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Background—The causes of aortic regurgitation (AR) severe enough to warrant aortic valve replacement (AVR) have received little attention in the last 20 years.

Methods and Results—We analyzed the causes of pure AR in 268 patients >20 years of age having isolated AVR at Baylor University Medical Center from 1993 to 2005 that was unassociated with mitral stenosis, mitral valve replacement, or a previous operation involving a cardiac valve or ascending aorta. In 122 patients (46%), the AR resulted from a problem with the aortic valve: congenital malformation unassociated with infective endocarditis, 66 patients (54%); infective endocarditis, 46 patients (38%; 15 with bicuspid valves); probable rheumatic heart disease, 8 patients (6%); and miscellaneous, 2 patients (2%). In the other 146 patients (54%), the AR was the consequence of a condition affecting the ascending aorta: dissection, 28 patients (19%); the Marfan syndrome or its forme fruste variety, 15 patients (10%); aortitis, 12 patients (8%), and in the remaining 91 patients (62%), the cause of the AR was not determined. This latter group was the oldest (mean age 66 years), 83 (91%) had hypertension, 26 (29%) had small calcific deposits in the valve cusps, and 46 (51%) had simultaneous coronary artery bypass grafting.

Conclusions—The causes of pure AR severe enough to warrant isolated AVR are diverse. The most common category in this study was “cause unclear.” (Circulation. 2006;114:422-429.)

Key Words: bypass ■ calcium ■ coronary disease ■ hypertension ■ regurgitation

In contrast to aortic stenosis, which essentially has 3 causes (congenital, atherosclerotic, and rheumatic),1–3 pure aortic regurgitation (AR; no element of aortic stenosis) has multiple causes, some of which directly affect the aortic valve and others of which are due to problems with the aorta without direct involvement of the aortic valve. Furthermore, unlike aortic stenosis, which essentially is always a slowly progressing chronic condition, AR may develop acutely (acute AR) or over a prolonged period (chronic AR). This report analyzes the causes of pure AR in patients having isolated aortic valve replacement (AVR) at Baylor University Medical Center (Dallas, Texas) from 1993 to 2005.

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Methods

Since March 1993, all operatively excised cardiac valves and aortas submitted to the surgical pathology division of the department of pathology have been examined and described by one of us (W.C.R.). Additionally, the preoperative cardiac catheterization and echocardiographic data, and often pertinent clinical records and operative notes, on most of these patients have been obtained.

The present study was limited to patients who, before AVR, had either no gradient or a negative gradient between peak systolic left ventricular and peak systolic aortic pressures or at least a transvalvular peak systolic pressure gradient of ≤10 mm Hg. Patients with associated mitral valve disease that required mitral replacement or repair or insertion of an annular ring, patients <20 years of age at the time of AVR, patients with a previous operation involving the ascending aorta or a cardiac valve, and patients with associated ventricular septal defect or discrete subaortic stenosis or hypertrophic cardiomyopathy were excluded. Mild degrees of mitral regurgitation preoperatively did not exclude patients from inclusion in the present study.

Most operatively excised valves and most operatively excised aortas were weighed (all by W.C.R.) on an Ohaus scale (Ohaus Corporation, Florham Park, NJ) accurate to 2 decimal places. All operatively excised valves and most aortas were photographed. The valves that contained vegetations were sectioned and processed in

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alcohols and xylene, and sections were cut and stained, one with hematoxylin-eosin and another with the Gram method. All aortas were also processed for histological study and, after they were cut, were stained, one with hematoxylin-eosin and another by the Movat method.

The study protocol was approved by the Institutional Review Board of Baylor University Medical Center.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

**Figure 1.** Congenitally bicuspid aortic valves unassociated with infective endocarditis in 4 men. Upper left, Age 53 years. The valve was devoid of calcific deposits and weighed 1.69 g. Upper right, Age 56 years. The valve weighed 1.65 g. Lower left, Age 66 years. The valve weighed 1.05 g. Lower right, Age 71 years. The valve weighed 2.43 g. The last 3 valves had calcific deposits on both cusps, mainly in their raphe.

