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Transcatheter aortic valve replacement for bicuspid valves – from anatomy all the way to the treatment

Implante transcater de válvula aórtica para válvulas bicúspides: da anatomia ao tratamento

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ABSTRACT – The transcatheter aortic valve implantation has revolutionized the treatment of symptomatic severe aortic stenosis in patients likely to have complications in the conventional surgery, particularly the elderly. However, almost all randomized clinical trials that assessed this therapeutical modality excluded patients with bicuspid aortic valve, due to the anatomic and technical particularities related to this condition. Enhanced understanding about the aspects inherent to percutaneous treatment of bicuspid aortic valve stenosis is crucial to obtain better clinical and hemodynamic results.

Keywords: Transcatheter aortic valve replacement; Aortic valve stenosis; Aortic valve; Heart valve diseases

RESUMO – O implante transcater de válvula aórtica revolucionou o tratamento da estenose aórtica grave sintomática em pacientes propensos a complicações com a cirurgia convencional, notadamente os idosos. Entretanto, a quase totalidade dos ensaios clínicos randomizados que avaliaram essa modalidade terapêutica excluiu pacientes portadores de válvula aórtica bicúspide, dadas as particularidades anatômicas e técnicas que envolvem essa condição. Uma maior compreensão sobre os aspectos inerentes ao tratamento percutâneo da estenose aórtica em valvas bicúspides é fundamental para a obtenção de melhores resultados clínicos e hemodinâmicos.

Descritores: Substituição da valva aórtica transcater; Estenose da valva aórtica; Valva aórtica; Doenças das valvas cardíacas

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BACKGROUND

Transcatheter aortic valve replacement (TAVR) completely changed the treatment of aortic stenosis (AS) in the past decade. The literature on the topic is wide and has modified the most recent guidelines^{1,2} regarding the management of aortic valvular disease. Almost all randomized trials that underlie these guidelines routinely excluded bicuspid aortic valves (BAV) for several reasons, including anatomical and procedural issues. With the decrease of age and risk profile of the patients referred for TAVR, it is likely that the Heart Teams will have to treat more BAV patients. A comprehensive understanding of the BAV will be crucial to achieve better clinical and hemodynamic outcomes.

PREVALENCE

Bicuspid aortic valve is the most common congenital heart abnormality, mainly affecting males, with an estimated prevalence of approximately 1% of the general population and 2% to 5% of patients with AS.^{3,4} This type of anatomy accounts for the majority of surgical aortic valve replacements (SAVR) in patients aged under 70 years. One study on surgically excised valves demonstrated that approximately 20% of the population aged over 80 years and submitted to surgery had bicuspid

anatomy.⁵ Bicuspid aortic valve often has a familial occurrence, consistent with an autosomal dominant inheritance, which justifies echocardiographic screening in first-degree relatives.⁶

ANATOMY

Congenital bicuspid valves can be stenotic with commissural fusion but they usually cause no hemodynamic repercussion during childhood. The turbulent flow may lead to leaflet trauma and fibrosis, followed by calcification and significant orifice reduction at adulthood.

Bicuspid aortic valve may combine heavily calcified leaflets, large annulus and dilated ascending aorta that can lead to procedure-related complications, such as moderate/severe paravalvular regurgitation, transcatheter heart valve malposition, annular rupture, stroke, aortic dissection, and accelerated structural valve deterioration. These complications were frequently met with first generation devices and the literature shows improved outcomes with the second generation, due to repositioning features and sealing skirts, associated with better implant techniques by more experienced operators.⁷ The Sievers classification has been frequently used to identify different types of morphology in BAV, and is based on number of raphe (fused area of two underdeveloped cusps turning into a malformed commissure between them), position of cusps or raphe and functional status of the valve (Figure 1). Type 1, with a raphe between left and right cusps, is the most frequently observed, with an incidence of approximately 70%, followed by an equal distribution of types 0 and 1 (R-N).⁸

Source: adaptado de Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg.* 2007;133(5):1226-33. Table 1, Schematic presentation (as viewed from the surgeon's position with the left coronary sinus on the left side) of the classification system of BAVs with one main and two subcategories, including the number of specimens (percent in parenthesis); p. 1.230.

