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## Comparison of eight prosthetic aortic valves in a cadaver model

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Drs Kresh, Entwistle, Youdelman, Wechsler, and  
Hirose (left to right)

**Objectives:** Proper valve selection is critical to ensure appropriate valve replacement for patients, because implantation of a small valve might place the patient at risk for persistent gradients. Labeled valve size is not the same as millimeter measure of prosthetic valve diameters or the annulus into which it will fit. Studies that use the labeled valve size in lieu of actual measured diameter in millimeters to compare different valves might be misleading. Using human cadaver hearts, we sized the aortic annulus with 8 commonly used prosthetic aortic valve sizers and compared the valves using geometric orifice area. This novel method for comparing prosthetic valves allowed us to evaluate multiple valves for implantation into the same annulus.

**Methods:** Aortic annular area was determined in 66 cadavers. Valve sizers for 8 prosthetic valves were used to determine the appropriate valve for aortic valve replacement. Regression analyses were performed to compare the relationship between geometric orifice area and aortic annular area.

**Results:** Tissue valves had a larger orifice area for any annular size but were not different at small sizes. Supra-annular valves were larger than intra-annular valves for the small annulus, but this relationship was not uniform with increasing annular size.

**Conclusions:** Labeled valve size relates unpredictably to annular size and orifice area. No advantage in geometric orifice area could be demonstrated between these tissue valves at small annular sizes. Valves with the steepest slope on regression analysis might provide a larger benefit with upsizing with respect to geometric orifice area.

Valve selection is critical to ensure appropriate valve replacement for a given patient, because implantation of a valve that is too small places the patient at risk for persistent gradients.<sup>1-6</sup>

Labeled valve size is not the same as a millimeter measure of the prosthetic valve diameter or the aortic annulus into which it will fit.<sup>7-11</sup> Valve sizers are made slightly larger than the corresponding valve to avoid problems seating the valve after sutures have been placed. Studies that use the labeled valve size in lieu of the actual measured diameter in millimeters to compare different valves might be misleading.<sup>7</sup>

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**Abbreviations and Acronyms**

- AVR = aortic valve replacement
- EOA = effective orifice area
- GOA = geometric orifice area

Furthermore, there is some small variability in the construction of these valves that further adds to the difficulty in comparing different products.

A standard sizer that gives the actual measurement of the aortic annulus in calibrated 1-mm increments is not used in general practice. After echocardiographic estimation of valve size, the surgeon evaluates the aortic annulus in the operating room using sizers provided by the manufacturers. These manufacturer-provided sizers do not always share the shape of the aortic annulus or the prosthesis to be inserted and are intentionally made slightly larger than the corresponding valve to avoid problems with implantation once sutures have been placed. These factors can lead to implantation of a valve that might be inadequate to relieve valvular stenosis in the small aortic root, despite a labeled valve size that would indicate otherwise.

Patients with a small aortic root carry a risk of patient-prosthesis mismatch.<sup>1</sup> A larger valve can be placed into a small aortic root by performing an aortic root enlargement procedure.<sup>12,13</sup> However, this might increase operative mortality.<sup>14</sup> Although the clinical relevance of patient-prosthesis mismatch remains controversial,<sup>15-17</sup> a small valve might not completely relieve aortic stenosis, might maintain increased left ventricular workload, and might contribute to adverse patient outcomes.<sup>2-5</sup>

Using human cadaver hearts, we sized the aortic annulus for aortic valve replacement (AVR) with 8 commonly used prosthetic aortic valves and compared the valves on the basis of geometric orifice area (GOA). This novel method for comparing prosthetic valves allowed multiple valves to be evaluated on the same annulus.

**Materials and Methods**

Between January 1 and September 30, 2005, all deaths referred to the medical examiner in our institution were evaluated for the study. Cadavers were excluded from the study for previous valve surgery, assist device implantation, heart transplantation, advanced decay, or a delay of 2 hours or more after the heart was removed from the body. Postmortem examinations were performed by a pathologist and mortician in the department of pathology at our institution. The heart was removed from the chest and submerged in a cool bath until examination.

