

# Comparison of the Structure of the Aortic Valve and Ascending Aorta in Adults Having Aortic Valve Replacement for Aortic Stenosis Versus for Pure Aortic Regurgitation and Resection of the Ascending Aorta for Aneurysm

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**Background**—There is debate concerning whether an aneurysmal ascending aorta should be replaced when associated with a dysfunctional aortic valve that is to be replaced. To examine this issue, we divided the patients by type of aortic valve dysfunction—either aortic stenosis (AS) or pure aortic regurgitation (AR)—something not previously undertaken.

**Methods and Results**—Of 122 patients with ascending aortic aneurysm (unassociated with aortitis or acute dissection), the aortic valve was congenitally malformed (unicuspid or bicuspid) in 58 (98%) of the 59 AS patients, and in 38 (60%) of the 63 pure AR patients. Ascending aortic medial elastic fiber loss (EFL) (graded 0 to 4+) was zero or 1+ in 53 (90%) of the AS patients, in 20 (53%) of the 38 AR patients with bicuspid valves, and in all 12 AR patients with tricuspid valves unassociated with the Marfan syndrome. An unadjusted analysis showed that, among the 96 patients with congenitally malformed valves, the 38 AR patients had a significantly higher likelihood of 2+ to 4+ EFL than the 58 AS patients (crude odds ratio: 8.78; 95% confidence interval: 2.95, 28.13).

**Conclusions**—These data strongly suggest that the type of aortic valve dysfunction—AS versus pure AR—is very helpful in predicting loss of aortic medial elastic fibers in patients with ascending aortic aneurysms and aortic valve disease. (*Circulation*. 2011;123:896-903.)

**Key Words:** aortic surgery ■ aortic valve regurgitation ■ aortic valve replacement ■ aortic valve stenosis ■ bicuspid aortic valve

Many patients with isolated aortic valve disease have some dilatation of the ascending aorta.<sup>1–10</sup> The dilatation in some of these patients is to such an extent that it is considered aneurysmal. In the later group of patients operative intervention frequently includes not only aortic valve replacement (AVR), but also replacement of the ascending aorta or at least “tailoring” (aortoplasty) with or without wrapping of this portion of aorta. Some thoughtful students recommend resection of the ascending aorta if its diameter is  $\geq 5.0$  cm or has an increase of 0.5 cm/y, and other similarly thoughtful students recommend a more conservative approach (aortoplasty with or without wrapping) to the dilated ascending aorta.<sup>11–17</sup> No previous study has attempted to find the proper approach to this problem by comparing patients based on whether the aortic valve is stenotic or purely regurgitant. Such is the purpose of the present study, because resection of the associated ascending aortic aneurysm com-

bined with AVR is a far more complicated operation than is isolated AVR. The present study compares the structure of the aortic valve and of the operatively excised portion of aneurysmal ascending aorta in patients with aortic stenosis (AS) ( $\pm$  aortic regurgitation [AR]) versus those with pure AR in an attempt to evaluate whether aneurysmectomy is actually warranted.

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## Methods

### Data Collection

The surgical pathology files of the cardiovascular laboratory, a part of the pathology department of Baylor University Medical Center at Dallas, TX, were searched for patients having operatively excised aortic valves with or without resection of varying portions of ascending aorta. From January 1995 to July 2009, a total of 1688 patients had AVR without replacement or repair of the mitral valve:

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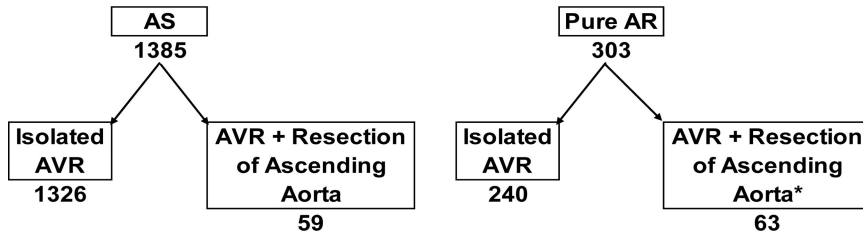
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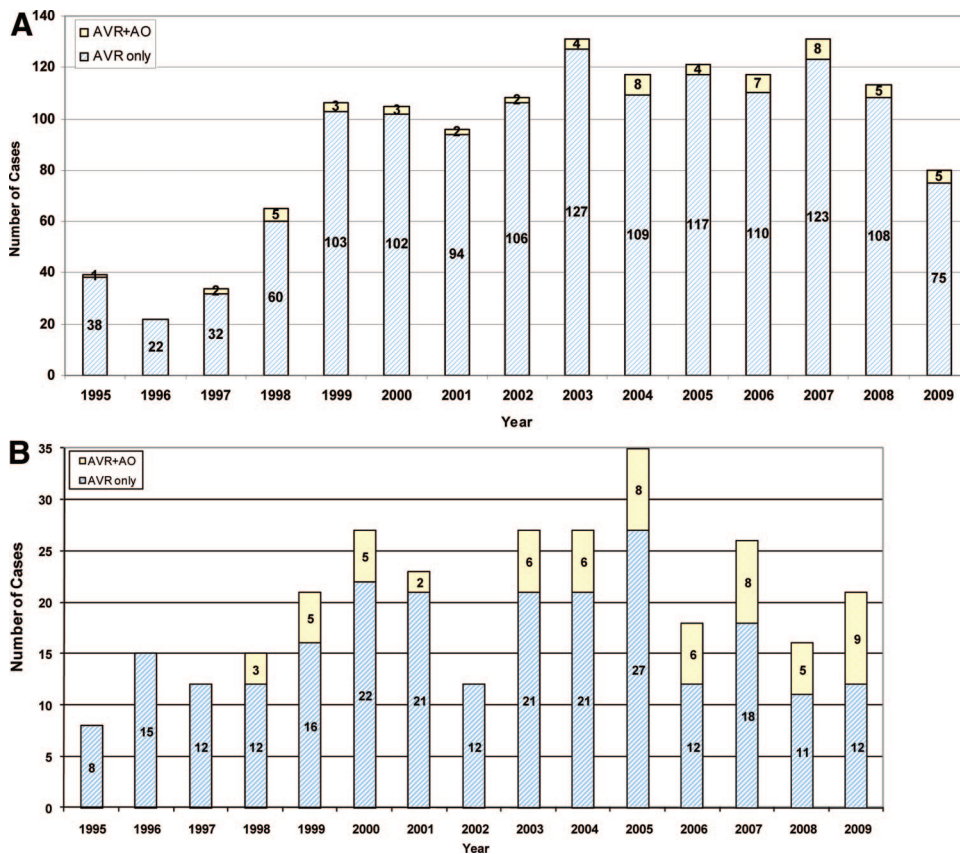
**Figure 1.** Numbers of patients with aortic stenosis (AS) or pure aortic regurgitation (AR) having aortic valve replacement (AVR) with or without resection of ascending aorta at Baylor University Medical Center in Dallas from 1995 through July 2009. \*Excludes patients with acute aortic dissection and patients with aortitis (syphilis or giant-cell aortitis).

