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EDITORIAL COMMENT

Bicuspid Aortic Valve

Any Room for TAVR?*

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Bicuspid aortic valve (BAV) disease is the most common congenital cardiac defect, with a prevalence estimated between 0.5% and 2% (1,2). The earliest description of BAV is attributed to Leonardo da Vinci, who sketched the bicuspid variant of the aortic valve over 400 years ago (3). In the last 100 years, various authors have reported the clinical sequelae of this common congenital disease, namely aortic stenosis or incompetence, endocarditis, aortic aneurysm formation, and aortic dissection (1,2,4).

There are several variants of this valve anomaly. Generally, BAV without any redundant tissue tends to develop stenosis, whereas valves with more redundant tissue usually develop valvular incompetence (3). The incidence of aortic stenosis complicating BAV in an autopsy series ranges from 15% to 75% (1). Progression of BAV stenosis is age related, with fibrosis beginning in the second decade and calcification progressing significantly after the fourth decade. Among octogenarians and nonagenarians undergoing surgical aortic valve replacement (AVR), 22% and 18%, respectively, were found to have BAV (5). Bicuspid aortopathy (i.e., dilation of any or all segments of the proximal aorta from the aortic root to the aortic arch) is the most common nonvalvular finding and is present in up to 50% of affected persons (2,6). Abnormal dilation of the ascending aorta is secondary to abnormalities of the aortic media and becomes of surgical interest when the aortic diameter exceeds 4.5 cm (6). Aortic media changes are present independent of whether the valve is functionally normal, stenotic, or incompetent. Ascending aorta pathology is an expression of the genetic basis of BAV and may justify a more complex surgical treatment (2).

All these differences between BAV and senile aortic valve stenosis affecting tricuspid aortic valves may justify the reason why BAV stenosis has been considered a contraindication for transcatheter AVR (TAVR) in most studies. The specific concerns regarding TAVR for BAV include:

1. An elliptically shaped annulus that may impair valve positioning and sealing.
2. Asymmetrical and heavy calcification of leaflets may impede valve expansion and valve hemodynamics (e.g., higher transvalvular gradients and paravalvular leak).
3. Presence of aortic disease increases the risk of dissection or rupture during valvuloplasty, postdilatation, or implantation of balloon-expandable valves.
4. Fused commissures are susceptible to disruption during balloon valvuloplasty, resulting in severe aortic regurgitation.
5. Underexpansion and/or a non-circular shape of the transcatheter heart valve may affect long-term durability.

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Despite these concerns, we cannot dismiss the fact that there are patients with severe aortic stenoses who are not suitable surgical candidates and are found to have BAV disease who would benefit from TAVR. However, until now, data regarding the feasibility of TAVR in BAV have been limited to small case series (7). The registry presented in this issue of the *Journal* is the largest collection of patients treated

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with TAVR who have a BAV (8). The authors collected data for 139 patients treated with TAVR in 12 centers over 9 years. The diagnosis of BAV was established by transesophageal echocardiography in all patients, and in 63% of the patients, multislice computed tomography (MSCT) also was performed. Despite advanced multimodal imaging techniques, the diagnosis of BAV remained uncertain in 19 patients (13.7%). The self-expandable transcatheter heart valve (THV) (CoreValve, Medtronic Inc., Minneapolis, Minnesota) was implanted in 91 patients (65%), whereas the balloon-expandable THV (Sapien, Edwards Lifesciences, Inc., Irvine, California) was implanted in 48 patients. The procedures were performed using transfemoral access in 78.5% of the patients. There were no clinical differences between the 2 groups of patients, except for a higher prevalence of atrial fibrillation (30% vs. 15%, respectively) in patients treated with the self-expandable valve. Overall, this population should be considered at intermediate risk, with a Society of Thoracic Surgeons predicted risk of mortality of 5%, whereas it was 11.8% in the PARTNER 1A (Placement of AoRTic TraNscathetER Valve) trial (9) and 7.3% in the CoreValve pivotal trial (10). As expected, the mean diameter of the valves used was 27.8 mm, which was relatively large (valve diameters were 28.5 mm for the self-expandable THV, where oversizing is less of an issue). There was a need for a second valve in 4 versus 1 patient, who received balloon-expandable valve implants. The procedural mortality was numerically higher for the self-expandable THV (4.9% vs. 2.1%, respectively; $p = 0.66$), whereas the 1-year mortality rate was lower for the self-expandable THV (12.5% vs. 20.8%, respectively; $p = 0.12$). The 30-day incidence of stroke was approximately 2%, with no differences between the 2 valves. The procedure was effective in most patients, with a 30-day combined efficacy endpoint achieved in 85% of the patients. The mean aortic valve area increased from 0.6 cm^2 to 1.7 cm^2 when assessed by echocardiography at 30 days. Significant post-implantation aortic regurgitation grade ≥2 was present in 28.4% of patients. Important findings regarding this parameter are: 1) significant aortic regurgitation decreased to 17.4% when preprocedural annular assessment was performed by MSCT; 2) significant aortic regurgitation was 2 times more frequent following implantation of the self-expandable THV than the balloon-expandable THV (32.2% vs. 19.6%, respectively; $p = 0.11$); and 3) MSCT evaluation was performed in 77.1% of patients who received balloon-expandable valve implants versus 56% of patients treated with the self-expandable valve ($p = 0.02$). Interestingly, significant aortic regurgitation was more frequent when the baseline BAV anatomy was type 0 (no raphe, classic bicuspid aortic valve).

The main conclusions we can draw from this important study are:

1. TAVR with first-generation aortic valves is feasible in selected patients with BAV (device success of 90%, 1-year mortality of 17.5%, 30-day incidence of stroke of 2%).
2. The incidence of significant aortic regurgitation is high at 28.4% (9% in the CoreValve pivotal trial and 12.2% in the PARTNER 1A trial).
3. When accurate sizing is performed using MSCT, the incidence of aortic regurgitation decreases to 17%.
4. The small number of patients and the fact that MSCT was more frequently used with the balloon-expandable valve than with the self-expandable valve does not allow us to make hypotheses regarding the most suitable first-generation valve for BAV.

IMPACT OF THIS STUDY ON TAVR

Unless next-generation transcatheter valves show better performance regarding prevention of residual aortic regurgitation, the incidence of significant aortic regurgitation following first-generation transcatheter valves implantation, even with full MSCT evaluation, is too high to extend TAVR to BAV unless the patient is truly inoperable or has an unacceptably high surgical risk. However, the current study does set a benchmark for next-generation TAVR devices and does demonstrate the feasibility of TAVR in BAV. The presence of significant aortic root dilation, not present in this study, probably demands complete surgical correction rather than TAVR, and a question mark remains regarding TAVR when aortic regurgitation is the main defect. The results presented reinforce the suggestion that BAV is predominantly a disease of the "young patient" and thus remains in the surgical domain. Nevertheless, we cannot dismiss the fact that approximately 20% of elderly patients with critical aortic stenosis have BAV and that it is in these high-risk elderly patients where the role of TAVR needs to be clearly defined. To conclude, we can state that the study presented in this issue of the *Journal* gives us a realistic perspective of TAVR in BAV and defines areas of improvement if the goal is to continue to treat more patients in a less invasive way.

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