**Figure 2.** Congenitally quadricuspid aortic valves in 2 women. Left, Age 79 years. The valve weighed 0.57 g. Right, Age 53 years. The valve weighed 1.13 g.
The study included all patients having AVR for pure AR who met the above criteria and had AVR from March 24, 1993, to March 31, 2005. A total of 268 patients aged 21 to 84 years (mean 57 years) met the above criteria, and the findings in these patients are summarized in Table 1. The 268 patients were divided into 2 major groups: those in whom the AR was secondary to a problem with the valve \( (n = 122, 46\%) \) and those in whom the AR was secondary to a problem with the ascending aorta (nonvalve; \( n = 146, 54\% \)). Of the 268 patients, 48 (18\%) had acute AR, which in 27 was due to active infective endocarditis and in 21 to acute aortic dissection; the remaining 220 patients had chronic AR.

Hemodynamic or echocardiographic data were available in 235 (88\%) of the 268 patients: One hundred thirty-seven patients had both cardiac catheterization data and echocardiographic data available; 40 other patients had only cardiac catheterization data available, and 58 others had only echocardiographic data available. Of the 177 patients with hemodynamic data from cardiac catheterization, 67 (38\%) had transvalvular peak systolic pressure gradients that varied from 1 to 10 mm Hg.

Of the 268 operatively excised aortic valves, the valve was weighed in 226 patients, and its weight ranged from 0.48 to 2.99 g (mean 1.22 g) in the men and from 0.31 to 2.50 g (mean 0.81 g) in the women. Of the 91 patients in whom portions of ascending aorta were resected, the resected specimens were weighed on the same scales in 63 (69\%) and ranged from 0.40 to 60 g (median 13 g) in the men and from 0.40 to 37 g (median 13 g) in the women. Whether the ascending aorta was resected was determined by its size, by its appearance, and by the operator. Of the latter 63 patients, the aorta weighed \( \geq 4 \) g in 13 patients and \( \geq 4 \) g in 50 patients.

### Table 1. Causes of AR in Patients Having Isolated AVR at Baylor University Medical Center (1993–2005)

<table>
<thead>
<tr>
<th>Cause of AR</th>
<th>Total</th>
<th>Ages at Operation, Range (Mean), y</th>
<th>M</th>
<th>F</th>
<th>Acute</th>
<th>Chronic</th>
<th>SH</th>
<th>CMN (3+ or 4+)</th>
<th>Examined</th>
<th>Histologically</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve (122 [46%])</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Congenital malformation without</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicuspid</td>
<td>59 (22%)</td>
<td>22–77 (55)</td>
<td>49</td>
<td>10</td>
<td>0</td>
<td>59</td>
<td>39 (66%)</td>
<td>18 (31%)</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Quadricuspid</td>
<td>2 (1%)</td>
<td>53–79 (66)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1 (50%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>5 (2%)</td>
<td>33–48 (40)</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>2 (40%)</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>46 (17%)</td>
<td>21–82 (45)</td>
<td>31</td>
<td>15</td>
<td>27</td>
<td>19</td>
<td>29 (63%)</td>
<td>7 (15%)</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Rheumatic?</td>
<td>8 (3%)</td>
<td>25–63 (47)</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>8</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2 (1%)</td>
<td>24–42 (33)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2 (100%)</td>
<td>1 (50%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nonvalve (146 [54%])</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>28 (10%)</td>
<td>25–78 (58)</td>
<td>20</td>
<td>8</td>
<td>21</td>
<td>7</td>
<td>22 (79%)</td>
<td>5* (17%)</td>
<td>28</td>
<td>20</td>
</tr>
<tr>
<td>Marfan or forme fruste</td>
<td>15 (6%)</td>
<td>21–71 (47)</td>
<td>9</td>
<td>6</td>
<td>6</td>
<td>15</td>
<td>10 (67%)</td>
<td>11 (7%)</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Aortitis</td>
<td>12 (4%)</td>
<td>35–82 (66)</td>
<td>5</td>
<td>7</td>
<td>0</td>
<td>12</td>
<td>10 (83%)</td>
<td>5 (42%)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Cause unclear</td>
<td>91 (34%)</td>
<td>50–84 (66)</td>
<td>58</td>
<td>33</td>
<td>0</td>
<td>91</td>
<td>83 (91%)</td>
<td>46 (51%)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>268 (100%)</td>
<td>21–84 (57)</td>
<td>182 (68%)</td>
<td>86 (32%)</td>
<td>48 (18%)</td>
<td>220 (82%)</td>
<td>203 (76%)</td>
<td>86 (32%)</td>
<td>91 (34%)</td>
<td>76</td>
</tr>
</tbody>
</table>

