Preparatory Balloon Aortic Valvuloplasty
During Transcatheter Aortic Valve Implantation for Improved Valve Sizing

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Objectives This study sought to evaluate whether supra-aortic angiography during preparatory balloon aortic valvuloplasty (BAV) improves valve sizing.

Background Current recommendations for valve size selection are based on annular measurements by transesophageal echocardiography and computed tomography, but paravalvular aortic regurgitation (PAR) is a frequent problem.

Methods Data of 270 consecutive patients with either conventional sizing (group 1, n = 167) or balloon aortic valvuloplasty–based sizing (group 2, n = 103) were compared. PAR was graded angiographically and quantitatively using several hemodynamic indices.

Results PAR was observed in 113 patients of group 1 and 41 patients of group 2 (67.7% vs. 39.8%, p < 0.001). More than mild PAR was found in 24 (14.4%) patients of group 1 and 8 (7.8%) patients of group 2. According to pre-interventional imaging, 40 (39%) patients had a borderline annulus size, raising uncertainty regarding valve size selection. Balloon sizing resulted in selection of the bigger prosthesis in 30 (29%) and the smaller prosthesis in the remaining patients, and only 1 of these 40 patients had more than mild PAR. As predicted by the hemodynamic indices of PAR, mortality at 30 days and 1 year was less in group 2 than in group 1 (5.8% vs. 9%, p = 0.2 and 10.6% vs. 20%, p = 0.01).

Conclusions Preparatory balloon aortic valvuloplasty during transcatheter aortic valve implantation improves valve size selection, reduces the associated PAR, and increases survival in borderline cases. (J Am Coll Cardiol Intv 2013;6:965–71) © 2013 by the American College of Cardiology Foundation
Paravalvular aortic regurgitation (PAR) after transcatheter aortic valve implantation (TAVI) is associated with increased in-hospital mortality and unfavorable long-term outcome (1). Reduction of PAR by appropriate valve size selection is key. Current recommendations for valve size selection are based on transesophageal echocardiography, but multislice computed tomography (MSCT) is increasingly used (2). The choice of correct prosthesis size based on pre-interventional imaging of annular size can be difficult, and relevant PAR with negative impact on survival still results in up to 20% of cases (1–15). TAVI generally requires preparatory balloon aortic valvuloplasty (BAV) to facilitate the prosthesis implantation and expansion. Accurate annular sizing remains challenging and is a prerequisite for reduction of PAR and associated mortality. The purpose of the present study, therefore, was to evaluate whether supra-aortic angiography during BAV improves valve size selection and reduces PAR especially in cases with borderline annulus size.

## Methods

### Patient population.
Data from 270 consecutive high-risk patients with symptomatic aortic valve stenosis who underwent transfemoral or transsubclavian TAVI using the Medtronic CoreValve (MCV) (Medtronic Inc., Minneapolis, Minneapolis; n = 104 [38.5%]) or the Edwards Sapien (Edwards Lifesciences Inc., Irvine, California; n = 166 [61.5%]) bioprosthesis were analyzed: 167 patients underwent conventional sizing by echocardiography (conventional sizing) and were compared with 103 subsequent patients, in whom BAV was additionally used for valve size selection (balloon sizing). The decision for TAVI was made by an interdisciplinary heart team (10,12,16–19). TAVI procedures were performed according to standard techniques (16,18,19).

### Valve size selection.
There is an overlap between 2 different prosthesis sizes for both the MCV and the Edwards Sapien bioprostheses where valve size selection is left to the physician’s choice. For conventional sizing (group 1), the choice of the prosthetic size was based on pre-interventional transesophageal echocardiography (TEE) by an experienced investigator (2–10). For balloon sizing (group 2), patients underwent preparatory BAV (Z-MED balloon, NuMED, Inc., Hopkinton, New York or Edwards balloon) during TAVI. Supra-aortic angiography during BAV was used to measure the size of the aortic annulus. At the time of full balloon inflation, supra-aortic angiography was performed perpendicular to the native valve plane in a slight cranial/left anterior oblique projection over a 6-F pigtail catheter (Cordis Corporation, East Bridgewater, New Jersey) placed in the noncoronary cusp. Contrast regurgitation into the left ventricle after injection of 20 ml of contrast at a flow rate of 10 ml/s served to indicate annulus size underestimation by TEE and resulted in the selection of a bigger prosthesis (Fig. 1, Online Video 1). For TAVI using the Edwards Sapien bioprosthesis, balloon sizing was performed with a 23-mm Edwards balloon for selection between the 23- and 26-mm valve and with a 25-mm Z-MED balloon for selection between the 26- and 29-mm valve. For TAVI using the MCV, balloon sizing was performed with a 23-mm Z-MED balloon for selection between the 26- and 29-mm valve and with a 25-mm Z-MED balloon for selection between the 29- and 31-mm valve. In order to achieve a 23-mm diameter using the 23-mm Edwards balloon or the 23-mm Z-MED balloon, inflation with 21 ml of saline/contrast mixture was necessary. In order to achieve a 25-mm diameter using the 25-mm Z-MED balloon inflation with 22 ml was necessary. A diameter of 26 mm was achieved by inflating the 25-mm Z-MED balloon with 23 ml of saline/contrast mixture. Of note, a 26-mm balloon was not available in our catheterization laboratory at that time. The volume needed to achieve a certain diameter was calibrated in vitro using a saline/contrast medium mix. To evaluate the congruence between the aortic annulus and the device, we also calculated the “cover index” as a ratio of: 100 × (prosthesis diameter – TEE annulus diameter)/prosthesis diameter (7).

