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Left Ventricular Echocardiographic and Histologic Changes: Impact of Chronic Unloading by an Implantable Ventricular Assist Device

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Objectives. **We studied the effects of chronic left ventricular unloading by a ventricular assist device and assessed left ventricular morphologic and histologic changes.**

Background. **The implantable left ventricular assist device has been effective as a "bridge" to cardiac transplantation. Although there are reports documenting its circulatory support, little is known about the effects of chronic left ventricular unloading on the heart itself.**

Methods. **We performed intraoperative transesophageal echocardiography at the insertion and explantation of a HeartMate left ventricular assist device in 19 patients with end-stage heart failure. They were supported by the assist device for 3 to 153 days (mean [±SD] 68 ± 33). Measurements were taken retrospectively to obtain left atrial and ventricular diameters and interventricular septal and posterior wall thicknesses. Histologic examinations were made from the left ventricular myocardial specimens of 15 patients at the times of insertion and explantation for heart transplantation. Insertion and explantation specimens were compared qualitatively (0 to 3 scale) for wavy fibers, contraction band necrosis and fibrosis, with quantitative measurement of minimal myocyte diameter across the nucleus.**

Results. **Left atrial and left ventricular diastolic and systolic diameters decreased immediately after insertion of the left ventricular assist device (from 46 to 35, 63 to 41 and 59 to 36 mm, respectively, all $p < 0.001$). Left ventricular wall thickness increased from 10 to 14 mm ($p < 0.001$) for the interventricular septum and from 10 to 13 mm for the posterior wall ($p < 0.001$). No echocardiographic measurements showed significant subsequent changes at the chronic stage. Myocardial histologic findings demonstrated a reduction in myocyte damage (from 1.9 to 0.5, $p < 0.001$, for wavy fiber and from 1.3 to 0.2, $p < 0.01$, for contraction band necrosis) and an increase in fibrosis (from 1.3 to 1.9, $p < 0.05$), but without significant change in myocyte diameter (from 15.6 to 16.8 μm, $p = 0.065$).**

Conclusions. **Left ventricular unloading with the implantable assist device induces an immediate increase in wall thickness, consistent with the reduction in chamber size, thereby decreasing wall stress. Chronic unloading allows myocardial healing and fibrosis without evidence for ongoing myocyte damage or atrophy. Left ventricular assist device insertion may have a role in "resting" the ventricle for selected patients with heart failure.**

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Cardiac transplantation has become a widely accepted treatment for end-stage heart disease. However, the demand for donor hearts is much higher than the supply (1–3), and many patients die while awaiting transplantation. Thus, the left ventricular assist device has been important as a "bridge" to cardiac transplantation (4–6), and a variety of devices have been used for this purpose (4–9). There have been several reports regarding hemodynamic or peripheral organ responses to the ventricular assist device (4,5,8,10). However, little is known about the impact of the device on the left ventricle itself. The left ventricular assist device provides remarkable unloading to the ventricle, and the aortic valve typically does not even open during function of the device (8). Therefore, some changes may be induced in the left ventricular structure and histology (11). Because some forms of heart failure are potentially reversible, it is important to determine the effect of long-term ventricular unloading on the left ventricular structure and histology.

The HeartMate (1000IP, Thermo Cardiosystems Inc.) is an implanted left ventricular assist device. It has been reported to provide consistent hemodynamic support with sustained reduction in both left ventricular preload and afterload without serious adverse effects (5,6,8,12). In the present study, echocardiographic observations were done in patients before and after HeartMate insertion to determine the effect of ventricular unloading on the left ventricular structure. In addition, to determine the impact on myocardial microstructure, histologic examinations were performed in left ventricular specimens

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obtained before ventricular assist device insertion and at the time of explantation and subsequent cardiac transplantation.

Methods

Study patients. Nineteen patients with end-stage heart failure who underwent HeartMate left ventricular assist device insertion as a "bridge" to cardiac transplantation were studied (17 men, 2 women; 35 to 62 years old, mean age [±SD] 50 ± 8; idiopathic dilated cardiomyopathy in 7, ischemic cardiomyopathy in 12). Despite inotropic (19 patients), ventilatory (14 patients) and intraaortic balloon pump (16 patients) support, mean cardiac index was 1.60 ± 0.27 liters/min per m^2 (range 1.17 to 2.05) at assist device insertion.

