6)	3 (20.0)	4 (80.0)
ARB	5 (71.4)	0 (0.0)	1 (20.0)
ACE inhibitor/ARB	7 (100.0)	3 (18.8)	5 (83.3)
Aldosterone inhibitor	6 (85.7)	8 (53.3)	4 (80.0)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; BNP, brain-type natriuretic peptide; BSA, body surface area; CHF, chronic heart failure; NA, not available.

[a] $p < 0.05$ vs full-support group.

[b] $p < 0.05$ vs no-support group.

[c] $p < 0.05$ (0.045).

$p = 0.01$ vs control). There was an average 76-ml reduction in V_{30}. This degree of reverse remodeling is slightly lower than that reported previously for the HeartMate I pulsatile device (average decrease for V_{30}: 98 ml).[5] In contrast, patients receiving partial support had an average heart size in between the full-support and no-support patients (V_{30}: 173.1 ± 42.7 ml).

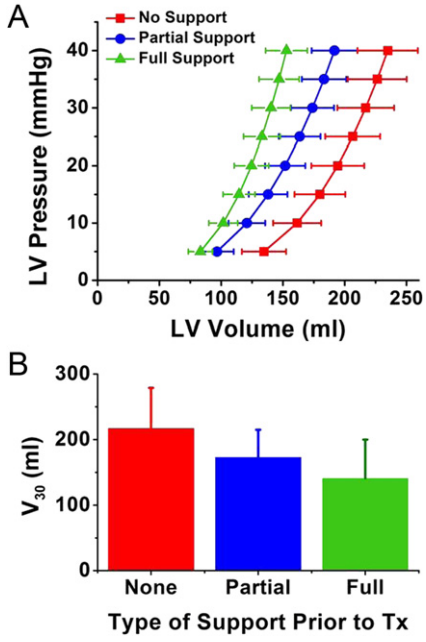

Figure 1 (A) Group-averaged passive, ex vivo pressure–volume relations from patients receiving full support, partial support or no mechanical support prior to transplantation. (B) Average V_{30} (volume on the PVR yielding a pressure of 30 mm Hg) for each patient group.

A potential limitation is the shorter duration of support for the partial-support device. Therefore, only hearts supported for >45 days were included. An earlier study has shown that reverse remodeling process is complete by this point.[5]

Despite the fact that pulsatile devices are more effective at unloading the ventricle than continuous-flow devices, clinical effectiveness in terms of hemodynamic support, recovery of exercise tolerance, and improvement in quality of life are comparable.[4] This suggests that choosing the mode of assist becomes relevant only if the goal of providing support is aimed at myocardial recovery. In this regard, it is critical to note that, although reverse remodeling is very common, recovery is very rare.

Despite these findings, improved understanding of the determinants of reverse remodeling remains a priority because this is what will ultimately contribute to development of strategies to enhance recovery.

Disclosure statement

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