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Durability of transcatheter aortic valve implantation in bicuspid aortic valve stenosis: the last missing piece?

Eric Van Belle[1,2]*, MD, PhD; Flavien Vincent[1,2], MD, PhD

1. Department of Interventional Cardiology for Coronary, Valves and Structural Heart Diseases, Institut Cœur Poumon, Cardiology, CHU Lille, Lille, France; 2. Inserm, U1011, Institut Pasteur de Lille, EGID, Université de Lille, Lille, France

Transfemoral transcatheter aortic valve implantation (TAVI) has demonstrated similar results as well as superiority over surgical aortic valve replacement (SAVR) in low-to-high surgical risk elderly patients with tricuspid aortic valve (TAV) stenosis[1]. TAVI is now the gold standard for patients at high surgical risk or who are deemed inoperable and is favoured over SAVR in patients at intermediate risk who are suitable for a transfemoral approach[1]. Conversely, the European Society of Cardiology (ESC) guidelines recommend surgery as the preferred option for patients with severe aortic stenosis (AS) and a bicuspid aortic valve (BAV) anatomy as these patients were excluded from previous randomised controlled trials (RCTs)[1].

Despite the lack of randomised comparative studies with SAVR, TAVI is already frequently used in AS patients with BAV. In 2020, they represented ≥10% of patients undergoing TAVI in the Western population[2]. This use is supported by several registries, including the very large Society of Thoracic Surgeons (STS) registry, which shows that for BAV patients considered suitable for TAVI, the acute results and 1-year follow-up of those receiving either the balloon-expandable (BE) SAPIEN 3 (Edwards Lifesciences) or the self-expanding (SE) Evolut-R/Pro (Medtronic) transcatheter heart valve (THV) are as good as patients with tricuspid AS receiving the same THV[3,4]. These favourable results were recently confirmed in BAV patients at low surgical risk[2,5]. As a result, the BE-THV SAPIEN 3 and the SE-THV Evolut-R/Pro have received Food and Drug Administration (FDA) and "European Conformity" (CE) approval for all surgical risk, regardless of the valve anatomy, and the precaution regarding BAV has recently been removed from its commercial labelling[6].

To guarantee good acute procedural and 1-year results, several aspects have been clarified during the last few years. First, we must avoid proposing TAVI for patients with type 1 BAV with both calcified raphe and excessive calcified leaflets[7]; second, we must avoid proposing TAVI for patients in whom surgery of the aortic root is required; third, the procedure should be feasible through transfemoral access; fourth, the size of the device should be adapted to the smallest diameter of the aortic root-aortic valve complex which, in 20% of cases, is a few mm above the annular plane, and finally, we may consider using embolic protection devices, particularly in younger patients[6].

It is important to remember that in Western countries, BAV is frequent among patients with AS requiring valve replacement, regardless of age. They represent 28% of those >80 years old and 42% of those between 70 and 80 years old[8]. It is also important

* *Corresponding author: Department of Cardiology, Institut Cœur Poumon, Centre Hospitalier Universitaire de Lille, Bd Professeur Jules Leclercq, 59037 Lille, France. E-mail: ericvanbelle@aol.com*

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to remember that the vast majority of those BAV patients undergoing SAVR undergo a relatively "simple surgery" including bioprosthetic replacement without combined aortic root surgery[6]. Therefore, in BAV patients undergoing such "minimal" SAVR, TAVI has the potential to provide the same medical service.

One important reason not to propose TAVI for more BAV patients is the lack of information concerning long-term results and THV-durability in this very peculiar context. Such data are indeed scarce and limited to valve haemodynamic performance over a relatively short period of time[9]. In the BAVARD registry, 30 days post-TAVR, the indexed effective orifice area (EOA) was smaller in BAV patients than in TAV patients, but the incidence of severe prosthesis-patient mismatch was similar[10]. In the STS/ACC TVT registry, the 1-year mean gradient and rate of ≥moderate paravalvular regurgitation (PVR) were similar between BAV and TAV patients treated with the SAPIEN 3[4]. The BAVARD registry was also reassuring on the overall THV stent circularity. However, THVs were more constrained and underexpanded in BAV patients compared to TAV patients[10]. As prosthesis expansion could impact the THV durability and promote leaflet thrombosis, these findings raised concerns about a potential acceleration of the structural valve degeneration process in BAV patients[6]. A recent CT-scan study found hypoattenuated leaflet thickening in 10% of BAV patients 30 days post-TAVR, which is comparable to the findings of previous TAV studies[9].

