Left Ventricular Ejection Performance, Wall Stress, and Contractile State in Aortic Regurgitation Before and After Aortic Valve Replacement

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Left ventricular ejection performance, wall stress, and contractile state were evaluated in 35 patients with chronic aortic regurgitation. Cineangiography and pressure measurements were obtained before and a mean of 26 months after aortic valve replacement, and data were compared with those from 30 normal control subjects. The relation between quantitative changes in wall stress and changes in ejection fraction after surgery was determined. Preoperatively, end-systolic stress was elevated in patients with aortic regurgitation (218±45 vs. 160±23 kdynes/cm² [mean±SD] for control subjects, p<0.01), and ejection fraction was depressed (0.46±0.11 vs. 0.65±0.05, p<0.01). End-systolic stress decreased postoperatively (151±41 kdynes/cm², p<0.01) and ejection fraction increased (0.58±0.11, p<0.01). The magnitude of increase in ejection fraction correlated significantly and negatively (r=-0.65) with the quantitative change in end-systolic stress after surgery. Contractile function, as assessed by the ejection phase index--end-systolic stress relation, did not significantly change: 23 of 35 patients preoperatively and 18 of 35 patients postoperatively had values that clearly fell below the 95% confidence limit of the ejection fraction--end-systolic stress relation for controls. After surgery, individual ejection fraction--end-systolic stress relationships demonstrated a shift parallel to the regression curve for the control subjects. Moreover, persistent postoperative left ventricular hypertrophy was significantly associated with persistent contractile dysfunction. Thus, late improvement in left ventricular ejection performance after aortic valve replacement can be attributed to the reduction in end-systolic stress. Contractile function itself was not improved by surgery. Persistent postoperative hypertrophy may be a marker for myocardial contractile dysfunction. (Circulation 1990;82:798–807)

In chronic aortic regurgitation (AR), afterload mismatch has been suggested as a cause of impaired pump performance.1,2 Recently, however, Wisenbaugh et al3 reported that extensive hypertrophy and depressed contractility, rather than inadequate hypertrophy with afterload mismatch, were the major causes of impaired pump performance. Thus, debate continues about preoperative left ventricular contractile state in aortic regurgitation.

Many studies of AR have shown that pump performance generally improves after aortic valve replacement, even if it is moderately impaired preoperatively.4–12 However, postoperative contractile state was not assessed in these earlier studies because no load-independent index of contractile function was available for clinical use. Therefore, the purpose of the present study was to evaluate the preoperative and postoperative contractile states in patients with AR by methods recently developed for assessing myocardial contractile function.5,13–15 and to examine the relation between postoperative alterations in ejection performance and loading conditions.

Methods

Patients

All patients with isolated, chronic AR who underwent aortic valve replacement at Osaka University...
Hospital between July 1978 and December 1987 were reviewed. Patients with any of the following characteristics were excluded: aortic stenosis (mean gradient, >5 mm Hg), mitral stenosis (mean gradient, >5 mm Hg), greater than trace mitral regurgitation, or evidence of significant coronary artery disease (50% or greater stenosis). Of the 69 patients identified, 35 patients underwent cardiac catheterization before and more than 6 months after aortic valve replacement and had left ventriculograms which allowed volume and stress analysis. There were 30 men and five women, ranging in age from 15 to 60 years (mean, 43 years). Twenty-nine patients underwent surgery because of significant cardiac symptoms (functional class II to IV, New York Heart Association classification) despite extensive medical treatment. The remaining six patients were subjectively asymptomatic (functional class I), and aortic valve replacement was recommended because of consistent evidence of cardiac enlargement on the basis of serial chest roentgenograms or echocardiography. No patient was denied surgery because of severity of preoperative left ventricular dysfunction.

Postoperative cardiac catheterization was performed a mean of 26 months (range, 6–80 months) after surgery. The indications for postoperative catheterization were not selective, but all patients were free of any signs of perioperative myocardial infarction and signs of coronary artery disease during the follow-up period. The purpose of repeat catheterization and the invasive nature of the tests were explained in detail to all patients. Patients who gave informed consent underwent the postoperative study. None had complications from either preoperative or postoperative catheterization.