The heart was placed in a container, and the aorta was transected 2 cm above the sinotubular junction. The aorta was then transected just above the ostia of the coronary arteries in a horizontal plane. The degree of calcification of the aorta, the aortic valve cusps, and the aortic annulus was assessed. After removal of the valve cusps, the annulus was measured with cylindrical plastic sizers with 1-mm increments (standard sizer) to record true annular size. The annulus was defined as the narrowest area associated with the aortic root after removal of the cusps. Valve sizers corresponding to the 8 valves were then used to size each valve according to the instructions for use provided by the manufacturers. The corresponding valve size was then recorded, as appropriate, for AVR. After these measurements were taken, a postexperimental measurement using the standard sizer was taken to evaluate for annular stretch.

The valves in this study were 5 mechanical valves, including the CarboMedics Standard and Top Hat (CarboMedics, Austin, Tex), the ATS AP (ATS Medical, Minneapolis, Minn), and the St

**TABLE 1. Background characteristics of 66 study subjects**

Characteristic	No. (%) or mean ± SD	No. (%)	No. (%)
Male sex	33 (50%)		
Female sex	33 (50%)		
Age (y)	65 ± 16		
Race			
White	35 (53%)		
Black	25 (38%)		
Hispanic	3 (5%)		
Other	3 (5%)		
Weight (kg)	90.9 ± 29.5		
Body surface area (m <sup>2</sup> )	2.04 ± 0.36		
Heart weight (g)	537.7 ± 185.3		
Bicuspid valve	1 (1.5%)		
Degree of calcification	None to mild	Mild to moderate	Moderate to severe
Aortic calcification	51 (77%)	14 (21%)	1 (1.5%)
Leaflet calcification	50 (75%)	15 (22%)	1 (1.5%)
Annular calcification	45 (68%)	21 (31%)	0 (0.0%)

SD, Standard deviation.

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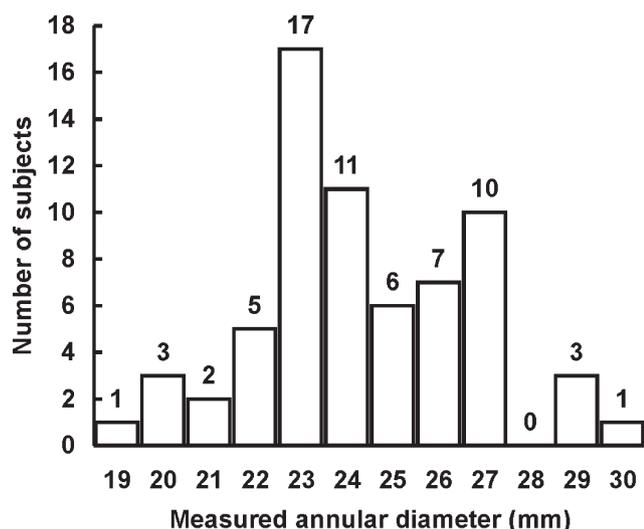


Figure 1. Number of subjects at each measured annular diameter (n = 66).

Jude Standard and Regent (St Jude Medical, St Paul, Minn), and 3 stented tissue valves, including the Carpentier–Edwards Perimount Pericardial Model 2700 and Perimount Magna Model 3000 (Edwards Lifescience, Irvine, Calif) and the Medtronic Mosaic Model 305 (Medtronic, Minneapolis, Minn). The Carbomedics Top Hat, ATS AP, and St Jude Regent valves are manufactured to be placed in a supra-annular position. The CarboMedics and St Jude Standard valves are designed for intra-annular placement.

The GOA of each valve was used for analysis by using values for GOA that were acquired from each company. Deviation of the labeled valve size from the measured annular size by using the standard sizer was calculated and analyzed with a paired *t* test. The relationship between GOA and measured annular size in each valve was analyzed by means of linear regression (PSI-Plot, Pearl River, NY). The data for the Carbomedics Top Hat for measured annular areas of 5.72 cm<sup>2</sup> (diameter, 27 mm) or larger was not included in the analysis because the largest available size is 27 (4 subjects were excluded from the analysis).