SH indicates systemic hypertension; M, male; F, female; CMN, cystic medial necrosis; and BAV, bicuspid aortic valve.

Cystic medial necrosis is used here to refer to the magnitude of loss of elastic fibers in the aorta’s media.

*Four other patients had CABG due to extension of the aortic dissection into a coronary artery.
†One additional patient had CABG due to extension of the aortic dissection into a coronary artery.
‡No. of cases with aortic valve weight.

### Results

The study included all patients having AVR for pure AR who met the above criteria and had AVR from March 24, 1993, to March 31, 2005. A total of 268 patients aged 21 to 84 years (mean 57 years) met the above criteria, and the findings in these patients are summarized in Table 1. The 268 patients were divided into 2 major groups: those in whom the AR was secondary to a problem with the valve (n=122, 46\%) and those in whom the AR was secondary to a problem with the ascending aorta (nonvalve; n=146, 54\%). Of the 268 patients, 48 (18\%) had acute AR, which in 27 was due to active infective endocarditis and in 21 to acute aortic dissection; the remaining 220 patients had chronic AR.

Hemodynamic or echocardiographic data were available in 235 (88\%) of the 268 patients: One hundred thirty-seven patients had both cardiac catheterization data and echocardiographic data available; 40 other patients had only cardiac catheterization data available, and 58 others had only echocardiographic data available. Of the 177 patients with hemodynamic data from cardiac catheterization, 67 (38\%) had transvalvular peak systolic pressure gradients that varied from 1 to 10 mm Hg.

Of the 268 operatively excised aortic valves, the valve was weighed in 226 patients, and its weight ranged from 0.48 to 2.99 g (mean 1.22 g) in the men and from 0.31 to 2.50 g (mean 0.81 g) in the women. Of the 91 patients in whom portions of ascending aorta were resected, the resected specimens were weighed on the same scales in 63 (69\%) and ranged from 0.40 to 60 g (median 13 g) in the men and from 0.40 to 37 g (median 13 g) in the women. Whether the ascending aorta was resected was determined by its size, by its appearance, and by the operator. Of the latter 63 patients, the aorta weighed \( \geq 4 \) g in 13 patients and \( \geq 4 \) g in 50 patients.

### Valve Problem

#### Congenital Malformation of the Aortic Valve

**Unassociated With Infective Endocarditis**

This group included 59 patients with congenitally bicuspid aortic valves (Figure 1), 2 with quadricuspid valves (Figure 2), and 5 with tricuspid valves (Figure 3). At operation in each of the latter 5 patients, 1 or 2 of the 3 aortic valve cusps was described as being prolapsed such that the free margins of the cusps did not coapt with each other at the same cephalad level. Examination of the operatively excised valves in these 5 patients did not disclose cuspal inequality but indeed similar-sized cusps. In other words, examination of the operatively excised valves in these 5 patients did not allow us to determine or predict which cusps had prolapsed. In 19 (32\%) of the 59 patients with congenitally bicuspid aortic valves, the ascending aorta was dilated, and a large portion (>4 g) of it was resected. Histological study of the
resected aorta showed severe loss of medial elastic fibers in 11 cases (58%).

**Infective Endocarditis**

In 46 patients, the cause of the pure AR was infective endocarditis (Figure 4), which was active in 27 patients (59%) and healed in 19 (41%). Each of the 27 patients with active infective endocarditis had an acute onset of AR, whereas each of the 19 patients with healed infective endocarditis had chronic AR. Of these 46 patients, 15 (33%) had the infection superimposed on a 2-cuspid aortic valve, and in the other 31 patients (67%), the infection involved a 3-cuspid aortic valve.

