Increased Left Ventricular Mass After Thoracotomy and Pericardiectomy
A Role for Relief of Pericardial Constraint?

Marc D. Tischler, MD; Michaelann Rowan, RN; and Martin M. LeWinter, MD

Background. Myocardial stretch and increased ventricular filling can lead to increased rates of myocardial protein synthesis. In animal studies, left ventricular mass increases after pericardiectomy, suggesting relief of a biologically meaningful restraining role and a resultant stimulus for growth. The present study was designed to test the hypothesis that combined thoracotomy and pericardiectomy leads to left ventricular hypertrophy in patients with normal left ventricular ejection fraction undergoing elective bypass surgery.

Methods and Results. Twenty-five patients with normal left ventricular ejection fraction without active myocardial ischemia underwent Doppler and quantitative two-dimensional echocardiography 1 day before and 6 weeks and 7 months after elective coronary artery bypass surgery. The pericardium was left widely incised in all patients. Left ventricular end-systolic volume, end-diastolic volume, stroke volume, ejection fraction, end-systolic circumferential wall stress, and mass were measured. Left ventricular end-diastolic volume index increased from 51±11 mL/m² to 62±14 mL/m² (p<0.05) at 6 weeks and to 66±14 mL/m² (p<0.05 versus baseline, p=NS versus 6 weeks) at 7 months. Left ventricular mass index increased from 109±23 g/m² to 127±24 g/m² (p<0.05) at 6 weeks and to 131±23 g/m² (p<0.05 versus baseline, p=NS versus 6 weeks) at 7 months. There were no changes in systolic or diastolic blood pressures, end-systolic circumferential wall stress, or end-systolic volume.

Conclusions. Patients with normal left ventricular ejection fraction develop increases in left ventricular end-diastolic volume and mass after coronary artery bypass surgery. These findings support the hypothesis that the increase in left ventricular end-diastolic volume associated with thoracotomy and pericardiectomy leads to myocardial growth and an increase in left ventricular mass. (Circulation 1993;87:1921-1927)

Key Words • bypass surgery • echocardiography • hypertrophy

In animal models, the intact pericardium restricts cardiac chamber dilation and can reduce the ability to increase stroke volume.1-9 In open-chest dogs at low normal cardiac volumes, this effect is most likely relatively small. At volumes approaching the high end of the physiological range, the left ventricular end-diastolic pressure–volume relation clearly shifts downward and to the right after pericardiectomy; this effect becomes marked at supranormal volumes. The in situ pericardium has a number of attachments to adjacent structures. In closed-chest dogs, the influence of the pericardium on filling may differ from open-chest conditions,10,11 suggesting that these attachments, along with the fact that the heart and pericardium are enclosed within the cardiac fossa, modify the pericardial effect on filling.

Investigations of the effect of the pericardium on cardiac function in human subjects have been very limited and thus far confined to the operating room. One study using radionuclide-derived volumes and the pulmonary capillary wedge pressure as a measure of left ventricular filling pressure failed to demonstrate any significant acute effect of pericardiectomy on diastolic compliance or left ventricular function curves in the normal heart.12 In contrast, other investigators13,14 using flat balloons to measure pericardial pressure have reported that the normal pericardium contributes significantly to intracavitary filling pressures. Janicki15 studied patients with chronic, dilated heart failure and found that right and left heart filling pressures increased with a one-to-one relation during moderate exercise. This pattern of equal increases in filling pressure was correlated with both an abnormal plateau in stroke volume and the onset of symptoms.15 These data suggest that these subjects were more dependent on dilation of the heart during exercise to maintain stroke volume, a mechanism that could be blunted to the extent that the pericardium and its associated effects on ventricular interaction limit dilation of the cardiac chambers. However, these results cannot necessarily be extrapolated to normal subjects.

