EuroIntervention 2022;18:790-792

TAVI in younger patients with bicuspid aortic stenosis: pros and cons

Daniel J. Blackman[1]*, MD, MRCP; Noman Ali[1], PhD, MRCP; Michael A. Borger[2]**, MD, PhD

1. Leeds Teaching Hospitals NHS Trust, Leeds, UK; 2. University Clinic of Cardiac Surgery, Leipzig Heart Center, Leipzig, Germany

Pros: safety and efficacy of TAVI in BAV

Daniel J. Blackman, MD, MRCP; Noman Ali, PhD, MRCP

There are a number of specific considerations when performing transcatheter aortic valve implantation (TAVI) in younger patients because of the need to consider lifetime management when life expectancy is measured in decades. We address each in turn, outlining how bicuspid anatomy may be advantageous for lifetime management, and describe the growing evidence supporting the safety and efficacy of TAVI in bicuspid aortic valves (BAV).

Valve durability: Valve durability remains the most important factor when considering TAVI in younger patients. A principal determinant of durability is the size of the implanted transcatheter heart valve (THV), with larger effective orifice areas being associated with lower rates of structural valve deterioration (SVD)[1]. Patients with BAV tend to have larger annular dimensions than those with tricuspid anatomy[2], allowing for implantation of larger THV, which should translate to better valve durability.

Redo TAVI: Whilst improved durability of the index THV can delay the onset of haemodynamically significant SVD, the ability to safely perform subsequent valve-in-valve interventions is critically important. The key factor determining the feasibility of redo TAVI is the risk of coronary obstruction from the "neoskirt" created by the displaced THV leaflets, either through direct ostial occlusion or sinus sequestration. Patients with BAV have larger aortic dimensions, sinuses of Valsalva (SOV) and sinotubular junction (STJ)[2], which reduce the risk of coronary obstruction with TAV-in-TAV, making revalving feasible in the majority of patients.

Coronary access post-TAVI: Preserving coronary access is a key consideration in younger patients where the probability of coronary artery disease requiring intervention over a lifetime is increased. The principal reason for challenging coronary access post-TAVI is the close proximity of the THV frame to the walls of the aorta at the STJ and coronary ostia. Larger aortic root dimensions in BAV patients, including the diameter and height of the SOV and STJ, mean that coronary access either above or alongside the THV frame should be more easily achieved. Coronary access is likely to be even more challenging after redo TAVI due to the creation of the "neoskirt". Again, larger STJ and SOV dimensions mean that coronary catheterisation can be more readily achieved.

*Corresponding authors: *St. James's University Hospital, Beckett Street, Leeds, West Yorkshire, LS9 7TF, UK.*
E-mail: daniel.blackman1@nhs.net
***University Clinic of Cardiac Surgery, Leipzig Heart Center, Struempellstrasse 39, 04289 Leipzig, Germany.*
E-mail: michael.borger@helios-gesundheit.de

DOI: 10.4244/EIJ-E-22-00042

Permanent pacemaker implantation: The long-term negative consequences of permanent pacemaker implantation (PPM) post-TAVI are undoubtedly greater in patients with a longer life-expectancy, including adverse remodelling with reduced LV systolic function, greater requirement for generator changes and lead revision, and increased risk of pacemaker-related complications. Minimising interaction with the left ventricular outflow tract (LVOT) is key to reducing the risk of conduction disturbance. Current guidelines support higher implantation of THV in bicuspid anatomy[3], using the leaflets and raphe for anchoring and sealing, hence minimising LVOT interaction, which should translate to a lower risk of PPM.