1385 (82%) had AS ( $\pm$  AR) and 303 (18%) had pure AR (no element of stenosis) (Figure 1). Of the 1385 patients having AVR for AS unassociated with mitral valve disease, 1326 (96%) had no operative resection of the ascending aorta, and the other 59 had portions of a dilated ( $>4.5$  cm in diameter) ascending aorta excised. Of the 303 patients having AVR for pure AR, 240 (79%) had no operative resection of ascending aorta and 63 (21%) had portions of a dilated ( $>4.5$  cm) ascending aorta resected. Patients having resection of the ascending aorta for aneurysm without AVR ( $n=67$ ) and patients with aortitis (syphilis or giant-cell aortitis) and acute dissection involving the ascending aorta were not included in these numbers. The frequency of resection of the ascending aorta in the patients with AS and pure AR during each year of the study is shown in Figure 2. The present study is limited to the 122 patients who had AVR and resection of portions of the ascending aorta for aneurysm: 59 had AS and 63 had pure AR.

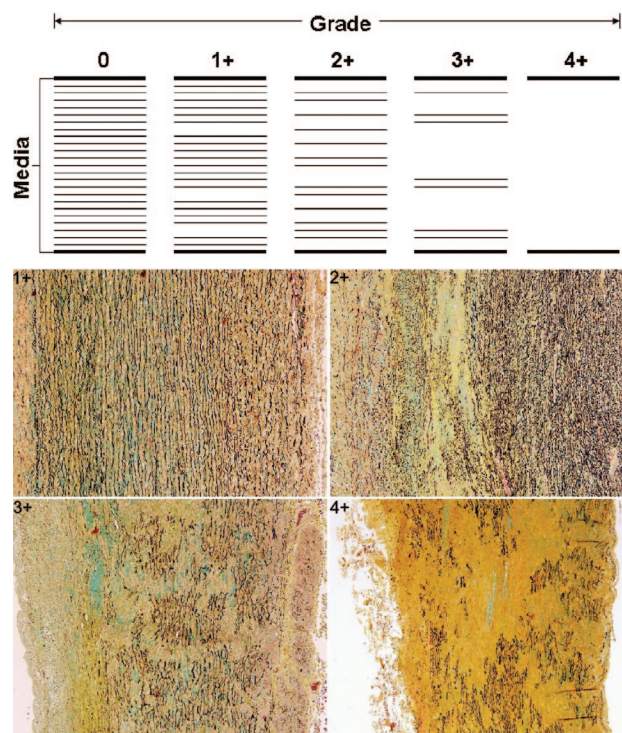
All operatively excised aortic valves and ascending aortas were examined and described. All aortic valves and all portions of ascending aorta excised were weighed (by W.C.R.), and many of them were photographed.<sup>18</sup> Histological sections were prepared on all aortas: at least one paraffin section was stained by hematoxylin-eosin and another was stained by the Movat method. All histological

sections were examined (by W.C.R.) initially to prepare the surgical report, and later, all together, as part of the present study. The total lengths in centimeters of the sections of aorta on each Movat-stained slide were measured and recorded. The degree of loss of elastic fibers in the aortic media from examination of the Movat-stained slides was graded 0 to 4+: grade 0 or 1+ represented no loss or minimal loss or mild fragmentation of elastic fibers; grade 4+ represented complete loss of elastic fibers in some full-thickness portions of media; grades 2 and 3 were intermediate (Figure 3).

