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EDITORIAL COMMENT

TAVR for Stenotic Bicuspid Aortic Valve

Feasible, Continuously Improving Results With Another Red Flag*

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Bicuspid aortic valves (BAVs) were systematically excluded from randomized studies that established the noninferiority of the percutaneous approach (transcatheter aortic valve replacement [TAVR]) in comparison with conventional surgical aortic valve replacement (SAVR) for the treatment of severe aortic stenosis (AS) (1,2). This initial precaution was clearly appropriate given the characteristics and known prevalence of BAV in clinical practice.

Indeed, BAV is a specific entity with its own developmental and pathophysiological mechanisms, morphologic features, and outcomes. BAV results from a congenital malformation of the embryonic outflow of the primitive heart tube. Neural crest cells from rhombomeres migrate early through the pharyngeal arches toward the outflow of the heart tube. They organize the formation of normal sigmoid arterial valves, participate in the arterialization of the distal outflow from which the intrapericardial arterial and pulmonary trunks derive, and contribute to the ventriculoarterial junction (3). Failure of this developmental process may account for a malformation complex of variable severity where, for our purpose, the abnormally formed aortic valve is pivotal.

The complex morphology of these valves was first accurately described by Anderson with reference to tricuspid aortic valves (TAVs), as reported by Sutton et al. (4). These valves were subsequently categorized into different types according to the number of leaflets and raphe (5). At the stage of severe calcific AS, the shape of the orifice and the amount of calcification of BAVs strikingly differ from TAV stenosis (**Figure 1**). From these (nearly trivial) observations emerge the true challenges of TAVR in patients with BAVs.

First, the elliptical and asymmetrical (both in shape and depth) residual orifice may impede the deployment of a circular valved device. Second, the huge calcifications that characterize these valves are unevenly distributed (i.e., maximal at the level of the raphe), frequently invade the fibrous and muscular subvalvular left ventricular outflow tract, and may be subjected to "caseous" transformation. As such they may impede valve orifice opening and are of major embolic concern during deployment of a percutaneous valve.

WHAT DO WE KNOW FROM CLINICAL EXPERIENCE?

So far, only short-term data from limited clinical series or registries (6) are available. These data showed that TAVR is feasible in stenotic BAVs. However, TAVR in BAVs appears more demanding and riskier, takes longer, and requires more pre- and post-dilation. Initial results in moderate- to high-risk patients were encouraging, but the high incidence of paravalvular leaks and pacemaker implantation was worrying and negatively affected global outcomes (7,8). In experienced hands and with evolving devices, the paravalvular leaks could be reduced to very low levels, but the pacemaker rate persists in up to

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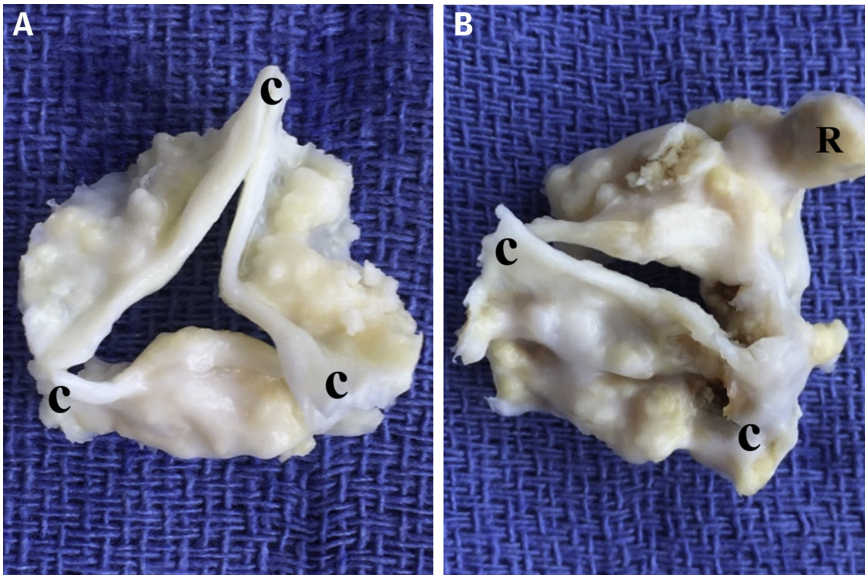
FIGURE 1 Pathoanatomy of Calcific TAV and BAV (Sievers Type 1 L/R)

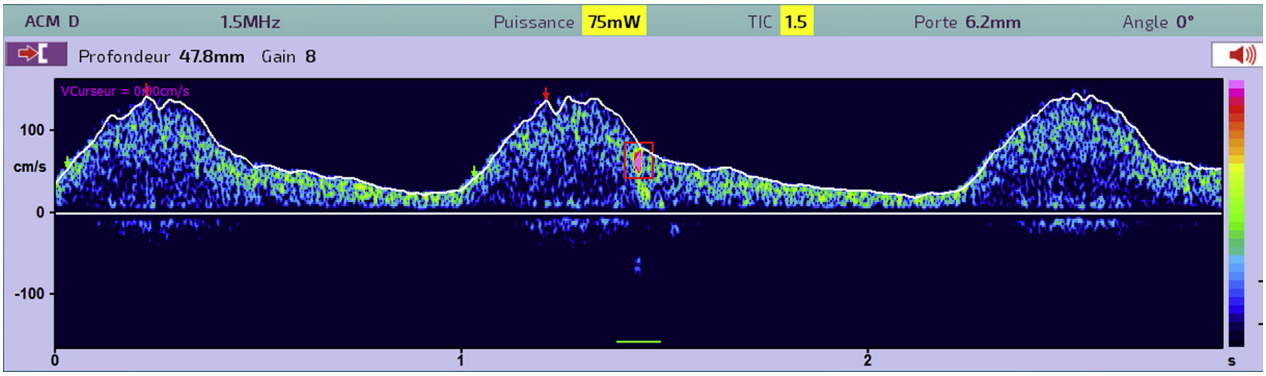


Resected specimen of a stenotic **(A)** tricuspid aortic valve (TAV) and **(B)** bicuspid aortic valve (BAV) as viewed from the aortic side. c = commissure; R = raphe.

