Coronary Atherosclerosis Is Associated With Left Ventricular Dysfunction and Dilatation in Aortic Stenosis

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Patients with aortic stenosis develop widely variable patterns of left ventricular hypertrophy and dysfunction. We postulated that coronary atherosclerosis (CAD) may be associated with impaired left ventricular function and chamber dilatation in patients with aortic stenosis. Left ventricular mass and volumes were quantified from two-dimensional echocardiography and correlated with coronary angiography in 78 patients with severe aortic stenosis and no previous myocardial infarction or regional wall motion abnormalities. Eighteen patients (group 1) had smooth coronary arteries, 25 patients had irregular coronary arteries with 50% or less stenosis (group 2), and 35 patients had obstructive CAD (group 3). Even though the calculated valve area was similar in all three study groups, group 1 patients had higher values for ejection fraction (65±9%, 51±17%, and 48±13%; p=0.0002), systolic mass-to-volume ratio (9.2±3.9, 5.6±2.8, and 5.2±2.2; p=0.0001), and cardiac index (2.9±0.7, 2.5±0.7, and 2.3±0.6 l/min·min⁻¹; p=0.015) than patients in groups 2 and 3, respectively (mean±SD). Mean circumferential wall stress was inversely related to severity of CAD. Multivariate analysis showed that CAD is an independent predictor of ejection fraction and mass-to-volume ratio in this group of patients. Thus, in an elderly population with severe aortic stenosis, patients with both obstructive and nonobstructive CAD have an increased incidence of left ventricular enlargement and systolic dysfunction. (Circulation 1990;82:2068-2074)

Patients with aortic stenosis display widely varying patterns of left ventricular hypertrophy and dysfunction.¹⁻⁵ Normal left ventricular systolic function and chamber size are preserved in some patients, whereas left ventricular enlargement and systolic dysfunction occur in others despite equivalent degrees of aortic stenosis.

Coronary artery disease (CAD) is present in a significant proportion of patients with aortic stenosis.⁶ Previous studies of left ventricular function in aortic stenosis excluded patients with obstructive CAD (≥50% stenoses) yet reported wide variations in systolic function in patients with nonobstructive CAD.¹⁻⁴ In patients with aortic stenosis and insignificant CAD, depressed systolic function in aortic stenosis has been ascribed to excessive afterload with inadequate hypertrophy²⁻⁷ or to impaired myocardial contractility.⁴ However, the proximate causes of inadequate hypertrophy and depressed contractility in aortic stenosis have not been defined.

Because coronary atherosclerosis, even in the nonobstructive form, has been shown to alter vascular reactivity and impair coronary flow,⁶⁻¹¹ we postulated that the presence of coronary atherosclerosis, even in the absence of myocardial infarction, may affect the pattern of left ventricular hypertrophy and impair left ventricular performance in aortic stenosis. Our study was designed to examine the relation between CAD and left ventricular function in aortic stenosis.

Methods

Study Population

The records of all patients with severe aortic stenosis (aortic valve area, 0.3–0.8 cm²) who underwent both diagnostic cardiac catheterization and echocardiography at Brigham and Women’s Hospital between July 1, 1986, and September 1, 1988, were analyzed. Patients with a clinical history of myocardial infarction, regional wall motion abnormality,
primary myocardial disease that preceded the diagnosis of severe aortic stenosis, more-than-mild aortic insufficiency by Doppler echocardiography, or other hemodynamically significant valvular heart disease or with technically inadequate echocardiograms were excluded from the study.

Records from 134 consecutive patients who underwent both diagnostic cardiac catheterization and echocardiography for symptoms or signs of severe aortic stenosis were reviewed. Fifty-six patients were excluded for one or more of the following reasons—echocardiograms that were technically inadequate for left ventricular volume and mass measurement (14 patients); more-than-mild (1+) aortic regurgitation or significant mitral valvular disease (30 patients); either a history of myocardial infarction or regional wall motion abnormality on echocardiography (29 patients); and a history of dilated cardiomyopathy (three patients—adriamycin induced in one, and alcohol related in two) that preceded the diagnosis of aortic stenosis. Thus, 78 patients fulfilled the entry criteria for this study.

