Transcatheter Aortic Valve Implantation for Patients With Severe Bicuspid Aortic Valve Stenosis

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Background—Bicuspid aortic valve (BAV) is regarded as a relative contraindication to transcatheter aortic valve implantation attributable to the risk of uneven expansion of the bioprosthesis. The purpose of this study was to evaluate the efficacy and safety of transcatheter aortic valve implantation in patients with BAV.

Methods and Results—Of 470 patients included in our prospective transcatheter aortic valve implantation database (October 2006–January 2012), 229 consecutive patients undergoing both echocardiography and multidetector computed tomography were analyzed. We compared clinical outcomes in patients with vs patients without BAV. In this series of 229 patients, BAV was detected by multidetector computed tomography in 21 patients (9.2%). BAV was identified by transthoracic and transoesophageal echocardiography in only 9 of these 21 patients. Patients were 83.1±6.6 years old, and European system for cardiac operative risk evaluation score was 20.0%±11.4%. The BAV group was similar to the non-BAV group except for diabetes mellitus (4.8% vs 24.0%; P=0.05). The aortic annulus diameter in BAV patients was not significantly larger by multidetector computed tomography (24.7±3.0 vs 23.7±1.9 mm; P=0.07). The CoreValve was used more frequently in the BAV group (47.6% vs 16.3%; P=0.002). There was no significant difference in device success (100% vs 92.8%; P=0.37), risk of annulus rupture (0% vs 1.4%; P=1.00), or valve migration (0% vs 1.4%; P=1.00) in BAV patients compared with non-BAV patients. Postprocedural mean gradient (10.0±3.4 vs 9.7±4.1 mm Hg; P=0.58), aortic regurgitation ≥2 of 4 (19.0% vs 14.9%; P=0.54), 30-day mortality (4.8% vs 8.2%; P=1.00), and 30-day combined safety end point (14.3% vs 13.5%; P=1.00) were also similar in both groups.

Conclusions—in selected BAV patients, transcatheter aortic valve implantation may be associated with low complication rate, efficacy, and acceptable outcomes similar to those in non-BAV patients. (Circ Cardiovasc Interv. 2013;6:284-291.)

Key Words: aortic stenosis ■ bicuspid aortic valve ■ computed tomography ■ echocardiography ■ transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) for treatment of aortic stenosis (AS) in high-risk patients has emerged as a promising therapeutic alternative to conventional surgical aortic valve replacement. Although the basic technique is reaching relative maturity, there is a paucity of data regarding patients who have not been included in recent clinical trials.

Bicuspid aortic valve (BAV) is a relatively common anomaly that is reported in 0.5% to 2.0% of the general population and has been observed in ≥50% of aortic valves resected during surgical aortic valve replacement. This anatomic variation is considered an exclusion criterion in most clinical trials because of the risk of uneven expansion and subsequent malfunction of the bioprosthesis.

Although initial TAVI experience in patients with BAV has been described in several reports, few data are available on the comparative feasibility and efficacy of TAVI in BAV compared with non-BAV.

The purpose of this study was to evaluate the efficacy and safety of TAVI in patients with the anatomic variation of the aortic valve described as BAV (in patients with BAV anatomy).

Methods

Study Sample and Design

From October 2006, consecutive high-risk patients with symptomatic severe AS who had undergone TAVI at our institution were prospectively included in our TAVI database. Patients with severe symptomatic AS (valve area ≤1.0 cm²) were considered candidates for TAVI if they had a logistic European system for cardiac operative risk evaluation score >20%, or if surgery was deemed to be of excessive risk because...
WHAT IS KNOWN

- Bicuspid aortic valve is considered an exclusion criterion in most clinical trials of transcatheter aortic valve implantation because of the risk of uneven expansion and subsequent malfunction of the bioprosthesis.
- Few data are available on the comparative feasibility and efficacy of transcatheter aortic valve implantation in bicuspid aortic valve.

WHAT THE STUDY ADDS

- This article describes the results of transcatheter aortic valve implantation in bicuspid aortic valve patients who underwent systematic multidetector computed tomography before the procedure.
- In selected patients, transcatheter aortic valve implantation may be associated with low complication rate, therapeutic efficacy, and acceptable outcomes similar to those in nonbicuspid aortic valve patients.