25% of the cases (9). This finding led Guyton and Padala (10) to temper the interventional enthusiasm by further raising the issues of incomplete and asymmetrical valve expansion and the resulting suboptimal hemodynamic features that will certainly affect valve durability.

Inherent in any cardiovascular intervention, the stroke rate in TAVR for TAVs that was initially at 5% to 10% in very high risk patients is now as low as 0.5% to 0.9% in the latest randomized trials performed in low-risk patients (1,2). Although cerebral embolic protection devices may actually capture debris (e.g., foreign body material, endothelium, calcific debris, myocardial tissue), in 98% of TAVR-treated patients, BAV is associated with a higher risk of dislodging particles ≥1,000 μm) (11). Accordingly, the overt

FIGURE 2 Transcranial Flow Doppler Recording of the Left Mean Cerebral Artery During TAVR Deployment



Recording of a particular solid embolus **(red square).** ACM D = right middle cerebral artery; porte = gate; profondeur = depth; puissance = power; TAVR = transcatheter aortic valve replacement; TIC = thermal index.

stroke rate remains higher in BAV compared with TAV (2.5% vs. 1.6%) (12). This is possibly related to the higher calcium load of BAV (13) and to the more challenging placement, deployment, and repositioning of devices known as major sources of any emboli (11). High-intensity transient signals (HITS) recorded by serial transcranial Doppler examination have been proposed as surrogates for cerebral micro-embolization (14). HITS may correspond to solid or gaseous emboli. In our experience, we have observed (using recognition algorithms) "solid HITS" in 89% of patients predominantly during valve implantation and deployment (**Figure 2**) (C. Douin, M. Sprynger, P. Lancellotti, unpublished data, June 2020). At the same time, it is increasingly realized that central nervous system (CNS) injuries are under-reported. With the availability of T_3-diffusion-weighted magnetic resonance imaging (DW-MRI), new silent lesions can be detected in most if not all patients undergoing TAVR for TAV stenosis (15). The tissue-based paradigm for CNS injury assessment therefore raises major concerns with regard to the significance of these so called "silent" or "covert" brain injuries. These areas of CNS white matter infarction are mostly without immediate neurological expression but seem causally linked to at least accelerated cognitive decline (16).

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WHAT IS NEW?

In this issue of the *Journal,* Fan et al. (17) bring to our attention important DW-MRI data on CNS lesions or injuries in patients with BAVs who have severe AS treated with TAVR. DW-MRI was performed for baseline imaging and within the post-procedure optimal window.

Fan et al. (17) showed that patients with BAVs have an overt stroke rate slightly higher than that of patients with TAVs (2.4% vs. 1.7%) and comparable to already published data (12). In addition, patients with BAVs experienced more new silent brain injuries after TAVR in terms of both number and volume of lesions. This resulted in a nearly 3 times higher incidence of lesions larger than 1 cm^3 in BAVs than in TAVs (28.6% vs. 10.9%). These data were derived from the analysis of a single-institution cohort of 204 consecutive patients, including 83 BAVs (76 years; Society of Thoracic Surgeons score 6.0 ± 3.6) and 121 TAVs (79 years; Society of Thoracic Surgeons score 7.1 ± 4.2). A higher proportion of patients with BAVs were treated with self-expandable valves.

These results must be interpreted cautiously in the context of a series of older adult Asian patients with BAVs (high prevalence of type 0) who had severe AS, were at intermediate risk, and were selected for TAVR by the heart team without randomization of TAVR devices.

Be that as it may, and before the multiple mechanisms of these lesions and their clinical impact are fully understood, we share the suggestions of Fan et al. (17) that an efficient embolic protection strategy is required. Specific device improvements are also needed, as well as procedure refinements. Finally, we concur as physicians with the cautious indications for TAVR in patients with BAVs as implicitly suggested here. Indeed, at a time when TAVR appears as a new paradigm for the treatment of severe AS in TAV regardless of the risk category (1,2), patients with a BAVs deserve special attention for optimal care. They are much younger than their TAV counterparts and are predominantly at lower risk according to current scoring systems. As such, both their lifestyle and life expectancy expose them to every unresolved issue of TAVR, namely suboptimal valve deployment and possibly accelerated valve failure, a need for pacemakers, and worrying neurological risk.

In this context, the option of modern SAVR, which is not exempt from CNS injury, either (18), but which may guarantee a properly fixed prosthesis and, as required, management of associated disease of the "BAV complex" (e.g., ascending aorta, impeachment of the anterior mitral leaflet, left ventricular outflow tract anomalies), is both efficient and currently performed mini-invasively. These 2 features confer the high value of SAVR in selected patients with BAVs without compromising late outcome.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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