Catheterization Techniques

Right and left heart catheterization was performed in all patients using the percutaneous femoral approach and standard Judkins technique. The aortic valve was crossed in a retrograde manner in 63 patients, whereas valve crossing was not attempted or was unsuccessful in 15 patients. In patients whose aortic valves were not crossed, a transaortic gradient of more than 60 mm Hg by Doppler echocardiography was required for inclusion into the study. Hemodynamic data were recorded using standard fluid-filled manometers. Right atrial, right ventricular, and pulmonary arterial and pulmonary capillary wedge pressures were recorded in all patients along with systemic arterial pressure. Simultaneous recordings of left ventricular and systemic arterial pressures were available in 63 patients whose aortic valves were crossed. Cardiac output and index were measured in all patients using the Fick method with measured oxygen consumption. Aortic valve area was calculated using the Gorlin formula.12

All 78 patients underwent coronary angiography. Coronary angiograms were reviewed by two cardiologists independently of each other. Based on the results of the angiograms, the patients were divided into three groups. Group 1 (CAD score 1) had smooth epicardial coronary arteries throughout, group 2 (CAD score 2) had irregular epicardial vessels with no more than 50% stenosis in any of the three major arteries, and group III (CAD score 3) had obstructive CAD with more than 50% stenosis in at least one artery. In eight cases, a discrepancy existed between the opinions of the two cardiologists. These angiograms were reviewed by a third cardiologist whose opinion was binding. All three cardiologists were blinded to the results of echocardiographic measurements.

Of the 78 study patients, 18 had smooth coronary arteries (group 1), 25 had irregular coronary arteries (group 2), and 35 had obstructive CAD (group 3). Of the 56 patients who were excluded from the study, 12 had smooth coronary arteries, 18 had irregular coronary arteries, and 26 had obstructive CAD. Of the 15 patients whose valve gradients were not measured at cardiac catheterization, six were in group 1, three were in group 2, and six were in group 3. In 18 patients who underwent balloon valvuloplasty, echocardiograms were performed in the cardiac catheterization laboratory simultaneously with hemodynamic recordings immediately before aortic valvuloplasty, as reported previously for 15 patients.6 In all other patients, the two studies were separated by 3.5±5.3 days (median, 1.5 days; range, 0–30 days), and no intervention was performed between the studies.

Echocardiographic Measurements

Two-dimensional Doppler echocardiograms were obtained in all patients in the supine position from the apex and left and right parasternal transducer views using a Hewlett-Packard 77020 AC/AR phased-array ultrasonoscope with a 2.5-mHz transducer. Left ventricular end-diastolic length (LVEDL) and left ventricular end-systolic length (LVESL) were measured in the apical four-chamber view from the apical endocardium to the middle of the mitral anulus. End diastole was defined as the frame coincident with the peak of the R wave on a simultaneous electrocardiogram, and end systole was timed to the smallest left ventricular chamber dimension. End-diastolic and end-systolic epicardial and endocardial areas were measured from the parasternal short-axis views of the left ventricle at the high papillary muscle level. The epicardial left ventricular boundary was digitized to include the right side of the interventricular septum to measure end-diastolic and end-systolic total areas (EDA, and ESA, respectively). The endocardial left ventricular border was digitized to measure end-diastolic and end-systolic cavity areas (EDA, and ESC, respectively). Volumes were calculated designating papillary muscles as cavity, and left ventricular mass was calculated to include papillary muscles as myocardial area. All measurements were made using a Freeland off-line analysis software package, CineView Version 2.0 by Good Technologies, Inc. Left ventricular myocardial area was calculated as A−A. Left ventricular volume and mass were calculated using the % area multiplied by length method.13–15 From the above measurements, the following parameters were calculated:

\[ \text{LVEDV (ml) =} 5/6 \text{ LVEDA} \times \text{LVEDL} \]

\[ \text{LVESV (ml) =} 5/6 \text{ LVESA} \times \text{LVESL} \]

\[ \text{LVEF} = \text{LVEDV} - \text{LVESV/LVEDV} \]

\[ \text{LVM at end diastole (ml) =} 1.055 \times \left( \% \text{LVEDA} \times (\text{LVEDL}+1) - \% \text{LVEDA} \times \text{LVEDL} \right) \]
LVM/V_{sys} (g/ml) = LVM/LVESV

where LVEDV is left ventricular end-diastolic volume, LVESV is left ventricular end-systolic volume, LVEF is left ventricular ejection fraction, LV is left ventricular mass, and V_{sys} is systolic volume.

In 18 patients undergoing aortic valvuloplasty in whom simultaneous hemodynamic and echocardiographic measurements were available, the following additional measurements were made. Left ventricular afterload was quantified as end-systolic circumferential wall stress with simultaneously measured peak systolic left ventricular pressure (LVSP) under resting conditions to estimate the end-systolic pressure as previously validated.\(^{14,16-18}\) Left ventricular circumferential wall stress \((\sigma_{cs}, 10^3 \text{ dynes/cm}^2)\) equals:

\[
\frac{1.33LVSP \cdot \sqrt{LVES_c}}{\sqrt{LVESA_t - \sqrt{LVES_c}}}
\left\{1 - \frac{(LVESA_c)^{3/2}}{\pi (0.5LVESL)^2 \left[\sqrt{LVESA_t} + \sqrt{LVES_c}\right]}\right\}
\]

All echocardiographic measurements were made by a cardiologist blinded to the results of coronary angiography.

**Statistics**

\(\chi^2\) analysis was used to identify differences in categorical variables (sex, angina, syncope, congestive heart failure, or hypertension) among groups 1, 2, and 3. One-way analysis of variance (ANOVA) was performed to identify differences in continuous variables (age and duration of symptoms) among the three patient groups and to identify the effect of CAD on echocardiographic and hemodynamic variables. If a significant result was obtained by ANOVA, Scheffe’s test for multiple comparisons was used to identify significant differences for each variable among the three groups of patients.\(^{19}\) Multivariate analysis was performed with multiple linear regression (Statview 512\(^+\), Calabasas, Calif.) to define the clinical and hemodynamic correlates of the mass-to-volume ratio and ejection fraction. Of the variables evaluated (CAD score 1, 2, or 3), aortic valve area, mean aortic gradient at cardiac catheterization, left ventricular systolic pressure, duration of all cardiac symptoms, history of hypertension, left ventricular end-diastolic pressure, age, aortic valve area index, and body surface area), those found to have borderline significance on linear correlation \((p<0.25)\) were included in the multivariate analysis.\(^{19}\) Values are given as mean ± SD.

**Results**

**Study Population**

Thirty-two men and 46 women were entered into the study. Mean age of the study population was 74 ± 9 years. Symptoms included angina (41 patients), syncope (11 patients), and congestive heart failure (50 patients). Patients were grouped according to coronary anatomy. Eighteen patients had smooth coronary arteries (group 1), 25 patients had irregular coronary arteries with stenosis equal to or less than 50% (group 2), and 35 patients had obstructive CAD (group 3). Despite the differences in coronary anatomy, the groups were well matched: no significant differences emerged among the three groups with respect to sex, age, or proportion of patients presenting with angina, syncope, or congestive heart failure. Total duration of all cardiac symptoms (angina, congestive heart failure, or exertional syncope) was similar in all three study groups (Table 1).