Vascular Access and Valve Selection

Patients were selected to undergo TAVI via the transfemoral approach or alternative approaches depending on the size, calcification, and tortuosity of the ilio-femoral arterial access, as described previously.9 The valve prosthesis type was selected according to the mean annulus diameter calculated by MDCT. The Edwards valve was used in patients with a diameter between 18 and 24.5 mm, and the CoreValve was used for annular diameters of 20 to 26.5 mm. For historical reasons (the Edwards valve was first introduced in 2006), the Edwards valve was used preferentially in patients who had an annulus diameter of 20 to 24.5 mm and who were amenable to treatment with either valve. The CoreValve prosthesis was implanted in patients whose annulus size was >24.5 mm, or patients with borderline ilio-femoral access, as described previously.9 These measurements were then translated into semiquantitative and multifactorial grades, including circumferential extent of paravalvular regurgitation as follows: (0) none; (1) trivial; (2) mild; (3) moderate; and (4) severe. All Doppler measurements were evaluated as the average of at least 3 cycles in patients with sinus rhythm or >5 cycles in those with atrial fibrillation. Consensus was obtained between 2 operators when there were discrepancies.

MDCT

All examinations were performed using a Philips Brilliance 64-slice MDCT (Philips Medical). Technical parameters were standard: gantry rotation time 330 ms; axial coverage 40 mm (64 x 0.625 mm); 120 kV tube voltage; 850–900 mAs intensity without modulation; and temporal resolution 165 ms. Retrospective ECG gating was used. Contrast enhancement was achieved with 50 to 80 mL of Iomeprol 400 mg/mL (Iomeron). A bolus tracking method was used in the descending aorta to achieve optimal synchronization. Additional β-blockers were not administered to any patients because of potential hemodynamic hazards in patients with tight AS. The thickness of reconstructed images was 0.67 mm. All data were transferred to an offline postprocessing dedicated workstation (Extended Brilliance Workspace; Philips Medical).

The midsystolic phase of the cardiac cycle was selected (20% or 30% of R-R interval of the electrocardiogramm spikes).

The measurement of the aortic annulus diameter was performed in the oblique plane that includes the nadirs of all 3 aortic cusps and perpendicular to the aortic root axis as previously described.11,12 In this plane, the virtual annulus ring appears oval, allowing 2 orthogonal diameters (long-axis and short-axis) to be measured.

The annulus surface area was then traced with a caliper, and the MDCT-measured mean geometric annulus diameter was derived as follows: annulus diameter calculated by CT = 2√(annulus surface area/r). This value represents the average of all annulus diameters, according to a previously described method.11 The degree of calcification of the aortic valve was evaluated in mid-diastole using a simple linear regression method between calcification and blood densities and was described precisely and validated in our previous report.14

The assessors investigating echocardiography and MDCT were blinded to the results of the previous examination.

Definition of BAV

In this study, a BAV was defined as a deformed aortic valve with 2 functional cusps forming a valve mechanism with <3 zones of parallel apposition between cusps according to a previous report.13 The classification into types depends on the number of raphes that are classified into 3 types: type 0, valves with no raphes; type 1, valves with 1 raphe; and type 2, valves with 2 raphes. Abnormal aortic valves with 2 raphes, resulting in a restricted orifice area extending from the periphery to the center, was included in the BAV group (type 2, valve with 2 raphes) and were not considered to be unicusp. The diagnosis was made by TTE and TEE, and by MDCT independently. The suspected cases of BAV in patients examined by echocardiography alone were excluded from the BAV group if 3 cusps with 3 commissural openings were observed by MDCT. Commissural fusion with a raphe <3-mm-long was considered not significant according to the previous study by Roberts et al.3

Procedures

All patients were using aspirin (160 mg) and clopidogrel (75 mg) daily before TAVI or were administered a loading dose of clopidogrel (300–600 mg) before or immediately after the procedure. A bolus of intravenous heparin (70 IU/kg) was administered at the start of each procedure to achieve an activated clotting time of 250 to 300 seconds, and the activated clotting time was measured every 30 minutes thereafter. All
procedures were performed by experienced interventional cardiologists according to our standard operating procedures, as previously described.9

**Postprocedural Care**
All patients were observed in the intensive care unit for at least 24 hours after Edwards valve implantation and for 72 hours after CoreValve implantation (in patients with no previous pacemaker). Dual antiplatelet therapy was continued for 6 months (except in patients using coumadin who had only 1 antiplatelet treatment) and, thereafter, aspirin was continued indefinitely.

**End Point Definitions**
The main end points of this study were all-cause 30-day mortality, a 30-day safety composite end point, and device success as defined by the valve academic research consortium criteria.16

The combined 30-day safety end point included the following: all-cause mortality; major stroke; life-threatening (or disabling) bleeding; acute kidney injury stage 3 (including renal replacement therapy); periprocedural myocardial infarction; major vascular complications; and further intervention attributable to valve dysfunction.