**Probable Rheumatic Heart Disease**

In 8 patients, the pure AR was attributed to rheumatic heart disease (Figure 5). Each of the 3 cusps in each of these 8 patients was quite thickened, mainly by fibrous tissue, but in 3 of the 8 patients, the cusps also contained small calcific deposits. Cardiac catheterization in 5 of these 8 patients disclosed small (2 to 9 mm Hg) peak systolic pressure gradients between left ventricle and aorta. None of these 8 patients had hemodynamic or echocardiographic evidence of mitral stenosis, although mild mitral regurgitation was present in several of them.

**Miscellaneous**

Two patients had 3-cuspid aortic valves that were mildly and focally thickened by fibrous tissue. No abnormalities of the aorta were described. One patient, a 24-year-old woman, had the Behçet syndrome with multiple noncardiovascular problems. The other patient, a 42-year-old obese woman, took phentermine-fenfluramine, and the AR was believed to be related to that medication. Histologically, however, no features of the phentermine-fenfluramine (carcinoid) valve lesion were evident.

**Aortic (Nonvalve) Problem**

**Aortic Dissection With Tear in Ascending Aorta**

In 28 patients, the AR was secondary to aortic dissection, acute in 21 (75%) and healed in 7 (25%; Figure 6). Portions of ascending aorta were excised in all 21 cases with acute dissection and were weighed in 10 cases; the resected aorta weighed from 0.40 to 51 g (median 13 g). Histologically, the number of patients with a clear loss of medial elastic fibers was 3. In 7 with healed dissection, the 6 resected aortas weighed from 11 to 60 g (mean 38 g); histologically, the media contained a normal number of elastic fibers in 5 and were severely deficient in elastic fibers in 2 patients.

**The Marfan Syndrome and Forme Fruste Varieties of It**

Pure AR was attributed to the Marfan syndrome in 15 patients. The resected ascending aorta weighed from 6 to 24 g (mean 13 g); portions of the resected aortas in 13 cases submitted for histological study showed massive loss of medial elastic fibers with normal intima and adventitia, which resulted in an aortic wall that was thinner than normal, and each of them had intima-media tears, without dissection in 14 and with dissection in 1.

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**TABLE 1. Continued**

<table>
<thead>
<tr>
<th>BAV</th>
<th>Calcium Deposits on AV Cusps</th>
<th>Aortic Valve Weight (g), Range (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
</tr>
<tr>
<td>59</td>
<td>31</td>
<td>0.52–2.99 (1.42)</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>1.11–1.40 (1.23)</td>
</tr>
<tr>
<td>15</td>
<td>8</td>
<td>0.77–2.31 (1.53)</td>
</tr>
<tr>
<td>0</td>
<td>3</td>
<td>1.10–2.45 (1.81)</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0.55</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>0.51–1.19 (0.81)</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>0.73–1.01 (0.94)</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>0.63–0.79 (0.70)</td>
</tr>
<tr>
<td>0</td>
<td>26</td>
<td>0.48–2.13 (1.08)</td>
</tr>
<tr>
<td>77 (29%)</td>
<td>76/263 (29%)</td>
<td>0.48–2.99 (1.22)</td>
</tr>
</tbody>
</table>

151‡ | 75‡

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Figure 3. Congenitally malformed tricuspid aortic valves. Left, In a 33-year-old woman, the valve weighed 0.34 g. Middle, In a 44-year-old man, the valve weighed 1.11 g. Right, In a 33-year-old man, the valve weighed 1.19 g. Which of these cusps were attached more caudally than normal was not discernible after the cusps had been excised.
Diffuse Aortitis
The AR was secondary to diffuse aortitis of the ascending aorta in 12 patients (Figure 7): granulomatous in 3 and nongranulomatous in 9. Eight (aged 42 to 82 years [mean 67 years]) of the latter 9 patients had typical histological features of syphilis; the ninth, aged 35 years, was believed to have Takayasu arteritis. In the 3 patients with granulomatous aortitis, its cause was not determined. The only difference between these 2 types of aortitis was the presence of multinucleated giant cells in 1 group and their absence in the other group. In both groups, both the intima and the adventitia were considerably thickened, mainly by fibrous tissue. The resected ascending aorta weighed from 0.40 to 25 g (median 18 g). Of these 12 patients, 8 were ≥65 years of age.

