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Editorial

Bicuspid aortic valve: one of the last remaining challenges for the percutaneous treatment of aortic valve disease

Válvula aórtica bicúspide: uno de los últimos retos para el tratamiento percutáneo de la valvulopatía aórtica

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From the outset, randomized trials comparing transcatheter aortic valve implantation (TAVI) and surgery have consistently excluded patients with bicuspid aortic valve (BAV). This is at least partly because BAVs frequently possess anatomical characteristics that predispose patients to worse outcomes after TAVI, such as larger and more elliptical aortic annuli and asymmetric leaflet calcification.[1] Another noteworthy anatomical characteristic is that 3 distinct BAV morphologies have been reported.[2] Depending on the type and degree of raphe calcification, these morphologies can confer an elevated risk of incomplete valve expansion, paravalvular leaks, and higher gradients after implantation (bicommissural type).[3,4] Furthermore, there are additional technical difficulties concerning aortic annulus measurement when selecting the size of the prosthesis to be implanted: at the annular level, such as in trileaflet aortic valves, and at the supraannular level (intercommissural distance). The presence of a BAV can also be associated with concomitant dilatation of the ascending aorta (less frequently in the "tricommissural" type), which can affect the long-term outcomes of TAVI. Another distinctive feature of BAVs, as shown in comparative studies of patients with tricuspid valves, is the type of patient presenting with severe BAV stenosis. These patients are generally younger and male and have lower surgical risk (Society of Thoracic Surgeons [STS] score) and cardiac comorbidity. The comparative studies found no differences in mortality but did link BAVs to lower device success, higher incidence of moderate or severe residual aortic regurgitation,[5,6] and an increased rate of stroke.[7]

Given the lack of randomized studies comparing TAVI and surgery in the context of BAV, the available data are derived from registries. These studies[8,9] show favorable outcomes for TAVI and associations with lower short-term mortality and incidence of major adverse cardiac events.[10] In addition, TAVI is linked to lower rates of infarction, bleeding, and vascular complications and a shorter hospital stay. On the other hand, patients undergoing TAVI exhibit a greater need for pacemakers.

Few studies have compared the different types of prosthesis in patients with BAV. A notable study by Amat-Santos et al.,[11] recently published in *Revista Española de Cardiología*, not only sheds light on an aspect of aortic valve disease that still lacks scientific evidence, but also presents clinical outcomes for a balloon-expandable valve with little related clinical data: the Myval prosthesis (Meril Life Sciences Pvt. Ltd, India). The study involved a multicenter registry of 360 consecutive patients with BAV treated with the latest-generation balloon-expandable prostheses SAPIEN 3 Ultra (S3U; Edwards Lifesciences, United States) (n = 129) and Myval (n = 122) and the self-expanding Evolut PRO+ (EP+; Medtronic, United States) (n = 109). The primary endpoint was 30-day device success, defined according to the Academic Research Consortium-3 consensus as a composite of freedom from mortality, surgery, or intervention related to the device, or a major vascular or access-related or cardiac structural complication, and intended valve performance (mean gradient $<$ 20 mmHg and less than moderate aortic regurgitation).

Using a propensity score adjustment of 3 groups (TriMatch analysis), the authors found that the primary endpoint at 30 days of follow-up was significantly more common in the Myval group than in the S3U group (100% vs 87.5%; $P = .0002$) and in the EP+ group (81.3%; $P < .001$). The main difference between the Myval and EP+ valves was the higher rate of moderate or greater aortic regurgitation with the self-expanding valve. These findings are in line with those of a study performed by Mangieri et al.[12] comparing 353 patients with BAV treated with SAPIEN 3 vs patients treated with Evolut R/Evolut PRO. Device success was similar for the 2 prostheses. However, at 1 year of follow-up, the self-expanding valve group showed a significantly higher rate of moderate/severe paravalvular leaks (9.3% vs 0%; $P = .043$).

Another novel aspect of the study by Amat-Santos et al. is the comparison of 2 balloon-expandable valves, the SAPIEN and Myval, in patients with BAV. Device success was higher in the Myval group, largely due to higher residual gradients. This was despite the lower use of small or intermediate prostheses in the S3U group (16.3%) than in the other groups (32.5% in Myval and 31.3% in EP+), even though these devices are the sizes most strongly associated

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with prosthesis-patient mismatch.[13] Amat-Santos et al. note that the use of intermediate-sized prostheses (in 25%) might have favorably influenced the residual gradient.[11] However, the rates of prosthesis-patient mismatch for intermediate or larger prostheses, with clinical repercussions, were 0% in the S3U and Myval groups and 1% in the EP+ group. Another factor potentially influencing these outcomes was the lower percentage of predilatation in the SAPIEN 3 group than in the comparison groups: 44% vs 70.1% in the Myval group and 79.2% in the EP+ group. This may be particularly important in light of the anatomical characteristics of the treated valves: about 90% of the patients had type 1 bicuspid valves characterized by eccentricity and moderately sized and highly calcified annuli (> 4000 Agatston units). Thus, the lower rate of predilatation in this type of valve could also have contributed to a lower expansion of the prosthesis in the S3U group and, thus, a gradient increase.

Another major result is that the secondary safety endpoint was significantly better in the Myval group than in the other groups: S3U (85% vs 70%; $P = .031$) and EP+ (67.5%; $P = .022$). This result was influenced by the frequency of stroke in the S3U group (7.7%), which was high for low-risk patients (STS score, 2.2). This represents an inherent limitation of this type of study because, despite propensity score adjustment and the excellent study group balance, the S3U group had a significantly higher incidence of porcelain aorta than the Myval and EP+ groups, a factor that is associated with a higher incidence of post-TAVI stroke.[14]

In conclusion, the study by Amat-Santos et al.[11] demonstrates not only the safety of these 3 valves in patients with BAV, but also the weaknesses of the latest-generation balloon-expandable S3U pump, such as the gradient increase after TAVI,[15] and of the self-expanding supraannular EP+ valve, such as residual aortic regurgitation, particularly for elliptical aortic annuli.[16] In addition, the results show a possible advantage of the Myval valve, particularly in complex anatomies such as those of BAV: the greater variety of prosthesis sizes enable a more precise adaptation to the size of the aortic annulus. Undoubtedly, the management of BAV remains a challenge and one of the last frontiers for the percutaneous treatment of aortic valve disease. Further studies are required to determine the optimal approach for achieving the best short- and long-term outcomes.

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