R: right; L: left; N: noncoronary.

Figure 1. Sievers classification.

Computed tomography and sizing

Multidetector computed tomography (MDCT) is the gold standard for sizing AV, however the methodology remains controversial. Current practice basically employs

two different methods: a standard annular-based sizing and/or supra-annular sizing at the level of the commissures (intercommissural distance – ICD). The BAVARD Multicenter Registry retrospectively analyzed the second-generation prosthesis geometry after implantation by MDCT in BAV, and compared the results with tricuspid valves⁹. The study had several interesting conclusions and recommended sizing according to annulus and ICD (4mm above the annulus) morphologies: tubular and flare sizing based on the annulus (88% of population of the study) and taper sizing based on the ICD (Figure 2). This study also highlighted second generation transcatheter heart valve (THV) similarly reshapes the aortic annulus in tricuspid and bicuspid valves. A more recent publication proposed a new algorithm for sizing stenotic BAV under evaluation for TAVR.¹⁰ It is based on three variables: the ratio between raphe length and annulus diameter; calcium burden; calcium distribution in relation to the raphe. This study has several methodological limitations but some interesting points, such as the use of raphe length and calcium burden for a more proper evaluation of THV sizing. Both studies have a common aspect – underexpansion of implanted devices in BAV found in postprocedural analysis by MDCT. This systematic underexpansion may have implications for sizing and potential complications, such as leaflet thrombosis. In terms of sizing, as opposed to what is regularly applied to tricuspid anatomies, in BAV, when the annulus is in a grey zone between two valve sizes, we may select the smallest. Minimal oversize seems to be efficient in BAV. It is clear that preprocedural planning with a precise sizing by MDCT is a crucial step for achieving success during BAV procedures.

Source: adapted from Tchetché D, de Biase C, van Gils L, Parma R, Ochala A, Lefevre T, et al. Bicuspid aortic valve anatomy and relationship with devices: The BAVARD Multicenter Registry. *Circ Cardiovasc Interv.* 2019;12(1):e007107. doi: 10.1161/CIRCINTERVENTIONS.118.007107. Figure 4, Various configuration of the landing zone in bicuspid patients and simplified sizing algorithm. ICD indicates intercommissural distance; p. 8.

ICD: intercommissural distance.

Figure 2. BAVARD Study scheme: various configurations of the landing zone in bicuspid valves and simplified algorithm.

CLINICAL EVIDENCE

As previously mentioned, BAV patients have been systematically excluded from pivotal randomized trials. Retrospective studies were published in the past years with very heterogeneous clinical and echocardiographic results. In common, these analyses showed that, as compared with tricuspid aortic valve (TAV), bicuspid valve has more paravalvular leak (PVL), permanent pacemaker rates, but not higher incidence of hard endpoints, such as death and stroke.⁷ The first data comparing early versus new generation THV demonstrated a remarkable improvement of these endpoints and device success rate,¹¹ paving the way to new studies showing better outcomes regarding mortality, disabling stroke, pacemaker rates and PVL $\geq$ moderate, suggesting a more adequate sizing leading to proper device choice and refinement of the implant technique (Table 1). The first multicenter, prospective trial has been recently presented (Evolut Low Risk Bicuspid Trial), with a cohort of 150 BAV low-risk patients using the self-expandable Evolut R/Evolut PRO devices. With a mean age of 70.3 $\pm$ 5.5 years and The Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) of 1.4 $\pm$ 0.6, the primary safety endpoint combining all-cause mortality or disabling stroke at 30 days was 1.3% (all-cause mortality: 0.7%; disabling stroke: 0.7%). This study also highlighted some practical issues, such as 91% of predilation, 30% of cerebral embolic protection devices and implant of more than 41% of the largest THV available (Evolut R 34mm), corroborating the findings of larger annulus in bicuspid anatomies. The permanent pacemaker rate was 14.7%, with one case of coronary obstruction and no cases of moderate/severe PVL. Another prospective registry (BIVOLUT-X) confirmed these findings in a cohort of patients treated with the Evolut Pro device. Despite the increasing data published in the last years, there is still a lack of evidence from randomized studies that can substantially support the treatment of BAV patients, especially those at lower risk.

