Regression of Coronary Artery Dimensions After Successful Aortic Valve Replacement

Bruno Villari, MD; Otto M. Hess, MD; Christoph Meier, BS; Antonella Pucillo, BS; Antonio Gaglione, MD; Marco Turina, MD; and Hans P. Krayenbuehl, MD

Background. The effect of regression of myocardial hypertrophy on coronary artery dimensions was evaluated in patients with aortic valve disease who underwent valve replacement.

Methods and Results. Cross-sectional area (CSA) of the three major coronary arteries (left anterior descending [LAD], left circumflex [LCx], and right coronary artery) was determined by quantitative coronary arteriography in 15 patients with aortic valve disease before and 38 months (range, 14–113 months) after successful aortic valve replacement. Twelve normal subjects served as controls. Left ventricular (LV) angiographic mass was calculated according to the method of Rackley. CSA of the left coronary artery was larger in aortic valve disease than in controls (LAD, 15 versus 8 mm², p<0.001; LCx, 14 versus 6 mm², p<0.001). After valve replacement, CSA of the left coronary artery decreased (LAD, 12 mm², p<0.05 versus before surgery; LCx, 11 mm², p<0.05 versus before surgery) but remained significantly larger than in controls. CSA of the right coronary artery in patients with aortic valve disease was not different from controls. LV muscle mass was significantly increased in aortic valve disease patients before (364 g) and after (350 g) valve replacement compared with controls (135 g). The appropriateness of coronary artery size with respect to muscle mass was evaluated by normalizing CSA of the left coronary artery (LAD+LCx) per 100 g of LV muscle mass (mm²/100 g). This index amounted to 11 mm²/100 g in controls, to 8 mm²/100 g in preoperative patients (p<0.05 versus controls), and to 10 mm²/100 g in postoperative patients with aortic valve disease (p=NS versus controls).

Conclusions. In patients with aortic valve disease, CSA of the proximal LAD and LCx is increased, but this increase is not sufficient to keep CSA per 100 g of LV mass within normal limits. The postoperative decrease in muscle mass is associated with a decrease in the size of LAD and LCx, whereas the size of the right coronary artery remains unchanged. In contrast to the preoperative state, the residually hypertrophied LV myocardium after aortic valve replacement is supplied by an enlarged but adequately sized LAD and LCx. (Circulation 1992;85:972–978)

Key Words • coronary artery dimensions • left ventricular hypertrophy • aortic valve disease • aortic valve replacement

The increase in coronary artery dimensions with left ventricular (LV) hypertrophy has been shown to represent an adaptive response to maintain coronary flow velocity and shear stress constant.1–3 Shear stress at the endothelial surface is directly proportional to blood flow velocity and is inversely proportional to the radius of the lumen.4 In aortic valve disease, resting coronary blood flow per 100 g of ventricular mass is similar to that in controls.5 This observation could suggest that the relation between coronary artery dimensions and muscle mass is probably also constant if one assumes flow velocity to be the same in the normal and hypertrophied ventricle.1,2,5–9 This hypothesis was tested in the present study by evaluation of coronary artery dimensions and LV mass in patients with aortic valve disease. Furthermore, the effect of postoperative regression of LV hypertrophy on coronary cross-sectional area has been assessed.

Methods

Fifteen patients (mean age, 55±7 years; range, 42–67 years) with aortic valve disease were studied before and 38±36 months (range, 14–113 months) after successful aortic valve replacement. Twelve normal subjects (mean age, 52±8 years; range, 38–65 years) served as controls. Body surface area was not different between controls (1.85±0.22 m²) and patients with aortic valve disease before surgery (1.83±0.20 m²) and after surgery (1.84±0.19 m²).

Cardiac Catheterization

Premedication consisted of chlordiazepoxide (10 mg p.o.) 1 hour before catheterization. Vasoactive substances were withheld for 24 hours before catheterization. LV pressure was measured transeptally with an 8.5F Brockenbrough catheter, whereas aortic pressure was determined through an 8F pigtail catheter introduced retrogradely from the right femoral artery. Pulmonary artery pressure was measured with a 7F Cour-

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nand catheter. Mean coronary perfusion pressure was calculated as mean aortic pressure minus mean right atrial pressure. Mean systolic pressure gradient and aortic valve area were calculated according to standard formulas. Aortic regurgitation was assessed by thermodilution technique.