HeartMate device. The HeartMate 1000IP device is an implantable, pneumatically driven, pusher-plate type pump (5,6,8). The pump housing is placed in the patient's left upper abdominal wall, and the pneumatic drive line is connected to an external console. A plug of the left ventricular apex is cored, and the inflow cannula is inserted into the apex. The outflow 25-mm Dacron graft is anastomosed to the proximal ascending aorta. Porcine bioprosthetic valves are used for both inflow and outflow conduits. Blood drains from the left ventricle through the inflow valved conduit into the pump by a pressure difference between the left ventricle and the pump and then is ejected through the outflow conduit into the ascending aorta. The maximal stroke volume of the pump is 85 ml with a maximal flow of ~11 liters/min (5,6,8). The pump is driven in either a fixed-rate (adjustable beats/min) or an automatic mode. In the automatic mode, the pusher-plate automatically ejects when the pump chamber is 90% filled, allowing natural adjustments in cardiac output to the physical demand. The device was typically driven in the automatic mode shortly after weaning from cardiopulmonary bypass during the entire period of ventricular assist, achieving significant unloading of the heart until explantation and cardiac transplantation. At the time of orthotopic cardiac transplantation, recipient cardiectomy and pump removal were performed. The left ventricular apical core from the time of insertion and the explanted recipient heart were available for pathologic examination and histologic comparison.

Echocardiography. Intraoperative transesophageal echocardiography was performed at HeartMate insertion and at its explantation and subsequent heart transplantation with a commercially available echocardiographic system (Hewlett-Packard Sonos OR and Sonos 1500) or Acuson 128XP. All images were recorded on 0.5-in. VHS videotape and were reviewed retrospectively for evaluation of wall motion and chamber measurements using two-dimensional and M-mode modalities (13,14). The presence of aortic regurgitation was assessed by color Doppler echocardiography. Measurements included left atrial systolic diameter, measured between the lateral atrial wall and atrial septum in the basal four-chamber transesophageal view; left ventricular diastolic and systolic diameters and diastolic interventricular septal thickness and left ventricular posterior wall thickness, measured either transgastrically or basally. Fractional shortening of the left ventricle was calculated as

$$\text{Fractional shortening (\%)} = [(Dd - Ds)/Dd] \times 100,$$

where Dd and Ds are left ventricular diastolic and systolic diameters, respectively. Anatomic landmarks (papillary muscle, aortic and mitral valves) were used to ensure that measurements were made at the same left ventricular or atrial level. Measured data were divided into three groups according to the time of observation, as follows: 1) before cardiopulmonary bypass, at the time of left ventricular assist device insertion (baseline stage); 2) immediately after insertion, when the hemodynamic variables were stable (after pump stage); and 3) just before assist device explantation and subsequent heart transplantation (chronic stage).

