Early postoperative changes in left ventricular chamber size, architecture, and function in aortic stenosis and aortic regurgitation and their relation to intraoperative changes in afterload: a prospective two-dimensional echocardiographic study

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ABSTRACT We prospectively studied 16 patients with isolated aortic stenosis and eight with isolated aortic regurgitation undergoing aortic valve replacement, using two-dimensional echocardiography preoperatively, intraoperatively, and 41 ± 7 days postoperatively to (1) calculate the intraoperative change in afterload, (2) quantify the postoperative changes in left ventricular chamber size, architecture, load and function, (3) determine whether the postoperative left ventricular remodeling correlated with the intraoperative change in afterload in aortic stenosis and aortic regurgitation, and (4) assess whether preoperative afterload excess precluded postoperative improvement in left ventricular function. Preoperative left ventricular mass, end-systolic meridional and circumferential wall stresses, ejection fraction, and stress-shortening relations in patients with aortic stenosis and aortic regurgitation were similar. However, our patients with aortic regurgitation had severe systolic dysfunction, with ejection fraction less than 55% in all but one patient, compared with only 10 of 16 patients with aortic stenosis. Left ventricular end-diastolic volume, mass/volume ratio, and chamber shape were significantly different in patients with aortic stenosis and aortic regurgitation (174 ± 64 vs 294 ± 140 ml, p < .01; 1.81 ± 0.63 vs 1.14 ± 0.18, p < .01; and 0.59 ± 0.09 vs 0.69 ± 0.09, p < .05, respectively). Intraoperative end-systolic meridional and circumferential stresses fell significantly in patients with aortic stenosis but remained unchanged in those with aortic regurgitation. The changes in left ventricular volume and ejection fraction during early postoperative remodeling (6 weeks) correlated with the intraoperative change in afterload in patients with aortic stenosis. In contrast, there was no intraoperative change in afterload in patients with aortic regurgitation and no significant changes in left ventricular volume, architecture, or function at 6 weeks or at 6 months. The differences in left ventricular remodeling and changes in function between patients with aortic stenosis and aortic regurgitation in the early postoperative period most probably relates to the major difference in intraoperative reduction in afterload, although a contributory role may have been played by the preoperative left ventricular dysfunction in those with aortic regurgitation that was underestimated by measurement of ejection fraction.


LEFT VENTRICULAR FUNCTION after aortic valve replacement is dependent on the complex interaction of a number of preoperative factors, important among which are myocardial contractility, left ventricular afterload, chamber architecture, and the extent of irreversible interstitial fibrosis.1-14 Routine measurements of preoperative left ventricular function and symptomatic functional classification may not accurately predict "late" postoperative left ventricular function.15-19 Currently, ejection fraction is the index of left ventricular function most frequently used in clinical decision making and for recommending operation in patients with aortic valve disease.20-34 However, because of its marked dependence on left ventricular loading conditions, ejection fraction may not accurately reflect intrinsic left ventricular performance.23, 32, 33, 35 In aor-
tic stenosis, for example, ejection fraction may be decreased due to afterload excess even when muscle function is normal, whereas it may be normal in aortic regurgitation when myocardial contractility is depressed. Thus primary reliance on preoperative ejection fraction in patients with aortic valve disease may not permit optimal timing of surgical intervention.

Left ventricular afterload, which is the counterforce that myocardial shortening must overcome to result in ejection, is an important regulator of left ventricular mass, geometry, and chamber function and is directly related to myocardial oxygen consumption. We therefore reasoned that the intraoperative reduction in afterload achieved by aortic valve replacement might be a potential determinant of postoperative left ventricular remodeling and chamber function. Accordingly, we performed a prospective longitudinal study in patients with isolated aortic stenosis or isolated aortic regurgitation undergoing valve replacement, using two-dimensional echocardiography serially during operation and postoperatively to achieve three goals: (1) to measure specifically the intraoperative change in afterload from before to after bypass, (2) to compare the magnitude of the intraoperative change in afterload in aortic stenosis and aortic regurgitation and to assess whether it correlated with the postoperative changes in left ventricular size, chamber architecture, and function, and (3) to assess whether preoperative afterload excess precluded postoperative left ventricular remodeling and improvement in function and might therefore prove useful in identifying patients who would not benefit from surgery.