The ascending aortas in 19 necropsy cases were selected to serve as controls for this study. None had cardiac valve disease or dilated ascending aortas. The 19 patients ranged in age from 28 to 82 years (mean: 61 years); 10 were women and 9 were men. Twelve had died of cardiac causes (coronary artery disease events in 10; amyloidosis in 1, and lymphocytic myocarditis in 1), and 7 had died of noncardiac and nonvascular causes. Sections of ascending aorta, both perpendicular to the long axis and parallel to it, were prepared from each control subject. In each of the 19 cases, one section was stained by hematoxylin-eosin, another by Movat, and another by elastic van Gieson methods. The lengths of the aorta examined histologically were measured in centimeters.



**Figure 2.** A, Numbers of patients with aortic stenosis having aortic valve replacement (AVR) with and without resection of the ascending aorta. B, Numbers of patients with pure aortic regurgitation having AVR with and without resection of the ascending aorta during each year of the study. The year 2009 included only 7 months; all others were 12 months. AO indicates aorta.



**Figure 3.** Diagram showing the grading system used in the study. Top, Diagram showing the zero to 4+ loss of medial elastic fibers. The top dark line represents the internal elastic membrane and the bottom dark line, the external elastic membrane. The elastic fibers in the media are represented by the lighter lines (see text for explanation). The photographs, each  $\times 100$  and stained by Movat, show medial elastic fiber loss (EFL) 1+ (middle left) to 4+ (lower right).

The clinical records, including admission note and/or discharge summary, echocardiographic and cardiac catheterization reports, and operative records, were sought from the patients' medical charts and/or from the Baylor University Medical Center Apollo cardiovascular database (Apollo Advance C/S version 4.2.13, LUMEDX Corp, Oakland, CA).

Excluded from this study were (1) patients with AR secondary to aortitis (usually syphilis) and those with acute aortic dissection, (2) patients who had had a previous cardiac operation or previous aortotomy, (3) patients who had had a Ross procedure performed, (4) patients who had mitral valve replacement or repair in addition to AVR and ascending aortic replacement or aortoplasty, (5) patients  $\leq 20$  years of age, and (6) patients with active infective endocarditis.

### Statistical Analysis

Descriptive statistics (percentage, mean, and standard deviation), crude comparisons based on  $\chi^2$  statistics, and plots were used to describe the patient cohort. In addition, crude odds ratios and 95% confidence intervals were estimated to describe the association between loss of medial elastic fibers (2+, 3+, or 4+) and the type of dysfunction of the aortic valve (AS versus pure AR) in the 96 patients with congenitally malformed aortic valves and in 19 healthy controls (necropsy subjects with grossly normal ascending aortas and normal aortic valves). Computationally, loss of medial elastic fibers was collapsed into two clinically relevant categories: (1) no or minimal loss of elastic fibers (grade 0 or 1+ representing no loss or minimal loss or mild fragmentation of elastic fibers), and (2) loss of elastic fibers (grade 2+, 3+, or 4+ representing a significant loss of elastic fibers in some portions of media). All analyses were done using the SAS 9.2 (SAS Institute Inc., Cary, NC) and R (R Foundation for Statistical Computing, Vienna, Austria).

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

### Results

Findings in the 122 patients are summarized in the Table and Figure 4. A qualitative comparison of the degree of loss of medial elastic fibers at the initial examination of the Movat-stained sections with the reexamination of the Movat-stained sections showed only minimal discrepancies: some cases called normal at the initial examination were occasionally called 1+ on reexamination or vice versa; sections classified as 2+ or 3+ or 4+ initially were classified similarly on reexamination.

### Control Subjects

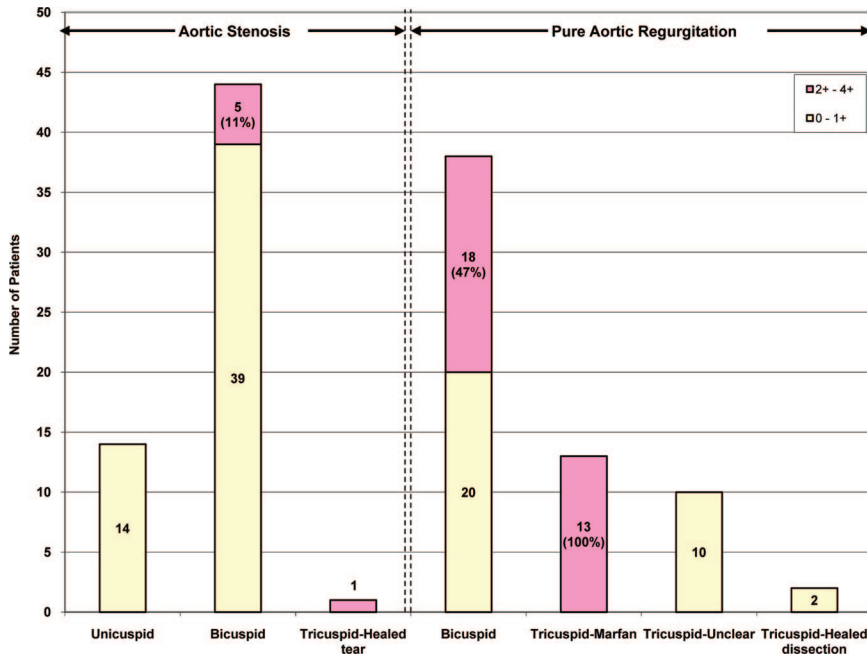
Examination of the Movat- and elastic van Gieson-stained sections of aorta in the 19 control subjects disclosed no