Medications

Preoperative cardiac medications included digoxin (23 patients), diuretics (11), long-acting nitrates (seven), calcium-channel blockers (four), propranolol (three), and captopril (one). After surgery, medical therapy consisted of administration of digoxin (29 patients), diuretics (11), nitrates (three), calcium-channel blockers (three), and propranolol (one). Hence, cardiac medications in use before and after surgery were not significantly different. Two patients were considered to have systemic hypertension postoperatively, which was controlled with medical therapy. Four patients in whom borderline hypertension was suspected received nitrates or calcium-channel blockers.

All medications were withheld for at least 12–24 hours before catheterization.

Preoperative Cardiac Catheterization

Right and retrograde left heart catheterizations were performed in all patients. Premedication consisted of meperidine hydrochloride (1 mg/kg i.m.) and hydroxyzine (1 mg/kg i.m.). Cardiac output was determined by the dye-dilution method. An 8F micromanometer-tipped angiographic catheter (Millar Instruments, Inc., Houston) was used in nine patients to allow simultaneous high-fidelity recording of left ventricular pressure during contrast ventriculography. In the remaining 26 patients, well-flushed fluid-filled catheters connected to a Statham P23Db or P23ID transducer (Spectramed Inc., Cardiovascular Products Division, Oxnard, Calif.) were used. Aortic pressure and left ventricular pressure were recorded immediately before left ventriculography, during which time there was no change in heart rate.

In the nine patients in whom the Millar catheter was used, the time delay in transmission of pressure through the fluid-filled catheter was about 10 msec, with the difference in peak left ventricular systolic pressure (LVSP) being less than 5 mm Hg. The LVSP recorded just before ventriculography was virtually identical to the pressure measured during contrast injection in these patients. Pressure tracings were recorded at a paper speed of 100 mm/sec with an eight-channel optical recording system. Left ventriculography was carried out using biplane 35 mm cineangiography (30° right anterior oblique and 60° left anterior oblique projections) in 29 patients, and single-plane 35 mm cineangiography (30° right anterior oblique projection) in six patients. Aortic root angiography was performed on all patients to estimate the degree of aortic regurgitation. All patients more than 40 years old, those experiencing chest pain on exertion, and those suspected of having coronary artery disease underwent coronary arteriography.

Postoperative Studies

The left ventricle was catheterized postoperatively using the transseptal technique in all patients. Preoperative and postoperative studies were performed using the same equipment and the same catheter manometer systems; a micromanometer-tipped angiographic catheter was introduced transseptally into the left ventricle in the same nine patients.

Simultaneous left ventricular and aortic pressures were recorded immediately before left ventriculography. In addition, aortic pressure was recorded during ventriculography in all patients through a fluid-filled catheter (8F pigtail) placed in the ascending aorta. We did not see any significant changes in either pressure or heart rate at the time of these two recordings. Precise synchronization between aortic pressure and cineventriculography was made possible by a cine frame marker, which recorded a mark for each film exposure (60/sec) on the simultaneous pressure recordings. Two patients with atrial fibrillation preoperatively exhibited sinus rhythm after surgery.

Aortic root angiography was repeated in all patients. No patient had a paravalvular leak. Coronary arteriography was performed if clinically indicated.

All prosthetic valves were considered to be functioning normally. Simultaneous aortic and left ventricular pressure measurements demonstrated peak systolic gradients across the prosthetic valve of less than 10 mm Hg in 30 patients, 10–20 mm Hg in three
patients and more than 20 mm Hg (22 and 30 mm Hg) in two patients.

