EDITORIAL COMMENT

“Prophylactic” Valve Replacement for Mild Aortic Valve Disease at Time of Surgery for Other Cardiovascular Disease? . . . No*

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The issue of prophylactic aortic valve replacement (AVR) or repair at time of open-heart surgery for other cardiovascular surgery arises in several clinical situations. For example, at the time of surgery for 1) rheumatic mitral valve disease, 2) coronary artery disease (CAD) and 3) ascending aortic disease.

Severe aortic valve disease. Aortic valve replacement is recommended in selected asymptomatic patients with isolated severe aortic stenosis (AS), aortic regurgitation (AR), AS/AR (1–3). Thus, there is probably no controversy that if AS or AR is severe, “prophylactic” AVR should be performed at time of other valvular, cardiac, coronary and ascending aortic surgery.

Mild aortic valve disease. RHEUMATIC MITRAL VALVE DISEASE. Sir William Broadbent (4) stated 100 years ago that “The age of the patient at the time when the lesion is acquired is the most important consideration in prognosis. . . .” This was confirmed in the study of Goldschlager et al. (5) and also in the current era by the seminal study of Bonow et al. (6).

More recently, Spagnuolo et al. (7) reported on 174 “young” patients with rheumatic heart disease from Irvington House and Bellevue Hospitals, New York, who were entered into the registry from 1952 through 1966. Patients in the “low-risk” group (probably those with less than severe AR) (Table 1) had an outcome that was better than that of a patient with a prosthetic heart valve (please see following section).

In this issue of the Journal, Vaturi et al. (8) report on the natural history of mild AVD in 131 patients aged 61 ± 12 years, and followed from 1975 to 1992 for 13 ± 7 years (range 1 to 33 years, median 13 years) after surgery for rheumatic mitral valve disease. Of 131 patients, 59 (42%) had AVD (mild in all); 52 of the 59 (88%) had AR, 1 had AS and 6 (10%) had mixed AS/AR. At the end of follow up, 96 (73%) of the patients had AVD; 63 of the 96 (66%) had AR, 6 (6%) had AS and 27 (28%) had AS/AR. Severe AS or AR was present in only 2 and 1 patients, respectively; all 3 initially were in the AS/AR group. It is of interest that of the 6 patients who required surgery on follow up, 4 were primarily for re-operation of the mitral valve and only 2 for severe AS. There are limitations to the study of Vaturi et al. (8). Of 424 patients with rheumatic mitral valve disease, 83 patients died during the first year (64 in-hospital deaths and 19 died during one year follow-up) and 200 patients had inadequate follow-up, leaving 131 patients in the study who were a select group. Nevertheless, the study of Vaturi et al. (8) is useful; it confirms that even in the current era, and even in older patients with rheumatic mitral valve disease, AR and not AS is the more common lesion, and mild aortic valve disease (AVD) rarely progresses to severe AVD over a long follow-up period. Therefore, patients with mild AVD at time of surgery for rheumatic mitral valve disease should not have surgery for the AVD.

CORONARY BYPASS SURGERY. In developed countries, rheumatic fever and rheumatic heart disease are uncommon, if not rare. Thus, the major clinical issue in these countries relates to the need for “prophylactic” AVR for mild AS at time of coronary bypass surgery (CBS).

In 1994, Collins and Aranki (9) described 44 patients with previous CBS who subsequently had AVR (AS was “mild to moderate” at the time of CBS) and had a high operative mortality (19.2%) (Table 2). The study of Collins and Aranki (9) has served the useful purpose of drawing attention to the clinical problem of management of associated AVD. Subsequently, Odell et al. (10) and Fighali et al. (11) have also shown a higher operative mortality of 17% and 14%, respectively, for subsequent AVR (Table 2). In the study of Odell et al. (10), 30/145 (21%) patients also had other cardiac/vascular procedures in addition to repeat CBS at time of AVR.

However, three subsequent studies of Fiore et al. (12), Hoff et al. (13), Sundt et al. (14), and their co-workers (Table 2) have failed to confirm these findings. Fiore et al. (12) showed the operative mortality in 28 patients for AVR subsequent to CBS was 18%, compared with 9.1% for initial CBS and AVR in 175 patients. The difference was not statistically significant, and the 10-year survival after AVR was also not significantly different. Hoff et al. (13) reported on 23 patients undergoing AVR subsequent to CBS; there was no hospital mortality, and the five-year actuarial survival after AVR was 71%. Sundt et al. (14) described 52 patients who had AVR subsequent to CBS; the hospital mortality was 7.7% compared with 6.3% (p = NS) in 427 patients.