Muscle bath and isolated heart experiments indicate that myocardial stretch and increased ventricular filling can lead to an increased rate of myocardial protein synthesis.16 Recently, we have reported that minor increases in left ventricular end-diastolic volume can lead to a significant increase in left ventricular mass in human subjects after relief of mitral stenosis.17 Simi-
larly, if pericardiomy leads to an increase in left ventricular end-diastolic volume by virtue of relief of a restraining effect, this in turn could lead to myocardial growth and an increase in left ventricular mass. Left ventricular mass increases after pericardiomy in animal models, but similar information in humans is lacking. Accordingly, the purpose of the present investigation was to test the hypothesis that thoracotomy and pericardiomy lead to increased left ventricular mass in patients with normal left ventricular ejection fraction undergoing coronary artery bypass surgery.

Methods

Patients

Between August 1991 and February 1992, 353 coronary artery bypass surgeries were performed at the Medical Center Hospital of Vermont. Two hundred seventeen patients were excluded because of documented left ventricular systolic dysfunction (left ventricular ejection fraction <50%). Sixty-five patients had unstable coronary syndromes requiring therapy with intravenous nitroglycerin and/or heparin. These patients were excluded because of the uncertain effect of acute ischemic syndromes on ventricular geometry and function. An additional 41 patients were admitted for same-day surgery and could not have an index echocardiogram. The remaining 31 patients had normal left ventricular ejection fractions and stable angina pectoris. No patient was receiving either intravenous nitroglycerin or heparin, and none had experienced chest pain within 48 hours of the index study. Two patients declined to participate in the study. Four patients had unsatisfactory echocardiographic windows. The remaining 25 patients comprised the study group. Thirteen patients had prior myocardial infarction, 10 of whom had regional wall motion abnormalities detected by left ventriculography. Myocardial infarction occurred from 13 days to 10 years (20±35 months) before the index echocardiogram. Five infarctions occurred within 2 months of bypass surgery. The mean ejection fraction measured by left ventriculography at the time of diagnostic left heart catheterization was 66±8%. Ten patients had three-vessel coronary artery disease, 12 had two-vessel disease, and three patients had one-vessel disease.

Coronary Artery Bypass Surgery

Patients underwent a variety of revascularization procedures depending on the underlying coronary anatomy. In all cases, the surgical approach was through a median sternotomy. The pericardium was opened longitudinally from apex to base and sutured laterally to fully expose the heart. The pericardium was left widely open in all cases. No patient had ECG or enzymatic evidence of myocardial infarction in the first 72 hours after surgery.

Echocardiography

All patients had baseline two-dimensional and Doppler echocardiography performed 1 day before coronary artery bypass grafting (CABG) and again 6 weeks (6±1; range, 4–8) and 7 months (7±1; range, 5–9) after surgery. Blood pressure was measured at the time of the echocardiographic examinations using a cuff sphygmo-

manometer. Two-dimensional and Doppler echocardiographic examinations were performed in the left lateral decubitus position using an Acuson phased-array ultrasonoscope device (Acuson XP-5) with a 2.5-MHz transducer. Parasternal short-axis and long-axis and apical two- and four-chamber images were recorded.

Two-dimensional Echocardiograms

All echocardiograms were analyzed in random sequence by a single investigator blinded to all clinical information. Using a Microsonics Image-Vue Workstation (Nova Microsonics Inc., Mahwah, N.J.), three to five cardiac cycles were digitized at end systole (time of smallest cavity area) and end diastole (R wave peak). Left ventricular mass, end-systolic, end-diastolic, and stroke volumes, and ejection fraction were calculated as previously described. Left ventricular volumes were calculated by the short-axis area-length method:

\[ \text{LVESV} = \frac{5}{6} \times A_s \times L_s \]

\[ \text{LVEDV} = \frac{5}{6} \times A_d \times L_d \]

where LVESV and LVEDV are left ventricular end-systolic and end-diastolic volumes, \( A_s \) and \( A_d \) are end-systolic and end-diastolic cavity areas in which the papillary muscles are regarded as part of the left ventricular cavity, and \( L_s \) and \( L_d \) are left ventricular end-systolic and end-diastolic lengths, respectively. Left ventricular mass was estimated as

\[ \text{mass} = 1.055 \times \frac{5}{6} (A_d - A_s) L \]

where \( L \) is the distance from the mitral annulus to the apical endocardium in diastole, \( A_s \) is the total left ventricular short-axis area enclosed by the left ventricular epicardium and the right side of the septum at the level of the papillary muscles, and \( A_d \) is the end-diastolic cavity area in which the papillary muscles are regarded as part of the left ventricular wall. All volumes and masses were indexed to body surface area.