Figure 4. Infective endocarditis. Upper left, Acute infection in a bicuspid valve in a 41-year-old man. Upper right, Acute infection in a tricuspid valve in a 40-year-old man. The valve weighed 1 g. Lower left, Healed infection with cuspal perforations in a bicuspid valve in a 27-year-old man. The valve weighed 0.86 g. Lower right, Healed infection with cuspal perforations in a tricuspid valve in a 69-year-old man. The valve weighed 0.96 g.

Figure 5. Probable rheumatic heart disease. Left, Tricuspid valve in a 60-year-old man. The valve weighed 2.06 g. Right, Tricuspid valve in a 55-year-old man. The valve weighed 1.52 g. The cusps in both patients are thickened by fibrous tissue.

Cause Unclear
Each patient in this group had 3-cuspid aortic valves (Figure 8). Seven, aged from 51 to 81 years (mean 67 years), had a portion of the ascending aorta excised (weight 1 to 31 g [median 12 g]), but 3 were small biopsies. In all 7, the aorta histologically was normal. Most of them had mildly dilated aortas, probably the result of aging alone. Of these 91 patients, 83 (91%) had either a history of systemic hypertension or a directly or indirectly measured peak systolic systemic pressure >140 mm Hg. Of these 91 patients, 46 (51%) also had coronary artery bypass grafting at the time of AVR.

Figure 6. Aortic dissection. Left, Cross section of a portion of ascending aorta in an acute dissection in a 42-year-old man. The partition between the false channel (FC) and the true channel (TC) buckled into the lumen of the TC. Right, Cross section of a portion of ascending aorta in a healed dissection in a 79-year-old man. The FC is filled with a thrombus and is larger than the TC.
Discussion

The present study describes causes of pure (no element of stenosis) AR in 268 patients having isolated AVR unassociated with mitral stenosis or mitral valve replacement. The patients were divided into 2 groups: those in whom the cause of the AR was a problem with the valve (46%) and those in whom the cause was a problem with the aorta (54%). Hemodynamic or echocardiographic data were available in 235 patients (88%). All excised valves and ascending aortas were examined by the same physician (W.C.R.), who has been examining operatively excised aortic valves for 45 years.

Several findings in the present study were surprising to the authors, the main one being the high frequency with which we were unable to determine the cause of the AR, an occurrence in 91 patients (34% of the total or 62% of the 146 patients in whom the AR was considered the consequence of a problem with the aorta). The ages of these 91 patients were among the oldest of any of the groups, namely, 50 to 84 years (mean 66 years), and all 91 had tricuspid aortic valves. Although probably all had some degree of dilatation of the ascending aorta, mainly due to aging, only 4 had significant portions of the ascending aorta resected, and in each of them, it was histologically normal. Of these 91 patients, at least 83 (91%) had either a transvalvular peak systolic aortic pressure >140 mm Hg, an end-diastolic aortic pressure >90 mm Hg, or both. It appears reasonable to believe that the systemic hypertension in some way caused or at least contributed to the AR in these patients. The operatively excised aortic valve cusps contained small calcific deposits in 26 (29%) of these 91 patients, but the valve weights were relatively small (mean 0.73 g in women and 1.08 g in men). Almost certainly, some of these 91 patients had a cardiac operation primarily because of severe coronary artery disease; 46 (51%) of these 91 patients had CABG. Nevertheless, the degree of AR appears to have been similar in the patients with versus those without simultaneous coronary bypass. In 79 of these 91 patients, the degree of AR was classified by either aortic angiography or echocardiography; the AR was severe in 67 (85%) and mild to moderate in 12 (15%).