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undergoing simultaneous CBS and AVR. There is incomplete information about various parameters in most of the studies (9–14) (Table 2).

The important issues to be considered in these studies include the following:

1. The studies described patients who had AVR after CBS. At the time of initial CBS, patients were said to have had mild/moderate AS or “no AS” (9–14). However, none of these studies provided any data on patients who had mild AS or “no AS” at time of initial CBS but who subsequently have not needed AVR (15).

2. The number of patients who needed AVR after CBS was quite small. For example, in the Collins study (9), 22 patients who initially had CBS at their own institution needed AVR over a period of 17 years, which averages 1.3 patients per year. Overall, it seems that at each of these institutions, about two to four patients each year had AVR following CBS, which is a very small number compared with the total number of patients undergoing isolated CBS or even combined CBS and AVR.

3. There is a price to be paid for performing AVR for mild AS at time of CBS. This includes a higher operative mortality for combined CBS and AVR (approximately a doubling of operative mortality as compared to isolated CBS) (9), and late mortality (up to approximately 2% to 4%/year) (18,19) and morbidity including reoperation for prosthetic valve malfunction (up to approximately 2% to 6%/year) (18,19). The average time from initial CBS to subsequent AVR in the cited studies was about eight years (Table 2) (9–14).

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**Table 1.** Outcome of Rheumatic AR in “Young” Patients

<table>
<thead>
<tr>
<th>Cumulative high-risk group†</th>
<th></th>
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<tbody>
<tr>
<td>Mortality at 6 years</td>
<td>30%</td>
</tr>
<tr>
<td>Angina at 7 years</td>
<td>60%</td>
</tr>
<tr>
<td>Heart failure at 6 years</td>
<td>60%</td>
</tr>
<tr>
<td>Mortality or angina or heart failure at 6 years</td>
<td>87%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cumulative low-risk group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality at 6 years</td>
<td>0%</td>
</tr>
<tr>
<td>at 15 years</td>
<td>5%*</td>
</tr>
<tr>
<td>Angina at 5 years</td>
<td>2%</td>
</tr>
<tr>
<td>Heart failure at 6 years</td>
<td>2%</td>
</tr>
<tr>
<td>at 15 years</td>
<td>5%</td>
</tr>
<tr>
<td>Mortality or angina or heart failure at 15 years</td>
<td>8%</td>
</tr>
</tbody>
</table>

*The only patient (of the 72 patients) in this subgroup who died had developed two of the three risk factors described above. †Patients were considered to be in a cumulative high-risk group if they had systolic blood pressure >140 mm Hg or diastolic blood pressure <40 mm Hg, moderate or marked left ventricular enlargement on chest x-ray and two of three ECG abnormalities (S in V5 + R in V4 ≥51 mm, ST segment depression or T wave inversion in left ventricular leads). Adapted from Spagnuolo et al. (7).

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**Table 2.** Data on Patients Who Had AVR Subsequent to CBS

<table>
<thead>
<tr>
<th></th>
<th>Collins et al. (9) 1994</th>
<th>Odell et al. (10) 1996</th>
<th>Fighali et al. (11) 1995</th>
<th>Fiore et al. (12) 1996</th>
<th>Hoff et al. (13) 1996</th>
<th>Sundt III (14) 1997</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>44</td>
<td>145</td>
<td>104</td>
<td>28</td>
<td>23</td>
<td>52</td>
</tr>
<tr>
<td>Time: CBS to AVR (yrs)</td>
<td>8–164 mo. (68)</td>
<td>9.0 ± 3</td>
<td>8 ± 4</td>
<td>2–17 (7.6)</td>
<td>7.8 ± 4.0</td>
<td></td>
</tr>
<tr>
<td>Age, yrs</td>
<td>52–83 (73)</td>
<td>71 ± 7.6</td>
<td>67 ± 9</td>
<td>70.4 ± 9.1</td>
<td>56–85 (69)</td>
<td>72.9 ± 6.2</td>
</tr>
<tr>
<td>Angina</td>
<td>38%</td>
<td>—</td>
<td>66%</td>
<td>Avg. Class 1.7</td>
<td>—</td>
<td>100%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>24%</td>
<td>9%</td>
<td>70%</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Heart failure + angina</td>
<td>36%</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>NYHA: FC III–IV</td>
<td>—</td>
<td>76%</td>
<td>59%</td>
<td>Avg. Class 2.7</td>
<td>—</td>
<td>53%</td>
</tr>
<tr>
<td>LV dysfunction</td>
<td>—</td>
<td>—</td>
<td>53%</td>
<td>Score 8.3 ± 3.8</td>
<td>—</td>
<td>78%</td>
</tr>
<tr>
<td>Repeat CBS</td>
<td>50%</td>
<td>46%</td>
<td>57%</td>
<td>75%</td>
<td>50%</td>
<td>—</td>
</tr>
<tr>
<td>Op. mortality</td>
<td>18.2%</td>
<td>17%</td>
<td>14%</td>
<td>18%</td>
<td>None (0%)</td>
<td>7.7%</td>
</tr>
<tr>
<td>Post op.</td>
<td>—</td>
<td>—</td>
<td>14%</td>
<td>1.1%</td>
<td>4%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>—</td>
<td>—</td>
<td>4%</td>
<td>—</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>Heart failure</td>
<td>—</td>
<td>—</td>
<td>YES</td>
<td>—</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>—</td>
<td>—</td>
<td>YES</td>
<td>8.7%</td>
<td>9%</td>
<td>15%</td>
</tr>
<tr>
<td>Significant complications</td>
<td>45%</td>
<td>56%</td>
<td>61%</td>
<td>—</td>
<td>22%</td>
<td>—</td>
</tr>
<tr>
<td>Causes of death</td>
<td>Low cardiac CO</td>
<td>—</td>
<td>75%</td>
<td>Combined</td>
<td>12%</td>
<td>100%</td>
</tr>
<tr>
<td>Sudden death</td>
<td>—</td>
<td>25%</td>
<td>80%</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