**Echocardiographic Measurements**

Echocardiographic studies showed no significant difference in total left ventricular mass among the groups. However, the pattern of left ventricular hypertrophy, expressed as mass-to-volume ratio in systole, was related to the presence of CAD. The patients with entirely smooth coronary arteries (group 1) had greater mass-to-volume ratios (i.e., less chamber dilation) than those with minimal CAD (group 2) or obstructive CAD (group 3): 9.2 ± 3.9, 5.6 ± 2.8, and 5.2 ± 2.2, respectively \((p=0.0001)\) (Figure 1). Although much overlap is present in the data, low values for mass-to-volume ratio were seen predominantly in patients with obstructive or nonobstructive CAD. Similarly, left ventricular ejection fraction was greater in...
patients with no CAD than in patients with mild or obstructive CAD: 65±9%, 51±17%, and 48±13%, respectively (p=0.0002) (Figure 2). Although most patients had normal ejection fractions, a greater proportion of patients with diminished ejection fractions was found in groups 2 and 3. Cardiac index also tended to diminish in patients in groups 2 and 3 compared with those in group 1: 2.9±0.7, 2.5±0.7, and 2.3±0.6, respectively (p=0.015). Mean transaortic pressure gradient was higher in patients in group 1 than in patients in groups 2 and 3: 70±24, 54±14, and 51±16, respectively (p=0.009). Left ventricular circumferential wall stress tended to increase in patients with CAD, with values of 121±41, 162±45, and 255±129×10^3 dynes/cm^2 in patients in groups 1, 2, and 3, respectively (p=0.046) (Figure 3). Patients with smooth coronary arteries (group 1) tended to have lower values for left ventricular systolic volume than did patients with irregular coronary arteries (group 2) or those with obstructive CAD (group 3): 36±21, 68±42, and 69±55 ml/m2, respectively. These data suggest that the presence of CAD in aortic stenosis is associated with chamber dilatation and inadequate wall thickness, leading to elevated wall stress. We also found a correlation between peak circumferential wall stress and ejection fraction. An inverse linear relation exists between these two parameters in patients with aortic stenosis (ejection fraction = -0.001·systolic pressure + 0.82; r^2=0.50; p=0.001), suggesting that depressed left ventricular performance is associated with elevated afterload.

In contrast to its relation with systolic parameters, CAD score was not significantly associated with diastolic measurements. Left ventricular end-diastolic volume index (59±27, 70±21, and 72±38 ml/m^2) and left ventricular end-diastolic pressure (21±8, 23±20, and 24±10 mm Hg for groups 1, 2, and 3, respectively) showed only a trend toward an increase with CAD score (Table 2).

**Multivariate Analysis**

To identify the determinants of ejection fraction and systolic mass-to-volume ratio in aortic stenosis, we used multivariate analysis to examine the effects of CAD score, aortic valve area, mean gradient, left ventricular systolic pressure, symptom duration, history of hypertension, left ventricular end-diastolic pressure, age, aortic valve index, and body surface area (Table 3). Of these variables, CAD score, left ventricular systolic pressure, and a history of hypertension each correlated independently with systolic mass-to-volume ratio and with ejection fraction. The multivariate model may account for approximately 40% of the variance in the measurement of mass-to-volume ratio (r^2=0.43, p=0.0001) and ejection fraction (r^2=0.38, p=0.0002). When the variables with nonsignificant probability values were removed from the multivariate model, the significant factors (CAD score, left ventricular systolic pressure, and history of hypertension) still accounted for approximately 40% of the variance in the measurement of mass-to-volume ratio (r^2=0.39, p=0.0001) and ejection fraction (r^2=0.40, p=0.0001). Both CAD score and a history of hypertension were inversely related to the
parameters (negative $\beta$ coefficient). Patient age, gender, duration of symptoms, and aortic valve area were not associated with ejection fraction or systolic mass-to-volume ratio.

**Discussion**

The results of the present study suggest that coronary atherosclerosis in the absence of myocardial infarction may be associated with left ventricular dilatation and impaired systolic function in elderly patients with severe aortic stenosis. Patients with smooth coronary arteries tend to have concentric left ventricular hypertrophy and preservation of systolic function.