**Table. Ascending Aortic Replacement or Aortoplasty for Aneurysm (4.5 to 7.5 cm) with Simultaneous Aortic Valve Replacement for Either Aortic Stenosis or for Pure Aortic Regurgitation**

Aortic Valve Structure	Patients, No. (%)	Age (Years), Range (Mean)	Sex		Weights (g) of Aortic Valve, Range (Mean±SD)	Weights (g) of Ascending Aorta, Range (Mean±SD)	Centimeters of Ascending Aorta Examined	Loss of Medial Elastic Fibers in Ascending Aorta					Concomitant Coronary Artery Bypass Grafting
			M	F				0	1+	2+	3+	4+	
Aortic Stenosis													
Unicuspid	14 (24)	41–70 (50)	10	4	0.97–8.00 (3.48±1.84)	1.0–23.0 (12.3±6.0)	7–22 (15)	8	6	0	0	0	1
Bicuspid	44 (75)	44–78 (63)	37	7	1.16–17.9 (4.10±3.15)	0.5–31.4 (13.7±8.6)	2–24 (14)	18	21	4	1	0	14
Tricuspid	1 (1)	78	1	0	2.16	11.2	25	0	0	0	0	1	0
								26	27	4	1	1	
SUBTOTAL	59	41–80 (61)	48	11	0.97–17.85 (3.91±2.86)	0.5–31.4 (13.3±8.0)	2–25 (13)	53 (90%)		6 (10%)			15
Pure Aortic Regurgitation													
Unicuspid	0	...	...	...	...	...	...	...	...	...	...	...	...
Bicuspid	38 (60)	22–72 (53)	33	5	0.52–2.38 (1.23±0.42)	1.1–22.6 (13.1±5.4)	4–23 (14)	9	11	4	13	1	8
Tricuspid													
Marfan-like	13 (21)	34–71 (56)	7	6	0.35–1.01 (0.80±0.20)	1.2–26.5 (13.0±7.5)	5–30 (16)	0	0	0	5	8	4
Unclear	10 (16)	52–83 (68)	9	1	0.55–1.82 (0.88±0.37)	2.2–30.7 (11.8±9.1)	4–28 (14)	2	8	0	0	0	2
Healed dissection	2 (3)	54, 79	1	1	0.35, 0.93	2.89, –	15, 21	2	...	...	...	...	0
								13	19	4	18	9	
SUBTOTAL	63	22–83 (57)	50	13	0.35–2.38 (1.07±0.42)	1.1–30.7 (12.7±6.5)	4–30 (14)	32 (51%)		31 (49%)			14

F indicates female; M, male; SD, standard deviation.





**Figure 4.** Frequency of 0 to 1+ and 2+ to 4+ loss of aortic medial elastic fibers among the 7 patient groups with aortic stenosis or pure aortic regurgitation.

discrepancies in the degree of medial EFL or the lack thereof between the 2 stains in any subject (Figure 5). The degree of EFL in all 19 control subjects was either zero or 1+. Specifically, no subject had 2+, 3+, or 4+ EFL. The numbers of centimeters of ascending aorta examined from the Movat-stained sections ranged from 4 to 16 cm (mean, 10).

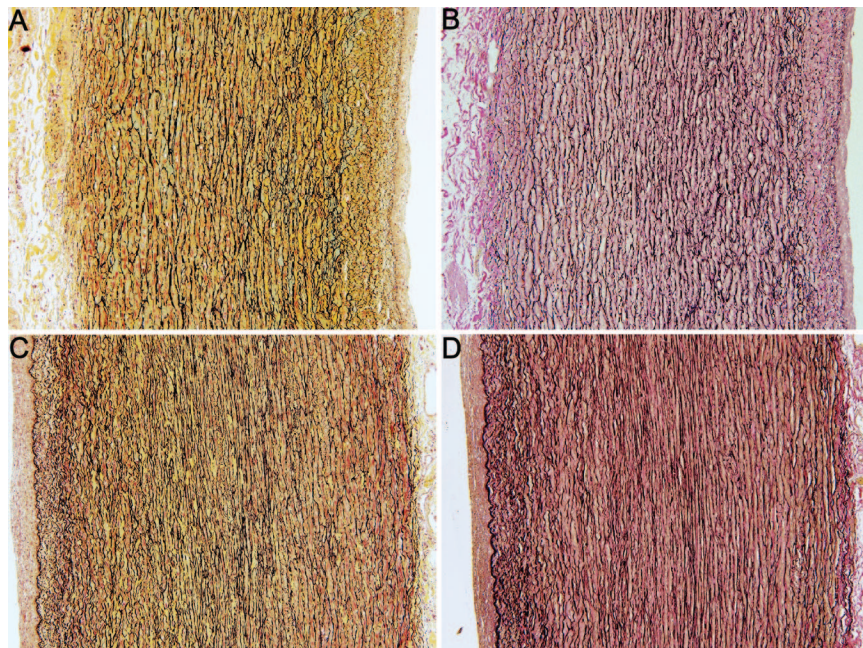
### Aortic Stenosis

Of the 59 patients with AS, 58 had a congenitally malformed aortic valve: unicuspid in 14 (unicommissural in 13 and acommisural in 1<sup>19,20</sup>) (Figure 6), 44 (75%) had a congenitally bicuspid aortic valve (Figure 6),<sup>21</sup> and one (1%), a tricuspid aortic valve. The later patient had a healed tear without dissection involving the ascending aorta. The unicus-