— = Data not stated; avg. = average; CO = cardiac output; op. = operation.
4. At subsequent AVR, 46% to 75% of the patients needed repeat CBS. Thus, if the patients initially had CBS and AVR, about 50% (Table 2) would presumably have needed reoperation anyway for graft atherosclerosis, progression of native CAD or both.

5. Many of the centers in the cited studies are referral centers. In two studies, 50% (9) and 43% (10) of the patients had their initial CBS elsewhere. Thus, the initial evaluation of AS and subsequent follow up presumably also occurred elsewhere. A large number of patients at time of subsequent AVR had heart failure, were in NYHA Functional classes III and IV and had reduced LV ejection fraction (9–14). Would a more careful follow up and earlier appropriate therapy have reduced these and other adverse factors and thus lowered the subsequent hospital mortality for the AVR? Will the operative mortality of AVR subsequent to CBS be lower in the late 1990s?

6. The assessment of severity of AS was not uniform (9–14). Is it possible that the assessment of the severity of AS at time of initial CBS and also at time of subsequent AVR may have been incorrect? For example, in one study, the aortic valve area (AVA) at time of initial CBS averaged 1.05 cm² (12), and some patients needed subsequent AVR within two months. In another study, the AVA at initial CBS was as low as 0.9 cm², and patients needed subsequent AVR within eight months (9). Thus, it is probable that in some patients severity of AS was not correctly diagnosed and AVR should have been performed at time of initial CBS.

At the time of subsequent AVR, in one study the only symptom was angina in 38%, the AVA was up to 1.7 cm² and 50% of the patients needed repeat CBS (9), and the AS was graded as mild to moderate. In another study, all patients had angina, aortic valve gradient (were the gradients mean or peak?) was 36 ± 27 mm Hg (some must have had very small gradients), and vein grafts demonstrated angiographic disease and vein grafts 7 to 10 years old were routinely replaced (14). Thus, it is probable that at time of subsequent AVR, some patients had mild AS, and angina was due to progression of CAD/graft atherosclerosis.

7. A careful review is needed to learn what is meant by “no AS,” the limitations of gradients obtained by Doppler ultrasound and the assessment of severity of AS by gradients, what criteria should be used to grade severity of AS and the progression of severity of AS.

In some studies, patients were graded as having “no AS” or no abnormality of the aortic valve at time of initial CBS, but the criteria used to make these diagnoses were not provided (14). Patients who have an ejection systolic murmur across the LV outflow tract may have a normal valve, a thickened valve or calcified valve or a stenotic valve. One needs to distinguish these three conditions. An aortic valve may be diseased but the orifice of the aortic valve has to be narrowed by up to approximately 50% before a measurable pressure gradient is present (20) when pressure gradients are directly measured. Thus, the presence of no gradient or a small gradient does not mean the valve is not stenotic. In one prospective study, the diagnosis of aortic “sclerosis” (a subjective evaluation) and of AS by echocardiography/Doppler could not be confirmed on re-analysis in 27% and 20%, respectively (21). Thus, one has to be very careful about the diagnosis of no AS in patients with diseased valves.