Device success was defined as follows: successful vascular access, delivery, and deployment of the device and successful retrieval of the delivery system; correct positioning of the device in the proper anatomic location; intended performance of the prosthetic heart valve with aortic valve area >1.2 cm² and mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s, without moderate or severe prosthetic valve AR; and only 1 valve implanted in the proper anatomic location.

**Statistical Analysis**
Quantitative variables are expressed as mean±standard deviation and qualitative variables are expressed as numbers and percentages. Comparison of quantitative variables was performed with an unpaired Student t test or Wilcoxon rank-sum test, depending on variable distribution. The Fisher exact test was used to compare qualitative variables. Statistical significance was defined as P<0.05. The data were analyzed using SPSS statistics 20.0 (SPSS, Chicago, IL).

**Results**
**Patient Characteristics**
Of 470 consecutive patients treated with TAVI between October 2006 and January 2012, 229 patients who underwent MDCT examination before TAVI were included in the study reported here. The remaining 241 patients who underwent TEE and TTE as the only modalities before TAVI were excluded from this study. Among them, only 2 suspicious cases of BAV were included (0.8%). This low proportion of BAV in the early phase of our experience is probably related to the fact that BAV was considered a relative contraindication to TAVI and that only echo was used and not MDCT.

The mean age of the entire sample was 83.1±6.6 years (Table 1). Congestive heart failure class III/IV was prevalent in 88.2%, coronary artery disease was prevalent in 57.2%, previous coronary artery bypass grafting was prevalent in 13.1%, and 59.4% of patients had significant renal dysfunction (estimated glomerular filtration rate <60 mL/min). The mean logistic European system for cardiac operative risk evaluation score was 20.0%±11.4%. The mean pressure gradient across the aortic valve was 48.1±17.1 mm Hg, and the mean CT-measured aortic annulus size was 23.8±2.0 mm.

BAV was observed in 21 cases by MDCT (9 cases were diagnosed by TTE or TEE, whereas 6 BAV-suspected cases were diagnosed by TTE/TEE were excluded because commisural opening between all 3 cusps was observed by MDCT). Of the 9 patients with BAV detected by echocardiography, 3 cases were diagnosed by both transthoracic and TEE, and 6 were detected by TEE alone.

The BAV group consisted of type 1 L-R (16 cases), type 1 R-N (1 case), type 1 L-N (1 case), and type 2 L-R and L-N (3 cases) according to the previously described criteria.15 The