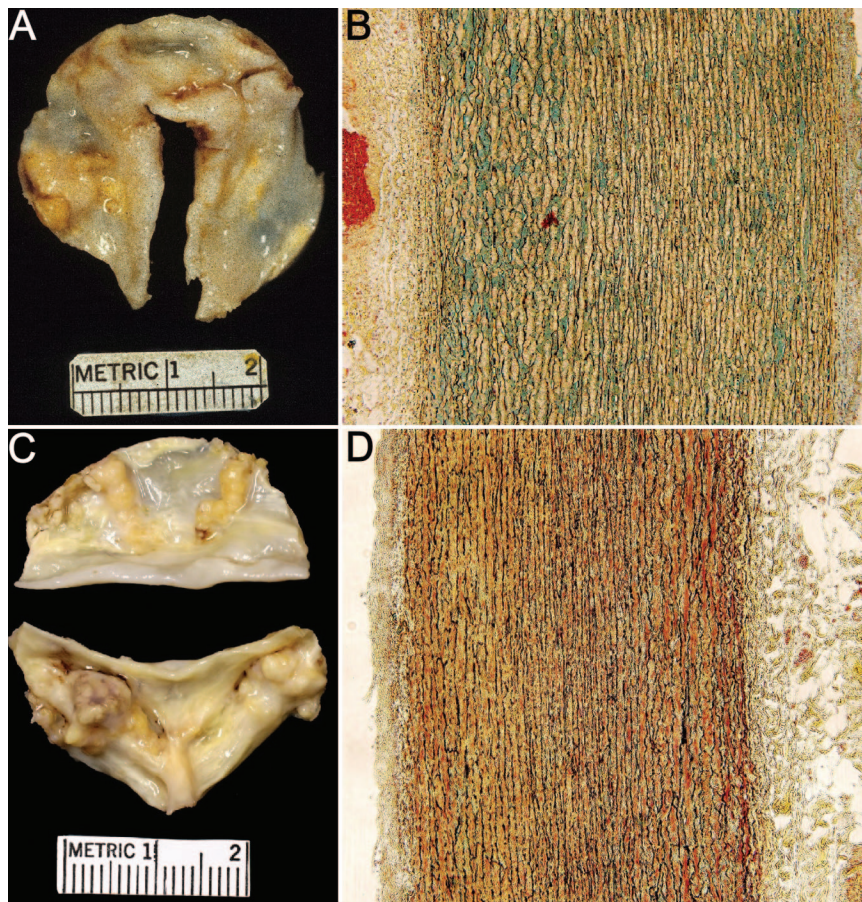
pid aortic valves were heavier than the bicuspid valves, which were heavier than the tricuspid valves in both men and women.<sup>18</sup>

At cardiac catheterization (34 patients), the peak systolic pressure gradient between left ventricle and aorta ranged from 11 to 125 mm Hg (average,  $48 \pm 31$  mm Hg), the cardiac indexes, from 0.87 to  $3.47 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$  (average,  $2.71 \pm 0.71 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ), and the aortic valve areas, from 0.47 to  $1.27 \text{ cm}^2$  (average,  $0.79 \pm 0.23 \text{ cm}^2$ ).

The largest diameter of ascending aorta preoperatively determined by echocardiography, computed tomography, or MRI in the 59 patients ranged from 4.5 to 6.7 cm (mean,  $5.3 \pm 0.5$  cm): these diameters were larger in the men than in the women (mean, 5.4 cm versus mean, 4.9 cm). The weights



**Figure 5.** Photograph of normal aorta in a 42-year-old woman (A, B) and in a 74-year-old man (C, D). A and C were stained by the Movat method ( $\times 100$ ) and C and D, by the elastic van Gieson method ( $\times 100$ ).



**Figure 6.** Photograph of an operatively excised unicommissural unicuspid stenotic (and regurgitant) aortic valve (A) and histological section (B) of the histologically normal aorta in a 41-year-old woman. Photograph of operatively excised congenitally bicuspid stenotic aortic valve (C) and histological section (D) of ascending aorta in a 77-year-old man showing 1+/4+ loss of medial elastic fibers. Both B and D are Movat stains,  $\times 100$ .