Measurements and Calculations

Left ventricular volumes were computed by the area-length method using the regression equation for the right anterior oblique projection as derived by Wynne et al. Correction factors for ventricular measurements were derived from grids positioned at the center of the ventricle. Premature ventricular contractions and postextrasystolic beats were excluded, and the earliest well-opacified beat (second to fourth cardiac cycle) following contrast injection (diatrizoate 76%, 36–51 ml) was chosen for analysis. Earlier studies have demonstrated that myocardial performance is not altered during the five beats following injection of contrast material. In two patients with atrial fibrillation, left ventricular volumes were calculated as the average of three consecutive cardiac cycles. End-systolic volume (ESV) was defined as the smallest ventricular volume, and end-diastolic volume (EDV) as the largest ventricular volume, as identified from serial frames. Ejection fraction (EF) was calculated as (EDV−ESV)/EDV. Left ventricular mass was determined at end-diastole by the method of Rackley et al. Wall thickness was measured at the middle third portion of the anterior wall in the right anterior oblique view for the end-diastolic frame. Volumes and mass were indexed for body surface area.

To determine the ejection phase velocity index, the rate of ventricular volume reduction during ejection, we measured the mean normalized systolic ejection rate at the midwall (MNSERme) as:

\[ \text{MNSER}_{\text{me}} = \frac{V_{\text{ed}} - V_{\text{es}}}{V_{\text{ed}} \times \text{ET}_c} = (1 - \frac{V_{\text{es}}}{V_{\text{ed}}})/\text{ET}_c \]

where \( V_{\text{ed}} \) and \( V_{\text{es}} \) = midwall volumes at end-diastole and end-systole, respectively, and \( \text{ET}_c = \) ejection time corrected for heart rate. Midwall volume was defined as:

\[ V = (\pi/6)(L+h)(D+h)^2 \]

where \( L = \) the ventricular long axis, \( D = \) the diameter computed as \( D = 4A/\pi L \), where \( A = \) area, and \( h = \) wall thickness. \( \text{ET}_c \) was measured as the time from the initial rise of the aortic pressure tracing to the nadir of the dicrotic notch and was rate-corrected to a heart rate of 60 beats/min by dividing by the square root of the RR interval. Midwall rather than endocardial dimensions were used for the analysis of velocity, since the endocardial shortening is significantly influenced by the dimension:thickness ratio. It is well established that the left ventricular dimension:thickness ratio changes significantly in patients with aortic regurgitation after aortic valve replacement.

End-systolic circumferential wall stress (ESS) was calculated from Mirsky’s formula as:

\[ \text{ESS} = 1332 \times \left( \frac{P}{h_{es}} \right) \left( 1 - \frac{b^2}{2a^2} - \frac{h_{es}}{2b} + \frac{h_{es}^2}{8a^2} \right) \]

where \( P = \) end-systolic pressure, \( h_{es} = \) end-systolic wall thickness, and \( a \) and \( b = \) the end-systolic semimajor axis \( ([L+h_{es}]^2) \) and end-systolic semiminor axis \( ([D+h_{es}]^2) \), respectively, at the midwall. End-systolic wall thickness was calculated from ESV and left ventricular mass, which was assumed to be constant, according to the method of Hugenholtz et al. End-systolic pressure was defined as the aortic diastolic pressure. As another measure of afterload, peak systolic circumferential wall stress (PSS) was calculated using the formula of Mirsky et al and the method of Gaasch et al using, in the latter, the end-diastolic and end-systolic left ventricular dimensions from cineangiography, wall thickness, and peak left ventricular pressure. Although this method is based on several assumptions, the values of peak stress calculated in patients with aortic valve disease were highly concordant \((r=0.95)\) with the maximum wall stress obtained from the frame-by-frame analysis.

End-diastolic stress (EDS) was also calculated from Mirsky’s formula, where \( P = \) end-diastolic pressure, \( h = \) end-diastolic wall thickness, and \( a \) and \( b = \) the end-diastolic semimajor axis and end-diastolic semiminor axis, respectively, at the midwall. Left ventricular end-diastolic pressure (LVEDP) was measured after the a wave. To minimize error in stress calculations in patients with atrial fibrillation, we carefully matched pressure and volume by the RR interval obtained from electrocardiographic recordings made before and during angiography.