Left ventricular end-systolic circumferential wall stress was estimated according to the method of Mirkovsky:

\[ \sigma_c (\text{kdyne/cm}^2) = \frac{1.33 \times \frac{A_e^{3/2}}{A_e^{1/2} - A_s^{1/2}} \times \left(1 - \frac{A_e^{3/2}}{\pi (0.5 L_s)^2 (A_e^{1/2} + A_t^{1/2})}\right)} \]

where 1.33 is a constant used to convert mm Hg to kdyne/cm², and \( P = \) peak left ventricular pressure in mm Hg. Peak left ventricular pressure was estimated from the systolic cuff blood pressure. This method has been demonstrated to correlate extremely well with estimates of wall stress based on high-fidelity invasive end-systolic pressure measurements.

Doppler Echocardiograms

Pulsed-wave Doppler sampling of transmitral flow was recorded from the apical four-chamber view with the sample volume located below the mitral valve annulus and above the leaflet tips (parallel to flow). Transmitral Doppler velocity flow profiles were digitized and analyzed. A minimum of three spectral envelopes were analyzed and averaged for each measurement. Modal peak velocities (E velocity and A velocity) and velocity time integrals were calculated. The early diastolic velocity time integral (VTI E) and late diastolic velocity time integral (VTI A) were calculated.

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The atrial filling fraction (AFF) was defined by $VTI_A/(VTI_e+VTI_a)$.

**Statistical Analysis**

All data are presented as mean±1 SD. Comparisons between patients before and at different intervals after bypass surgery were performed by repeated-measures ANOVA with and without covariates. A trial by group interactions of the ANOVA within the repeated-measures structure was used to explore the effects of a history of myocardial infarction as well as postoperative discontinuation of β-blocker or calcium channel antagonist. In cases where significant $F$ values were detected, the Student-Newman-Keuls test for multiple comparisons was used to identify significant differences for each variable. Differences were considered significant if the null hypothesis could be rejected at the 0.05 probability level.

**Results**

**Patients**

Patients included 17 men and eight women whose mean age was 62±11 years (range, 33–78). All patients returned for 6-week and 7-month examinations. At the time of the baseline examination, 24 (96%) were taking antianginal medications, including nitrates ($n=11$), β-blockers ($n=16$), and calcium channel antagonists ($n=13$). At the 6-week study, 12 patients (48%) were taking antianginal medications. These included β-blockers ($n=12$) and calcium channel antagonists ($n=1$). At the 7-month examination, seven patients (28%) were taking a β-blocker and one was taking a calcium channel antagonist.

The mean hematocrit decreased from 39.8±4.8% before surgery to 35.2±3.5% before discharge ($p<0.05$). The blood urea nitrogen (16±6 versus 20±10 mg/dL, $p=\text{NS}$) and serum creatinine (1.1±0.3 versus 1.1±0.3, $p=\text{NS}$) did not change.

**Systolic and Diastolic Blood Pressures**

Six weeks after bypass surgery, the mean systolic blood pressure was unchanged compared with preoperative values (130±19 at 6 weeks versus 132±26 mm Hg after surgery, $p=\text{NS}$). The systolic blood pressure at 7 months was also unchanged (141±25 mm Hg, $p=\text{NS}$). Diastolic blood pressure 6 weeks (76±10 mm Hg, $p=\text{NS}$) and 7 months (77±13 mm Hg, $p=\text{NS}$) after surgery was also unchanged from the preoperative value (76±10 mm Hg). The trial by group interactions of the ANOVA did not reveal any significant serial systolic blood pressure or diastolic blood pressure pattern differences between those withdrawn from β-blockers or calcium channel antagonists compared with other subjects.