of the operatively excised ascending aortas ranged from 0.5 to 31.4 g (mean,  $13.3 \pm 8.0$  g; median, 13.6 g). In 40 (68%) of the 59 patients, the operatively excised portion of aorta was  $>10$  g. The ascending aorta was replaced in 49 (83%) of the 59 patients and in these patients the excised aortas ranged from 0.5 to 31.4 g (mean,  $15.8 \pm 6.6$  g; median, 15.4 g); in the other 10 patients the ascending aorta was not replaced but made smaller by excising a longitudinal portion of it (“tailoring”). The excised portions of aortas ranged from 0.6 to 6.3 g (mean,  $2.2 \pm 2.1$  g; median, 1.1 g). The maximal diameter of ascending aorta was similar in the 49 patients having replacement and in the 10 having only “tailoring” of the ascending aorta ( $5.4 \pm 0.5$  cm versus  $5.1 \pm 0.5$  cm). The lengths of the ascending aorta examined in the 59 patients ranged from 2 to 24 cm (mean, 13 cm). No section had inflammatory cells in the aortic wall. (The Movat method stains the elastic fibers black, making their absence and their presence easily discernible.) In 53 (90%) of the 59 patients, the medial elastic fibers were normal (grade 0) or only minimally decreased in number (grade 1); in 4 patients (7%), the loss of medial elastic fibers was grade 2, and in 2 patients (3%), either grade 3 or 4+.

During the 14 years that the 59 patients underwent operation, 8 (14%) have died: 3 early (days 1, 2, and 12 postoperatively) and the other 5 from 276 to 1939 days (mean, 1168 days = 3.2 years) postoperatively. Of these 8 patients, 4 were among the 15 who had simultaneous coronary artery bypass grafting. Their ages at operation ranged from 59 to 77 years

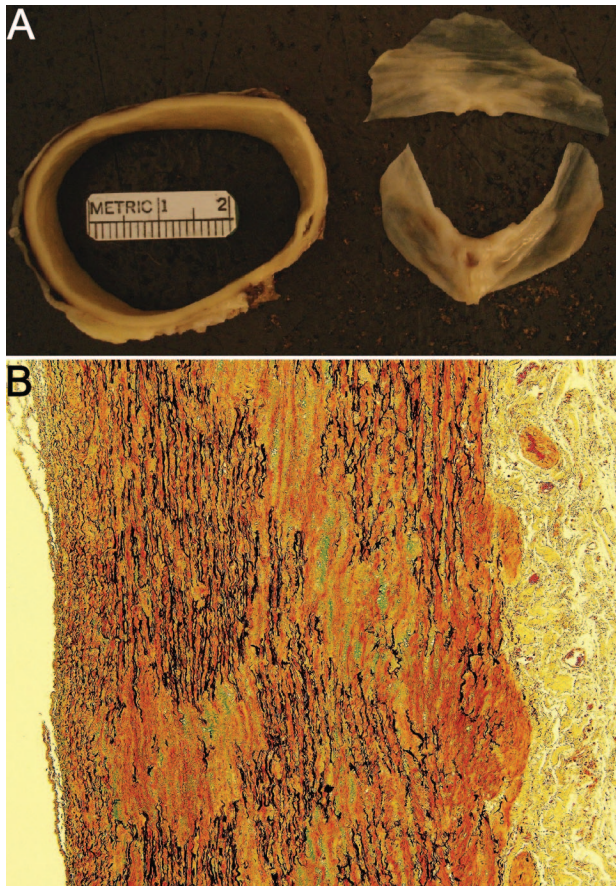
(mean, 67 years) and their ages at death ranged from 59 to 81 years (mean, 70 years). All 8 had bicuspid aortic valves and, of them, 7 had replacement of the ascending aorta with a graft and 1 had aortoplasty. The aortic valve was replaced with a bioprosthesis in 27 patients, a mechanical prosthesis in 29, and a homograft in 3.

### Pure Aortic Regurgitation

These 63 patients were divided into 2 major groups: (1) those with congenitally bicuspid aortic valves, 38 patients (60%), and (2) those with tricuspid aortic valves, 25 patients (40%). Cardiac catheterization (22 patients) disclosed that the peak left ventricular systolic pressures ranged from 110 to 182 mm Hg (average,  $132 \pm 20$  mm Hg); the simultaneous peak aortic systolic pressures, from 112 to 176 mm Hg (mean,  $133 \pm 19$  mm Hg); the aortic end-diastolic pressures, from 52 to 90 mm Hg (average,  $69 \pm 9$  mm Hg), and the cardiac indexes, from  $1.74$  to  $3.79 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$  (average,  $2.84 \pm 0.77 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ). All patients had peak systolic pressure differences between left ventricle and aorta  $<10$  mm Hg. Of the 63 patients with pure AR, 59 (94%) had resection of much of the ascending aorta and a graft was inserted; the other 4 patients had small portions of ascending aorta excised (1.2 to 5.2 g [mean, 2.9 g]) and the aorta was “tailored” to a smaller size.