## Results

A total of 66 cadaver hearts (33 male and 33 female cadavers with a mean age of 65 ± 16 years) were studied (Table 1). Distribution of patients across measured annular size is shown in Figure 1. Deviation of the labeled valve size from the measured annular diameter is shown in Figure 2 for both mechanical valves (top) and bioprosthetic valves (bottom). Mechanical valves had significant differences in the labeled valve size from the measured annular diameter when comparing the products from different companies. (Figure 2, top). All mechanical valves except the CarboMedics Top Hat had labeled valve sizes smaller than the measured annular diameter into which that valve could be placed. All labeled valve sizes were statistically different from one

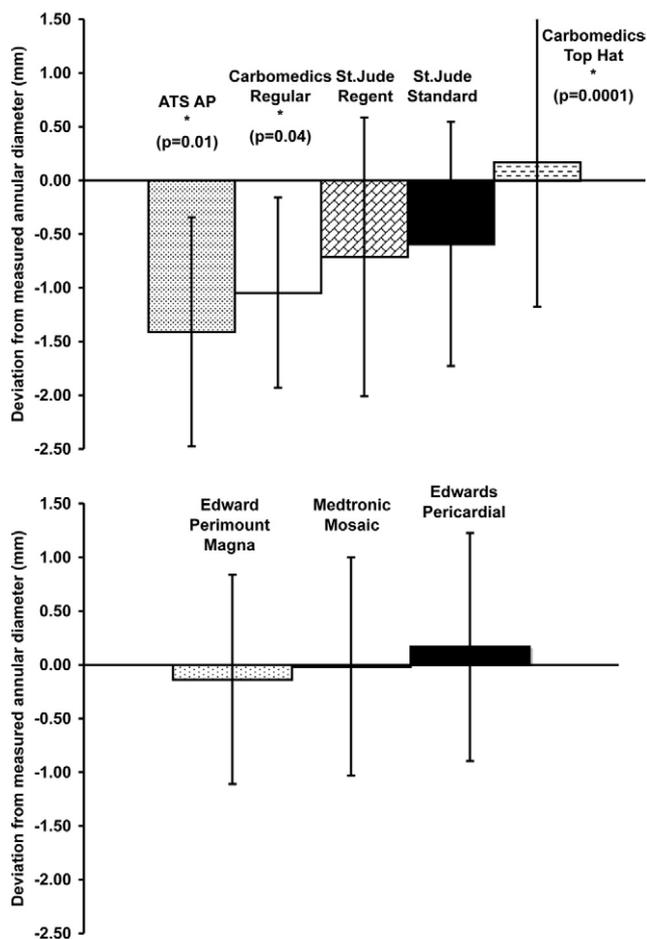
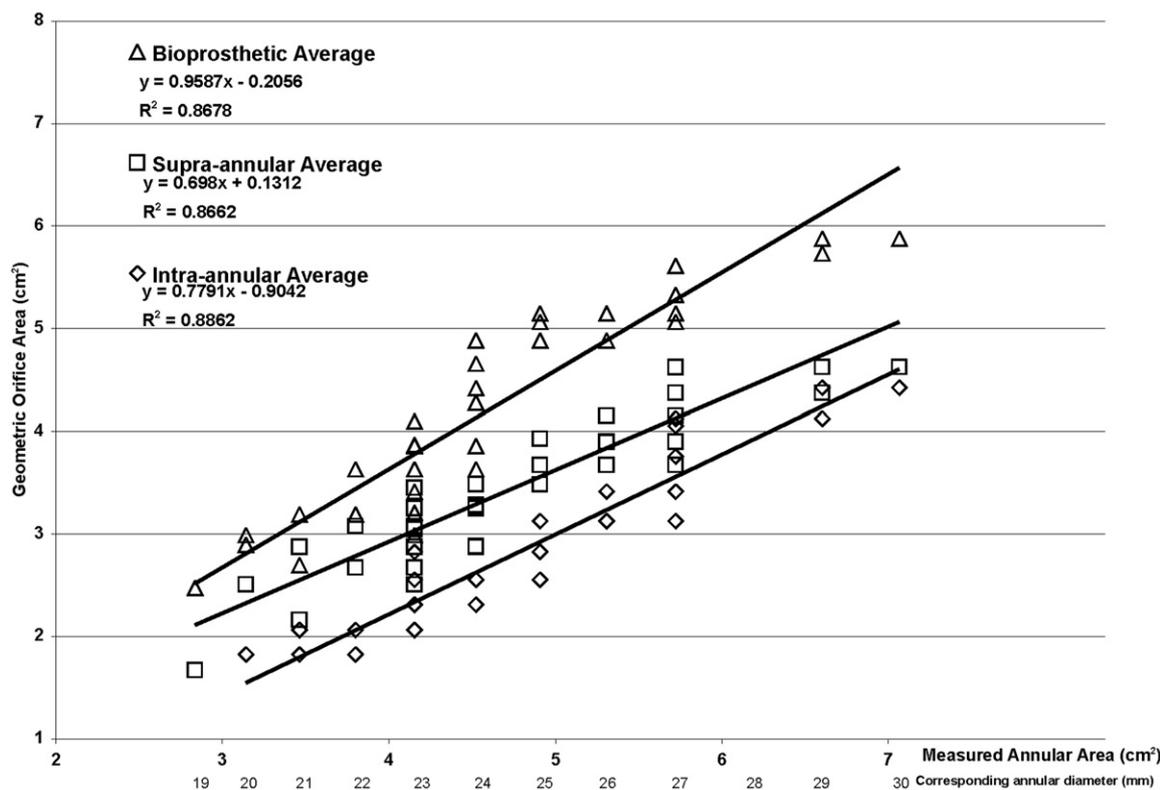