**Table 1. Baseline Characteristics of the Study Sample**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>BAV</th>
<th>Non-BAV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>229</td>
<td>21</td>
<td>208</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>83.1±6.6</td>
<td>82.0±7.0</td>
<td>83.2±6.5</td>
<td>0.29</td>
</tr>
<tr>
<td>Male sex</td>
<td>123 (53.7%)</td>
<td>12 (57.1%)</td>
<td>111 (53.4%)</td>
<td>0.82</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.0±4.3</td>
<td>24.7±4.1</td>
<td>26.1±4.3</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>51 (22.3%)</td>
<td>1 (4.8%)</td>
<td>50 (24.0%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>107 (46.7%)</td>
<td>9 (42.9%)</td>
<td>98 (47.1%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Hypertension</td>
<td>154 (67.2%)</td>
<td>12 (57.1%)</td>
<td>142 (68.3%)</td>
<td>0.33</td>
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<tr>
<td>Current smoker</td>
<td>6 (2.6%)</td>
<td>1 (4.8%)</td>
<td>5 (2.4%)</td>
<td>0.44</td>
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<td>NYHA class III/IV</td>
<td>202 (88.2%)</td>
<td>19 (90.5%)</td>
<td>183 (88.0%)</td>
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</tr>
<tr>
<td>Coronary artery disease</td>
<td>131 (57.2%)</td>
<td>10 (47.6%)</td>
<td>121 (58.2%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Previous MI</td>
<td>19 (8.3%)</td>
<td>1 (4.8%)</td>
<td>18 (8.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>51 (22.3%)</td>
<td>4 (19.0%)</td>
<td>47 (22.6%)</td>
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<tr>
<td>Previous CAVB</td>
<td>30 (13.1%)</td>
<td>2 (9.5%)</td>
<td>28 (13.5%)</td>
<td>1.00</td>
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<td>Peripheral artery disease</td>
<td>73 (31.9%)</td>
<td>5 (23.8%)</td>
<td>68 (32.7%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>14 (6.1%)</td>
<td>1 (4.8%)</td>
<td>13 (6.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>COPD</td>
<td>55 (24.0%)</td>
<td>5 (23.8%)</td>
<td>50 (24.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>eGFR, ml/Lmin</td>
<td>59.1±24.6</td>
<td>60.3±27.2</td>
<td>59.0±24.4</td>
<td>0.81</td>
</tr>
<tr>
<td>eGFR &lt;60 ml/Lmin</td>
<td>136 (59.4%)</td>
<td>12 (57.1%)</td>
<td>124 (59.6%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Logistic European score, %</td>
<td>20.0±11.4</td>
<td>19.9±11.9</td>
<td>20.1±11.4</td>
<td>0.90</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>0.65±0.13</td>
<td>0.67±0.11</td>
<td>0.65±0.14</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean pressure gradient, mm Hg</td>
<td>48.1±17.1</td>
<td>47.8±18.6</td>
<td>48.1±17.0</td>
<td>0.94</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>53.3±14.4</td>
<td>47.5±14.5</td>
<td>53.9±14.3</td>
<td>0.04</td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>60 (26.2%)</td>
<td>6 (28.6%)</td>
<td>54 (26.0%)</td>
<td>0.80</td>
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<tr>
<td>Aortic annulus size (TEE-measured), mm</td>
<td>22.6±2.0</td>
<td>23.4±2.7</td>
<td>22.5±1.9</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean aortic annulus size (CT-measured), mm</td>
<td>23.8±2.0</td>
<td>23.7±3.0</td>
<td>23.7±1.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Short-axis annulus size (CT-measured), mm</td>
<td>22.0±2.0</td>
<td>22.7±2.8</td>
<td>21.9±1.9</td>
<td>0.09</td>
</tr>
<tr>
<td>Long-axis annulus size (CT-measured), mm</td>
<td>26.5±2.5</td>
<td>27.4±3.1</td>
<td>26.4±2.5</td>
<td>0.06</td>
</tr>
<tr>
<td>Long/short Diam-CT ratio</td>
<td>1.21±0.08</td>
<td>1.21±0.07</td>
<td>1.21±0.08</td>
<td>0.53</td>
</tr>
<tr>
<td>Circumference, mm</td>
<td>75.6±6.8</td>
<td>75.7±9.5</td>
<td>74.3±6.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Aortic valve calcification degree, %</td>
<td>28.7±11.4</td>
<td>32.2±10.1</td>
<td>28.4±11.9</td>
<td>0.39</td>
</tr>
<tr>
<td>Length of raphe (CT), mm</td>
<td>—</td>
<td>12.7±2.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Aortic regurgitation (0–4)</td>
<td>0.84±0.70</td>
<td>0.95±0.74</td>
<td>0.83±0.70</td>
<td>0.98</td>
</tr>
<tr>
<td>Mitral regurgitation (0–4)</td>
<td>0.81±0.69</td>
<td>0.74±0.87</td>
<td>0.82±0.67</td>
<td>0.72</td>
</tr>
<tr>
<td>Ascending aorta size, mm</td>
<td>36.1±4.3</td>
<td>38.3±3.4</td>
<td>35.8±4.3</td>
<td>0.01</td>
</tr>
</tbody>
</table>

BAV indicates bicuspid aortic valve; BMI, body mass index; CAVB, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; CT, computed tomography; Diam-CT, annulus diameter measured by CT; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; TEE, transesophageal echocardiography. Values are expressed as n (%) or mean±SD.
mean length of raphe measured by CT was 12.7±2.7 mm (range, 7–16 mm), which is in line with the previous report. A calcium bridge across 2 cusps was observed in 15 cases (71.4%) by MDCT. Figure 1 shows examples of BAV that echocardiography failed to identify (Figure 1A and 1B show case 1; Figure 1C and 1D show case 2). In both cases, the presence of a calcium bridge across 2 cusps was observed (Figure 1B and 1D).

In the BAV group, patients had a lower incidence of diabetes mellitus (4.8% vs 24.0%, P=0.05), and there was a trend toward larger mean annulus diameter measured by CT (24.7±3.0 vs 23.7±1.9 mm; P=0.07) and long-axis annulus diameter measured by CT (27.4±3.1 vs 26.4±2.5 mm; P=0.06). The logistic European system for cardiac operative risk evaluation score was similar in both groups (19.9±11.9 vs 20.1±11.4%; P=0.90). There was no significant difference between the groups in the grade of preprocedural AR (0.95±0.74 vs 0.83±0.70; P=0.98). The size of the ascending aorta was significantly larger in the BAV group compared with the non-BAV group (38.3±3.4 vs 35.8±4.3 mm; P=0.01).