In several studies, the severity of AS was assessed by echocardiography and Doppler ultrasound. It must be remembered that “None of the echocardiographic techniques measures intravascular pressure directly” (21). The formula used for aortic valve gradient (AVG) is $\Delta P = 4v^2$, which is a simplification of the Bernoulli equation (21):

$$\frac{1}{2} p (v^2) = p_1 - p_2 = \text{Convective} + \text{Flow} + \text{Viscous}$$

$$\text{Acceleration} + \text{Acceleration} + \text{Friction}$$

Several assumptions are made to calculate valve gradient by Doppler ultrasound. These include eliminating the flow acceleration and viscous friction factors, and ignoring the proximal velocity (22), and that energy losses, nonuniform velocity profiles, unsteady flow and omission of the upstream velocity also affect the accuracy of Doppler assessments of pressure drop (23).

Gradients obtained by Doppler estimate gradients at the level of the valve whereas gradients obtained a few centimeters distal to the aortic valve after pressure recovery has occurred are more meaningful for the circulation (24).

Doppler gradients are liable to be incorrect in patients with high cardiac output and in those with small annuli and eccentric orifices (23). The latter two conditions occur frequently in older patients (>60 years), especially if the stenosis is judged to be moderate (23). In the cited studies at the time of CBS, the patients were in their sixties (Table 2).

The gradient across an aortic valve is related to flow across the valve in systole and is a per beat, and not a per minute, function (25). Thus, AVG is related to forward stroke volume from the LV and to systolic ejection time both of which are a function of heart rate, and of LV preload, afterload and myocardial contractility (3,26,27). In addition, because of two obstructions in-series (stenotic aortic valve and systemic arterial resistance), the gradient is also influenced by systolic pressure proximal to the distal stenosis, that is, in the ascending aorta. Thus, AVGs, no matter how they are obtained, may change within minutes and do decrease over months of follow-up (Fig. 1). Otto et al. (28) have documented that AVG may not even increase when the AV stenosis worsens.

In 636 patients studied by cardiac catheterization over a 10-year period, no AVG (peak or mean) was found that was both sensitive and specific for severe AS. A mean gradient of $\geq 50$ mm Hg or a peak gradient of $\geq 60$ mm Hg were “specific” with a 90% or more positive predictive value.
The severity of AS can be graded on the basis of AVA obtained at cardiac catheterization and the subsequent natural history data on follow-up. These are extensively referenced in the cited review (Table 3) (26,27). The calculation of AVA by the method of Gorlin and Gorlin (34) was criticized 45 years ago (35), but it is still widely used, is clinically useful and has stood the test of time (26,27).

Progression of severity of AS has been cited as an issue that should be considered for recommending AVR at time of initial CBS. Progression has been assessed by changes in pressure gradients and AVA. The pressure gradient is said to increase by 10 to 15 mm Hg/year (28,36–43). In some patients it increases by as much as 15 to 19 mm Hg/year, while others show little or no change or even an actual decrease (Fig. 1).

AVAs are said to decrease by 0.1 to 0.3 cm²/year (42–46) and the average rate of change has ranged from 0.10 to 0.15 cm²/year. The 95% confidence limit of Echocardiographic-Doppler derived AVA to that obtained by cardiac catheterization ranges from ±0.4 to 0.8 cm² (26,27). A small AVA by Doppler ultrasound may result partly from measured small LV outflow tract, which can lead to an erroneous overestimation of the severity of AS (17). Moreover, Otto et al. (28) have documented that although stenosis severity progresses more rapidly in patients who develop symptoms requiring AVR, these patients cannot be identified at the initial study.

There are problems with the evaluations of progression of severity of AS. Progression of AS is not uniform in all age groups, it is more rapid in older patients and in those with calcific (“degenerative”) AS (46). In the studies that had repeat cardiac catheterization to assess progression of AS, (38,40,42,44–47) there presumably had to be a clinical reason to repeat the cardiac catheterization. In most of the echo-Doppler studies, the data were obtained from a retrospective review of patient records rather than as a prospective study of consecutive unselected patients. The follow-up study in some patients has been as little as two to three months, (42) (Fig. 1) 3, (43) 4, (46) 6, (28,40) 7, (38) 11, (41) 12 (39) and 13 (36) months and the initial change in AVG/AVA were then extrapolated to calculate percent change per year (linearized rate). However, progression of