### PAR severity.
The severity of residual PAR was graded qualitatively by the amount of regurgitating contrast medium during supra-aortic angiography after final device deployment and catheter removal using the Sellers criteria (12,14,20): absent 0/4; mild 1/4; moderate 2/4; moderate-to-severe 3/4; and severe 4/4. Simultaneous left ventricular (LV) and aortic pressures were recorded at 50 mmHg and averaged over 3 representative cardiac cycles after the procedure. The aortic regurgitation index (AR index) as the ratio of the gradient between diastolic aortic pressure and left ventricular end-diastolic pressure (LVEDP) to systolic blood pressure × 100 (11), the pressure gradient between diastolic aortic pressure (DAP) and left ventricular end-diastolic pressure (ΔP_{DAP–LVEDP}) (14), and the myocardial
supply-demand ratio (DPTI:SPTI) (15) from planimetric integration of the diastolic pressure time integral (DPTI) and systolic pressure time integral (SPTI) were calculated. An AR index $<25$, a $\Delta P_{DAP-LVEDP} \leq 18$ mm Hg, and a DPTI:SPTI $\leq 0.7$ have been previously proposed as cutoff values for increased mortality associated with PAR after TAVI.

**Endpoint.** The primary endpoint was mortality over the duration of the study according to Valve Academic Research Consortium II definitions (19). All patients were followed for at least 1 year.

**Post-interventional protocol.** After TAVI, patients were transferred for 24 h to an intensive care unit for post-interventional monitoring. Besides the clinical examination, electrocardiogram, body temperature, and chest x-ray, all blood parameters, which had already been determined at the initial examination, were determined again. Follow-up examinations were performed 3 months and 1 year after discharge.

**Statistical analysis.** Categorical data are presented as frequencies and percentages; continuous variables are presented as mean $\pm$ SD. The normal distribution of the variables was tested by the Shapiro-Wilk test (p-Wert $\geq 0.1$). Comparisons were made with 2-sided chi-square tests or 2-sided Fisher exact tests for categorical variables and 1-way analysis of variance for continuous variables, using Bonferroni correction for multiple testing. Analysis of variance and the Student $t$ test were used to compare normally distributed variables (age, aortic annulus, weight, height) and the Mann-Whitney $U$ test was used compare the other non-normally distributed variables between the 2 groups. A $p$ value of $<0.05$ was considered significant. Survival analyses for conventional and balloon sizing were performed by the Kaplan-Meier method, with patients censored as of the last date known alive. All statistical analyses were performed using SPSS (version 17.0, SPSS, Chicago, Illinois).

**Results**

**Baseline and procedural characteristics.** Our study cohort represents a typical TAVI patient population at high risk for open-heart surgery (logistic EuroSCORE [European System for Cardiac Operative Risk Evaluation]: 21.0 $\pm$ 12.8%, STS [Society of Thoracic Surgeons] score: 7.7 $\pm$ 6.7%) with symptomatic aortic stenosis (aortic valve area: 0.63 $\pm$ 0.2 cm$^2$, transvalvular gradient: 55.7 $\pm$ 9.6 mm Hg). There were no significant differences in baseline and procedural characteristics between the retrospective conventional-sizing group and the balloon-sizing group (Tables 1 and 2).

**BAV for valve size selection.** For 63 (61%) patients of group 2 who had a distinct annulus size, balloon sizing was used to confirm annular sizing based on the pre-interventional TEE. In all 63 patients, absence of contrast regurgitation into the LV after balloon inflation confirmed annulus sizing by TEE and resulted in the implantation of the expected valve size (Fig. 2).