Histologic examination. To determine the histologic changes that accompanied these ventricular structural changes, myocardial specimens from 14 patients who successfully underwent cardiac transplantation (mean duration of left ventricular assist device support 73 days) and 1 patient who died from fungal sepsis after 70 days of support were studied. Of the 15 patients studied, 6 had dilated cardiomyopathy, and 9 had ischemic cardiomyopathy. The left ventricular myocardial specimens were obtained from the cored left ventricular apex at the time of insertion (mean volume 5.8 ± 4.3 cm^3, range from 1.5 × 0.8 × 0.5 to 4.5 × 3.5 × 1.0 cm) and from the left ventricle of the explanted heart at the time of transplantation (mean weight 489 ± 75 g). These samples were fixed in buffered formalin, embedded in paraffin, cut in 4-μm sections and stained with hematoxylin and eosin. One section from each of the insertion and explantation specimens was examined histologically. Sections examined from the left ventricle of the explanted heart were chosen from areas adjacent to the apex, far enough away from the inflow cannula to avoid secondary histologic changes that might be associated with the cannula itself. Because histologic assessment was performed retrospectively, apical tissue was not always available. The examination included qualitative (0 to 3 scale) assessment of wavy fibers, contraction band necrosis and fibrosis as a measure of myocardial injury. Features were graded as 0 = absent; 1 = mild (findings occupied <10% of the tissue sample); 2 = moderate (findings occupied from 10% to 30% of the tissue sample); and 3 = prominent (findings occupied >30%) (15). The presence or absence of acute myocardial necrosis was also noted. Acute myocardial necrosis and fibrosis are histologic features that can be observed in both dilated and ischemic cardiomyopathy. Wavy fibers and contraction band necrosis are features that are indicative of myocardial ischemia. The presence of wavy fibers and contraction band necrosis was evaluated in all patients to assess the presence of acute ischemic changes. In addition, minimal myocyte diameter across the nucleus was measured at a magnification of 1,000× using the Bioquant system (W. Nuchsbaum, Inc.) connected to a personal computer (Gateway 4DX-66U, Gateway) (16). An average of 100 myocytes were analyzed per section.

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Table 1. Changes in Echocardiographic Measurements

	Baseline Stage (n = 19)	After Pump Stage (n = 12)	Chronic Stage (n = 16)
LAD (mm)	46 ± 6	35 ± 5*	37 ± 4*
Dd (mm)	63 ± 15	41 ± 9*	41 ± 8*
Ds (mm)	59 ± 15	36 ± 9*	36 ± 10*
FS (%)	7 ± 3	11 ± 10	12 ± 11
IVST (mm)	10 ± 2	14 ± 2*	12 ± 2*
PWT (mm)	10 ± 2	13 ± 2*	13 ± 2*

*$p < 0.001$ versus baseline stage. Data presented are mean value ± SD. Dd = left ventricular diastolic diameter; Ds = left ventricular systolic diameter; FS = percent fractional shortening; IVST = interventricular septal thickness; LAD = left atrial systolic diameter; PWT = left ventricular posterior wall thickness.

Statistical analysis. Results are expressed as mean value ± SD. Comparison of differences among the three stages was done with analysis of variance and the Bonferroni *t* test. Comparison of wall thickness changes between akinetic and other segments and comparison of histologic indexes between dilated and ischemic cardiomyopathy were done with unpaired *t* testing. Least-squares linear regression analysis was used to correlate wall thickness with left ventricular diameter. To assess the cause of left ventricular assist device-induced increase in wall thickness, we developed a mathematical model quantifying the change in wall thickness required to preserve wall mass as cavity diameter changes in a thick-walled spherical shell (see Appendix). The predicted slope of the diameter (D)–thickness (T) relation (dT/dD) was compared with observed changes in patients. Results were considered significant at $p < 0.05$.

Results

Results of HeartMate insertion. Mean cardiac index (pump index) increased from 1.60 ± 0.27 to 2.99 ± 0.40 liters/min per m^2 ($p < 0.05$) after left ventricular assist device insertion. Duration of support ranged from 3 to 153 days (mean 68 ± 33). One patient died of multiple organ failure 3 days after device insertion and two patients of fungal sepsis after 44 and 70 days of support, respectively. Sixteen patients underwent orthotopic cardiac transplantation after 22 to 153 days of support (mean 66 ± 31).

Echocardiographic findings. Because we reviewed tapes retrospectively, some suboptimal recordings were excluded from the analysis. Thus, data from 19 patients (7 with dilated cardiomyopathy, 12 with ischemic cardiomyopathy) served as the baseline data; data from 14 (7 with dilated cardiomyopathy, 7 with ischemic cardiomyopathy) served as the after-pump data; and data from all 16 (6 with dilated cardiomyopathy, 10 with ischemic cardiomyopathy) who had cardiac transplantation served as the chronic stage data.