That systemic hypertension can cause AR severe enough to warrant AVR has been debated. Waller and colleagues in 1982 described 4 patients with severe AR from systemic hypertension (without aortic dissection) who underwent AVR, and they reviewed previously reported patients with systemic hypertension and pure AR. Of their 4 patients, the systemic arterial pressures =1 month postoperatively remained elevated in 2 of the 3 survivors. Among previous reports describing precordial murmurs consistent with AR in patients with systemic hypertension, Waller and colleagues found 7 studies that analyzed 79 patients with AR associated with systemic hypertension, and 17 had severe AR with evidence of considerable heart failure. In 11 of the 17 patients, systemic hypertension appeared to be the only reasonable cause of the AR. Barlow and Kincaid-Smith studied 100 patients with systemic hypertension and peak systolic pressures >180 mm Hg; 9 had diastolic blowing murmurs consistent with AR. Their report and reports of others pointed out that among hypertensive patients, the higher the systemic arterial pressure, the greater the chance that AR would develop. Among patients with similar levels of systemic arterial pressure, older patients had a higher frequency of AR than did younger patients. Of patients of similar age and with similar blood pressures, those with systemic hypertension of longer duration had a higher frequency of AR than did those with hypertension of shorter duration. Among the few patients with severe AR due to systemic hypertension, arterial diastolic pressure is usually >60 mm Hg; nevertheless, the pulse pressure is high (often >100 mm Hg).

Another finding, not unexpected, was the high frequency of a congenitally bicuspid aortic valve, which occurred in 77 (29%) of the 268 patients, including 74 (61%) of the 122 patients in whom the AR was a consequence of a valve problem and 3 (2%) of the 146 patients in whom the AR appeared to be the consequence of a problem with the aorta. All 3 of the latter patients were among the 28 patients with aortic dissection. Thus, 11% of the patients in whom the AR resulted from aortic dissection had a congenitally bicuspid aortic valve. Of the 74 patients with a congenitally bicuspid aortic valve, the AR in 59 (80%) was in patients who had never had a clinical event compatible with active or healed infective endocarditis and 15 (33%) were in the 46 patients in whom the AR appeared to result from active or healed infective endocarditis superimposed on a congenitally bicuspid aortic valve. Small calcific deposits were present in 34 (44%) of the 77 congenitally bicuspid aortic valves. The calcific deposits usually were localized to the raphe. Although its high frequency in patients with aortic valve stenosis is well appreciated, the bicuspid aortic valve as a cause of pure AR—at least, when unassociated with infective endocarditis—is less well appreciated. Indeed, that a bicuspid aortic valve could cause AR severe enough to warrant AVR in the absence of active or healed infective endocarditis was not described initially until 1981.

Figure 7. Diffuse aortitis. Valve and a portion of an ascending aorta in a 69-year-old man with syphilis. The aortic wall is thickened, and the intimal surface is 100% involved by the process. The tricuspid aortic valve is essentially normal and weighed 0.83 g.
In addition to the findings of a congenitally bicuspid aortic valve in 77 patients, 7 other patients had congenitally malformed aortic valves. Two had quadricuspid valves, and 5 had tricuspid aortic valves. In each of the latter 5 patients, 1 or 2 of the 3 cusps was attached more caudally than usual such that the free margins of these cusps did not coapt with the normally attached cusp(s), which resulted in prolapse. The prolapsed cusp, however, was usually similar in size to the nonprolapsed cusps, just attached more caudally. That a tricuspid aortic valve can be congenitally malformed or malpositioned is not a well-recognized cause of AR.

Portions of the ascending aorta were resected in 91 (34%) of the 268 patients, and in 63 of them, the excised portion of aorta was weighed (range 0.40 to 60 g [median 13 g] in men and 0.40 to 37 g [median 13 g] in women); in 13 patients (21%), the excised portion of aorta weighed >4 g, and in the other 50 patients, it weighed <4 g. Ascending aortas having features of the Marfan syndrome, aortitis (usually syphilis), and acute or healed dissection were excised. Patients having AR secondary to congenitally bicuspid aortic valves unassociated with infective endocarditis often (22 [37%] of 59 patients) had portions of the aorta excised, and the aortas histologically usually had evidence of loss of medial elastic fibers.