Figure 2. Mean deviation of number label from measured annular diameter with standard deviation error bars in 5 mechanical valves (top) and 3 stented tissue valves (bottom). Asterisks indicate statistically significant deviation from the number label compared with the measured annular diameter (n = 66).

another, with the exception of the relationship between the St Jude Standard and Regent ( $-0.59 \pm 1.14$  and  $-0.71 \pm 1.30$  cm, respectively). The 3 stented bioprosthetic valves demonstrated greater parity with the measured annular diameter than the mechanical valves (Figure 2, bottom). There was a small but significant difference between the Edwards Pericardial and the Magna ( $P = .017$ ).

Twenty-nine percent (19/66) of the specimens had an increase in annular size, as measured before and after the experimental protocol. There was a small but significant difference between average pre-experimental and post-experimental measured annular size ( $24.3 \pm 2.3$  and  $24.6 \pm 2.3$  mm diameter, respectively,  $P = .00003$ , and  $4.68 \pm 0.904$  and  $4.78 \pm 0.903$  cm<sup>2</sup> area, respectively,  $P = .00004$ ).

Grouping valves by type and implantation position, the bioprosthetic valves had a larger GOA compared with that



**Figure 3.** Regression analysis for the 3 different valve types: bioprosthetic, supra-annular mechanical, and intra-annular mechanical aortic valves (n = 66). Measured annular area is the largest standard size that could fit into the annulus (in square centimeters). Corresponding annular diameter is the diameter of this size in millimeters.

of the supra-annular mechanical valves, which had larger GOAs than those of the intra-annular mechanical valves (Figure 3). Regression equations for each prosthetic valve showing measured annular area versus GOA are shown in Figures 4 and 5. The data for measured annular sizes of greater than 27 mm were not included in the analysis for the CarboMedics Top Hat because the largest labeled valve size is 27, and therefore there would be no increase in GOA beyond 27 for the Top Hat, which would inappropriately skew the data.

There was no difference in GOA demonstrated for the 3 bioprosthetic valves in the small annular sizes (area, 2.83–3.46 cm<sup>2</sup>; diameter, 19–21 mm). With increasing size, the Magna had the greatest increase in GOA relative to measured annular area, translating into the steepest slope compared with the others. The Magna was followed by the Pericardial and then the Mosaic.