As shown in Table 1, before HeartMate insertion, left atrial and ventricular dilation and thin ventricular walls were found in all patients except two who had an acute myocardial infarction and normal diastolic ventricular diameter. After insertion, the aortic valve did not open in any patient, demonstrating significant left ventricular afterload reduction. Mild to moderate aortic regurgitation was seen in two patients, and ventricular preload reduction was considered to be incomplete in these patients. Figure 1 shows representative echocardiographic observations before and after the assist device insertion. With left ventricular assist device insertion, left atrial systolic diameter decreased from 46 ± 6 to 35 ± 5 mm, left ventricular diastolic diameter from 63 ± 15 to 41 ± 9 mm, and systolic diameter from 59 ± 15 to 36 ± 9 mm, all highly significant ($p < 0.001$). Wall thickness increased significantly from 10 ± 2 to 14 ± 2 mm for interventricular septal thickness and from 10 ± 2 to 13 ± 2 mm for posterior wall thickness ($p < 0.001$). At the chronic stage, chamber size and wall thickness showed no significant changes from those obtained after pump stage.

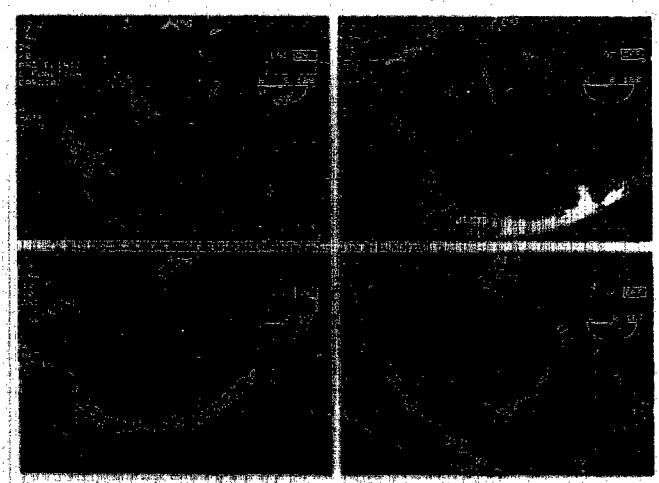


Figure 1. Left ventricular morphologic changes by left ventricular assist device insertion observed by transesophageal echocardiography. **Upper panels**, Basal four-chamber transesophageal views before (**left**) and after support (**right**). **Lower panels**, Transgastric short-axis views before (**left**) and after support (**right**).

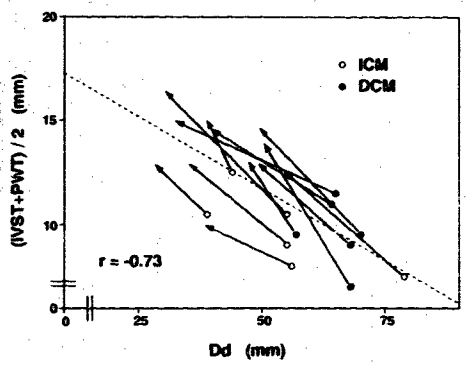


Figure 2. Changes of left ventricular diastolic diameter (Dd) and mean wall thickness of interventricular septum and posterior wall [(IVST + PWT)/2] before and immediately after assist device insertion. Arrows = intraoperative change of each point from the prepump (baseline) to the postpump stage. DCM = dilated cardiomyopathy; ICM = ischemic cardiomyopathy.

When the baseline data of wall thicknesses were compared with the data at the left ventricular assist device explantation (chronic stage), akinetic or dyskinetic walls demonstrated less increase in diastolic wall thickness (mean change 1 ± 1 mm, six segments [four from patients with dilated cardiomyopathy, and two from patients with ischemic cardiomyopathy]) than those with any degree of contractility (mean change 4 ± 2 mm, 19 segments [7 from patients with dilated cardiomyopathy, 12 from patients with ischemic cardiomyopathy], $p < 0.001$). Figure 2 shows the relation between left ventricular diastolic diameter and mean wall thickness obtained as an average of septal and posterior wall thicknesses before and after pump in 12 patients with complete data on both the dimension and wall thickness. There was a significant negative correlation between these variables, irrespective of the etiology of the disease ($r = -0.73$, $p < 0.001$, Fig. 2). Average left ventricular diastolic diameter in these 12 patients decreased from 60 to 41 mm, and mean wall thickness increased from 10 to 14 mm. Thus, the average increase of wall thickness was 0.21 mm/1-mm decrease in diastolic diameter. This finding was similar to the predicted value of 0.21 mm predicted for a thick-walled sphere (see Appendix), demonstrating that most of the change in wall thickness was explained by conservation of mass rather than by any fundamental change in cellular size. Fractional shortening did not show significant changes before and after left ventricular assist device insertion.