All measurements and calculations were processed using a digital plotting table (PC-8875, NEC, Tokyo) connected to a small computer (PC-9801, NEC). The intraobserver (K.T.) and interobserver variabilities (K.T. vs. K.S.) of volume and wall thickness measurements were evaluated by the end-diastolic frames of 20 ventriculograms. For volume measurements, intraobserver variability was \( 2.3 \pm 1.5 \% \) (mean±SD) and interobserver variability was \( 3.6 \pm 3.6 \% \). For wall thickness measurements, intraobserver variability was \( 3.6 \pm 2.8 \% \) and intraobserver variability was \( 6.5 \pm 4.6 \% \).

Surgical Technique

All patients underwent aortic valve replacement with a Björk-Shiley tilting disc prosthesis within 3 months of preoperative catheterization. The average aortic cross-clamp time was \( 68 \pm 21 \) minutes. In addition to systemic hypothermia, myocardial protection during the surgery was provided by a cold potassium cardioplegic solution and topical cooling with ice slush. The dose of cardioplegic solution was determined by methods previously reported. No patient had evidence of perioperative myocardial infarction.

Normal Subjects

For purposes of comparison, normal values for quantitative angiographic and left ventricular function data were obtained from 30 normal subjects who
Their pain. Hemodynamic compared by unpaired were undergone catheterization had using Student’s isons. The changes and with AR rate heart in lower postoperatively, LVEDP and EF were or compared with AR patients. Left ventricular EDVI and ESVI were higher than in controls preoperatively, and both decreased significantly postoperatively.

**Statistics**

Values are given as mean±SD. Comparisons of preoperative and postoperative data were made using Student’s paired t test. Unmatched variables were compared by unpaired t test. Multiple comparisons among regression lines were made by analysis of covariance. The association between preoperative data and the magnitude of postoperative change in left ventricular EF was tested by linear regression analysis. The relations between changes in ESS, end-diastolic and end-systolic volume indexes (EDVI and ESVI), or left ventricular mass index (LVMI) and changes in EF after surgery were also tested by linear regression analysis.

**Results**

**Hemodynamic and Volume Data**

Heart rates did not differ between controls and patients with AR before surgery (Table 1). LVSP and LVEDP were higher and the cardiac index was lower in the AR group compared with controls. The heart rate and LVSP did not change significantly postoperatively, while LVEDP decreased and cardiac index increased significantly in the AR patients. Left ventricular EDVI and ESVI were higher than in controls preoperatively, and both decreased significantly postoperatively.

**Stress and Ejection Performance**

ESS, which was used as a measure of afterload and was elevated in the AR group, decreased after aortic valve replacement (Table 2). Similarly, PSS decreased significantly. EDS, which was used as a measure of preload and was also higher in AR, decreased after surgery. The EF, which was depressed preoperatively, showed a significant increase postoperatively.

There was a significant negative correlation \(r=-0.65, p<0.001\) between the magnitude of increase in EF after surgery and the change in ESS (Figure 1), indicating a strong association between a long-term decrease in afterload and an improvement in pump performance after aortic valve replacement. The postoperative increase in EF was also related to the decrease in the ESVI \(r=0.35, p<0.05\), but was not related to changes in the EDVI \(r=0.19\), EDS \(r=0.10\), or LVMI \(r=0.22\). The increase in EF after valve replacement was also unrelated to the preoperative regurgitant volume/EDV ratio \(r=0.16\).