Materials and methods

Population. The study population consisted of 24 patients who underwent aortic valve replacement. Patients were included in this study only if they fulfilled all of the following criteria: (1) clinically severe isolated aortic stenosis or severe isolated aortic regurgitation confirmed at preoperative diagnostic cardiac catheterization, (2) no other valvular heart disease, (3) normal coronary arteries demonstrated by selective coronary arteriography, (4) absence of segmental left ventricular wall motion abnormalities on contrast left ventricular angiography and/or two-dimensional echocardiography, (5) no history of hypertension or myocardial infarction.

Aortic stenosis. Sixteen patients had isolated severe aortic stenosis, of whom five were women. Their ages ranged from 44 to 84 years (mean 68). Preoperative hemodynamics at cardiac catheterization demonstrated resting left ventricular outflow tract gradients of 30 to 120 mm Hg (mean 78), calculated aortic valve areas from 0.31 to 0.82 cm² (mean 0.47), left ventricular end-diastolic pressures from 20 to 45 mm Hg (mean 29), cardiac index of 1.4 to 2.4 liters/min/m² (mean 2.1), and echocardiographically determined ejection fraction below 55% in 10 of 16 patients (table 1). All patients were in NYHA symptom class III or IV.

Aortic regurgitation. Eight patients had isolated severe aortic regurgitation, one of whom was a woman. Their ages ranged from 28 to 79 years (mean 48). Preoperative hemodynamics at cardiac catheterization demonstrated left ventricular end-diastolic pressures ranging from 12 to 34 mm Hg (mean 28), cardiac index of 1.8 to 2.9 liters/min/m² (mean 2.4), and ejection fractions below 55% in all but one patient (table 1). Thus our aortic regurgitation population was unusual in that it was characterized by severely abnormal systolic function in seven of eight patients. All patients were in NYHA symptom class III or IV.

Medications were discontinued 12 to 24 hr before surgery. Informed consent was obtained from each patient included in this study.

Data acquisition

Preoperative studies (closed chest). High-quality two-dimensional left ventricular echocardiograms were obtained from the apical four-chamber and parasternal short-axis views on the day before surgery. Short-axis views were recorded at high papillary muscle level, i.e., where the papillary muscles are free standing in the left ventricular cavity and separate from the left ventricular wall.

Electrocardiographic lead II was recorded simultaneously with the two dimensional echocardiograms in each patient.

Intraoperative (open chest)

Preebypass. After induction of anesthesia, a radial arterial catheter was introduced and a No. 5F Swan-Ganz catheter was positioned in the pulmonary artery. The radial arterial and pulmonary arterial catheters were calibrated at 0 to 200 and 0 to 40 mm Hg, respectively. After thoracotomy, pacing electrodes were attached to the right atrium in all patients.

After right atrial and aortic cannulation but before the onset of cardiopulmonary bypass, a sterile No. 5F Millar micromanometer, previously calibrated from 0 to 100 mm Hg at 37°C, was introduced via the right superior pulmonic vein and advanced across the mitral valve into the body of the left ventricle so that its tip was free and did not provoke ventricular ectopic activity. The output of the left ventricular micromanometer was fed into an isolated amplifier to ensure the patients' electrical safety.

### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>LV end-diastolic pressure (mm Hg)</th>
<th>LV outflow pressure gradient (mm Hg)</th>
<th>Cardiac index (l/min/m²)</th>
<th>Aortic valve orifice area (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic stenosis</td>
<td>16</td>
<td>20–45 (mean 29)</td>
<td>30–120 (mean 78)</td>
<td>1.4–2.4 (mean 2.1)</td>
<td>0.31–0.82 (mean 0.4)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>7</td>
<td>12–34 (mean 28)</td>
<td>—</td>
<td>1.8–2.9 (mean 2.4)</td>
<td>—</td>
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LV = left ventricular.
Left ventricular micromanometer, right atrial, and pulmonary arterial pressure signals, along with the lead II ECG, were fed via a custom-built, isolated four-channel amplifier interface into an Irex system 2. The amplified signals were displayed on the CRT and records were obtained on the multichannel strip-chart recorder at paper speeds of 50 or 100 mm/sec.