The study by Zhou et al, published in the present issue of EuroIntervention, reports on the 3-year clinical and echocardiography outcomes of 246 consecutive patients undergoing TAVI, mostly treated with SE-THVs (82.9%) in a Chinese centre[11].

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The present study has several important limitations. First, it reports data from a single centre. Second, it reports data from an Asian population with a higher frequency of BAV than is found in Western countries and with a different proportion of BAV subtypes (0 versus 1)[6]. Third, among the SE-THVs which were used in the study besides the CoreValve (Medtronic) family, several are not available in Western countries, including the supra-annular Venus A (Venus Medtech), the VitaFlow (MicroPort), and the intra-annular TaurusOne (Peijia) THVs. It is also unfortunate that the proportion of patients treated with each of these three different SE-THVs is not reported.

Still the authors should be congratulated as it is the first study to report on the 3-year clinical and echocardiography outcomes in BAV patients undergoing TAVI[11], for they add several important pieces of information. The study demonstrates that at 3 years, survival (87.2% versus 79.6%; p=0.11), transvalvular gradient (10.76±5.15 mmHg versus 10.33±4.74 mmHg; p=0.64), and paravalvular leak ≥moderate (3.9% versus 6.5%; p=036) are similar between BAV (n=109) and TAV (n=137) patients. It further shows a progressive and continuous decrease of left ventricular mass over the 3-year time period.

As the proportion of type 0/type 1 BAV is very different between Western (15%/85%) and Asian (60%/40%) AS patients undergoing TAVI[6], it is also very reassuring to observe that the 3-year clinical outcome and valve haemodynamic performance, as evaluated by echocardiography, were similar in patients with type 0 or type 1 BAV.

Also interesting is the subgroup analysis restricted to the 204 patients treated with an SE-THV showing no sign of degradation in haemodynamic performance at 3 years in BAV as compared to TAV patients. This information is also reassuring in the context of the recent report that, in TAV patients, structural valve deterioration at 5 years is less frequent in patients undergoing TAVI than in those undergoing SAVR (2.6% versus 4.4%). This was recently reported, but not yet published, in the combined analysis of the 2 pivotal randomised studies comparing SE-THVs (CoreValve and Evolut TAVI systems).

Such very favourable results are encouraging and will have to be confirmed in larger patient populations, as well as in BAV patients from Western countries. It will also be very important to report long-term outcomes and valve durability of BE-THVs, as they are often preferred over SE-THVs in this population[6], whereas their durability has recently been questioned in TAV patients[12,13].

If the favourable results reported in the present study are confirmed, TAVI could become the treatment of choice for most AS patients with BAV. While BAV already represents 10% of patients undergoing TAVI in Western countries[6], this proportion could climb to 40% if the use is extended to patients in the 70-80 year-old range.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sadaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention.* 2022;17:e1126-96.

2. Makkar RR, Yoon SH, Chakravarty T, Kapadia SR, Krishnaswamy A, Shah PB, Kaneko T, Skipper ER, Rinaldi M, Babaliaros V, Vemulapalli S, Trento A, Cheng W, Kodali S, Mack MJ, Leon MB, Thourani VH. Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke Among Patients at Low Surgical Risk. *JAMA.* 2021;326:1034-44.

3. Forrest JK, Kaple RK, Ramlawi B, Gleason TG, Meduri CU, Yakubov SJ, Jilaihawi H, Liu F, Reardon MJ. Transcatheter Aortic Valve Replacement in Bicuspid Versus Tricuspid Aortic Valves From the STS/ACC TVT Registry. *JACC Cardiovasc Interv.* 2020;13:1749-59.

4. Makkar RR, Yoon SH, Leon MB, Chakravarty T, Rinaldi M, Shah PB, Skipper ER, Thourani VH, Babaliaros V, Cheng W, Trento A, Vemulapalli S, Kapadia SR, Kodali S, Mack MJ, Tang GHL, Kaneko T. Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke. *JAMA.* 2019;321:2193-202.