In cases of borderline annulus size, balloon sizing was used for valve size selection. According to pre-interventional
imaging by TEE, 40 (39%) patients had a borderline annulus size. Balloon sizing performed in these cases revealed an underestimation of annulus size in 30 patients (29%), so that on-table the bigger prosthesis was selected, whereas the smaller prosthesis was chosen in the remaining patients, resulting in only 1 of these 40 patients with at least moderate PAR (Fig. 2). Of note, there were no complications associated with angiography during BAV. Specifically, there were no annulus ruptures associated with balloon sizing.

**PAR after TAVI.** The angiographic assessment of post-procedural PAR revealed a lower frequency of PAR in the balloon sizing than in the retrospective conventional sizing group (Table 3A). At least mild PAR was observed in 113 patients of the retrospective conventional-sizing group and 41 patients of the balloon-sizing group. Severe PAR did not occur in any of our study patients (67.7% vs. 39.8%, p < 0.001).

An AR index <25, a pressure difference ≤18 mm Hg, and a DPTI:SPTI <0.7 were observed less often in patients who underwent balloon sizing than in those who underwent conventional sizing (Table 3B). There was a tendency toward a lower cover index in the retrospective conventional-sizing group compared with the balloon-sizing cohort but without significance (6.4 ± 5% vs. 6.8 ± 6%, respectively, p = 0.6). Correcting maneuvers for PAR treatment in the retrospective conventional-sizing group have been described before (14). Twenty-three patients underwent post-dilation with an improvement in PAR grade to <2/4 in 13 (54%) of them. One patient with severe PAR due to low implantation of a MCV underwent post-deployment repositioning by snaring, which resulted in PAR improvement to 1/4. In the balloon-sizing cohort, 10 patients underwent post-dilation with an improvement in PAR grade to <2/4 in 2 (20%) of them. The reduced rate of

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 270)</th>
<th>Conventional Sizing (n = 167)</th>
<th>Balloon Sizing (n = 103)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>80.9 ± 6.2</td>
<td>80.7 ± 6.6</td>
<td>81.5 ± 5.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Male</td>
<td>110 (40.7)</td>
<td>70 (41.9)</td>
<td>40 (38.8)</td>
<td>0.7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>75.5 ± 13.2</td>
<td>75.2 ± 14.2</td>
<td>76.3 ± 14.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.4 ± 7.4</td>
<td>166.2 ± 8.3</td>
<td>167.1 ± 6.4</td>
<td>0.31</td>
</tr>
<tr>
<td>Logistic EuroSCORE, %</td>
<td>17.9 (16.0, 27.1)</td>
<td>18.3 (16.1, 26.7)</td>
<td>16.8 (15.7, 27.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>STS score, %</td>
<td>7.3 (6.7, 9.1)</td>
<td>7.2 (6.8, 8.7)</td>
<td>7.5 (7.1, 9.3)</td>
<td>0.6</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>0.61 (0.5, 0.7)</td>
<td>0.60 (0.5, 0.7)</td>
<td>0.65 (0.5, 0.8)</td>
<td>0.15</td>
</tr>
<tr>
<td>Mean transvalvular PG, mm Hg</td>
<td>54.7 (46.0, 61.0)</td>
<td>55.0 (48.0, 63.0)</td>
<td>54.0 (47.0, 60.0)</td>
<td>0.2</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>22.9 ± 1.9</td>
<td>22.8 ± 1.4</td>
<td>23.1 ± 1.4</td>
<td>0.08</td>
</tr>
<tr>
<td>CAD</td>
<td>174 (64.4)</td>
<td>105 (62.9)</td>
<td>69 (66.9)</td>
<td>0.5</td>
</tr>
<tr>
<td>Prior MI</td>
<td>10 (3.7)</td>
<td>4 (2.4)</td>
<td>6 (5.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>107 (39.6)</td>
<td>62 (37.1)</td>
<td>45 (43.7)</td>
<td>0.4</td>
</tr>
<tr>
<td>Prior heart surgery</td>
<td>47 (17.4)</td>
<td>28 (16.8)</td>
<td>19 (18.4)</td>
<td>0.75</td>
</tr>
<tr>
<td>PVD</td>
<td>38 (14.0)</td>
<td>25 (15.0)</td>
<td>13 (12.6)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD, n (%), or median (interquartile range).

CAD = coronary artery disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; PG = pressure gradient; PVD = peripheral vascular disease; STS = Society of Thoracic Surgeons.