### Table 2. Procedural Characteristics of the Study Sample

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>BAV</th>
<th>Non-BAV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>229</td>
<td>21</td>
<td>208</td>
<td></td>
</tr>
<tr>
<td>Edwards</td>
<td>185 (80.8%)</td>
<td>11 (52.4%)</td>
<td>174 (83.7%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Transfemoral</td>
<td>84 (36.7%)</td>
<td>5 (23.8%)</td>
<td>79 (38.0%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Transapical</td>
<td>40 (17.5%)</td>
<td>3 (14.3%)</td>
<td>37 (17.8%)</td>
<td></td>
</tr>
<tr>
<td>Transaortic</td>
<td>61 (26.6%)</td>
<td>3 (14.3%)</td>
<td>58 (27.9%)</td>
<td></td>
</tr>
<tr>
<td>CoreValve</td>
<td>44 (19.7%)</td>
<td>10 (47.6%)</td>
<td>34 (16.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Transfemoral</td>
<td>34 (14.8%)</td>
<td>8 (38.1%)</td>
<td>26 (12.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Transsubclavian</td>
<td>3 (1.3%)</td>
<td>0</td>
<td>3 (1.4%)</td>
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</tr>
<tr>
<td>Transaortic</td>
<td>7 (3.1%)</td>
<td>2 (9.5%)</td>
<td>5 (2.4%)</td>
<td></td>
</tr>
<tr>
<td>Valve size, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edwards, 23 mm</td>
<td>26.5±2.2</td>
<td>27.8±3.0</td>
<td>26.4±2.1</td>
<td>0.06</td>
</tr>
<tr>
<td>26 mm</td>
<td>115 (50.2%)</td>
<td>2 (9.5%)</td>
<td>113 (54.3%)</td>
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</tr>
<tr>
<td>29 mm</td>
<td>29 (12.7%)</td>
<td>4 (19.0%)</td>
<td>25 (13.5%)</td>
<td></td>
</tr>
<tr>
<td>CoreValve, 26 mm</td>
<td>3 (1.3%)</td>
<td>0</td>
<td>3 (1.4%)</td>
<td>0.33</td>
</tr>
<tr>
<td>29 mm</td>
<td>28 (12.2%)</td>
<td>5 (23.8%)</td>
<td>23 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>31 mm</td>
<td>13 (5.7%)</td>
<td>5 (23.8%)</td>
<td>8 (3.8%)</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as n (%) or mean±SD. BAV indicates bicuspid aortic valve.

### Procedural Characteristics

The Edwards valve was used in 80.8% of cases, the CoreValve was used in 19.7%, and the procedure was performed via the transfemoral approach in 51.5% of cases (Table 2). The most commonly used implant was the Edwards 26-mm valve (50.2%).

The CoreValve was more frequently used in the BAV group compared with the non-BAV group (47.6% vs 16.3%; P=0.002). There was no difference in the access site between the groups. The selected valve size tended to be significantly larger in the BAV group (27.8±3.0 vs 26.4±2.1 mm; P=0.06).

Both types of TAVI bioprostheses were used equally (11 Edwards valves and 10 CoreValves) in the BAV group.

### CT Images of TAVI for BAVs

Representative images of both the Edwards valve and CoreValve are shown in Figures 2 and 3.
Postprocedural Outcomes
A periprocedural cerebrovascular accident was observed in 2.6% cases and valve migration was observed in 1.3% of cases (Table 3). The mean pressure gradient was 9.8±4.1 mm Hg, and postprocedural AR grade ≥2 was reported in 15.3%. New pacemaker implantation was required in 7.9% (5.4% with Edwards and 18.2% with CoreValve), and 30-day mortality and combined safety end point were 7.9% and 13.5%, respectively.

There was no significant difference in the incidence of periprocedural complications (Table 3). No annulus rupture or valve migration was observed in the BA V group. Conversion to open heart surgery was not required in the BA V group.

Similar mean pressure gradient was achieved in both groups (10.0±3.4 vs 9.7±4.1 mm Hg; P=0.58), and no significant difference was observed in the incidence of postprocedural AR grade ≥2 (19.0% vs 14.9%; P=0.54). Device success was achieved similarly in both groups (100% vs 92.8%; P=0.37). There was no significant difference in the incidence of 30-day mortality (4.8% vs 8.2%; P=1.00) and 30-day combined safety end point (14.3% vs 13.5%; P=1.00).

In the BA V group, the postprocedural mean pressure gradient was similar in the Edwards valve and CoreValve recipients alike (9.8±3.9 vs 9.2±5.4 mm Hg; P=0.43).