**Two-dimensional Echocardiography**

Preoperative ejection fraction measured by two-dimensional echocardiography (62±7%) was similar to that measured by left ventriculography (66±8%, $p=\text{NS}$) (Table 1). Six weeks after surgery, there were significant increases in left ventricular end-diastolic volume (22%, Figure 1) and mass indexes (17%, Figure 2). The end-systolic volume index (Figure 3) did not change significantly. End-systolic circumferential wall stress did not change at 6 weeks or 7 months. There was an initial increase in ejection fraction to 67±10% that was not statistically significant. At 7 months, ejection fraction was 69±8%, significantly greater than that recorded before surgery. End-diastolic volume (29%) and mass (20%) were still significantly greater than preoperative values. There were no significant interval changes between the 6-week and 7-month studies. When patients with myocardial infarction within 2 months of bypass were excluded, there were no significant changes in overall results. As was the case for systolic and diastolic blood pressures, no interactions between discontinuation of medications and ejection fraction were detected. In addition, the serial increases in left ventricular mass and mass index were not influenced by a history of myocardial infarction (Figure 4) or medication discontinuation.

**Table 1. Echocardiographic Variables**

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>6 Weeks</th>
<th>7 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cohort (n=25)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVESEV (mL)</td>
<td>38±13</td>
<td>40±18</td>
<td>39±14</td>
</tr>
<tr>
<td>LVESEVI (mL/m²)</td>
<td>19±6</td>
<td>20±9</td>
<td>20±7</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>100±26</td>
<td>119±20*</td>
<td>126±27*</td>
</tr>
<tr>
<td>LVEDVI (mL/m²)</td>
<td>51±11</td>
<td>62±14*</td>
<td>66±14*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62±7</td>
<td>67±10</td>
<td>69±8*</td>
</tr>
<tr>
<td>σ (kdyne/cm²)</td>
<td>187±26</td>
<td>192±22</td>
<td>190±19</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>216±56</td>
<td>248±61*</td>
<td>254±61*</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>109±23</td>
<td>127±24*</td>
<td>131±23*</td>
</tr>
</tbody>
</table>

No infarction within 2 months of bypass (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>6 Weeks</th>
<th>7 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVESEV (mL/m²)</td>
<td>19±6</td>
<td>21±10</td>
<td>21±8</td>
</tr>
<tr>
<td>LVEDVI (mL/m²)</td>
<td>50±11</td>
<td>62±14*</td>
<td>66±14*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62±7</td>
<td>65±10</td>
<td>69±9*</td>
</tr>
<tr>
<td>σ (kdyne/cm²)</td>
<td>186±29</td>
<td>192±24</td>
<td>186±17</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>111±23</td>
<td>129±24*</td>
<td>133±22*</td>
</tr>
</tbody>
</table>

LVESEV, left ventricular end-systolic volume; LVESEVI, left ventricular end-systolic volume index; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; σ = end-systolic circumferential wall stress; LV, left ventricle.

*p<0.05 vs. preoperative values.

![Figure 1. Plot of left ventricular (LV) end-diastolic volume index before surgery and 6 weeks and 7 months after coronary artery bypass surgery.](http://circ.ahajournals.org/content/111/7/1923/F1.large.jpg)
continuation (Figure 5). Left ventricular mass index before surgery (113±18 versus 106±27 g/m², p=NS), at 6 weeks (130±18 versus 124±29 g/m², p=NS), and at 7 months (136±19 versus 126±27 g/m², p=NS) was similar in patients with and without prior myocardial infarction, respectively, and exhibited comparable serial increases over time (Figure 4). Similarly, the serial increases in left ventricular mass index from baseline (114±21 versus 104±24 g/m², p=NS) to 6 weeks (130±23 versus 124±25 g/m², p=NS) and 7 months (132±21 versus 130±26 g/m², p=NS) were the same in patients who did or did not have medications discontinued after surgery (Figure 5). When time-dependent systolic blood pressure covariate values were used, significant covariate effects (p<0.05) were observed for left ventricular mass and mass index. However, the biological significance of these statistical relations is minimal, since in all cases the covariance-adjusted means differed by <1.2% from the unadjusted means.