### Table 2. Procedural Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 270)</th>
<th>Conventional Sizing (n = 167)</th>
<th>Balloon Sizing (n = 103)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfemoral</td>
<td>260 (96.3)</td>
<td>158 (94.6)</td>
<td>102 (99)</td>
<td>0.095</td>
</tr>
<tr>
<td>Transsubclavian</td>
<td>10 (3.7)</td>
<td>9 (5.4)</td>
<td>1 (1.0)</td>
<td>0.095</td>
</tr>
<tr>
<td>CoreValve</td>
<td>104 (38.5)</td>
<td>88 (52.7)</td>
<td>16 (15.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Edwards</td>
<td>166 (61.5)</td>
<td>79 (47.3)</td>
<td>87 (84.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Procedural duration, min</td>
<td>71.1 (53.0–101.0)</td>
<td>72.0 (55.0–105.0)</td>
<td>69.2 (50.0–95.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>13.5 (10.6–17.9)</td>
<td>13.1 (10.3–17.5)</td>
<td>14.0 (11.1–18.5)</td>
<td>0.1</td>
</tr>
<tr>
<td>Contrast amount, ml</td>
<td>175 (130.0–207.0)</td>
<td>173.5 (130.0–205.0)</td>
<td>179.6 (137.0–210.0)</td>
<td>0.4</td>
</tr>
<tr>
<td>Post-procedural transvalvular mean PG, mm Hg</td>
<td>9.3 (7.0–14.0)</td>
<td>9.0 (6.0–13.0)</td>
<td>9.7 (7.3–13.9)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Values are n (%) or median (interquartile range).

PG = pressure gradient.
post-dilation due to the reduced incidence of PAR in the balloon-sizing group did not significantly affect stroke rate.

**PAR and associated mortality in relation to the sizing method.** Mortality at 30 days and 1 year was less in patients who underwent additional balloon sizing in comparison to those who underwent conventional sizing (5.8% vs. 9%, p = 0.2, and 10.6% vs. 20%, p = 0.01) (Fig. 3).

## Discussion

The present study is the first to demonstrate that supra-aortic angiography during preparatory BAV improves valve size selection and reduces PAR and the associated mortality after TAVI. Qualitatively, the frequency of post-procedural PAR was lower in patients who underwent additional balloon sizing in comparison to those who underwent conventional sizing (5.8% vs. 9%, p = 0.2, and 10.6% vs. 20%, p = 0.01) (Fig. 3).

### Use of preparatory BAV for improved valve size selection.

Due to conflicting measurements obtained with multimodal imaging, asymmetric calcifications, or eccentric leaflets, there can be uncertainties regarding the optimal valve size selection for TAVI. When measurements of the aortic annulus are ambiguous between 2 different available prosthesis sizes, valve size selection based only on indirect annular sizing, or eccentric leaflets, there can be uncertainties regarding the optimal valve size selection for TAVI. Although recent data show a correlation between echocardiographic and MSCT sizing, results between these methods are not identical (2). The calculation of the annular diameter from maximum/minimum cross-sectional diameter but also cross-sectional area has been proposed for more accurate sizing; however, radiation exposure and contrast medium injection are important limitations (2). In a recent analysis, computed tomography sizing recommendations resulted in mean annular oversizing of 13.9% (27).

### Table 3. Assessment of PAR Severity

<table>
<thead>
<tr>
<th>A</th>
<th>Conventional Sizing (n = 167)</th>
<th>Balloon Sizing (n = 103)</th>
<th>p Value</th>
<th>B</th>
<th>Conventional Sizing (n = 167)</th>
<th>Balloon Sizing (n = 103)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent (0/4)</td>
<td>54 pts (32.3%)</td>
<td>62 pts (60.2%)</td>
<td>&lt;0.0001</td>
<td>AR index &lt; 25</td>
<td>45 (26.9%)</td>
<td>16 (15.5%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Trace or mild (1/4)</td>
<td>89 pts (53.3%)</td>
<td>33 pts (32%)</td>
<td>&lt;0.0001</td>
<td>DPTI:SPTI ≤ 0.7</td>
<td>20 (11.9%)</td>
<td>5 (4.8%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Moderate (2/4)</td>
<td>21 pts (12.6%)</td>
<td>7 pts (6.8%)</td>
<td>&lt;0.0001</td>
<td>ΔPp-DAP-LVEDP ≤ 18 mm Hg</td>
<td>44 (26.3%)</td>
<td>15 (14.5%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Moderate-to-severe (3/4)</td>
<td>3 pts (1.8%)</td>
<td>1 pts (1.0%)</td>
<td>&lt;0.0001</td>
<td>DPTI:SPTI ≤ 0.7</td>
<td>20 (11.9%)</td>
<td>5 (4.8%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Severe (4/4)</td>
<td>0 pts (0%)</td>
<td>0 pts (0%)</td>
<td>&lt;0.0001</td>
<td>DPTI:SPTI ≤ 0.7</td>
<td>20 (11.9%)</td>
<td>5 (4.8%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