**Table 1. Hemodynamic and Volume Data in Patients With Aortic Regurgitation and Normal Subjects**

<table>
<thead>
<tr>
<th></th>
<th>HR (beats/min)</th>
<th>LVSP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>CI (l/min/m²)</th>
<th>EDVI (ml/m²)</th>
<th>ESVI (ml/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic regurgitation (n=35)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>82±18</td>
<td>142±21</td>
<td>16±7</td>
<td>2.80±0.87</td>
<td>246±86</td>
<td>137±70</td>
</tr>
<tr>
<td>Postoperative</td>
<td>79±17</td>
<td>140±23</td>
<td>8±3</td>
<td>3.47±0.95</td>
<td>102±30</td>
<td>45±25</td>
</tr>
<tr>
<td>(p^*)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Normal subjects (n=30)</td>
<td>77±14</td>
<td>120±17</td>
<td>9±4</td>
<td>3.68±1.01</td>
<td>80±10</td>
<td>28±6</td>
</tr>
<tr>
<td>(p^#)</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are given as mean±SD.
*Comparison of preoperative with postoperative values.
†Compared with preoperative values in patients with aortic regurgitation.
‡Compared with postoperative values in patients with aortic regurgitation.

HR, heart rate; LVSP, left ventricular peak systolic pressure; LVEDP, left ventricular end-diastolic pressure; CI, cardiac index; EDVI, end-diastolic volume index; ESVI, end-systolic volume index; NS, not significant.

**Table 2. Wall Stress and Ejection Performance in Patients With Aortic Regurgitation and Normal Subjects**

<table>
<thead>
<tr>
<th></th>
<th>ESS (kdyne/cm²)</th>
<th>PSS (kdyne/cm²)</th>
<th>EDS (kdyne/cm²)</th>
<th>EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic regurgitation (n=35)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>218±45</td>
<td>432±70</td>
<td>54±25</td>
<td>0.46±0.11</td>
</tr>
<tr>
<td>Postoperative</td>
<td>151±41</td>
<td>305±76</td>
<td>21±11</td>
<td>0.58±0.11</td>
</tr>
<tr>
<td>(p^*)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Normal subjects (n=30)</td>
<td>160±23</td>
<td>332±43</td>
<td>28±11</td>
<td>0.65±0.05</td>
</tr>
<tr>
<td>(p^#)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(p^\‡)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are given as mean±SD.
*Comparison of preoperative with postoperative values.
†Compared with preoperative values in patients with aortic regurgitation.
‡Compared with postoperative values in patients with aortic regurgitation.

ESS, end-systolic stress; PSS, peak systolic stress; EDS, end-diastolic stress; EF, ejection fraction; NS, not significant.
Interestingly, function pump and Preoperative systolic wall observed was ejection fraction (EF) and postoperative changes.

Preoperative and Postoperative Contractile States

A significant inverse relation between EF and ESS was observed in the normal control group (EF = 0.81 - 0.00096 * ESS, r = -0.65, p < 0.001) and in the AR group (EF = 0.78 - 0.00139 * ESS, r = -0.62, p < 0.001). Interestingly, comparison of the two population regressions by analysis of covariance showed no significant difference in the slopes of the regressions, indicating that the two lines were almost parallel. The intercept on the y-axis was significantly (p < 0.001) lower in the AR group than in the control group.

Preoperatively, 23 of the 35 patients with AR had EF values that fell below the 95% confidence limit of the EF-ESS relation for control subjects (Figure 2A). Postoperatively, 18 patients still had abnormal relations of EF to ESS that fell below the 95% confidence limit for control subjects. Although the disproportionate impairment of EF in relation to ESS was less frequent postoperatively than preoperatively, the difference was not statistically significant. As shown in Figure 2B, aortic valve replacement resulted in shifts in individual EF-ESS relations that were nearly parallel to the regression line for the control group, suggesting that significant changes in contractile state did not occur after surgery.

The velocity-stress relation has been suggested to be a preload-insensitive alternative to the shortening-stress relation, and analysis of its use did support the findings of the analysis using the EF-ESS relation. A significant negative correlation between MNSERmc and ESS was also observed in both the control group (MNSERmc = 1.71 - 0.0019 * ESS, r = -0.57, p < 0.001) and in the AR group (MNSERmc = 1.49 - 0.0021 * ESS, r = -0.43, p < 0.001). Comparison of the two population regressions by analysis of covariance showed no significant difference for the slopes but a significantly (p < 0.001) lower intercept for AR patients than for controls (Figure 3).