The intra-annular mechanical valves (CarboMedics and St Jude Standard valves) had nearly the same regression line. For the supra-annular valves, the St Jude Regent was larger than both the ATS AP and the CarboMedics Top Hat at smaller sizes. There was no difference between the AP

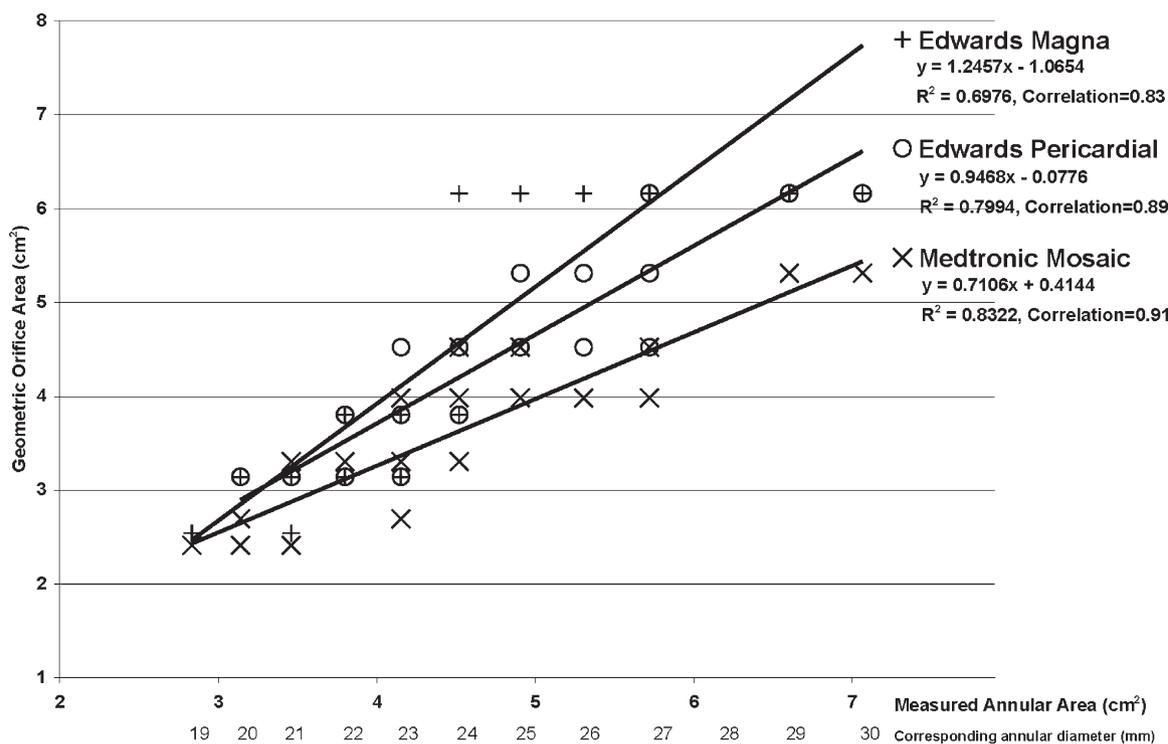
and the Top Hat at the smaller sizes, but the ATS AP had the steepest slope on regression analysis.

**Discussion**

Inconsistency of labeled valve sizes has been well documented and might contribute to misinformation and confusion.<sup>7-9</sup> In the worst-case scenario, patient-prosthesis mismatch<sup>1</sup> will occur and result in adverse patient outcomes.<sup>2-5</sup>

We used a novel method to compare prosthetic valves by using cadaver hearts as a surrogate for live human hearts. One difference in a cadaver heart compared with a patient undergoing AVR is the degree of aortic and valvular disease. In our study only a small number of patients had a similar degree of calcification compared with patients undergoing AVR for aortic stenosis (Table 1). However, a well-debrided aortic annulus should be similar to a normal cadaver annulus, making this a feasible model. This study could not be conducted in living subjects because of the potential for injury. Multiple passes with valve sizers and time added to an operation in which a patient is on cardiopulmonary bypass with the aorta crossclamped raise obvious ethical concerns.

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**Figure 4.** Relationship between the geometric orifice area and measured annular area in 3 stented bioprosthetic valves. Lines depict regression analysis (n = 66). Measured annular area is the largest standard size that could fit into the annulus (in square centimeters). Corresponding annular diameter is the diameter of this size in millimeters.