LV angiograms were recorded simultaneously in the right and left anterior oblique projections at a filming rate of 50 frames per second.10 LV volumes and ejection fraction were calculated by the “area–length” method.11 LV muscle mass was determined according to the method of Rackley et al.12

Selective left and right coronary angiography was done from the right femoral artery (Judkins technique, 8F catheters) with multiple views for optimal visualization of the coronary arteries.

Quantitative Coronary Arteriography

Quantitative evaluation of coronary angiograms was performed with a semiautomatic computer system.13,14 The system is based on a 35-mm film projector (Tagarno 35 CX), a slow-scan charge couple device camera (image digitation) developed at the Institute for Biomedical Engineering in Zurich, and a computer work station (Apollo DN 3000) for image storage and processing. Contour detection was done with a geometric–densitometric edge-detection algorithm13–18 (Figure 1). The methodology for computerized analysis of coronary angiograms has been described elsewhere.13–18

The proximal cross-sectional area of the three major coronary vessels (left anterior descending artery [LAD], left circumflex artery [LCx], and right coronary artery [RCA]) was measured in end-diastolic cine frames. The proximal cross-sectional area of the LAD and LCx was defined as the vessel segment immediately beyond the bifurcation of the left main coronary artery over a length of approximately 1 cm. The computer traced this segment automatically and calculated the mean area over this segment. A circular lumen was assumed because only patients with normal coronary arteries were included (Figure 1). The proximal cross-sectional area of the RCA was defined as the vessel segment 1–2 cm distal to the coronary ostium. Cross-sectional area of the distal RCA was also measured distal to the right marginal branches and proximal to the posterior descending coronary artery.1 A vessel segment over a length of approximately 1 cm was analyzed, and the mean cross-sectional area was calculated as for the left coronary artery (LCA). For each vessel segment, three measurements in different projections were made and averaged to correct for biological variations in coronary artery dimensions.14,19,20 Calibration was performed automatically with the proximal part of the 8F Judkins catheter as a scaling device.19,21

Left or right dominance was evaluated in all patients according to the guidelines of the American College of Cardiology and American Heart Association Task Force.22

As an index of the enlargement of the coronary arteries with respect to muscle mass, the cross-sectional area of the LCA (LAD+LCx) per 100 g angiographic mass was calculated.23

Statistics

Statistical comparisons of hemodynamic and angiographic data among controls and patients with aortic valve disease before and after surgery were carried out by a one-way ANOVA. When the analysis was significant, the Scheffé procedure was applied. Paired Student’s t test was used for comparing preoperative and postoperative data in patients with aortic valve disease. Comparison of type of coronary dominance between controls and patients with aortic valve disease was performed by the χ2 procedure. Linear regression analysis was carried out by the least-squares method; in all figures with linear regressions, the 95% confidence limits are included. Data in all tables and figures are reported as mean±1 SD.

Results

Eight patients had pure or predominant aortic stenosis (mean systolic pressure gradient, 69 mm Hg; range, 45–102 mm Hg; aortic valve area, 0.68 cm²; range, 0.58–1.0 cm²), and seven patients had pure or predominant aortic regurgitation (regurgitant fraction 59%, range 40–65%). After surgery, mean systolic pressure gradient was 23 mm Hg (20–31 mm Hg), and aortic valve area was >1.5 cm², whereas regurgitant fraction was minimal.

Hemodynamic and Angiographic Data

These data are included in Table 1. All patients were in sinus rhythm. Heart rate was similar in all three groups. LV peak systolic pressure was significantly higher before and also after surgery in patients with aortic valve disease than in controls but decreased from 182 mm Hg before surgery to 142 mm Hg after surgery. LV end-diastolic pressure and mean pulmonary arterial pressure were significantly higher in aortic valve disease before surgery than in controls. Mean coronary perfusion pressure was similar in controls and in patients with aortic valve disease before and after surgery.