Histologic findings. Florid changes of acute myocardial necrosis were found in 7 of 15 patients (2 with dilated cardiomyopathy, 5 with ischemic cardiomyopathy) at the time of insertion but in none at explantation. Inspection of myocardial tissue from left ventricular assist device insertion revealed prevalent wavy fibers and contraction band necrosis in both dilated and ischemic cardiomyopathy (Table 2). After chronic ventricular support, there was a significant decrease in myocardial injury with a significant reduction in scores of both wavy fibers and contraction band necrosis (from 1.9 to 0.5, $p < 0.001$, for wavy fiber and from 1.3 to 0.2, $p < 0.01$, for contraction band necrosis) (Fig. 3). When dilated cardiomyopathy was compared with ischemic cardiomyopathy, no significant difference was found in any variable at either insertion or explantation (Table 2). There was also no significant difference in the decrease in wavy fiber (mean change −1.7 ± 0.8 for dilated cardiomyopathy, −1.3 ± 0.7 for ischemic cardiomyopathy, $p = 0.341$) and contraction band necrosis (mean change −0.7 ± 1.0 for dilated cardiomyopathy, −1.3 ± 1.3 for ischemic cardiomyopathy, $p = 0.310$) between two groups. The mean fibrosis score increased, partly reflecting healing of acute myocardial necrosis (from 1.3 to 1.9, $p < 0.05$). Although myocyte diameter across the nucleus tended to increase after chronic support, it did not reach statistical significance as a whole (15.6 vs. 16.8 μm, $p = 0.065$) (Table 2).

Table 2. Histologic Features at Insertion and Explantation of Left Ventricular Assist Device

	Insertion	Explantation
Wavy fibers		
DCM	2.2 ± 0.7	0.5 ± 0.5*
ICM	1.8 ± 1.0	0.4 ± 0.5†
All	1.9 ± 0.9	0.5 ± 0.5†
Contraction band necrosis		
DCM	0.8 ± 1.0	0.2 ± 0.4
ICM	1.6 ± 1.2	0.2 ± 0.4‡
All	1.3 ± 1.2	0.2 ± 0.4*
Fibrosis		
DCM	0.8 ± 0.8	1.7 ± 0.8‡
ICM	1.6 ± 1.1	2 ± 0.7
All	1.3 ± 1.0	1.9 ± 0.7‡
Myocyte diameter (μm)		
DCM	16.1 ± 2.9	16.5 ± 2.9
ICM	15.3 ± 1.9	16.8 ± 1.6
All	15.6 ± 2.3	16.8 ± 2.1
Acute myocardial necrosis		
DCM	2/6 (33%)	0/6 (0%)
ICM	5/9 (56%)	0/9 (0%)
All	7/15 (47%)	0/15 (0%)

*$p < 0.01$, †$p < 0.001$, ‡$p < 0.05$ versus feature at left ventricular assist device insertion. No significance was found in any variable between dilated cardiomyopathy (DCM) and ischemic cardiomyopathy (ICM) either at insertion or at explantation. Data presented are mean value ± SD or number (%) of patients.