CT scan revealed the presence of a calcium bridge in 14 of the 21 patients; regardless of this anatomic structure, no significant difference was observed in mean pressure gradient (11.0±3.7 vs 8.3±2.9 mm Hg; P=0.20).

Follow-up
Among the 21 patients with BA V, 11 underwent TAVI more than a year ago and 2 patients died during the follow-up period (1 Edwards recipient because of an unknown cause on day 241 after the intervention and 1 CoreValve recipient with baseline chronic obstructive pulmonary disorder because of respiratory failure. Of the remaining 9 patients, 7 were in New York Heart Association class 1 and 2 were in New York Heart Association class in class 2.

A mean pressure gradient of 9.0±3.6 mm Hg as assessed by echocardiography was achieved in the 6 patients in whom follow-up data were available at 1 year. No mean pressure gradient ≥20 mm Hg was observed in any patient. No difference was observed between the 2 valves.

Discussion
To the best of our knowledge, this is the first article reporting the results of TAVI in cases of bicuspid AS in a large consecutive single-center series of patients who underwent systematic MDCT before the procedure. This study clearly shows that the diagnosis of bicuspid AS is often underestimated by echocardiography compared with MDCT and may sometimes be overestimated and that device success in patients with BA V is similar to non-BA V patients (100% vs 92.8%; P=0.37), as are 30-day mortality (4.8% vs 8.2%; P=1.00) and 30-day combined safety end points (14.3% vs 13.5%; P=1.00). Furthermore, postprocedural mean gradient (10.0±3.4 vs 9.7±4.1 mm Hg; P=0.58) and risk of postprocedural AR ≥2 (19.0% vs 14.9%; P=0.54) are also similar.

A BA V is a deformed aortic valve with 2 functional cusps forming a valve mechanism with <3 zones of parallel apposition between cusps. This anatomic variation is observed in >50% of resected aortic valves during surgical aortic valve replacement. However, BA V has been considered an
Table 3. Postprocedural Outcomes of the Study Sample

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>BAV</th>
<th>Non-BAV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>229</td>
<td>21</td>
<td>208</td>
<td></td>
</tr>
<tr>
<td>Transfusion ≥4 units</td>
<td>21 (9.2%)</td>
<td>2 (9.5%)</td>
<td>19 (9.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Bleeding (life-</td>
<td>24 (10.5%)</td>
<td>2 (9.5%)</td>
<td>22 (10.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>threatening)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding (major)</td>
<td>10 (4.4%)</td>
<td>1 (4.8%)</td>
<td>9 (4.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Bleeding (minor)</td>
<td>12 (5.2%)</td>
<td>1 (4.8%)</td>
<td>11 (5.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Periprocedural</td>
<td>1 (0.4%)</td>
<td>0</td>
<td>1 (0.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(≤72 hours)</td>
<td>6 (2.6%)</td>
<td>0</td>
<td>6 (2.9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Periprocedural</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cerebrovascular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>accident (≤72 hours)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annulus rupture</td>
<td>3 (1.3%)</td>
<td>0</td>
<td>3 (1.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Valve migration</td>
<td>3 (1.3%)</td>
<td>0</td>
<td>3 (1.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>5 (2.2%)</td>
<td>1 (4.8%)</td>
<td>4 (1.9%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Conversion to open</td>
<td>2 (0.9%)</td>
<td>0</td>
<td>2 (1.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>heart surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major vascular</td>
<td>10 (4.4%)</td>
<td>1 (4.8%)</td>
<td>9 (4.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>complication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pressure gradient,</td>
<td>9.8±4.1</td>
<td>10.0±3.4</td>
<td>9.7±4.1</td>
<td>0.58</td>
</tr>
<tr>
<td>mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, %</td>
<td>54.3±12.5</td>
<td>53.2±15.1</td>
<td>54.4±12.2</td>
<td>0.89</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>0.84±0.70</td>
<td>0.85±0.69</td>
<td>0.89±0.72</td>
<td>0.47</td>
</tr>
<tr>
<td>(0–4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic regurgitation ≥2</td>
<td>35 (15.3%)</td>
<td>4 (19.0%)</td>
<td>31 (14.9%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Aortic regurgitation ≥3</td>
<td>2 (0.9%)</td>
<td>0</td>
<td>2 (1.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>0.81±0.69</td>
<td>0.74±0.87</td>
<td>0.82±0.67</td>
<td>0.37</td>
</tr>
<tr>
<td>(0–4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New pacemaker</td>
<td>18 (7.9%)</td>
<td>3 (14.3%)</td>
<td>15 (7.2%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>24 (10.5%)</td>
<td>1 (4.8%)</td>
<td>23 (11.1%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Device success</td>
<td>214 (93.4%)</td>
<td>21 (100%)</td>
<td>193 (92.8%)</td>
<td>0.37</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>18 (7.9%)</td>
<td>1 (4.8%)</td>
<td>17 (8.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>30-day combined safety</td>
<td>31 (13.5%)</td>
<td>3 (14.3%)</td>
<td>28 (13.5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>end point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU stay, days</td>
<td>4.2±4.1</td>
<td>4.5±3.6</td>
<td>4.1±4.2</td>
<td>0.51</td>
</tr>
<tr>
<td>Hospital stay, days</td>
<td>10.6±5.9</td>
<td>8.5±3.6</td>
<td>11.0±6.2</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Values are expressed as n (%) or mean±SD. BAV indicates bicuspid aortic valve; ICU, intensive care unit; LVEF, left ventricular ejection fraction.