Significant overlap exists among the three groups with respect to systolic mass-to-volume ratio, ejection fraction, and wall stress, suggesting that factors other than atherosclerosis contribute to left ventricular dysfunction and changes in left ventricular geometry. However, multivariate analysis indicated that CAD is an independent predictor of left ventricular function and geometry in aortic stenosis in the elderly population. The analysis also suggested that both hypertension and CAD are associated with impaired left ventricular function in aortic stenosis. The ability of the left ventricle to generate systolic pressure at rest correlated with ejection fraction and systolic mass-to-volume ratio. This finding is consistent with the previously reported association between left ventricular systolic pressure and left ventricular mass-to-volume ratio in patients who undergo balloon aortic valvuloplasty.\(^5\)

Left ventricular function in aortic stenosis influences survival after surgery and therefore deserves considerable attention.\(^20\) It is well recognized that severe coronary disease may impair left ventricular function in the setting of aortic stenosis by producing myocardial infarction and regional wall motion abnormalities,\(^21\) but the relation between coronary disease and left ventricular function in the absence of myocardial infarction has not been fully investigated. Most studies have defined significant CAD as the presence of stenoses of more than 50%\(^3,22,23\) or of more than

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**Table 2. Left Ventricular Function and Hemodynamics**

<table>
<thead>
<tr>
<th></th>
<th>No CAD</th>
<th>Mild CAD</th>
<th>Obstructive CAD</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM (g)</td>
<td>282±100</td>
<td>308±82</td>
<td>280±83</td>
<td>NS</td>
</tr>
<tr>
<td>$M/V_{sv}$</td>
<td>9.2±3.9</td>
<td>5.6±2.8</td>
<td>5.2±2.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>65±9</td>
<td>51±17</td>
<td>48±13</td>
<td>0.0002</td>
</tr>
<tr>
<td>$\sigma_{ws}$ (10^9 dynes/cm^2)</td>
<td>121±41</td>
<td>162±45</td>
<td>255±129</td>
<td>0.046</td>
</tr>
<tr>
<td>LVV$_{sys}$ index (ml/m^2)</td>
<td>36±21</td>
<td>68±42</td>
<td>69±55</td>
<td>0.053</td>
</tr>
<tr>
<td>LVV$_{dia}$ index (ml/m^2)</td>
<td>59±27</td>
<td>70±21</td>
<td>72±38</td>
<td>NS</td>
</tr>
<tr>
<td>CI (l/min · m$^{-2}$)</td>
<td>2.9±0.7</td>
<td>2.5±0.7</td>
<td>2.3±0.6</td>
<td>0.015</td>
</tr>
<tr>
<td>Mean AVG (mm Hg)</td>
<td>70±24</td>
<td>54±14</td>
<td>52±16</td>
<td>0.009</td>
</tr>
<tr>
<td>PAWP (mm Hg)</td>
<td>19±3</td>
<td>19±3</td>
<td>20±3</td>
<td>NS</td>
</tr>
<tr>
<td>AVA (cm^2)</td>
<td>0.61±0.16</td>
<td>0.56±0.14</td>
<td>0.57±0.16</td>
<td>NS</td>
</tr>
<tr>
<td>LVSP (mm Hg)</td>
<td>219±24</td>
<td>199±25</td>
<td>202±39</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>21±8</td>
<td>23±20</td>
<td>24±10</td>
<td>NS</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; LVM, left ventricular mass; $M/V_{sv}$, left ventricular mass-to-volume ratio in systole; EF, left ventricular ejection fraction; $\sigma_{ws}$, mean circumferential left ventricular wall stress; LVV index, left ventricular volume index in systole (sys) or (dia); CI, cardiac index; AVG, aortic valve gradient; PAWP, pulmonary artery wedge pressure; AVA, aortic valve area; LVSP and LVEDP, left ventricular systolic and end-diastolic pressures, respectively.