### Table 3. Suggested Grading of the Degree of Aortic Stenosis

<table>
<thead>
<tr>
<th>Aortic Stenosis</th>
<th>AVA† (cm²)</th>
<th>AVA Index (cm²/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt; 1.5</td>
<td>&gt; 0.9</td>
</tr>
<tr>
<td>Moderate</td>
<td>&gt; 1.0 to 1.5</td>
<td>&gt; 0.6 to 0.9</td>
</tr>
<tr>
<td>Severe*</td>
<td>≤ 1.0</td>
<td>≤ 0.6</td>
</tr>
</tbody>
</table>

*Patients with an aortic valve area that is at a borderline value between the moderate and severe grades (0.9 to 1.1 cm²; 0.55 to 0.65 cm²/m²) should be individually considered for reasons discussed in the text. The AVA index was calculated on basis of an average BSA of 1.75 m². Criteria for AVA derived from natural history studies after cardiac catheterization. Reproduced with permission from Brener et al. (42).
149 patients with initial AVA of 1.5 cm² underwent AVR. The history study of Horstkotte and Loogen (48) showed that in many patients already had severe AS at the initial study (28,37–41,46). For example, in one study, 69% of the patients had severe AS at the initial study (37), and in one prospective natural history study (43), the median AVA at entry into the study and at final follow-up at time of AVR/death was about 1.0 cm². That is, many patients already had severe AS at entry into the study.

In brief, mild AS has a more benign outcome than valve replacement. Assessment of AVD and its severity is not without problems that must be recognized and taken into account. Performance of both noninvasive and invasive procedures, analyses of the data and overall evaluation of the patient should be done with care by skilled and experienced personnel. Clinical implications are as follows:

1. The severity of AS at the time of initial CBS should be carefully and accurately determined.
2. Patients with mild AS and no AS at time of CBS should not undergo AVR at time of initial CBS.
3. At time of initial CBS, it would be prudent to obtain an echocardiogram in all patients aged ≥55 to 60 years. If the valve is thickened, calcified, or is otherwise abnormal, the patients should have careful evaluation by skilled and experienced personnel of both their clinical status and of the valve.
4. After CBS, patients with valvular abnormality initially should be followed closely and carefully by appropriately experienced and skilled personnel for assessment of progression of AS and for evaluation of symptoms, heart failure and LV dysfunction. If any of these occur, patients must be treated promptly and appropriately. Patients must be treated aggressively for control of adverse factors for atherosclerosis which are common in such patients (21). Control of these risk factors is beneficial for slowing or delaying progression of atherosclerosis in native coronary vessels and grafts. These risk factors are common in older patients with calcific AS (17,21,43) and may have an etiologic relationship to the development of calcific AS in the older patient (21,49–53), either directly or as an autoimmune reaction to antigens present in the valve (49). Patients must stop smoking. Lipid abnormalities, hypertension and diabetes must be corrected, patients should take aspirin and appropriate hormone replacement therapy if indicated, provided there are no contraindications to their use. Regular exercise and attaining an ideal weight are also desirable, and on follow-up, one needs to carefully evaluate whether symptoms or abnormal findings are due to progression and development of severe AS or of atherosclerosis in the coronary arteries/grafts.

5. In clinical practice, the average rate of change of gradient and valve area is of very limited value. Patients must be individualized; they should be carefully evaluated and followed, particularly those in the older age group who
have mild calcific AS or have valve disease with no demonstrable gradient.

ASCENDING AORTIC DISEASE. In patients with dissecting aneurysm of the ascending aorta, AR usually implies that the dissection has extended down to the aortic root/annulus. Thus, these patients need aortic valve surgery at time of surgery for the aneurysm even if the AR is mild (54).

Moderate aortic valve disease. AORTIC REGURGITATION. With moderate AR, it may be difficult to maintain the patient on extracorporeal circulation or to wean them off bypass without AVR. This factor should be considered when recommending CBS.

AORTIC STENOSIS. Patients with AVA from >1.0 to 1.5 cm² are considered to have moderate AS (Table 3). Older patients with calcific AS have more rapid progression of severity of AS. Thus, it may be clinically prudent to perform AVR at time of initial CBS in some older patients (>60 years) with moderate calcific AS, especially if the AVA is from >1.0 to 1.3 cm² (from >0.60 to 0.75 cm²/m²). However, once again, clinical judgment is important because in small persons, AVA from >1.0 to 1.5 cm² may actually be mild AS, and in large people, AVA in this range may actually be severe AS. In such patients, correcting AVA for body size is of some help in clinical decision making.

REFERENCES

37. Nestico PF, De Pace NL, Kimbris D, Hakki AH, Khanderia B,