Of the 38 patients with bicuspid aortic valves (Figure 7), the maximal diameter of the ascending aorta ranged from 4.5 to 7.5 cm (mean,  $5.4 \pm 0.6$  cm). The loss of medial elastic





**Figure 7.** A, Photograph of operatively excised purely regurgitant congenitally bicuspid aortic valve and portion of resected aorta in a 54-year-old man. B, Histological section of ascending aorta (maximal diameter=6.7 cm) shows a 3+/4+ loss of medial elastic fibers (Movat stain,  $\times 100$ ).

fibers was zero or 1+ in 20 patients (53%); 2+ in 4 patients (10%), and 3+ or 4+ in 14 patients (37%). Comparison of the 20 patients with zero or 1+ loss of aortic medial elastic fibers with the 18 patients with 2+ to 4+ loss showed no significant differences in ages ( $54 \pm 9$  years versus  $52 \pm 13$  years); sex (men 16/20 [80%] versus men 17/18 [94%]); the presence of peak systolic aortic pressure  $>140$  mm Hg (12 versus 13 patients); average aortic peak systolic pressure ( $136 \pm 23$  mm Hg versus  $130 \pm 16$  mm Hg); aortic valve weight ( $1.09 \pm 0.32$  g versus  $1.39 \pm 0.47$  g); weight of excised aorta ( $11.47 \pm 5.72$  g versus  $14.84 \pm 4.63$  g), or centimeters of ascending aorta examined histologically ( $14.6 \pm 5.79$  cm versus  $13.2 \pm 3.49$  cm).

Of the 25 patients with tricuspid aortic valves, 13 (52%) had physical features of the Marfan syndrome or at least characteristic gross and histological features of this syndrome in the ascending aorta (forme fruste variety).<sup>22</sup> All 13 patients had either 3+ or 4+ loss of medial elastic fibers. These aortas were focally thinner than normal, and focal aortic medial tears without dissection were present in 2 of these 13 patients. In the other 10 patients with tricuspid aortic valves, the cause of the aneurysmal dilatation of ascending aorta was unclear. All 10 patients had either no loss of medial elastic fibers or only 1+ loss. Two other patients with tricuspid aortic valves

had healed aortic dissection with tears in the ascending aorta; histological study in them disclosed no loss of medial elastic fibers.

During the 11.4 years that the 63 patients underwent operation, 6 (10%) died: one on day 16 postoperatively and the other 5 from 434 to 2474 days (mean, 1143 days=3.13 years) postoperatively. Of these 6 patients, 4 were among the 14 who had simultaneous coronary artery bypass grafting. Their ages at operation ranged from 47 to 81 years (mean, 66 years) and their ages at death ranged from 54 to 85 years (mean, 69 years). Four of the 6 had tricuspid and 2 had bicuspid aortic valves. All 6 had replacement of the ascending aorta with a graft. The aortic valve was replaced with a bioprosthesis in 20 patients, a mechanical prosthesis in 42, and an allograft in 1.

### Unadjusted Comparison Among Patients with Congenitally Malformed Valves of Loss of Elastic Fibers Between Valve Groups

The 38 patients with pure AR and congenitally bicuspid valves had a much greater likelihood of significant (2+ to 4+) aortic medial EFL than the 58 patients with congenitally malformed aortic valves and AS (unadjusted OR: 8.78; 95%CI: 2.95, 28.13) (Figure 4). Moreover, patients with pure AR and congenitally bicuspid valves were 35 times more likely (unadjusted OR: 35.19; 95%CI: 1.98, 624.57) to have significant (2+ to 4+) loss of medial elastic fibers than normal controls. No significant differences in EFL were observed between the patients with AS and the control subjects (unadjusted OR: 4.01; 95%CI: 0.21, 75.92).

### Discussion

The present study focused on 122 patients with either AS (59 patients) or pure AR (63 patients) and an aneurysmally dilated ascending aorta ( $\geq 4.5$  cm), and all underwent AVR and resection of portions of ascending aorta. The purpose was to study histologically the structure of the aortic media in an attempt to determine whether replacement of the ascending aorta was actually warranted or if "tailoring" (reduction aortoplasty) would have been adequate. To help answer the question the patients were divided into 2 groups: those with AS ( $\pm$ AR) and those with pure AR (no element of AS). The method chosen to study the aorta was by elastic tissue stains such that the medial elastic fibers are blackened permitting their loss or lack thereof to be easily discernible and the findings reproducible.

The major and surprising finding of this study was that 90% (53 of 59 patients) of the patients with AS had no loss or only minimal (1+) loss of medial elastic fibers and 10% (6 of 59 patients) had a significant (defined as 2+ to 4+/4+) loss. Four of the latter 6 patients, however, had only a 2+ loss of medial elastic fibers and only 1 each a loss of 3+ or 4+. Additionally, all but one of the 59 AS patients had a congenitally malformed valve (either unicuspid or bicuspid). These findings support the view that patients with AS and an aneurysmally dilated ascending aorta infrequently need to have the aorta replaced with a graft.

In contrast to the patients with AS, those with pure AR had a much greater chance (nearly 50%) of having significant loss

of medial elastic fibers. Among the pure AR patients, 60% (38 of 63) had a congenitally bicuspid aortic valve and 47% (18 of 38) of them had a significant loss of medial elastic fibers. In contrast to the virtual absence (only 1 of 59 patients) of tricuspid aortic valves in the patients with AS, 40% (25 of 63) of the patients with pure AR had a tricuspid aortic valve. Among them, however, only those with the Marfan syndrome (characterized by dilatation of the sinuses of Valsalva as well as dilatation of at least the proximal tubular portion of ascending aorta)<sup>22</sup> had severe loss (100%) (13 of 13 patients) of medial elastic fibers. The 10 patients with tricuspid valves in whom the cause of the ascending aortic dilatation was unclear or undetermined had either no loss of medial elastic fibers or only 1+ loss (Such minimal loss may be simply related to the expected loss with aging.<sup>23</sup>). The remaining 2 patients with tricuspid aortic valves had healed aortic dissection but neither patient had detectable loss of medial elastic fibers. Thus, among the patients with pure AR, the ascending aorta clearly needs to be replaced if the patient has the Marfan syndrome or a forme fruste variety of it, but probably not so if the dilatation of the ascending aorta is limited to its tubular portion in the setting of a tricuspid aortic valve and patients with aortitis (giant cell or syphilis<sup>24</sup>) and acute dissection are excluded.