Discussion

Changes in left ventricular morphology. With the initiation of assist device pumping, all or part of the blood in the left ventricle drains into the device, and preload is significantly decreased. Thus, left atrial and ventricular size decreased immediately after insertion. Wall thickness increased linearly as the ventricular size decreased. Because these changes occurred in the period immediately after the insertion, development of true myocyte hypertrophy in response to changes in loading conditions could not explain these changes. In fact,

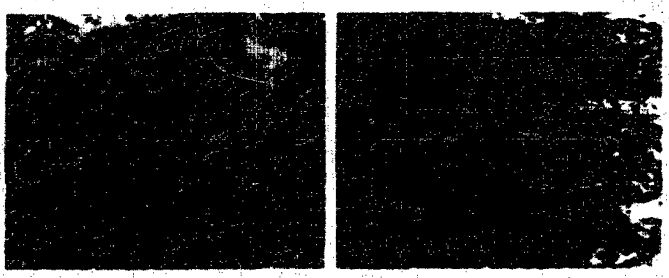


Figure 3. Representative histologic specimens obtained at insertion of a left ventricular assist device (**left**) and at explantation (**right**) (hematoxylin and eosin). **Wavy fibers** significantly visible at implantation disappeared at explantation.

actual myocyte diameter across the nucleus did not increase significantly after left ventricular assist device support (normal myocyte diameter 10 to 15 μm) (17), suggesting that myocyte hypertrophy was not a cause of the increase in wall thickness but rather geometric rearrangement of the tissue with reduction in chamber size. Indeed, mathematical modeling demonstrated that most of the increase in wall thickness can be simply explained by conservation of mass as the chamber diameter decreases (see Appendix).

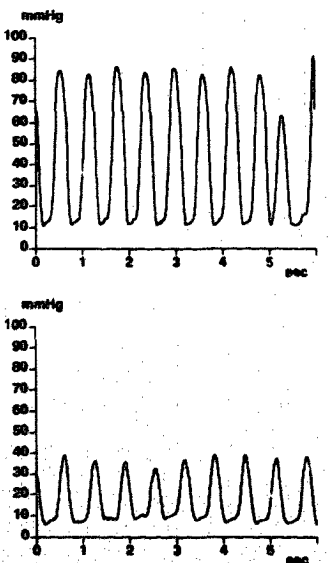
There have been several prior reports showing volume-induced changes in ventricular wall thickness clinically (18) and experimentally (19,20) that have similarly demonstrated an inverse relation between wall thickness and ventricular volume consistent with mass conservation. In an ex vivo rat model, for example, it was demonstrated that internal rearrangement of the ventricular wall fibers or side to side slippage of myocytes led to an increase in wall thickness, with the cleavage plane between fiber bundles becoming oriented increasingly perpendicular to the endocardial surface as the wall thickened (19). The same mechanism is applied to explain ventricular dilation and wall thinning in the noninfarcted area after myocardial infarction (21,22) or ventricular remodeling in ischemic cardiomyopathy (23). Examination of cardiomyopathic hearts fixed at varying degrees of distension might help to clarify the mechanism of the wall thickening.

Ventricular walls in dilated and ischemic cardiomyopathies are characteristically thin and hypocontractile with only slight thickening in systole. Little is known about whether this dysfunction is reversible to the point of recovering normal systolic thickening. In the present study, we showed that thin cardiomyopathic walls could thicken (at least passively) if they had any degree of contractility. In contrast, myocardium that was considered nonviable (thinned, akinetic, and hyperechoic) seemed incapable of increasing its thickness at all. According to the mechanism of volume-induced change in wall thickness mentioned before, as long as there is viable myocardial tissue, internal rearrangement of myocardial fibers could occur, and ventricular walls could thicken.

After left ventricular assist device insertion, afterload decreased as well as preload because the pressure in the inlet cannula is much lower than the aortic pressure. This was evidenced by the closed aortic valve throughout the cardiac cycle during the device functioning. Figure 4 shows representative change in left ventricular pressure after left ventricular assist device insertion, which was recorded using a 5F micromanometer-tipped catheter (Millar Mikro-Tip model SPC-751, Millar Instruments) inserted from the right pulmonary vein. Left ventricular systolic pressure decreased to ~40 mm Hg after insertion. The triad of increased wall thickness, decreased chamber size and decrease in intracavitary pressure all led to a dramatic reduction in left ventricular wall stress, "resting" the myocardium, which may be of value in occasional patients with reversible cardiomyopathies.