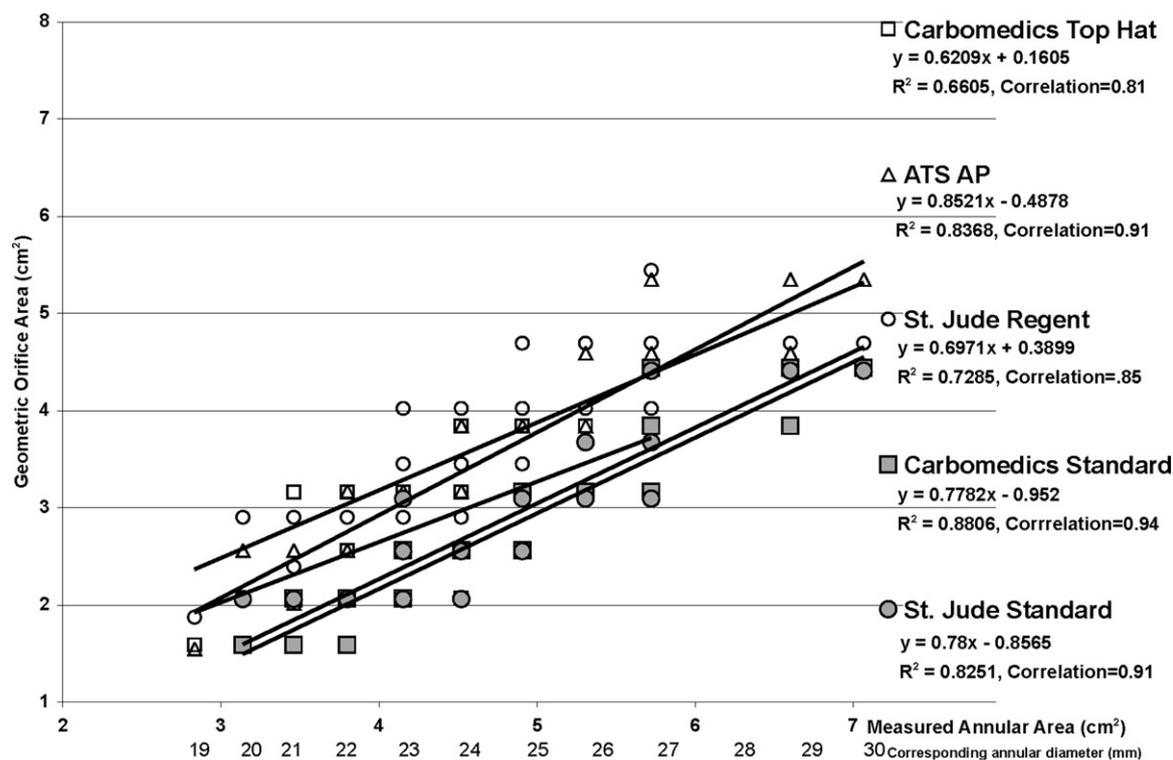
We sized the same aorta for every valve and used GOA to compare the valves, thereby removing the labeled valve size and hemodynamic variability from the comparison. GOA is a measure of the area of flow based on the internal diameter of a valve and is an appropriate tool for comparison between valves. Unlike effective orifice area (EOA), GOA does not require complex hemodynamic measurements and calculations that have inherent variability related to heart rate, blood pressure, ejection fraction, and echocardiographer variability. However, GOA does not take into account obstruction to flow caused by the leaflets in the bioprosthetic valves or the leaflet suspension apparatus, resistance to leaflet movement, and opening angle in the mechanical valves. The advantage of using GOA for analysis is that it allows for comparison between valves with a measurement that is reproducible and neither operator dependent nor hemodynamically variable. Large retrospective series studying orifice size<sup>18</sup> and others looking at EOA<sup>6,19</sup> have been conducted with results that do not demonstrate the superiority of one measurement methodology over the other. Multiple trials with EOA have shown that the incidence of echocardiographically determined patient–prosthesis mismatch is quite variable, estimated by Pibarot and Du-

mesnil<sup>20</sup> in a recent review to be 20% to 70%. This variability might, in itself, be due to the inherent variability in measuring EOA in patients who could actually have clinically similar orifice areas from a prosthetic valve.<sup>21</sup>