Doppler Echocardiography

The only Doppler parameter that demonstrated a statistically significant change at any time during the follow-up period was the peak A velocity at 6 weeks, which was significantly greater than that recorded before surgery but returned to baseline at 7 months (Table 2). The atrial velocity time integral did not change significantly during this period.

Discussion

Ventricular filling is restrained by the pericardium over a wide range of physiological conditions. However, the significance of this effect at physiological ventricular volumes in humans is uncertain. Since myocardial stretch and increased ventricular filling can lead to an increased rate of myocardial protein synthesis, we hypothesized that if pericardiectomy results in an increase in diastolic volume in humans, this would lead to an increase in left ventricular mass. We selected patients with normal preoperative left ventricular volumes, ejection fraction, and mass who were undergoing pericardiectomy as part of elective coronary artery bypass surgery. Our results indicate that left ventricular end-diastolic volume and mass do increase after bypass surgery. This effect is present 6 weeks after surgery, persists for at least 7 months, and is substantial, with the increase in mass averaging 17% at 6 weeks and 20% at 7 months.

FIGURE 3. Plot of left ventricular (LV) end-systolic volume index before surgery and 6 weeks and 7 months after coronary artery bypass surgery.

FIGURE 4. Graph of serial changes in left ventricular (LV) mass index in patients with (solid dots) and without (open dots) a history of myocardial infarction.

FIGURE 5. Graph of serial changes in left ventricular (LV) mass index in patients with (solid dots) and without (open dots) withdrawal of β-blockers and/or calcium channel antagonists during the follow-up period.
TABLE 2. Doppler Variables

<table>
<thead>
<tr>
<th></th>
<th>Before surgery</th>
<th>Period after bypass surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 Weeks</td>
<td>7 Months</td>
</tr>
<tr>
<td>E velocity</td>
<td>74±21</td>
<td>77±21</td>
</tr>
<tr>
<td>A velocity</td>
<td>78±22</td>
<td>90±35&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>E/A</td>
<td>1.00±0.37</td>
<td>0.93±0.33</td>
</tr>
<tr>
<td>VTI E</td>
<td>12.9±4.5</td>
<td>13.2±7.5</td>
</tr>
<tr>
<td>VTI A</td>
<td>9.7±3.6</td>
<td>9.6±4.2</td>
</tr>
<tr>
<td>VTI E/VTI A</td>
<td>1.48±0.65</td>
<td>1.44±0.54</td>
</tr>
<tr>
<td>AFF</td>
<td>0.42±0.09</td>
<td>0.42±0.08</td>
</tr>
</tbody>
</table>

E/A, E velocity/A velocity; VTI, velocity time integral; AFF, atrial filling fraction.

<sup>*</sup>p<0.05 vs. 1 month; <sup>†</sup>p<0.05 vs. 7 months; all other, p=NS.

There is no prior information available regarding the immediate or chronic effects of pericardiectomy or pericardiectomy on ventricular volume in human subjects. Left ventricular volume changes immediately after acute closure of a pericardiectomy have been described in human subjects,<sup>25,26</sup> however, these intraoperative observations cannot be extended to postoperative patients with closed chests. The effects of reclosing a pericardiectomy that has been traumatized in the operating room are not necessarily the reverse of opening the pericardiectomy. Furthermore, the in situ heart and pericardiectomy are enclosed within the cardiac fossa, consisting of the lungs, mediastinal structures, and bony thorax. These surrounding structures influence the interactions between the pericardiectomy and the ventricles.<sup>10,11</sup>

Crawford et al.<sup>27</sup> used biplane two-dimensional echocardiography to study closed-chest dogs before and after pericardiectomy. They detected significant increases in end-diastolic volume after pericardiectomy. The follow-up period was relatively brief (2 weeks), and left ventricular mass was not measured. Left ventricular mass has been reported to increase in rats after pericardiectomy,<sup>18,19</sup> but in both of these studies pericardiectomy was combined with exercise. Perhaps the best evidence of a physiologically meaningful restraining role in closed-chest animals is that pericardiectomy results in an increased maximal cardiac output during exercise in dogs.<sup>5</sup>