A 5 MHz two-dimensional echocardiographic transducer, sterilized in ethylene oxide at 100°C, was applied gently to the right ventricular epicardium at the base of the heart, from which position short-axis images of the left ventricle at high papillary muscle level were obtained with a two-dimensional ultrasonoscope during right atrial pacing at 100 beats/min and recorded on beta format videotape. The transducer was not applied directly to the left ventricle for the following reasons: (1) to avoid distorting the left ventricular cavity shape, which might invalidate the stress calculations, (2) to avoid compressing epicardial coronary arteries and interfering with coronary blood flow to the left ventricle, whose function we were assessing, and (3) to be able to use the right ventricle as an “offset” to obtain clear and complete left ventricular endocardial and epicardial images distant from the transducer artifact.

Postbypass. After aortic valve replacement when patients were hemodynamically stable and body core temperature was above 36°C, open-chest two-dimensional echocardiographic left ventricular images, left ventricular micromanometer, pulmonary arterial, and radial arterial pressures, and ECG were recorded simultaneously during right atrial pacing at 100 beats/min. Simultaneous records of radial arterial and left ventricular pressure were obtained to provide an estimate of the transprosthetic valve gradients.

Postoperative studies (closed chest). Postoperative studies were performed a mean of 42 ± 7 days after valve replacement. Two-dimensional left ventricular echocardiograms were recorded (closed chest) with simultaneous lead II ECG and cuff systolic arterial pressure measured at rest and at 1 min intervals after patients had been recumbent for 3 to 5 min. Cuff arterial systolic pressure was used to represent left ventricular end-systolic pressure.

We attempted to restudy all patients with aortic regurgitation at 6 months postoperatively. However, we were able to restudy only four patients. Of the remaining four, one had a hemorrhagic cerebrovascular accident (unrelated to her aortic valve replacement) and has since been admitted to a long-stay facility with a dense hemiplegia; three who live in another state are followed locally and are unavailable for follow-up echocardiographic studies.

Data analysis

Two-dimensional left ventricular echocardiograms. The left ventricular endocardial and epicardial borders in the short-axis and apical four-chamber views from five high-quality, stop-action, end-diastolic and end-systolic frames were traced with their calibration factors on clear plastic overlays from a flat, high-contrast scan converter. Tracings of endocardium and epicardium from each subject were digitized on a Hewlett Packard 9825A microcomputer to obtain the following data as described previously.

1. Total left ventricular short-axis area (A L) enclosed by the left ventricular epicardium and right side of the septum
2. Cavity area (A C) by two previously validated methods, in which the papillary muscles were regarded as part of the cavity for stress determinations and as the left ventricular wall for left ventricular volume and mass determinations
3. Muscle area (A m) obtained as described previously by subtracting A C (including papillary muscles) from A L, i.e., (A L – A C), for wall stress calculations
4. Left ventricular and epicardial lengths (L) traced from five end-diastolic and five end-systolic stop-action frames and digitized.

These values for A L, A m, A C, and L were utilized to calculate the following:

(1) End-diastolic and end-systolic volumes by the short-axis area length method (Appendix equation 1)
(2) Fractional shortening assessed as the percent change in left ventricular short-axis area
(3) Ejection fraction
(4) Left ventricular shape as the ratio of the short to long left ventricular axes
(5) Left ventricular muscle mass (LVM) (Appendix equation 2); the reproducibility and interobserver variability of left ventricular volume and mass determinations by two-dimensional echocardiography have been previously reported by our laboratory.
(6) Left ventricular end-systolic meridional wall stress (σ m) (Appendix equation 3) circumferential wall stress (σ c) (Appendix equation 4).
(7) Left ventricular end-systolic volume

The formulas used to calculate meridional and circumferential wall stresses were derived by Mirsky (Appendix equations 3 and 4). Meridional and circumferential stresses were calculated intraoperatively before and after bypass with micromanometer-derived left ventricular pressure and postoperatively with cuff systolic arterial pressure.

(8) Ratio of left ventricular mass to end-diastolic volume (LVM/LVEDV)

We also examined and compared stress-shortening and the stress-volume relations, i.e., the relationships between end-systolic meridional stress and ejection fraction and end-systolic meridional stress and end-systolic left ventricular volume, and between end-systolic circumferential wall stress and ejection fraction and end-systolic circumferential stress and end-systolic left ventricular volume in the populations with aortic stenosis and aortic regurgitation. In addition, we investigated the relationships between the intraoperative reduction in end-systolic wall stress and the postoperative changes in left ventricular chamber volume and left ventricular mass in patients with aortic stenosis and aortic regurgitation.