exclusion criterion in the majority of clinical trials because of the risk of uneven expansion and subsequent malfunction of the bioprosthesis.4,5

Imaging Modality for BAVs

Consensus between MDCT and TTE/TEE regarding diagnosis of BAV was achieved in only 9 cases (42.9% of the cases diagnosed by MDCT, 60% of which were diagnosed by TTE/TEE). Although the extended use of 3-dimensional-TEE can improve sensitivity and specificity in the detection of BAV, this is not always feasible and appropriate in seriously ill patients with severe AS, and the problem of artifacts remains unresolved even with 3-dimensional TEE, especially in patients with severely calcified aortic valves. The diagnostic value of MDCT for this anatomic variation remains unclear. However, in this study, the opening of a commissure between 2 cusps was clearly observed even in certain patients with BAV diagnosed by echocardiography, presumably because of better spatial resolution and less artifact caused by calcification compared with echocardiography. Furthermore, a calcium bridge characterized by calcification extending between 2 cusps was observed in 15 cases (71.4%) and was never breached in any of the 9 patients who underwent postprocedural MDCT. The presence of a calcium bridge may be regarded as a new finding that could improve diagnosis of BAV by MDCT. MDCT also has the advantage of allowing meticulous screening of concomitant aortic or vascular disease in BAV patients scheduled for TAVI.6 A published seminal study has clearly shown the almost perfect and more accurate agreement between MDCT and intraoperative findings (a gold standard) compared with echocardiography.7 The authors also indicated the limitations of echocardiography in depicting the type of aortic valve in the presence of extensive calcification,7 and our findings are in line with their data. Further improvement in 3-dimensional echocardiography resolution may help diagnosis of BAV in the future and may prove an interesting approach in patients with severe chronic kidney disease and in those for whom iodinated contrast media injection is contraindicated. Alternatively, magnetic resonance imaging offers a good visualization of the aortic valve anatomy and of the number of independent cusps, and enables measurements of annulus size and velocity. However, the depiction and quantification of calcifications remain very limited even though they are of crucial importance in this setting.

Patients with congenital bicuspid valves generally undergo operation at a much younger age. Therefore, it is probable that BAV patients with anatomy suitable for TAVI were included in this registry rather than any BAV patient. This potential selection bias may partly account for the fact that the ratio of long/short CT base diameter shows no difference between BAV and tricuspid valves.

TAVI in BAVs

Although initial results of TAVI in patients with BAV already have been reported,5,6,8 data are scarce with respect to the comparative outcomes of TAVI in patients with compared with patients without BAV. In our analysis, type 1 L-R was the most common subtype of BAV, which is in line with previous reports of surgical aortic valve replacement.15,18 The CoreValve was more frequently used in BAV compared with non-BAV, partly because of relatively larger mean CT-measured annulus diameters in BAV (24.7±3.0 vs 23.7±1.9; P=0.07) and partly because of operator preference.

In the postprocedural CT-images, both types of bioprosthesis tended to be oval, reflecting the anatomy of BAV (Figures 2C and 3B). Apparently, the postprocedural eccentricity index was higher with the CoreValve than with the Edwards valve; however, postprocedural MDCT was not performed systematically in all patients in the study reported here. Interestingly, the mean postprocedural pressure gradient (10.0±3.4 vs 9.7±4.1 mm Hg; P=0.58) as well as the incidence of postprocedural AR grade ≥2 (19.0% vs 14.9%; P=0.54) were not higher in BAV patients compared with non-BAV.
patients. Moreover, in the BAV group, there were no significant differences in postprocedural mean pressure gradient (9.3±3.2 vs 10.8±3.6 mm Hg; P=0.36) and postprocedural AR grade ≥2 (9.1% vs 30.0%; P=0.31) between the Edwards valve and CoreValve. The oval stent frame of the CoreValve is dissociated from the supra-annular location of the valve bioprosthesis, which may account for the absence of differences in hemodynamic performance.