Although many published reports have appeared in the past 15 years advocating either replacement of or tailoring of aneurysmally dilated ascending aortas associated with aortic valve dysfunction,<sup>12–17</sup> none have divided such patients according to the type of aortic valve dysfunction—either AS or pure AR—to determine proper therapy. The move to replace or tailor aneurysmally dilated ascending aortas is an occurrence that has taken place primarily in the past 15 or so years. Replacement of the aneurysmally dilated aorta in patients with AS—or even pure AR—was uncommon in the first 30 years (1960–1990) of aortic valve surgery. The present report supports the view that patients with AS and aneurysmally dilated ascending aortas infrequently need to have the aorta replaced, and only about half of the patients with pure AR, assuming exclusion of patients with aortitis and aortic dissection, need the aorta replaced.

Why did the study of the histological sections of ascending aorta focus only on medial elastic fibers when the wall of the ascending aorta also contains smooth-muscle cells, collagen, and some mucoid material? The reason is that examination of the elastic fiber structure is easily discernible and interpretation is highly reproducible. The grading of the degree of medial EFL when examined initially (when preparing the surgical pathology report) and then again altogether when reexamining the sections for the present study showed essentially no discordant interpretations. A few patients considered to have zero EFL initially were graded 1+ on reexamination and vice versa; all cases graded 2+, 3+, or 4+ initially were graded similarly on reexamination. When medial elastic fibers are lost, it appears that they are replaced by fibrous tissue and by small deposits of mucoid material, suggesting that the medial elastic fibers serve as a good marker of other changes in the aortic media.

Although numerous publications have appeared discussing patients with aortic valve disease associated with aneurysmal

dilatation of the ascending aorta, few have reported findings from histological examination of the operatively excised aorta, and none have divided the patients into those with pure AR as opposed to patients with AS. Several investigators<sup>25–29</sup> have used multiple histological features (fibrosis, atherosclerosis, medionecrosis, cystic medial necrosis, loss or disorientation or apoptosis of smooth-muscle cells, elastic fiber fragmentation or disruption or distances between fibers, inflammation, pooling of mucoid material) to describe the media of ascending aorta in patients with normal or dysfunctioning bicuspid and tricuspid aortic valves. With one exception,<sup>29</sup> these investigators found more aortic wall alterations in the patients with bicuspid compared with those with tricuspid aortic valves. We believe that trying to characterize the condition of the aortic wall in patients with medial disease with use of multiple criteria is too complex and not reproducible and that is why we limited our study to the degree (if any) of medial EFL.

The positive features of the present study are the following: (1) it was the first study to divide patients with aneurysm of the ascending aorta by type of aortic valve dysfunction—either AS or pure AR; (2) it described ascending aortic structure in patients with unicuspid aortic valves for the first time; (3) it was the first report where all valves and aortas were examined and classified both initially and all together later by the same investigator (W.C.R.); (4) it provided weights of all operatively excised aortic valves and aortas; (5) it included the number of centimeters of aorta examined histologically for the first time; (6) it used a system for grading the aortas (medial EFL on elastic tissue stain) that was highly reproducible, and (7) a relatively long follow-up after the operation was available.

The present study has limitations: (1) the amount of excised aorta varied, from 2 to 24 cm (mean, 13) and (2) hemodynamic data and specifically the transvalvular pressure gradients were not available in all of the AS patients; (3) given the relatively small cohort size the analysis of the association between loss of medial elastic fibers (2+, 3+, or 4+) and the type of valve, dysfunction may not have accounted for potential confounders. The weights of the operatively excised aortic valves, however, were available, and the weights correlate well with the peak systolic transvalvular pressure gradients.<sup>30</sup>

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## Disclosures

None.

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## CLINICAL PERSPECTIVE

There is debate whether an aneurysmal ascending aorta should be replaced when associated with a dysfunctioning aortic valve that is to be replaced. We examined this issue by dividing the patients by type of aortic valve dysfunction—either aortic stenosis (AS) or pure aortic regurgitation (AR)—something not done previously. Of the 59 AS patients, 58 (98%) had a congenitally malformed valve and 53 (90%) had only a zero or 1+ aortic medial elastic fiber loss (graded 0 to 4+). In contrast, of the 63 pure AR patients, 38 had a bicuspid valve and 20 of them had zero or 1+ EFL and 18 had 2+ to 4+ EFL; of the 25 with pure AR and tricuspid aortic valves, all 13 with the Marfan syndrome had severe (3+ or 4+) EFL and the 12 without this syndrome had either zero or 1+ EFL. These data strongly suggest that when ascending aortic aneurysm is associated with aortic valve disease, the type of valve dysfunction—AS or pure AR—is very helpful in predicting aortic medial elastic fiber loss.