Surgical procedures. Six patients had St. Jude mechanical prostheses sizes 21 to 25 mm (two with aortic regurgitation, four with aortic stenosis) and 18 had Carpentier-Edwards porcine prostheses sizes 23 to 27 mm (six with aortic regurgitation, 12 with aortic stenosis).

Cardiopulmonary bypass time varied from 73 to 150 min at 26°C to 28°C and was not different among patients with aortic stenosis (mean 101 ± 14 min) and aortic regurgitation (mean 103 ± 11 min). In all patients cold potassium cardiospecific solution was injected directly into both coronary ostia every 15 to 25 min, and cold solution was used externally to protect the myocardium from ischemia. No catecholamines or vasodilators were used before intraoperative measurements, since catecholamines alter myocardial contractile state and thereby render comparison of end-systolic wall stress before and after bypass uninterpretable.

Statistical methods. Differences between preoperative and postoperative measurements of left ventricular function within populations were tested for significance by paired t tests and between populations with unpaired t tests. Relationships between measurements of left ventricular function and load were examined by linear regression analysis.

Results

Preoperative left ventricular function (closed chest). Preoperative left ventricular end-diastolic and end-systo-
ic volumes in patients with aortic regurgitation were 294 ± 140 and 179 ± 105 ml, significantly greater than those in patients with aortic stenosis (174 ± 64 and 96 ± 66 ml; p < .01 and p < .02, respectively) (table 2). Left ventricular muscle mass was similar (328 ± 146 vs 279 ± 38 g, respectively) (table 2). Thus the ratio of muscle mass to end-diastolic volume was significantly lower in patients with aortic regurgitation (1.14 ± 0.18 vs 1.81 ± 0.63; p < .01) (table 2).

In addition, left ventricular end-diastolic chamber architecture expressed as the ratio of short/long chamber axes was 0.69 ± 0.09 in patients with aortic regurgitation and 0.59 ± 0.09 in those with aortic stenosis (p < .05), indicating that left ventricular shape was more spherical in aortic regurgitation.

Ejection fraction varied over the same range with mean values of 46 ± 18% in patients with aortic stenosis and 40 ± 12% in those with aortic regurgitation. Importantly, resting ejection fraction was depressed (defined as less than 55%) in the majority of patients with aortic stenosis (10/16, 63%) and in all but one patient with aortic regurgitation (7/8, 88%).

Intraoperative studies (open chest). In spite of the significant differences in left ventricular pressure, chamber volumes, and architecture between the groups with aortic stenosis and aortic regurgitation, left ventricular afterload assessed as end-systolic meridional and circumferential wall stresses was similar (78 ± 43 vs 100 ± 30 kdyne/cm² and 207 ± 76 vs 217 ± 50 kdyne/cm² in aortic stenosis and regurgitation, respectively) (table 2).

Before bypass there were close inverse linear correlations between ejection fraction and end-systolic meridional stress in the patients with aortic stenosis (r = - .85, slope = -0.352) and in those with aortic regurgitation (r = - .91, slope = -0.349) and between ejection fraction and end-systolic circumferential stress (r = - .84, slope = -0.197) in patients with aortic stenosis (r = - .91, slope = -0.213) and in those with aortic regurgitation (figure 1), indicating that preoperatively both stress shortening relations were similar in the two populations. End-systolic meridional and circumferential wall stresses decreased significantly after valve replacement in patients with aortic stenosis (figure 2). In contrast, there were no significant changes in the end-systolic meridional or circumferential wall stresses in patients with aortic regurgitation (figure 2). Left ventricular end-diastolic pressures in patients with aortic stenosis were significantly higher than in patients with aortic regurgitation before bypass (p < .05, table 1) and remained so after bypass in spite of a decrease in both populations.

The differences between left ventricular end-systolic pressure and peak radial arterial pressure recorded simultaneously after bypass varied between 0 and 12 mm Hg with a mean difference of 4.8 mm Hg and a standard deviation of 3.1 mm Hg. This similarity between left ventricular systolic and radial artery systolic pressures indicated that resting transprosthetic valve gradients were small. Thus we believed we could substitute arterial systolic pressure for left ventricular pressure to estimate end-systolic stress in patients with aortic prostheses studied postoperatively.