The ratio of ESS to ESVI (ESS/ESVI), another index for estimating contractile state, was depressed preoperatively in all patients with AR.
compared with control subjects and showed a significant increase after surgery (Figure 4). Postoperatively, 18 patients had normal values. However, the ESS/ESVI ratio remained abnormal in the other 17 patients. At postoperative evaluation, contractile performance estimated from the ESS/ESVI was concordant with that estimated from the EF-ESS relation.

Postoperative Regression of Left Ventricular Hypertrophy

LVMI decreased significantly from 280±110 to 175±65 g/cm² (p<0.001) after aortic valve replacement (Figure 5) but remained significantly higher than that of the normal subjects (96±13 g/m²). The time interval between surgery and postoperative catheterization did not correlate with the extent of regression of LVMI, expressed as a percentage of the preoperative value (r=0.17).

There was a strong inverse correlation between the postoperative LVMI and the postoperative ESS/ESVI ratio (r=−0.79), indicating that persistent postoperative hypertrophy is associated with persistent contractile dysfunction (Figure 6). Although the correlations were less strong, the postoperative LVMI was also related to the postoperative EDVI (r=0.63, p<0.001), the postoperative ESVI (r=0.69, p<0.001), and the postoperative EF (r=−0.48, p<0.01) (Figure 7). The postoperative LVMI was not related to the postoperative ESS (r=0.02) or the postoperative LVPS (r=0.05). The postoperative LVMI was also significantly correlated with the preoperative values for LVMI and the ESS/ESVI ratio (r=0.85 and r=0.75, respectively).

Discussion

Previous studies have shown that impaired pump performance in chronic AR generally improves and even returns to normal in many patients after aortic valve replacement.4−12 Mechanical unloading of the ventricle, rather than alterations in myocardial contractility following surgery, has been postulated as the mechanism responsible for improved pump performance. This hypothesis, proposed by Ross,1,27 has not clearly been confirmed by quantitative data of preoperative and postoperative left ventricular function, however. Moreover, changes in postoperative

**FIGURE 4.** Plots of preoperative (preop) and postoperative (postop) ratios of end-systolic wall stress to end-systolic volume index (ESS/ESVI) for the 35 patients with AR. The dashed line indicates the lower 95% confidence limit of values in 30 control subjects.

**FIGURE 5.** Plots of preoperative (preop) and postoperative (postop) left ventricular mass index (LVMI) for the 35 patients with AR. The dashed line indicates the upper 95% confidence limit of values in 30 normal subjects. One patient had persistent severe hypertrophy (LVMI of 463 g/m²) 9 months after surgery, despite a remarkable improvement in cardiac symptoms. He received a 29-mm Björk-Shiley tilting disc valve and had good prosthetic valve function. This patient died suddenly 25 months postoperatively; an autopsy was not performed.

**FIGURE 6.** Scatterplot of relation between postoperative (postop) end-systolic stress/volume ratio (ESS/ESVI) and postoperative left ventricular mass index. A strong negative correlation was noted, indicating that persistent postoperative hypertrophy after aortic valve replacement is associated with persistent left ventricular contractile dysfunction.
 contractility were not assessed in these earlier studies. A major finding in our study was the highly significant correlation between postoperative increase in EF and postoperative decrease in ESS. This finding supports the hypothesis that improved ejection performance is due to reduced afterload following aortic valve replacement.

Other important findings included the observation that contractile state, as assessed by the relation between afterload and either fiber shortening or velocity, did not change after surgery, and the observation that the contractile dysfunction seen in a substantial number of patients with AR persisted after aortic valve replacement. Moreover, we found that postoperative contractile dysfunction was associated with persistent left ventricular hypertrophy.