Effect of ventricular unloading on left ventricle morphometry. The effect of chronic unloading on myocyte structure and function is unknown because of few previous studies. In the current study, analysis of myocardial histologic findings demonstrated a reduction in myocyte damage after a mean of 73 days of ventricular unloading, irrespective of the etiology of the disease. Acute myocardial necrosis, observed at device insertion in patients with both ischemic and dilated cardiomyopathy, was accompanied by both wavy fibers and contraction band

Figure 4. Left ventricular pressure tracings before (**top**) and after (**bottom**) left ventricular assist device insertion.



necrosis. This finding suggests the presence of acute myocardial ischemia in both patient groups. The ischemic changes in patients with dilated cardiomyopathy may be caused by low flow states in the period immediately before device insertion. This is in agreement with a prior histologic report of patients with left ventricular assist device implantation, which suggested that myocardial injury was reduced after support (11). However, in contrast, near-complete unloading of the ventricle with a ventricular assist device has been reported to induce severe atrophy of the myocytes in experimental animals (24,25). Two factors may help explain this apparent discrepancy: 1) In our study, the left ventricular assist device was maintained in the automatic mode, enabling the ventricle to contract against a low afterload, yet still producing a low intraventricular systolic pressure (Fig. 4). This incomplete unloading may help prevent the myocytes from becoming atrophic. Thus, proper "resting" with incomplete unloading may be necessary for the recovery of the ventricular myocardium histologically and to avoid myocyte atrophy. A previous report demonstrating the importance of loading in reversing myocardial atrophy induced by unloading supports this (26), as does the concordance between the histologic findings of this study and previous ones (11,29). 2) Another reason for this discrepancy may be the difference of disease. Our patients all had end-stage heart failure from idiopathic or ischemic cardiomyopathy, whereas the experimental animals had no myocardial disease (24,25) and may have been at increased risk for disuse atrophy. Overall, however, these apparently discordant data point up the need for more basic investigation of this issue.

The histologic studies are limited by the small sample number. The data may also be affected by the fact that the implantation sample came from an apical core sample, which may have a greater tendency to have fibrosis and ischemic changes, especially in ischemic cardiomyopathy.

Clinical implications. In the present study, we showed that thin walls in cardiomyopathy became thicker after insertion of a left ventricular assist device in association with a dramatic reduction in chamber volume. This finding may suggest that wall thinning in cardiomyopathy is partly a result of loading conditions and may be reversed by appropriate load reduction therapy. Because mass conservation dictates some increase in wall thickness, our observation does not necessarily indicate myocardial viability. However, the fact that walls that were considered nonviable (echocardiographically scarred) showed less thickening suggests some relationship between the reversibility of wall thinning and myocardial viability. Side-to-side slippage of myocytes may not occur when the myocardium is totally scarred. In cardiomyopathy, the myocardial damage progresses and ends with myofibrillar lysis and interstitial fibrosis (27). Appropriate load reduction therapy, if initiated before development of fibrosis, may delay progression of myocardial damage by decreasing wall stress. This is supported by the histologic recovery demonstrated here.

We demonstrated obvious changes of the left ventricle both structurally and histologically after ventricular unloading with an assist device. Left ventricular improvement could not be expected in completely infarcted areas, because myocytes cannot regenerate once they die. Therefore, one might expect true recovery only in the borderline areas of ischemia and edema, which may be salvaged. Traditionally, the left ventricular assist device has been utilized as a "bridge" to cardiac transplantation. However, if some functional recovery were observed with the ventricular assist device, some cases might be weaned from a ventricular support, particularly those with myocarditis, as was shown in a previous report (28). Recently, three patients were weaned from the Novacor left ventricular assist device after several months of support (Portner P, Oakland, California, personal communication, May 1995). This suggests the feasibility of left ventricular assist devices serving not only as a "bridge" to transplantation but also as a treatment of certain types of heart failure. Moreover, a recent report by Frazier (29) of the first use of a vented electric HeartMate strongly suggest that left ventricular assist devices may improve cardiac function. Consistent with our present results, he showed improvement of ventricular configuration and myocardial histology in a patient with idiopathic dilated cardiomyopathy after long-term support. Although the patient died from a neurologic event after 503 days of support, his heart showed increased ejection fraction and decreased left ventricular diastolic diameter and could maintain circulation without vasopressor support even after the device support was discontinued. Because the demand for cardiac transplantation far exceeds the current donor supply (1–3), application of the left ventricular assist device as a treatment for reversible cardiomyopathies may be warranted. However, we should carefully assess the possibility of removal of the assist device in patients, because whether structural and histologic changes would be sustained after removal is unknown, as is the long-term prognosis. Further extensive studies are needed on this issue.