Postoperative studies (closed chest). Six weeks postoperatively both left ventricular end-diastolic volume and left ventricular end-systolic volume had decreased significantly in patients with aortic stenosis (figure 3). This was due in large part to the dramatic fall occurring in those patients with the largest preoperative volumes (>300 ml) since those with small preoperative left ventricular volumes (<100 ml) increased toward normal postoperatively as the left ventricular hypertrophy regressed. In contrast there was a small but not statistically significant reduction in diastolic and systolic volumes in patients with aortic regurgitation (figure 3).

Left ventricular mass, which was similar preoperatively, decreased in all but one patient with aortic stenosis by 6 weeks postoperatively but did not change significantly in patients with aortic regurgitation (figure 4). The changes in left ventricular mass and volume in patients with aortic stenosis over the same period were accompanied by minor alterations in

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**TABLE 2**

Preoperative left ventricular function assessed by two-dimensional echocardiography

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
<th>LVM (g)</th>
<th>Shape LV (short/long axis ratio)</th>
<th>LVM/EDV</th>
<th>EF (%)</th>
<th>ESS_m (dyne/cm² × 10⁹)</th>
<th>ESS_c (dyne/cm² × 10⁹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic stenosis</td>
<td>16</td>
<td>174 ± 64</td>
<td>96 ± 66</td>
<td>279 ± 38</td>
<td>0.59 ± 0.09</td>
<td>1.81 ± 0.63</td>
<td>46 ± 17</td>
<td>78 ± 43</td>
<td>207 ± 76</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>7</td>
<td>294 ± 140</td>
<td>179 ± 105</td>
<td>328 ± 146</td>
<td>0.69 ± 0.09</td>
<td>1.14 ± 0.18</td>
<td>40 ± 12</td>
<td>100 ± 30</td>
<td>217 ± 50</td>
</tr>
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</table>

EDV = end-diastolic volume; ESV = end-systolic volume; LVM = left ventricular mass; EF = ejection fraction; ESS_m = end-systolic meridional stress; ESS_c = end-systolic circumferential stress.

*p < .01; **p < .02; ***p < .05.
short/long axis ratio (0.59 ± 0.09 vs 0.57 ± 0.10) and mass/volume ratio (1.81 ± 0.63 vs 1.70 ± 0.45), although neither change was statistically significant. There were no significant changes in left ventricular short/long axis ratio in patients with aortic regurgitation (0.69 ± 0.09 before surgery vs 0.66 ± 0.11 at 6 weeks after surgery) or in left ventricular mass/volume ratio (1.14 ± 0.18 vs 1.29 ± 0.29 over the same period).

By 6 weeks, postoperative end-systolic meridional and circumferential wall stresses increased slightly but significantly from the intraoperative postbypass values in patients with aortic stenosis but did not change in those with aortic regurgitation (figure 5). Resting ejection fraction improved in patients with aortic stenosis, but there was no change or even a slight fall in patients with aortic regurgitation (figure 6).

Postoperatively, the slopes of the relations between ejection fraction and end-systolic meridional wall stress and between ejection fraction and end-systolic circumferential wall stress decreased slightly from preoperative levels in the population with aortic regurgitation but did not change in the patients with aortic stenosis. However, in the aortic stenosis group, as postoperative end-systolic stress fell, ejection fraction increased (figure 7). Furthermore, the slopes of the relationships between preoperative end-systolic volume and end-systolic meridional and circumferential stresses did not change postoperatively (at 6 weeks) in patients with aortic stenosis or in patients with aortic regurgitation (figures 8 and 9). The intraoperative fall in end-systolic meridional and end-systolic circumferential wall stress in patients with aortic stenosis correlated with the changes in end-systolic volume at 6 weeks postoperatively but did not correlate with the changes in left ventricular mass.