Mangano et al.<sup>12</sup> used first-pass radionuclide angiography and pulmonary capillary wedge pressure measurements to assess left ventricular systolic function and diastolic compliance in 15 patients intraoperatively before and immediately after pericardiectomy during coronary artery bypass surgery. The pericardiectomy did not have a significant effect on systolic function curves. As in the present investigation, end-systolic volume did not change after pericardiectomy. End-diastolic volume index increased to a degree that approached but did not achieve statistical significance, possibly because of the small sample size. Using this methodology, diastolic compliance was not significantly different before and after surgery.

In the present investigation, we detected no significant changes in Doppler indexes of diastolic function with the exception of the peak atrial velocity, which increased at 6 weeks compared with preoperative values but normalized by the end of the study. Left ventricular ejection fraction increased slightly but significantly during the follow-up period. The trial by group interactions of the ANOVA demonstrates that this increase was not related to the reduced use of β-blockers and calcium antagonists during the follow-up period. Therefore, the mechanism of the increase in ejection fraction must be related to alterations in either the intrinsic contractile performance of the left ventricle or loading conditions. Since we selected patients with stable coronary disease, it seems unlikely that an improvement in blood flow resulting in reversal of “stunned” or “hibernating” myocardium was the mechanism. It is also unlikely that significant surgically related neurohumoral changes were still present 7 months after surgery. With respect to altered loading conditions, ejection fraction is sensitive to both preload and afterload. End-diastolic volume increased; however, we have no way of knowing whether, in this chronic situation, preload was increased at the sarcomere level. Thus, increased preload is a potential explanation. Our index of end-systolic wall stress did not change after surgery, suggesting that changes in afterload were not responsible for the increased ejection fraction. However, this is a relatively crude index of afterload, and we therefore cannot completely exclude this possibility.

Limitations

Although we specifically selected patients with normal systolic function and no active evidence of ischemia, we cannot exclude the possibility that other factors related to the bypass procedure besides the pericardiectomy may have influenced the volumes and masses recorded. Potential confounding factors include postoperative changes in intravascular volume, changes in pharmacological therapy, changes in coronary turgor, longitudinal effects related to recovery of hibernating or stunned myocardium subjected to subclinical ischemia, neurohumoral changes, and variations in postoperative patterns of exercise.

While circulating blood volume was not specifically measured, several indirect measurements make this an unlikely explanation for the observed increases in left ventricular mass. Blood urea nitrogen and serum creatinine did not change after surgery. The hematocrit did decrease from preoperative to immediate predischarge values. However, this decrease was minimal and unlikely to have persisted in patients eating a balanced diet after surgery.

The effect of changes in pharmacotherapy must be evaluated in view of possible effects of β-blockers and calcium channel antagonists on left ventricular mass. However, the trial by group interactions of the ANOVA failed to detect a significant effect of medication withdrawal on blood pressure, ejection fraction, or left ventricular mass.

It is possible that coronary turgor increases sufficiently after revascularization to lead to measurable increases in left ventricular mass. Although turgor is generally discussed in association with abnormalities in diastolic distensibility and filling, experimentally induced coronary ischemia does lead to acute reductions in left ventricular wall thickness.<sup>28</sup> It is not entirely possible to exclude the possibility that surgical revascularization could increase the volume of blood in the walls of the heart sufficient to cause a measurable increase in wall thickness and mass calculations.
ever, such an effect would not explain the observed increase in end-diastolic volume and would require the presence of markedly reduced flow at rest before surgery. Our study design, by selecting only patients with normal global systolic function and nonacute symptoms, makes it unlikely that turgor would be significantly augmented after surgery.