No differences in ejection fraction were found among the three groups. LV end-diastolic volume was higher in aortic valve disease before and after surgery compared to controls. LV mass was also significantly increased in patients with aortic valve disease; however, a significant reduction in LV mass occurred after aortic valve replacement.

Coronary Artery Dimensions

Table 2 and Figure 2 show these dimensions. In seven patients of the control group, the RCA was dominant; the LCA was dominant in three, and a balanced type of distribution was present in two patients. Among patients with aortic valve disease, a right dominance was present in seven patients, a left dominance in five patients, and a balanced distribution in three patients. This type of distribution was not different by χ2 analysis between controls and patients with aortic valve disease.

Before surgery, the proximal cross-sectional areas of the LAD and the LCx were significantly larger in patients with aortic valve disease than in controls; after valve replacement, however, the dimensions of the LAD and LCx decreased significantly but still remained larger than in controls. The proximal and distal cross-sectional areas of the RCA were not different before and after surgery than in controls. Similar data were
obtained when patients were grouped according to coronary artery dominance; that is, the cross-sectional area of the LAD and LCx (but not the cross-sectional area of the RCA) was larger in patients with aortic valve disease before surgery than in controls, independent of the vessel dominance. Moreover, the decrease in size of the LAD and LCx after surgery was similar in the three types of coronary artery dominance.

The index of the appropriateness of LCA size per 100 g of LV muscle mass was significantly lower in aortic valve disease before surgery than in controls (8 versus 11 mm²/100 g) but became normal (10 mm²/100 g) after aortic valve replacement.

Correlations

Correlations (Table 3) were established using all data (n=42), including those of the controls as well as those from the patients with aortic valve disease before and after surgery. There was a significant correlation between cross-sectional area of the LCA and LV peak systolic and end-diastolic pressure (r=0.58 and r=0.68, respectively, p<0.001 for both), LV end-diastolic volume (r=0.66, p<0.001), and LV muscle mass (r=0.70, p<0.001; Table 3). Left coronary cross-sectional area was not correlated to ejection fraction or mean coronary perfusion pressure. Cross-sectional area of the proximal RCA was significantly correlated to LV end-diastolic pressure (r=0.46, p<0.01) and to mean pulmonary artery pressure (r=0.54, p<0.001; Figure 4), whereas it was not correlated to LV peak systolic pressure, end-diastolic volume, ejection fraction, LV muscle mass, or mean coronary perfusion pressure. Moreover, distal cross-sectional area of the RCA was not correlated to LV muscle mass (r=0.24, p=NS) but was weakly correlated to mean pulmonary artery pressure (r=0.34, p<0.05).

Discussion

Several experimental and clinical studies have reported a direct relation between LV muscle mass and coronary dimensions. This relation has been attributed to the constancy of blood flow per 100 g muscle mass in the presence of LV hypertrophy. Coronary artery dimensions seem not to increase proportionally to the increase in mass, however, as shown in the canine heart. The goal of the present study was to evaluate the adequacy of coronary artery enlargement in the presence of LV hypertrophy and to study the effect of postoperative regression of LV muscle mass after valve replacement on coronary artery dimensions of the LCA and the RCA.

### Table 1. Hemodynamic and Angiographic Data

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=12)</th>
<th>AVD-pre (n=15)</th>
<th>AVD-post (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>70±13</td>
<td>70±11</td>
<td>68±12</td>
</tr>
<tr>
<td>LVSP (mm Hg)</td>
<td>114±20</td>
<td>182±31*†</td>
<td>146±22‡</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>9±3</td>
<td>19±12‡</td>
<td>13±6</td>
</tr>
<tr>
<td>MPAP (mm Hg)</td>
<td>15±3</td>
<td>21±8‡</td>
<td>19±5</td>
</tr>
<tr>
<td>MCPP (mm Hg)</td>
<td>86±8</td>
<td>90±14</td>
<td>95±4</td>
</tr>
<tr>
<td>EF (%)</td>
<td>65±4</td>
<td>57±10</td>
<td>62±12</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>137±28</td>
<td>296±97*</td>
<td>197±39*</td>
</tr>
<tr>
<td>LMM (g)</td>
<td>136±30</td>
<td>364±102*†</td>
<td>250±100§</td>
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</table>

* p<0.001, † p<0.05, § p<0.01 vs. control; ‡ p<0.01 vs. AVD-post.