Study limitations. We demonstrated some structural and histologic recovery but not functional recovery of the left ventricle after long-term ventricular support with the assist device. Indeed, fractional shortening did not show significant changes after the insertion, but this may not necessarily indicate that there was no functional recovery with the device. Because fractional shortening is a load-sensitive index, it is not suitable for assessing cardiac function in a situation where loading conditions are dramatically changed as with left ventricular assist device. Evaluation with a load-insensitive index or with the left ventricular assist temporarily disabled may be needed to determine the functional recovery after the insertion.

In this retrospective study, some cases had suboptimal recordings for measurements of chamber diameter and wall thickness and were excluded from the analysis. Because the left ventricular assist device does not pump in a coordinated fashion with ventricular contraction, the left ventricular diastolic and systolic diameters did not always show maximal and minimal diameters, respectively. This might be one reason for the scattering of measured values.

The maximal period of the support was 153 days with a

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mean of 68 days in our patients. Therefore, we could not predict the consequences of a longer period of support. One report with three cases showed ventricular wall thinning after long-term implantation (6 to 12 weeks) with a left ventricular assist device (11), which may suggest that more prolonged support could result in different sequelae that might (or might not) be detrimental to the left ventricle. Thus, if it is possible for some patients to be weaned from the left ventricular assist device, determination of the optimal duration of support should be an aim of future studies.

Conclusions. Chronic ventricular unloading with an implantable left ventricular assist device significantly reduced left atrial and ventricular size, with an increase in wall thickness, thereby decreasing wall stress. Myocardial histology demonstrated a reduction in myocyte damage. Thus, the left ventricular assist device may have a role in "resting" the ventricle in selected patients with heart failure.

Appendix

Volume-Induced Changes in Left Ventricular Wall Thickness

We hypothesized that the increase in left ventricular wall thickness induced by ventricular volume decrease can be estimated mathematically.

Solving for thick-shelled spherical model. If the left ventricle can be assumed to be a thick-shelled sphere with an internal diameter of D and wall thickness of T, then left ventricular mass M can be obtained as follows:

$$M = \rho\pi/6[(D + 2T)^3 - D^3]$$

$$= \rho\pi/6(6D^2T + 12DT^2 + 8T^3),$$

where ρ = myocardial density. Left ventricular mass is thus a function of D and T [M(D, T)] and may vary with independent changes in either of these variables; $\partial M/\partial D$ and $\partial M/\partial T$. Left ventricular mass does not change simply by changing chamber volume. Therefore,

$$dM = 0 = (\partial M/\partial D)\, dD + (\partial M/\partial T)\, dT$$

$$= \rho\pi/6[(12DT + 12T^2)\, dD + (6D^2 + 24DT + 24T^2)\, dT].$$

Solving this equation for dT/dD,

$$dT/dD = -(2DT + 2T^2)/(D^2 + 4DT + 4T^2).$$

By dividing both numerator and denominator by D^2 and replacing T/D by ϵ,

$$dT/dD = -(2\epsilon + 2\epsilon^2)/(1 + 4\epsilon + 4\epsilon^2).$$

According to the data in Table 1, the baseline ϵ is ~0.16 (=10/63). Thus,

$$dT/dD = -0.21.$$

This means that when diastolic dimension decreases 1 mm, left ventricular wall thickness increases 0.21 mm. This value is almost identical to the actual change shown by the present study (Fig. 2).

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