The terms “stunned” and “hibernating” myocardium refer to reversible ischemic injury and functional impairment caused by decreased coronary flow, respectively. A variety of metabolic derangements develop during ischemia, including depletion of adenine nucleosides and inhibition of the glycolytic pathway. Genetic expression of specific proteins is also modified by myocardial ischemia. As discussed previously, myocardial stretch is an important independent stimulus to hypertrophy in vitro models. Thus, even though global systolic function was not impaired, we cannot exclude the possibility that restoration of flow resulted in recovery of stunned or hibernating myocardium and to metabolic effects or stretch, either of which might lead to myocardial growth and increased left ventricular mass.

There are a variety of neurohumoral factors that might affect left ventricular mass in the postoperative state. For example, angiotensin II directly leads to myocardial hypertrophy in some species. Similarly α-adrenergic stimulation has been implicated as a stimulus to myocardial growth. Cultured cardiac myocytes exhibit significant increases in cell surface area and volume without undergoing DNA synthesis or mitosis in response to α stimulation. Thus, bypass surgery could lead to perturbations in these or other neurohumoral axes that result in increased left ventricular mass independent of the mechanical effects of thoracotomy and pericardiotomy. However, as discussed earlier, any neurohumoral changes occurring during the postoperative period would likely have returned to normal by 7 months after surgery.

We cannot exclude the possibility that patients increased their physical activity after surgery to a degree capable of stimulating compensatory myocardial hypertrophy. However, detectable myocardial hypertrophy is generally associated with vigorous endurance exercise. Our patients were not enrolled in a formal postoperative rehabilitation program. Furthermore, the most significant increase in mass occurred during the first 6 weeks, a period when patients are convalescing from the immediate effects of surgery and restricting vigorous activity.

Finally, we do not have a control group to compare with our patients. The ideal control group would consist of patients having thoracotomy and bypass grafting without pericardiotomy, an obvious impossibility. Other means of approaching the problem of an appropriate control group would be to examine the effects of thoracotomy alone or revascularization alone. To the best of our knowledge, there is no existing evidence that thoracotomy alone leads to measurable myocardial hypertrophy. The effects of thoracotomy alone could be examined in patients having various types of noncardiac thoracic surgery. Technically, this approach would be limited by the poor echocardiographic windows associated with advanced lung disease in most such patients and by potential distortion of the cardiac fossa, which could diminish the reproducibility of quantitative echocardiographic measurements. Furthermore, few of these patients undergo a median sternotomy.

Although studying patients undergoing percutaneous angioplasty would allow us to examine the independent effects of revascularization and to assess the effect of increased physical activity after revascularization, it is unlikely that the modest amounts of regional hypertrophy that might be expected if revascularization itself induces growth would be detectable using the methodology used in this investigation. As a way to determine whether revascularization itself influenced the hypertrophy we detected, we compared left ventricular mass index in those patients having three-vessel bypass (n=10) with those having one- or two-vessel bypass (n=15). Preoperative and 7-month values were virtually identical in the two groups, increasing from 108±20 g/m² to 129±21 g/m² in the three-vessel group and from 112±27 g/m² to 133±25 g/m² in the one- and two-vessel groups. Thus, the extent of revascularization did not appear to influence the amount of hypertrophy. Thus, although it appears to be unlikely that any of these factors contributed to our findings, these data must nonetheless be interpreted in light of the fact that we did not have an appropriate control group with which to compare our results.

Conclusions

This study describes the changes in left ventricular volume, ejection fraction, and mass over 7 months in 25 patients with normal left ventricular systolic function who underwent open pericardiotomy as part of elective coronary artery bypass surgery. Left ventricular end-diastolic volume increased significantly 6 weeks after surgery and remained elevated at 7 months. This dilation was associated with a significant increase in left ventricular mass in the absence of changes in systolic or diastolic blood pressure. These findings suggest that thoracotomy and pericardiotomy lead to improved left ventricular filling in patients undergoing coronary artery bypass surgery and support the hypothesis that the increase in left ventricular end-diastolic volume associated with thoracotomy and pericardiotomy leads to myocardial growth and an increase in left ventricular mass.

References


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