To investigate whether the presence of left ventricular remodeling in aortic stenosis and the absence of remodeling in aortic regurgitation at 6 weeks were simply due to the fact that the time course of postoperative changes in aortic regurgitation was slower, we reassessed all the patients with aortic regurgitation who were available for follow-up at 6 months. We were able to study only four of the eight patients with aortic regurgitation at 6 months postoperatively. Although left ventricular end-diastolic and end-systolic volumes had decreased from preoperative values, these changes were not significant (255 ± 42 vs 177 ± 53 ml and 137 ± 47 vs 106 ± 43 ml, respectively). Furthermore, there were no significant changes in ejection fraction (47 ± 11% vs 42 ± 10%), left ventricular mass (285 ± 27 vs 291 ± 69 g) or meridional...
and circumferential end-systolic stress (89 ± 32 vs 93 ± 23 kdyne/cm² and 195 ± 48 vs 214 ± 43 kdyne/cm², respectively).

Discussion

The rationale for using open-chest, two-dimensional echocardiographic techniques, similar to those described previously, was twofold. First, we could calculate intraoperative changes in afterload (end-systolic wall stress) using high fidelity micromanometers to accurately measure left ventricular pressure, while keeping heart rate constant before and after bypass by right atrial pacing. Measurements of the intraoperative change in afterload were important because preoperative afterload may be normal in patients with compensated severe pressure or volume overload, since normalization of end-systolic stress appears to be the feedback loop that regulates left ventricular mass, geometry, and function. Second, by applying the transducer directly to the heart, we could obtain very high quality left ventricular images quickly, safely, and without prolonging cardiopulmonary bypass time.

Comparison of preoperative measurements of left ventricular function in our patients with aortic stenosis and aortic regurgitation demonstrated some remarkable similarities. For example, end-systolic meridional and circumferential wall stresses, left ventricular mass, ejection fraction, and cardiac indexes all varied over the same ranges with no significant differences in their respective mean values. Preoperative ejection fraction was depressed in the majority of patients with aortic stenosis and in all but one patient with aortic regurgitation. The major preoperative differences between patients with aortic stenosis and aortic regurgitation were in left ventricular chamber volumes, architecture, and preload.

Intraoperatively end-systolic meridional and circumferential wall stresses fell significantly in patients with aortic stenosis after valve replacement, whereas there was no change in patients with aortic regurgita-
Left ventricular mass fell significantly by 6 weeks after surgery in patients with aortic stenosis but remained unchanged in those with aortic regurgitation.

Left ventricular end-diastolic pressure, an estimate of preload, also decreased from before and after bypass but remained significantly higher in the patients with aortic stenosis.

At 6 weeks after aortic valve replacement, mean end-diastolic and end-systolic volumes had fallen significantly in patients with aortic stenosis. The changes in end-diastolic volume occurred largely as a result of the dramatic decrease in those patients whose preoperative volumes were greater than 300 ml. Furthermore, these postoperative changes in end-diastolic and end-systolic volume in patients with aortic stenosis correlated with the intraoperative reduction in end-systolic meridional and circumferential wall stresses. Over the same follow-up period, left ventricular mass fell by approximately 30% but there was no demonstrable correlation between the reduction in left ventricular mass and the intraoperative change in end-systolic stress. However, this may relate to the time course of regression of left ventricular hypertrophy, which is initially rapid and subsequently slower.10, 25, 51 Six weeks after valve replacement, left ventricular end-diastolic and end-systolic volumes, end-systolic wall stresses, and left ventricular mass in patients with aortic regurgitation had not changed significantly from preoperative values, nor had any of these variables changed at 6 months in the four patients restudied.

The early postoperative remodeling in patients with aortic stenosis was not associated with any alteration in cavity shape. The regression of left ventricular hypertrophy and concomitant changes in chamber volume occurred in such a way that left ventricular architecture and the mass/volume ratio did not alter significantly. Since the majority of patients with aortic stenosis had near-normal preoperative end-systolic stresses, the early intraoperative abolition of the left ventricular to aortic pressure gradient by valve replacement resulted in end-systolic stress falling to abnormally low levels after bypass, since left ventricular mass did not decrease as rapidly. Thus from immediately after bypass to 6 weeks after surgery, end-systolic meridional and circumferential stresses increased slightly but signifi-
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AORTIC STENOSIS

AORTIC REGURGITATION

FIGURE 6. Changes in ejection fraction from before to 6 weeks after surgery in patients with aortic stenosis and aortic regurgitation.

depressed preoperative ejection fraction in patients with aortic stenosis caused by excess afterload did not preclude postoperative improvement in pump function. By comparison, there were no changes in end-systolic stress or in ejection fraction in patients with aortic regurgitation.