AVD-pre, preoperative patients with aortic valve disease; AVD-post, postoperative patients with aortic valve disease; HR, heart rate; bpm, beats per minute; LVSP, left ventricular systolic pressure; LVEDP, left ventricular end-diastolic pressure; MPAP, mean pulmonary artery pressure; MCPP, mean coronary perfusion pressure; EF, ejection fraction; EDV, end-diastolic volume; LMM, left ventricular muscle mass.

### Table 2. Quantitative Coronary Arteriographic Data

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=12)</th>
<th>AVD-pre (n=15)</th>
<th>AVD-post (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSA_LAD (mm²)</td>
<td>7.8±3.6</td>
<td>15.1±3.8*†</td>
<td>11.9±3.8‡</td>
</tr>
<tr>
<td>CSA_LCA (mm²)</td>
<td>6.3±3.4</td>
<td>13.8±5.3*†</td>
<td>10.9±3.3‡</td>
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<tr>
<td>CSA_LCX (mm²)</td>
<td>9.0±4.7</td>
<td>12.0±5.3</td>
<td>10.1±4.0</td>
</tr>
<tr>
<td>f (mm²/100 g)</td>
<td>10.9±3.2</td>
<td>7.9±2.1†‡</td>
<td>10.1±4.0</td>
</tr>
</tbody>
</table>

*p<0.001, † p<0.05 vs. controls; ‡ p<0.05 vs. AVD-post.

AVD-pre, preoperative patients with aortic valve disease; AVD-post, postoperative patients with aortic valve disease; CSA_LAD, cross-sectional area of left anterior descending coronary artery; CSA_LCA, cross-sectional area of left circumflex artery; CSA_LCX, cross-sectional area of right coronary artery; f=(CSA_LAD+CSA_LCA)/LMM×100; LMM, left ventricular muscle mass.

**Figure 2.** Graph shows changes in coronary artery dimensions after valve replacement: Cross-sectional area of left anterior descending (LAD) and left circumflex (LCX) coronary artery decreased significantly after valve replacement but remained enlarged with respect to controls. The size of the right coronary artery (RCA) did not change. C, control; AVD-pre, aortic valve disease before surgery; AVD-post, aortic valve disease after surgery.
TABLE 3. Correlations Between Coronary Artery Dimensions and Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Cross-sectional area (mm²)</th>
<th>Left coronary (n=42)</th>
<th>Right coronary (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>vs. LVSP (mm Hg)</td>
<td>0.59 &lt;0.001</td>
<td>-0.10 NS</td>
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<tr>
<td>vs. LVEDP (mm Hg)</td>
<td>0.68 &lt;0.001</td>
<td>0.46 &lt;0.01</td>
</tr>
<tr>
<td>vs. MPAP (mm Hg)</td>
<td>0.39 &lt;0.05</td>
<td>0.54 &lt;0.001</td>
</tr>
<tr>
<td>vs. EF (%)</td>
<td>-0.28 NS</td>
<td>-0.08 NS</td>
</tr>
<tr>
<td>vs. LVEDV (ml)</td>
<td>0.66 &lt;0.001</td>
<td>0.29 NS</td>
</tr>
<tr>
<td>vs. LMM (g)</td>
<td>0.70 &lt;0.001</td>
<td>0.31 NS</td>
</tr>
<tr>
<td>vs. MCPP (mm Hg)</td>
<td>0.03 NS</td>
<td>0.03 NS</td>
</tr>
</tbody>
</table>

r, Correlation coefficient; p, probability (linear regression analysis); LVSP, left ventricular peak systolic pressure; LVEDP, left ventricular end-diastolic pressure; MPAP, mean pulmonary artery pressure; EF, ejection fraction; LVEDV, left ventricular end-diastolic volume; LMM, left ventricular muscle mass; MCPP, mean coronary perfusion pressure.