5. Deeb GM, Reardon MJ, Ramlawi B, Yakubov SJ, Chetcuti SJ, Kleiman NS, Mangi AA, Zahr F, Song HK, Gada H, Mumtaz M, Heiser J, Merhi W, Murrah CP, Noel T, Kirshner M, Byrne T, Ito S, Huang J, Forrest JK. Propensity-Matched 1-Year Outcomes Following Transcatheter Aortic Valve Replacement in Low-Risk Bicuspid and Tricuspid Patients. *JACC Cardiovasc Interv.* 2022;15:511-22.

6. Vincent F, Ternacle J, Denimal T, Shen M, Redfors B, Delhaye C, Simonato M, Debry N, Verdier B, Shahim B, Pamart T, Spillemaeker H, Schurtz G, Pontana F, Thourani VH, Pibarot P, Van Belle E. Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Stenosis. *Circulation.* 2021;143:1043-61.

7. Yoon SH, Kim WK, Dhoble A, Pio SM, Babaliaros V, Jilaihawi H, Pilgrim T, De Backer O, Bleiziffer S, Vincent F, Shmidt T, Butter C, Kamioka N, Eschenbach L, Renker M, Asami M, Lazkani M, Fujita B, Birs A, Barbanti M, Pershad A, Landes U, Oldemeyer B, Kitamura M, Oakley M, Ochiai T, Chakravarty T, Nakamura M, Ruile P,

Deuschl F, Berman D, Modine T, Ensminger S, Kornowski R, Lange R, McCabe JM, Williams MR, Whisenant B, Delgado V, Windecker S, Van Belle E, Sondergaard L, Chevalier B, Mack M, Bax JJ, Leon MB, Makkar RR; Bicuspid Aortic Valve Stenosis Transcatheter Aortic Valve Replacement Registry Investigators. Bicuspid Aortic Valve Morphology and Outcomes After Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol.* 2020;76:1018-30.

8. Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. *Circulation.* 2005;111:920-5.

9. Waksman R, Craig PE, Torguson R, Asch FM, Weissman G, Ruiz D, Gordon P, Ehsan A, Parikh P, Bilfinger T, Levitt R, Hahn C, Roberts D, Ingram M, Hanna N, Comas G, Zhang C, Ben-Dor I, Satler LF, Garcia-Garcia HM, Shults C, Rogers T. Transcatheter Aortic Valve Replacement in Low-Risk Patients with Symptomatic Severe Bicuspid Aortic Valve Stenosis. *JACC Cardiovasc Interv.* 2020;13:1019-27.

10. Tchetche D, de Biase C, van Gils L, Parma R, Ochala A, Lefevre T, Hovasse T, De Backer O, Sondergaard L, Bleiziffer S, Lange R, Kornowski R, Landes U, Norgaard BL, Biasco L, Philippart R, Molina-Martin de Nicolas J, Mylotte D, Lemee C, Dumonteil N, Van Mieghem NM. Bicuspid Aortic Valve Anatomy and Relationship With Devices: The BAVARD Multicenter Registry. *Circ Cardiovasc Interv.* 2019;12:e007107.

11. Zhou D, Yidilisi A, Fan J, Zhang Y, Dai H, Zhu G, Guo Y, He Y, Zhu Q, Lin X, Li H, Jiang J, Ng S, Li C, Ren K, Wang L, Liu X, Wang J. Three-year outcomes of transcatheter aortic valve implantation for bicuspid versus tricuspid aortic stenosis. *EuroIntervention.* 2022;18:193-202.

12. Pibarot P, Ternacle J, Jaber WA, Salaun E, Dahou A, Asch FM, Weissman NJ, Rodriguez L, Xu K, Annabi MS, Guzzetti E, Beaudoin J, Bernier M, Leipsic J, Blanke P, Clavel MA, Rogers E, Alu MC, Douglas PS, Makkar R, Miller DC, Kapadia SR, Mack MJ, Webb JG, Kodali SK, Smith CR, Herrmann HC, Thourani VH, Leon MB, Hahn RT, PARTNER 2 Investigators. Structural deterioration of transcatheter versus surgical aortic valve bioprostheses in the PARTNER-2 Trial. *J Am Coll Cardiol.* 2020;76:1830-43.

13. Van Belle E, Delhaye C, Vincent F. Structural Valve Deterioration at 5 Years of TAVR Versus SAVR: Half Full or Half Empty? *J Am Coll Cardiol.* 2020;76:1844-7.