**Alterations in Wall Stress and Ejection Performance**

Gault et al. reported that no change in velocity of circumferential shortening at maximal wall tension occurred after aortic valve replacement despite a return of wall tension to normal ranges. Pantely et al. found no change in peak equatorial wall stress or EF after surgery. In contrast, Schwarz et al. recently studied patients with AR who underwent aortic valve replacement during cardioplegic arrest and found a remarkable improvement in EF and a reduction in PSS. Our observations were similar to these findings. Although Schwarz et al. acknowledged that postoperative changes in ejection performance could be attributable to reduced afterload, they nonetheless concluded that a complete postoperative restoration of myocardial contractility accounted for improvements in ejection performance. However, the strong correlation found in our study between the magnitude of increase in EF and the change in ESS provides evidence that improvements in ejection performance were due at least in part to a reduction in afterload.

**Preoperative and Postoperative Myocardial Contractile Function**

Assessment of myocardial contractility in patients with chronic volume overload has been difficult because of the lack of a load-independent index of contractile function. Recently, the relations between ESS and either EF or ESV have been used to estimate contractile state in chronic myocardial overload. In the present study, therefore, preoperative and postoperative contractile states were determined by these two methods.

There was a marked discrepancy in the preoperative assessments using these different methods. Using the relation between EF and ESS, contractile state was found to be normal in 12 of the 35 patients and to be depressed in the remaining 23. On the other hand, when the ratio of ESS to ESV was used, contractile state appeared to be depressed in all patients. This discrepancy could be explained by the dependence of these methods on ventricular size and loading conditions. The EF-ESS relation takes afterload into account, but is affected by the level of preload. Therefore, contractile state may have been slightly overestimated by this measure in the setting of AR and an augmented preload.

On the other hand, the end-systolic stress-volume relation is shifted to the right with normal contractility in the setting of chronic volume overload. This implies that the ratio of stress to volume index at end-systole is dependent on the size of the ventricle, and that a reduced ESS/ESVI ratio can occur without indicating a depressed contractile state. Contractile function may thus have been underestimated by the preoperative ESS/ESVI ratio in some patients with AR.

However, although these methods represent load- and size-dependent measures of contractility, both demonstrated the existence of contractile dysfunction in a substantial number of preoperative patients. Our results are in part consistent with those obtained by Wisenbaugh et al., who found an inverse relation between EF and ESS in both control and patient groups. They concluded that contractile impairment, rather than afterload mismatch, was the major cause of pump dysfunction. In contrast to our study, they
showed a significant difference between the slopes of the regressions of control and patient groups by analysis of variance. However, we believe that the inverse relation between EF and afterload observed in the present study is consistent with the results of Wisenbaugh et al, and that the discrepancy arises from the larger number of patients in our study and the difference in the statistical methods used. In addition, differences in patient selection might be responsible for the seemingly different results. Our study included surgery patients who had larger left ventricular volumes and lower EFs than those studied by Wisenbaugh et al.

Postoperative assessments of contractility in our study using the two methods were in good agreement. Both consistently indicated impaired contractility in a number of patients after surgery. This close agreement may be explained by the fact that the postoperative decreases in ventricular size and preload reduced their relative contributions to calculated indices of contractile state.

Importantly, the contractile abnormalities as assessed by the EF-ESS relation appeared to be virtually unchanged postoperatively, because individual relations changed parallel to the normal regression line. In the presence of a postoperative reduction in preload, this finding might imply a slight increase in contractility. In the present study, however, analysis of the MNSE\textsubscript{r}-ESS relation, which has been suggested to be a preload-insensitive alternative to the shortening-ESS relation,\textsuperscript{15} also supported conclusions derived from EF-ESS analyses, namely, that contractile dysfunction was present in a substantial number of patients with AR, and significant changes in contractile state did not occur after aortic valve replacement.