The distribution of post-procedural PAR was associated with the sizing method (A). An AR index < 25, a Δp DAP-LVEDP ≤ 18 mm Hg and a DPTI:SPTI ≤ 0.7 were observed more frequently in the conventional than in the balloon-sizing group (B).

### Aortic annulus sizing in TAVI.

Accurate annulus measurements and the selection of the appropriate prosthesis size are critical in order to avoid valve migration, severe PAR, or annulus rupture (2). The aortic annulus can be measured by echocardiography, MSCT, or angiography. Recommendations for valve size selection are currently based on annular measurements by TEE. Recent studies, however, show an underestimation of the annulus size by echocardiography so that possibly undersized valves are implanted (2). Given the structure of the aortic root and semilunar-shaped cusps, 2-dimensional imaging possibly “cuts” the oval plane at many angles, resulting in inaccurate measurements (12,21). MSCT is increasingly used for annular sizing and provides additional anatomical information regarding the coronary arteries, the aortic valve area, and the distribution of aortic valve calcifications (2,22–25). Although recent data show a correlation between echocardiographic and MSCT sizing, results between these methods are not identical (2). The calculation of the annular diameter from maximum/minimum cross-sectional diameter but also cross-sectional area has been proposed for more accurate sizing; however, radiation exposure and contrast medium injection are important limitations (2). In a recent analysis, computed tomography sizing recommendations resulted in mean annular oversizing of 13.9% (27).
severity and therefore may serve in decision making on valve size selection, especially in cases with borderline annulus size.

TAVI generally requires preparatory BAV to facilitate the prosthesis implantation, and therefore balloon sizing cannot be considered as an additional risk factor for stroke. On the other hand, a reduced stroke rate was not observed due to decreased rate of post-dilation in the balloon-sizing group. In a recent study for the detection of procedural cerebral microembolization during TAVI, the majority of high-intensity transient signals (HITS) recorded by transcranial Doppler ultrasonography was seen during direct valve manipulation while positioning and implanting the prosthesis, revealing that the calcified aortic valve is the main source of emboli (28). In addition, the number of HITS during BAV was unexpectedly low, possibly due to the endothelial coverage preventing calcific debris from release and embolization at this stage of the procedure (28). Although this explanation remains speculative, it is supported by the relatively low stroke rates of 1% to 2% reported by the relatively low stroke rates of 1% to 2%.

Study limitations. Our data are derived from a retrospective analysis of consecutive patients and not from a prospective, randomized trial. We, therefore, cannot exclude that part of the observed benefit in group 2 versus group 1 is due to a learning curve and not specifically to the technique of balloon sizing. In addition, growing awareness of the clinical impact of relevant PAR and therefore focus on avoidance of annulus-to-prosthesis mismatch as well as better selection of TAVI patients could have also played a role in the observed benefit in group 2 and are consequently potential confounders of our current study. The characteristics of the self-expandable nitinol frame of the MCV permit the selection of the larger valve to avoid PAR in cases of borderline annulus size, but still complications such as atrioventricular block may result (30). Taking the significant discrepancies (31) between measurements using 2- and 3-dimensional imaging, but also the lack of sizing recommendations based on 3-dimensional imaging under consideration, we focused on the current manufacturer’s guidelines and used 2-dimensional TEE for annulus measurements. It remains hypothetical whether we would have potentially used the bigger valve in borderline cases without our current procedure of valve sizing, but it must be noted that in 10 of 40 patients with borderline annulus size, the smaller valve was ultimately chosen.

Conclusions

At least mild PAR and quantitative parameters of PAR severity, such as an AR index <25, a ΔP_{DAP-LVEDP} ≤18 mm Hg, and a DPTI:SPTI ≤0.7, all associated with an increased mortality, were observed less often in patients who underwent additional balloon sizing than in those who underwent only conventional sizing. Preparatory BAV during TAVI improves valve size selection, reduces PAR, and thus improves survival, especially in borderline cases.

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REFERENCES


Key Words: aortic regurgitation • balloon valvuloplasty • transcatheter aortic valve implantation.

APPENDIX

For an accompanying video, please see the online version of this article.