*One-way analysis of variance.

**Table 3. Univariate and Multivariate Analysis of Factors Associated With Mass-to-Volume Ratio and Ejection Fraction**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate $\beta$</th>
<th>Multivariate $\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass-to-volume ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD score</td>
<td>0.0001</td>
<td>-1.36</td>
</tr>
<tr>
<td>Aortic valve area</td>
<td>0.85</td>
<td>...</td>
</tr>
<tr>
<td>Mean gradient</td>
<td>0.003</td>
<td>0.017</td>
</tr>
<tr>
<td>LV systolic pressure</td>
<td>0.002</td>
<td>0.026</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>0.49</td>
<td>...</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>0.08</td>
<td>-1.79</td>
</tr>
<tr>
<td>LV end-diastolic pressure</td>
<td>0.85</td>
<td>...</td>
</tr>
<tr>
<td>Age</td>
<td>0.32</td>
<td>...</td>
</tr>
<tr>
<td>Aortic valve area index</td>
<td>0.51</td>
<td>...</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.27</td>
<td>...</td>
</tr>
<tr>
<td>(Multivariate intercept=3.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD score</td>
<td>0.0001</td>
<td>-0.085</td>
</tr>
<tr>
<td>Aortic valve area</td>
<td>0.27</td>
<td>...</td>
</tr>
<tr>
<td>Mean gradient</td>
<td>0.04</td>
<td>-0.001</td>
</tr>
<tr>
<td>LV systolic pressure</td>
<td>0.005</td>
<td>0.002</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>0.20</td>
<td>0.001</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>0.04</td>
<td>-0.107</td>
</tr>
<tr>
<td>LV end-diastolic pressure</td>
<td>0.81</td>
<td>...</td>
</tr>
<tr>
<td>Age</td>
<td>0.16</td>
<td>0.001</td>
</tr>
<tr>
<td>Aortic valve area index</td>
<td>0.43</td>
<td>...</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.67</td>
<td>...</td>
</tr>
<tr>
<td>(Multivariate intercept=0.47)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; LV, left ventricular.
60% and have thus grouped patients who have luminal irregularities with those who have smooth coronary arteries. In the present study, we separated patients with entirely smooth coronary arteries from those with luminal irregularities and stenoses of 50% or less. Alternatively, when we analyzed the data according to the formulation used in previous studies that defined only two groups of patients (those with luminal irregularities and stenoses of 50% or less are grouped with those who have smooth coronary arteries) and compared the results with data for those with obstructive CAD,1-4 we found no significant relation between coronary anatomy and left ventricular function or geometry.

Useful insights into left ventricular function in the setting of aortic stenosis have been gained by analyzing left ventricular ejection fraction as a function of wall stress. Gunther and Grossman7 observed that inappropriately high wall stress impairs left ventricular ejection performance in aortic stenosis in the absence of significant CAD. Huber et al6 used the peak velocity of shortening as an index of contractility and suggested that some patients with aortic stenosis have impaired contractility. However, it is not clear why some patients with severe aortic stenosis develop inappropriately high wall stress (due to chamber dilatation and inadequate wall thickness) or impaired contractility and others do not even when the severity of aortic stenosis is equivalent. Our data suggest that the presence of luminal irregularities without obstructions of more than 50% may be associated with chamber dilatation and impaired ejection fraction. In a smaller subset of patients, we observed that coronary disease is also associated with increased wall stress. Thus, coronary atherosclerosis appears to be associated with impaired ventricular performance and the development of inappropriately high afterload due to chamber dilatation and inadequate wall thickness.