We did not assess left ventricular contractility directly, before or after bypass, for fear of increasing operative risk because it required multiple load manipulations intraoperatively. We therefore compared the slopes of the preoperative end-systolic stress-volume and stress-shortening relationships with those obtained 6 weeks postoperatively. In patients with aortic stenosis the slopes of the end-systolic stress-shortening relationships were unchanged by valve replacement, but in individual patients, as wall stress decreased postoperatively ejection fraction increased. Likewise, the slopes of the preoperative and postoperative end-systolic stress-volume relations remained unchanged. The similarity in the slopes of these relationships before and after surgery in patients with aortic stenosis demonstrated that no overt myocardial damage resulted from cardiopulmonary bypass or valve replacement per se. The slopes of these same stress-shortening and stress-volume relationships decreased slightly after

FIGURE 7. Relationships between ejection fraction and end-systolic meridional wall stress and between ejection fraction and end-systolic circumferential wall stress in patients with aortic stenosis (top panels) and in those with aortic regurgitation (bottom panels) at 6 weeks postoperatively.
surgery in patients with aortic regurgitation, but these changes were not statistically significant.

Thus there was no detectable postoperative left ventricular remodeling and no change in ejection phase indexes of pump function from preoperative values in our patients with aortic regurgitation during the 6 week period of postoperative follow-up nor in the small number of patients restudied in 6 months. The striking difference between the postoperative courses of patients with aortic stenosis and those with aortic regurgitation has clinical relevance, since preoperative left ventricular mass, afterload, ejection fraction and stress-shortening relations, which are important conventional measures of left ventricular function, were indistinguishable preoperatively. The postoperative findings in our patients are not typical of the universal experience in patients with aortic regurgitation but are reminiscent of a recently identified subpopulation of patients with impaired preoperative left ventricular function who do not improve postoperatively.\[17, 26, 52\]

However, in spite of no objective change in postoperative left ventricular architecture or function, removal of the regurgitant volume by valve replacement was associated with amelioration of cardiac symptoms in the early postoperative period.

Possible causes of the discrepancy in postoperative left ventricular remodeling between patients with aortic stenosis and those with aortic regurgitation can be divided into preoperative, intraoperative, and postoperative factors. Preoperative left ventricular mass, afterload, ejection fraction, and end-systolic stress-shortening relations were similar in the groups with aortic stenosis and aortic regurgitation. However, the numerical similarity of ejection fraction in the two populations may not represent equivalent ventricular function because of the diametrically opposite tendency of ejection fraction to overestimate contractile function in aortic regurgitation and to underestimate it in aortic stenosis.\[23, 32\] Therefore the similarity in left ventricular function in patients with aortic stenosis and aortic regurgitation suggested by ejection fraction may have been more apparent than real and demonstrates that comparison of preoperative ejection fraction in volume and pressure overload is ill advised.

It may be that our patients with aortic regurgitation and decreased preoperative ejection fraction had al-
ready developed irreversible left ventricular dysfunction, and this could have accounted for the absence of postoperative improvement at early and late follow-up. Preoperative left architecture was considerably different in patients with aortic regurgitation in that the left ventricular cavity had a significantly larger volume, a more spherical shape, and a decreased mass-to-volume ratio, or a “mismatch” between left ventricular mass and volume. Nevertheless, these alterations in chamber architecture had resulted in similar left ventricular afterloads. A further difference in preoperative left ventricular function between the two groups was observed in left ventricular end-diastolic pressure, an estimate of preload, which was significantly lower in patients with aortic regurgitation and remained so postoperatively. However, it is unlikely that this difference was an important etiologic factor in the divergent postoperative courses.

The major intraoperative difference between the groups was the significant decrease in afterload in patients with aortic stenosis. This intraoperative change in afterload correlated with the changes in volume and function, indicating that it was most likely the stimulus to the postoperative left ventricular remodeling. This contention is supported by the observation that patients with aortic regurgitation in whom there was no change in afterload intraoperatively underwent no postoperative left ventricular remodeling at 6 weeks or 6 months. Thus the preoperative stimulus to left ventricular hypertrophy and dilatation in aortic regurgitation was unaffected by valve replacement in our patients. Other intraoperative factors that theoretically could have contributed to the discrepant postoperative courses in patients with aortic stenosis and aortic regurgitation include differences in the anesthetic agents used, myocardial preservation techniques, the duration of cardiopulmonary bypass, and the prosthetic valve types and sizes. However, the anesthesia protocol and the myocardial preservation techniques were standardized, and the duration of cardiopulmonary bypass, the valve types, and sizes were similar.