The data of the present study suggest that in LV hypertrophy from aortic valve disease, the luminal size of the proximal major branches of the LCA is increased, but this increase is not sufficient to keep the cross-sectional area of the LCA per 100 g of LV muscle mass within normal limits. The postoperative decrease of LV hypertrophy is associated with a decrease in the size of the LAD and LCx, whereas the size of the RCA did not change.

Appropriateness of Coronary Artery Dimensions

Cross-sectional area per 100 g muscle mass could not be maintained within normal limits in preoperative patients with aortic valve disease, indicating that coronary artery size in LV hypertrophy is inappropriate to LV muscle mass. Similar data have been reported in experimental studies by Stack et al.

These authors observed that the size of large epicardial coronary arteries does not increase in proportion to the changes in LV muscle mass induced by pressure overload. Marcus et al. have reported a significant reduction in coronary vasodilator reserve in dogs with LV hypertrophy caused by renal hypertension. This finding has been attributed either to an alteration in the wall-to-lumen ratio of the coronary resistance vessels or to an inadequate growth of the coronary arteries.

Exposure to chronically elevated perfusion pressure could result in medial thickening of the coronary arteries with a reduction in the wall-to-lumen ratio and, thus, a reduction in coronary flow reserve. Coronary perfusion pressure was normal before and after surgery in patients with aortic valve disease, suggesting that this factor is of minor importance for the difference in the size of the coronary vessels. Mueller and coworkers observed in dogs with renal hypertension that the functional cross-sectional area of the coronary bed does not increase proportionally to the degree of hypertrophy. These authors attributed the inadequate growth of the coronary bed during hypertrophy to anatomic or architectural alterations in the relation between the coronary microvasculature and the cardiac muscle. It must be realized that the proximal coronary arteries are enlarged in patients with LV hypertrophy because of the increased flow governed by the distal coronary arteries. The demand for blood flow as well as LV hypertrophy could stimulate the increase in coronary dimensions. The limitation to flow in the hypertrophied myocardium, however, is not a result of the inadequate growth of the large coronary arteries but rather of the resistance of the small coronary arteries (microvasculature). The resistance of the peripheral coronary arteries in patients with aortic valve disease is decreased, and, thus, resting blood flow is increased. Eberli and coworkers have recently reported that coronary resistance per 100 g of LV muscle mass is normal in patients with aortic valve disease before and after surgery. They concluded that systolic and diastolic compressive forces and structural changes of resistance vessels seem to contribute little to the altered coronary reserve in patients with aortic valve disease. Thus, the inadequate growth of the proximal coronary artery might be the result, but certainly not the cause, of the reduced coronary flow reserve in patients with LV hypertrophy.

Regression of Coronary Artery Dimensions After Aortic Valve Replacement

An important finding of our study is that there was a significant decrease in the dimensions of the LCA after successful aortic valve replacement. When LV hypertrophy regresses, oxygen demand lessens, flow decreases, and the proximal coronary arteries diminish in size. The reduction in left coronary dimension (~23%), however, was less (p<0.05) than the reduction in LV muscle mass (~34%). Despite this difference in percent decrease,
the postoperative ratio of cross-sectional area per 100 g muscle mass was close to that observed in controls. It must be realized, however, that the LCA is still significantly enlarged after valve replacement (Table 2, Figure 2), but this can be explained by the residual hypertrophy of the left ventricle. Thus, the LCA is enlarged after surgery but adequately sized to supply the residually hypertrophied myocardium. When the ratio of cross-sectional area per 100 g muscle mass was plotted against the time period (in months) after valve replacement, there was a reasonably good linear correlation \((r=0.67, p<0.01; \text{Figure 5})\), suggesting that time is an important factor for the normalization of the relation between luminal area and muscle mass.