Implantability of prosthetic valves is multifactorial. Patient morphology, including the size of the aorta, sinotubular junction, and degree of calcification, is highly variable. A less pliable calcified aorta might not have enough flexibility to allow placement of an optimally sized valve in the appropriate position. This could require either undersizing the valve to get it seated on the annulus or performing an aortic root enlargement procedure. These choices place the patient at increased risk for patient-prosthesis mismatch on the one hand and increased morbidity and mortality from additional surgical intervention on the other.<sup>12-14</sup>

Our study demonstrates that the manufacturer-labeled valve size does not predictably correspond to the size of the annulus into which the valve will fit. This makes comparisons on the basis of labeled valve size alone inappropriate and further reinforces the need for standardization in sizing.

These data do not demonstrate an advantage in GOA of one bioprosthetic valve over another at smaller sizes. This is of interest considering that the GOAs of the Pericardial and



**Figure 5. Relationships between geometric orifice area and measured annular area in 5 mechanical valves. Lines depict regression analysis (n = 66). Measured annular area is the largest standard size that could fit into the annulus (in square centimeters). Corresponding annular diameter is the diameter of this size in millimeters.**

the Magna are the same, and the external diameter differences are in the construction of the sewing ring, resulting in a smaller external diameter for the Magna. This is similar to the CarboMedics Standard and Top Hat, except that these 2 valves are significantly different in construction and have very different sizes, explaining the results in this study.

The intra-annular mechanical valves were essentially the same, and the supra-annular valves always had larger GOAs at the smaller sizes, with more variability at the larger sizes. Differences in GOA between the supra-annular valves and the intra-annular valves support the use of supra-annular valves to maximize GOA in patients with a small aortic annulus. The larger GOA of the bioprosthetic valves as a whole over the supra-annular mechanical valves could also be exploited in patients at high risk for patient-prosthesis mismatch.

The data support the superiority in GOA of the St Jude Regent valve at smaller annular sizes. We did not demonstrate a difference between the ATS AP and the CarboMedics Top Hat valves at small sizes.

The slope of these regression lines might have clinical significance in determining the benefits of upsizing any particular valve in a patient. The steeper slope of the ATS AP valve compared with the CarboMedics Top Hat valve,

for example, would yield a greater increase in GOA if upsizing is done. Our findings show that valves with the steepest slope on regression analysis provide the greatest increase in GOA with increasing valve size.

Valve sizers have a built-in safety margin of 0.5 to 0.8 mm to minimize the chances of a prosthesis not seating correctly after sutures have been placed. The safety margin is required because of the manufacturer's tolerance of  $\pm 0.5$  mm for the external diameter, which varies as a result of construction of individual sewing rings. This safety margin might be exaggerated in supra-annular valves, the sizers of which are sometimes more bulky, making it more difficult to place them in a small or heavily calcified narrow aorta. The differences seen in these data reflect the ability or inability to place the valve sizer into the aortic annulus. During this study, it became apparent that sizing an aortic annulus for supra-annular valves was often hampered by the construction of the valve sizers and ability to navigate a narrow or calcified aorta. These sizers are provided by the manufacturers and recommended for use during implantation; however, some sizers do not bear a resemblance to their corresponding prosthetic valve or the true shape of the aortic annulus.

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Some surgeons deviate from the practice of using the valve-specific sizers to choose a valve size in the operating room. These surgeons might be taking advantage of the built-in safety margin, routinely upsizing and sometimes implanting a valve with a corresponding sizer that might not fit into the annulus.

The results of future endeavors, including transapical and transfemoral AVR, will ultimately be judged by the ability to implant a prosthesis that results in adequate relief of aortic stenosis. Determination of pressure and flow dynamics for the 8 valves in this study under controlled conditions with a pulse duplicator might further elucidate the valve-dependent relationship between GOA and EOA and help to guide future investigations into valve replacement strategies.

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