A postoperative factor that may partially account for our inability to demonstrate left ventricular remodeling in aortic regurgitation is the relatively short follow-up period in our study in most of the patients. If the time course of regression of left ventricular hypertrophy and change in left ventricular architecture and function after correction of volume overload is slower than that
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occurring after correction of pressure overload, it is possible that over a longer follow-up, we may have identified findings consonant with those previously described in patients with aortic regurgitation at 6 months and 1 year postoperatively. However, in the four patients with aortic regurgitation we restudied at 6 months there were no significant changes in left ventricular volumes, mass, ejection fraction, or afterload from preoperative values. Furthermore, in the few early postoperative left ventricular studies that have been performed in patients with aortic regurgitation, changes in left ventricular volumes and ejection fractions were detectable within days. More likely, our patients with aortic regurgitation represent the same subgroup characterized by Zile et al., in whom preoperative left ventricular function is impaired and does not improve in spite of technically satisfactory valve replacement. These patients also have a high postoperative mortality from progressive left ventricular failure within 1 to 2 years.

We believe that in aortic stenosis, postoperative changes in chamber volume and ejection phase indexes of pump function correlate with the intraoperative reduction in afterload, which may thus be the stimulus to early postoperative left ventricular remodeling. Furthermore, decreased preoperative ejection fraction caused by excess afterload in aortic stenosis does not preclude postoperative improvement in left ventricular function. The postoperative outcome in our patients with aortic regurgitation in terms of left ventricular function and architecture was markedly different. However, our study cannot be regarded as representing patients with aortic regurgitation at large, since our patient group was small and preoperative pump function was seriously depressed. The failure of postoperative left ventricular remodeling and improvement in function in our patients with aortic regurgitation was probably caused by a combination of factors of which we believe two were important. First, the absence of any intraoperative change in afterload — so that the preoperative stimulus to left ventricular hypertrophy and dilatation was unchanged by valve replacement — and thus the left ventricle remained internally loaded postoperatively in spite of abolition of the regurgitant volume. Second, preoperative left ventricular function may have been already irreversibly depressed and therefore did not change postoperatively, related in part to serious overestimation of left ventricular contractile function by ejection fraction, which should not be relied upon to determine the timing of surgery in patients with aortic valve disease.

The failure of our patients with aortic regurgitation and severe preoperative left ventricular dysfunction to improve postoperatively either at early or late follow-up argues for earlier surgery to obviate the onset of irreversible myocardial damage because operative and late mortality in uncomplicated patients with aortic regurgitation is low.

We thank Miss Eileen Slattery of “Graphica” Philadelphia for the medical illustrations.

Appendix

Equation 1. Left ventricular volumes were calculated by the short-axis area × length method:

\[ V = \frac{5}{6} A_L L \]

Equation 2. Left ventricular muscle mass (LVM) was calculated as:

\[ LVM = 1.055 \times \frac{5}{6}(A_L - A_c) \]

The constant 1.055 is the density of myocardial muscle.

Equation 3. Left ventricular end-systolic meridional wall stress (\(\sigma_m\)) was calculated as:

\[ \sigma_m = \frac{1.33 \times P \times A_c}{A_L - A_c} \]

The constant 1.33 in equations 3 and 4 is the conversion factor from mm Hg to dyne/cm².

Equation 4. Left ventricular end-systolic circumferential wall stress (\(\sigma_c\)) was calculated as:

\[ \sigma_c = \frac{1.33 \times P \times A_c}{\sqrt{A_L - A_c}} \times 1 - \frac{A_c^{3/2}}{\pi (0.5 L)^2 (\sqrt{A_L} + \sqrt{A_c})} \]

References
12. Ross Jr: Afterload mismatch and preload reserve: a conceptual
Early postoperative changes in left ventricular chamber size, architecture, and function in aortic stenosis and aortic regurgitation and their relation to intraoperative changes in afterload: a prospective two-dimensional echocardiographic study.
M Sutton, T Plappert, A Spiegel, J Raichlen, P Douglas, N Reichek and L Edmunds

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