PROCEDURE RECOMMENDATIONS

The daily practice in cardiac catheterization laboratories varies much in different organizations. However, considering the anatomical features of BAV previously described, some steps are recommended to approach this specific scenario:

- General anesthesia or conscious sedation: indifferent, according to the current practice of the team. There is no data available supporting one strategy over another regarding clinical endpoints.
- Transesophageal echocardiography: not mandatory, but may be useful in very challenging BAV anatomies evaluating PVL and early identification of potential complications.
- Vascular access: percutaneous transfemoral approach is recommended.
- Guidewire: a stiffer pre-shaped wire like double-curved Lunderquist® is recommended, but other types, such as Confida or Safari, can also be used.
- Predilation: seems to be unanimous in this scenario, regardless the type of device to be used. A balloon sized according to the minimal diameter of the annulus is recommended. It is important to highlight that predilation should not be therapeutic, it just facilitates expansion in THV implanting.
- Device: there are no randomized data comparing the devices available for BAV. Second-generation devices proved to be safer and more effective as compared to the previous generation. Sealing skirt and the capacity to be repositionable and recapturable are interesting features that can aggregate value to the procedure.
- THV implant height: considering the landing zone can be from the annulus to 4 to 5mm above, due to the constraint points, a higher implant is recommended whenever possible, promoting a more adequate sealing.
- Post-dilation: depends on the hemodynamic result and degree of regurgitation after device deployment. If necessary, use a balloon sized by the mean annulus diameter in self-expandable devices, or extra volume overfilling on the balloon expandable devices.

Table 1. Cumulative data on bicuspid aortic valve patients treated with second generation transcatheter heart valve

Author	Population	Method	Age	STS	Device	Follow-up period	Death	Stroke*	PM	PVL
Yoon et al. ¹²	561	R	77.2 $\pm$ 8.2	4.6 $\pm$ 4.6	SE+BE	1 year	4.5%	NA	16.4%	NA
Perlman et al. ¹³	51	R	76.2 $\pm$ 9.3	5.2 $\pm$ 3.7	S3	30 days	3.9%	0	16.4%	23.5%
Reddy et al. ¹⁴	758	M	77.3	5	SE+BE+ME	30 days	3.7%	NA	17.9%	12.2%
Makkar et al. ¹⁵	2,691	M	74	4.9	S3	1 year	10.5%	3.4%	10%	3.2%
Halim et al. ¹⁶	3,705	R	74	3.8	SE+BE	1 year	12%	4.1%	NA	2.7%
Waksman et al. ¹⁷	61	P	68.6 $\pm$ 7.4	1.5 $\pm$ 0.6	SE+BE	30 days	0	0	13.1%	1.6%

* Refers to disabling events. STS: Society of Thoracic Surgeons; PM: permanent pacemaker; PVL: $\geq$ moderate paravalvular regurgitation; R: retrospective; SE: self-expandable transcatheter heart valve; BE: balloon-expandable transcatheter heart valve; M: meta-analysis; ME: mechanically-expanded transcatheter heart valve.

- Cerebral embolic protection devices: there is no specific data supporting use of these devices in BAV patients. However, the anatomical features with high calcium burden and association with aortopathy, especially in lower-risk and younger patients, seems to be an equation suitable for indication.

Postprocedural recommendations regarding immediate recovery, antithrombotic therapy, echocardiography and hospital discharge do not differ from TAV cases.

CONCLUSION

Bicuspid aortic valves remain one of the last frontiers for transcatheter aortic valve replacement. Collective knowledge about procedural techniques and clinical outcomes has constantly improved. A thorough multidetector computed tomography-guided anatomical assessment is mandatory for decision-making and identification of the optimal bicuspid candidates for transcatheter aortic valve replacement. Further studies are needed to better explore sizing, clinical outcomes, and durability.

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None.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: VE and DT; data collection: VE and DT; data interpretation: VE and DT text writing: VE and DT; approval of the final version to be published: VE and DT.

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