Comparison between the Edwards valve (11 cases) and the CoreValve (10 cases) showed that the former had stronger radial force and thus retained the same circular shape even in the presence of such uneven anatomic variations, allowing sufficient stent expansion for adequate valve function. The CoreValve bioprosthesis was positioned 12 mm higher than the lower end of the stent frame and seemed to be hindered by the BAV anatomy because of the lower radial force of the stent frame. Nevertheless, adequate postprocedural pressure gradient was achieved in all CoreValve and Edwards valve recipients alike. This observation suggests that the CoreValve bioprosthesis may function adequately despite its relatively oval shape at the level of the annulus. However, the possible impact of valve underexpansion on its long-term function remains unclear.

The frame and bioprosthesis shape may be affected by the position in which the prosthesis is implanted and the distance between the annulus plane and the native valve. In this report, the sample size was too small to allow any conclusion to be drawn about the differences between the 2 valves. Further investigation should provide interesting data.

BAV is known to be associated with concomitant aortic diseases, such as aortic root dilatation or aortic aneurysm, which tend to be related to type 2 morphology (2 raphes). In our study, type 2 BAV was identified in 3 cases (14.3%), and no patient had an ascending aortic diameter in excess of 45 mm. However, the mean ascending aortic diameter was larger (38.3±3.4 vs 35.8±4.3 mm; P=0.01) than in the non-BAV group. Screening for concomitant aortic or arterial disease and appropriate patient selection to exclude patients requiring surgical correction of aortic disease are essential before considering TAVI in this anatomic variation.

**Extension of Indications for BAV in TAVI**

Now that the TAVI technique has reached relative maturity, the extension of its indications is a highly important matter. Wider application of TAVI to patients with BAV may result in an increase in the number of treatable patients, especially in younger age groups. Despite the limited sample size of this study, we believe that our study may offer a glimpse into the future of this promising technique. Data allowing comparison between preprocedural and postprocedural MDCT images are currently being processed, and meticulous analysis will help us understand the mechanism of TAVI in BAV and the differences in performance of the various types of bioprosthesis.

**Study Limitations**

It is possible that some patients with bicuspid AS may have been excluded from TAVI (indication) because of an overly large mean diameter or maximal diameter of the annulus. No information is available about the BAV patients who were deemed ineligible for this procedure, because these cases were not included in our database. An important selection bias...
was taken into account in our study. As a rule, only patients with degenerated tricuspid AS are referred to our center for TAVI, because BAV is a recognized contraindication to this procedure. In such patients, BAV sometimes may be diagnosed by MDCT. CT sensitivity and specificity will need to be studied in larger unbiased AS populations and compared with TTE and (3-dimensional) TEE. Our study reports a retrospective single-center TAVI cohort of limited size. The diagnosis of BAV by MDCT still remains unestablished. Although 3-dimensional TEE was rarely performed for preprocedural screening in TAVI, echocardiography assessment was achieved by 2 independent experienced operators. In our study, no gold standard criterion (surgical specimen or pathology) was available to diagnose BAV. More precise criteria of bicuspidy need to be defined in larger studies taking into account the following factors: length of commissure fusion; degree; location; symmetry of calcification; presence of a calcification bridge; and other factors.

Further studies of larger patient populations are required to confirm our results.

Conclusions

In selected patients with BAV, TAVI may be associated with a low complication rate, therapeutic efficacy, and acceptable outcomes similar to those in non-BAV patients. Nevertheless, further studies with larger samples of patients as well as precise evaluation comparing preprocedural and postprocedural MDCT analysis are required to confirm our results.

Acknowledgments

The authors thank Catherine Dupic for her assistance in the preparation of this article.

Disclosures

Dr. Hayashida is a proctor for transfemoral-TAVI for Edwards. Dr Lefèvre is a proctor for transfemoral-TAVI for Edwards and is a consultant for Symetis and Directflow. Dr Chavalier is a consultant for Medtronic. Dr Romano is a proctor for transapical-TAVI for Edwards.


Transcatheter Aortic Valve Implantation for Patients With Severe Bicuspid Aortic Valve Stenosis

Kentaro Hayashida, Erik Bouvier, Thierry Lefèvre, Bernard Chevalier, Thomas Hovasse, Mauro Romano, Philippe Garot, Yusuke Watanabe, Arnaud Farge, Patrick Donzeau-Gouge, Bertrand Cormier and Marie-Claude Morice

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