There are few reported studies to which the present data can be compared. Roberts and colleagues7 in 1981 briefly described causes of pure AR in 177 patients, aged 18 to 70 years, having AVR at the National Heart, Lung, and Blood Institute from 1963 to 1979. Of the 177 patients fulfilling the same criteria as in the present study, these authors attributed the AR to rheumatic heart disease in 94 patients (53%); to infective endocarditis in 41 (23%; bicuspid aortic valve in 7 and tricuspid valve in 34); to the Marfan syndrome or its forme fruste variety in 15 (8%); to a congenitally bicuspid aortic valve unassociated with infective endocarditis in 13 (7%); to syphilis in 9 (5%); to aortic dissection in 2 (1%); and to trauma in 1 (<1%). Thus, there were no patients in whom the AR was attributed to an unclear cause.

Olson and colleagues8 in 1984 described 221 patients with “clinically pure aortic insufficiency” having AVR at the Mayo Clinic during the 4 years of 1965, 1970, 1975, and 1980. In contrast to the present study, however, these authors included patients who also had simultaneous mitral valve replacement (80 patients [36%]) or who were aged <20 years (8 patients), and none had the presence of pure AR confirmed by hemodynamic data, angiography, or echocardiography. Rheumatic heart disease was the most frequent cause of “clinically pure” AR in their patient population (100 [45%] of 221 patients). The second most common cause was “idiopathic aortic dilatation” (43/221 [19%]). We suspect that their group of “idiopathic aortic dilatation” would have been similar to our group classified as “cause unclear.” The Mayo clinic study did not provide information on blood pressure, and therefore, the frequency of hypertension in this group is not known. Their third most common cause of AR was congenitally bicuspid aortic valve unassociated with either infective endocarditis or aortic dissection (42/221 [19%]). Infective endocarditis was next (21/221 [10%], 9 of whom had a bicuspid aortic valve). Other causes included the Marfan syndrome (4 patients), aortic dissection (3 patients, each of whom had a bicuspid aortic valve), ankylosing spondylitis (3 patients), indeterminate (2 patients), and syphilis (1 patient). Their study did not include any information regarding coronary artery bypass grafting or resection of the ascending aorta, and there was no information regarding preoperative echocardiographic or hemodynamic data.

No previous studies have weighed operatively excised purely regurgitant aortic valves. Table 2 shows the range and mean weights of the purely regurgitant aortic valves in the present study and the weights for comparative

<table>
<thead>
<tr>
<th>Bicuspid</th>
<th>Tricuspid</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td></td>
</tr>
<tr>
<td>No. of cases with aortic valve weight</td>
<td>45</td>
</tr>
<tr>
<td>No. of cases with aortic valve weight</td>
<td>0.52–2.99 (1.39)</td>
</tr>
<tr>
<td>No. of cases with aortic valve weight</td>
<td>0.89–11.30 (3.57)</td>
</tr>
</tbody>
</table>

*Patients with infective endocarditis were excluded.
†Data from Roberts et al.2
purposes of operatively excised stenotic aortic valves—
(with or without associated AR). In both groups, the
mean weights were heavier in the men than in the wo-
men. The mean weights of the purely regurgitant valves
ranged from 39% to 54% of the mean weights of the
stenotic valves. The normal aortic valve in adults weighs
\( \approx 0.5 \) g.9

Disclosures

None.

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**CLINICAL PERSPECTIVE**

In the first 30 years of aortic valve replacement (AVR) for pure aortic regurgitation (AR), the cause of the AR was usually readily apparent. We reviewed causes of pure AR among 268 patients having AVR from 1993 to 2005. To our surprise, despite examining the operatively excised valves and occasionally portions of ascending aorta and the medical records, the cause of the AR was clear in 177 patients (66%) and unclear in 91 (34%). The frequency of simultaneous coronary bypass was much less in the clear-cause group than in the unclear-cause group (40/177 [23%] versus 46/91 [51%]).
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