The correlation between angiographic evidence of coronary disease and mass-to-volume ratio and ejection fraction suggests that atherosclerosis contributes to left ventricular dysfunction in aortic stenosis, perhaps by impairing coronary blood flow at rest and during stress. Although we did not measure coronary flow in the present study, we may review the relations among atherosclerosis, blood flow, and hypertrophy that have been reported in heart and other organ systems. In the two-kidney Goldblatt model of hypertension, the organ with intact arterial blood flow hypertrophies, whereas the kidney with blood flow impaired by stenosis does not.24 In heart, coronary flow reserve has been found to be diminished in aortic stenosis despite the presence of angiographically normal coronary arteries (i.e., with less than 50% stenoses).25 Impaired coronary flow reserve may lead to chronic left ventricular subendocardial ischemia, fibrosis, or impairment of left ventricular function. It is also true that conventional angiography can underestimate the extent and severity of coronary atherosclerosis.26,27 It is possible that the group 2 patients with luminal irregularities had disturbed regulation of coronary flow. One recent report suggested that patients with normal epicardial coronary arteries and impaired vasodilator reserve show evidence of left ventricular dysfunction, but it is not clear from the report whether patients with luminal irregularities and stenoses of less than 50% were included.28

Recent reports demonstrating that luminal irregularities are markers for endothelial dysfunction and impaired coronary vasomotion suggest another explanation for our findings. Ludmer et al6 demonstrated that irregular coronary segments constrict in response to acetylcholine, whereas smooth coronary arteries dilate in response to this stimulus. Other stimuli, such as exercise10 and the cold pressor test,9 also lead to vasoconstriction of irregular or obstructed segments and dilatation of smooth coronary segments. Cox et al11 recently demonstrated that flow-mediated dilatation is impaired in atherosclerosis, further confirming the evidence for impaired coronary vasomotion. Thus, the presence of luminal irregularities on the coronary arteriogram may be a marker for abnormal vasomotion under periods of stress. This may lead to disturbed regulation of coronary blood supply, particularly in settings of increased myocardial oxygen demand, and play a role in causing subendocardial ischemia. Stenoses that produce a 50% or less reduction in luminal diameter may become significant when compensatory arteriolar dilatation is limited; hypertrophy and cavity dilatation may then lead to abnormal wall stress and increased myocardial oxygen demand. Finally, the endothelium may be a source of growth factors for myocardial hypertrophy. If hypertrophy is inadequate, chamber dilatation and dysfunction may ensue.

Several limitations of this analysis require emphasis. One limitation of the present study is the lack of measurement of coronary flow and its reserve. We speculate that coronary flow reserve is impaired to a greater extent in patients with angiographic evidence of coronary disease than in those with smooth coronary arteries. Second, we could not control for the duration of aortic stenosis in the present study. However, the similarity of age, severity of aortic stenosis, and duration of symptoms (Table 1) minimizes but does not exclude the possibility that duration of aortic stenosis was different among the three groups of patients. Third, we used two-dimensional echocardiographic measurements to provide estimates for left ventricular mass, volume, and wall stress. Numerous investigations have demonstrated the ability of two-dimensional echocardiography to provide valid estimates of in vivo left ventricular mass, volume, and wall stress despite marked abnormalities in left ventricular shape.13-18 The method of calculating wall stress used in the present study has limitations, particularly regarding enlarged ventricles in which the absolute value of wall stress may not be accurate. Fourth, we presumed that patients in all three groups had similar degrees of aortic valve disease because the calculated aortic valve areas for
the three groups were nearly identical. Lower values for the valve gradient and cardiac index in the patients with CAD were attributed to the finding of impaired left ventricular function in these patients. Finally, most of the patients in the present study were elderly persons with calcific aortic stenosis. Therefore, the findings of the present study may not be applicable to younger patients with aortic stenosis.

In summary, this analysis suggests that patients with severe aortic stenosis and CAD have an increased incidence of impaired left ventricular systolic function. These findings may have an impact on clinical issues such as the timing of surgery and the expectation of improved left ventricular function after valve replacement.

References


Key Words • atherosclerosis • left ventricular dysfunction
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