**Left Versus Right Coronary Artery Dimensions**

Different patterns of changes in coronary artery size between the RCA and LCA have been observed in the present study. In fact, while the LCA seems to follow changes in LV mass, the RCA does not. Cross-sectional area of the proximal and distal RCA was directly related to mean pulmonary artery pressure, suggesting that the right coronary dimensions are influenced by the extent of pressure load and hence the right ventricular muscle mass.24 Because mean pulmonary artery pressure did not change after surgery (Table 1), it appears likely that right ventricular muscle mass remained essentially unchanged. No correlation to the LV mass was observed with the distal RCA dimensions.

**Limitations**

Determinants of coronary artery cross-sectional area other than muscle mass must also be addressed, such as age, body size, physical working capacity, vessel dominance, and coronary vasomotor tone.

1) Variable effects of age on LCA size have been reported.7,30 In the present study, a positive correlation was found in controls \((r=0.58, p<0.05)\) but a negative correlation in aortic valve disease \((r=0.55, p<0.05)\). Thus, no clear statement on the effect of age on coronary artery size can be made from the present data.

2) Body size may have a direct effect on coronary dimensions. Because no differences in body surface area between controls and patients with aortic valve disease were found in the present analysis, this factor is unlikely to have influenced the results of our study.

3) Physical working capacity has been reported to have a direct influence on coronary artery size.30 However, the postoperative decrease in cross-sectional area of the LCA was associated with an increase in physical working capacity31 from 74% to 90% \((p<0.01)\). Nevertheless, the still enlarged postoperative left coronary arteries could be related, at least in part, to the enhanced physical working capacity. It appears more likely, however, that the residual LV hypertrophy was caused by the prosthesis-related mild to moderate LV pressure overload rather than by physical conditioning.

4) Coronary dominance plays an important role as a determinant for the size of the proximal coronary arteries.32 It has been shown8 that myocardial territory size is closely correlated with the proximal coronary artery diameter. In the present analysis, however, coronary dominance was similar in control subjects and patients with aortic valve disease. Moreover, the same patterns of changes in the coronary dimensions were observed when patients were subgrouped according to left or right coronary dominance.

5) Another important factor that influences coronary artery dimension is coronary vasomotor tone. It can be assumed that coronary vasomotor tone as mediated by the nervous system was quite similar in controls and in patients with aortic valve disease, because heart rate was not different in the three groups, suggesting that “overall” autonomic nervous activity was similar (Table 1). We recognize, however, that humoral as well as endothelium-derived vasoactive factors may have varied among our patients.

**Pathophysiological Mechanisms**

It is unclear what the stimulating factor for increasing coronary cross-sectional area is. Some vessel growth factors could be responsible for the growth of the large epicardial arteries.33 Production of these growth factors could be stimulated by physical or mechanical factors.33 The reported reduction in coronary flow reserve in patients with aortic valve disease5 is related to the limitation of flow through the small peripheral coronary vessels. The relative contribution of the conducting arteries to the coronary resistance is small; thus, changes in these arteries would not limit flow unless significant stenoses are present.

**Conclusions**

In secondary hypertrophy from aortic valve disease, the cross-sectional area of the major branches of the LCA is increased, but this increase is not sufficient to keep the cross-sectional area of the LCA per 100 g of LV muscle mass within normal limits. The postoperative decrease of LV hypertrophy is associated with a decrease in the size of the LCA, whereas the size of the RCA did not change. In contrast to the preoperative state, the residually hypertrophied LV myocardium

**FIGURE 5. Scatterplot shows correlation between left coronary cross-sectional area per 100 g of left ventricular muscle mass (LMM) and time period after valve replacement (Follow-up) for the patients with aortic valve disease after surgery \((n=15)\). Dashed lines represent 95% confidence limits. Excluding the three patients with the longest follow-up period, the correlation remains significant \((r=0.61, p<0.05)\), but the slope of the correlation increases from 0.094 to 0.257.**
References


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