**Regression of Left Ventricular Hypertrophy**

We observed that LVMI decreased substantially after aortic valve replacement, although it did not return to normal. This decrease in LVMI appeared to occur rather rapidly after surgery so that there was no correlation between the duration of valve replacement and subsequent cardiac catheterization and the extent of regression of LVMI. Our findings are consistent with results of earlier echocardiographic\textsuperscript{6,8} and angiographic\textsuperscript{4,29} studies. The clinical importance of the incomplete regression of hypertrophy, its influences on myocardial contractile state, and its impact on long-term prognosis in patients remain to be determined.\textsuperscript{30} Incomplete regression after aortic valve replacement may be caused by the small residual gradient across the prosthetic aortic valve\textsuperscript{31} or by irreversible damage of the ventricular myocardium. Wisenbaugh et al,\textsuperscript{3} in their angiographic study of 16 patients with AR, found a strong inverse correlation between the maximum-stress-volume ratio and LVMI and concluded that extensive hypertrophy was associated with contractile dysfunction. Our data support the findings of Wisenbaugh et al and provide further evidence that persistent hypertrophy after aortic valve replacement is a marker for persistent contractile dysfunction.

**Methodological Limitations**

As measures of afterload, PSS, mean systolic stress (MSS), or, more recently, ESS have been used in the literature. Although ESS is considered to be the most appropriate measure of the afterload opposing left ventricular emptying, it would also be important to determine either PSS or MSS. In the present study, when using PSS instead of ESS, the postoperative change in EF was significantly correlated ($r=-0.52, p<0.002$) with the change in PSS. Furthermore, a weak but significant correlation between EF and PSS was observed for normal control subjects (EF=0.73–0.00024×PSS, $r=-0.37, p<0.05$) and patients with AR (EF=0.66–0.00038×PSS, $r=-0.30, p<0.02$). The results of comparison of the two regressions using analysis of covariance were qualitatively similar to those for EF and ESS. Thus, these findings did not appear to have altered our conclusions. An earlier study\textsuperscript{32} demonstrated a close correlation between PSS and MSS ($r=0.94$), and it is unlikely that the use of MSS as a measure of afterload would have led to different conclusions.

Estimation of preload, the sarcomere length at the beginning of contraction, has also been problematic. Although EDS, a measure of preload, substantially decreased postoperatively, this decrease might be affected by factors extrinsic to the left ventricle.\textsuperscript{33} The usefulness of the ejection phase index-ESS relation is limited by the extent to which corrections for preload are affected by these factors.\textsuperscript{34}

There are some problems inherent in our angiographic techniques. We used single plane angiography to calculate left ventricular volume. Although single plane angiography may overestimate true volume, the appropriate regression equation was used to correct for this problem. The validity of this method has been reported.\textsuperscript{16} Our wall stress measurements may be limited by the facts that: 1) pressure recordings were made just before but not simultaneously with the left ventriculography and some pressure changes could have occurred before the ventriculograms were recorded; 2) pressures were measured with fluid-filled catheters in many patients; 3) aortic diastolic pressure was substituted for end-systolic pressure to calculate ESS, and 4) some of the patients were in atrial fibrillation where beat-to-beat differences in stress and contractility are found. However, earlier studies have demonstrated that no serious error is introduced by these methods.\textsuperscript{35,36}

**Factors Influencing Ventricular Contractile State**

There are other factors possibly influencing left ventricular contractility after aortic valve replacement. Although systemic hypertension represents a potential cause of persistent hypertrophy and persistently depressed contractile state, only a few patients with hypertension were seen in this study. In addition, medical therapy might have some effect on
loading conditions and cardiac function. However, cardiac medications were not significantly changed between the preoperative and postoperative studies, and all medications were withheld for 12 to 24 hours before catheterization. Although we cannot exclude the possibility of some effect of these medications on our measurements, we believe alterations produced by medical therapy did not affect our conclusions to a significant degree.

The important influence of time since surgery on changes in left ventricular hypertrophy and function in patients with AR has been described. Some investigators have reported that regression of left ventricular hypertrophy ceases in most patients before the end of the first postoperative year. In contrast, the recent report of Monrad et al. indicated that the process of myocardial remodeling after aortic valve replacement may continue for many years. We cannot definitively exclude the possibility that a further reduction in left ventricular hypertrophy will occur with time in some patients if they continue to have normal prosthetic valve function. Therefore, the ultimate prognosis of our patients was not defined in the present study.

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References


**KEY WORDS**
- aortic regurgitation
- aortic valve replacement
- left ventricular function
- myocardial contractility
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