Evidence for TAVI in bicuspid anatomy: There is growing evidence demonstrating favourable outcomes following TAVI in younger BAV patients. PARTNER 3 and the Evolut Low Risk Trial adopted parallel registries which included BAV patients with low surgical risk treated with TAVI. Using propensity score matching, these patients were compared to those with tricuspid anatomy from the main trials[4,5]. The PARTNER 3 Bicuspid Registry found no difference in the composite primary endpoint of all-cause mortality, stroke and cardiovascular-related rehospitalisation at 1 year[4], whilst the Evolut Low Risk Trial substudy demonstrated no difference in all-cause mortality or disabling stroke at 1 year[5]. Both studies also showed no difference in haemodynamic echocardiographic parameters at 1 year.

While longer-term outcome studies would be welcomed, contemporary data with current-generation THV demonstrate that outcomes of TAVI among younger low-surgical risk patients with BAV are similar to those with tricuspid valves. Furthermore, the specific anatomical characteristics of BAV appear favourable in addressing critical lifetime management factors in younger patients undergoing TAVI.

Conflict of interest statement

D.J. Blackman is a consultant & proctor for Medtronic; and a consultant for Abbott Vascular, Boston Scientific, and Edwards Lifesciences. N. Ali has received speaker fees from Medtronic.

Cons: negative implications of BAV for TAVI

Michael A. Borger, MD, PhD

Surgical aortic valve replacement (SAVR) is the current gold standard for young patients with BAV disease and will remain that way for the foreseeable future. SAVR is recommended in aortic stenosis (AS) patients younger than 75 years of age in the current European valvular guidelines[6], and one of the principal reasons behind this recommendation is that a large proportion of young AS patients have BAV pathology. BAV morphology has important short- and long-term negative implications for TAVI, but negligible impact on SAVR.

BAV is associated with higher rates of several important complications post-TAVI when compared to patients with tricuspid aortic valve (TAV) stenosis, including paravalvular leak (PVL), pacemaker implantation, conversion to surgery and lack of procedural success[7]. Results for SAVR, by contrast, are largely independent of valve morphology. BAV status has never emerged as a risk factor in any SAVR risk scoring system (e.g., Society of Thoracic Surgeons [STS], EuroSCORE) and has rarely been a focus of surgical studies. However, Celik et al from Rotterdam recently compared results of BAV versus TAV in SAVR ± coronary bypass grafting patients (n=3,145) operated on between 1987 and 2016[8]. These investigators found significantly better survival in BAV patients, even after propensity- and age-matching. Twenty-year survival of BAV patients was 40%, as compared to only 18% for TAV patients[8].

These marked differences between SAVR and TAVI in BAV patients may be explained, in large part, by severe valve calcification and a non-spherical annular shape which are much more common in BAV than TAV. Excessive calcification and non-spherical annuli do not play a significant role in SAVR, since the surgeon is able to debride all calcium under direct visual inspection, and the annulus is forced to conform to the circular frame of the valve prosthesis. In contrast, retention of large amounts of calcium debris in non-spherical annuli during TAVI may have deleterious effects on short-term complications such as annular rupture, PVL, pacemaker requirement and increased gradients due to non-uniform expansion of the TAVI device, as well as long-term complications such as coronary access difficulties, accelerated valve degeneration due to non-uniform device expansion, and decreased space allowing for future TAV-in-TAV procedures.

Furthermore, it is commonly known that BAV is associated with aortopathy and aortic complications. For this reason, SAVR with replacement of the ascending aorta is recommended in AS patients with an ascending aorta >4.5 cm in diameter[6,9]. What is less known is that BAV is also associated with several coronary artery anomalies. The most frequent anomaly is a hypoplastic right coronary artery, whose ostium frequently lies close to the right non-coronary commissure and therefore may be at risk of occlusion during TAVI or future TAV-in-TAV procedures.

Lifetime management of AS patients is a topic that is gaining increasing attention within the medical and patient communities. One of the dictums of lifetime management is that, if SAVR is performed, the largest possible valve prosthesis should be implanted to lower the risk of patient-prosthesis mismatch and to facilitate future TAVI valve-in-valve procedures. BAV patients are known to have larger annuli than TAV patients, allowing the insertion of larger SAVR prostheses[8]. In addition, we know that SAVR post-TAVI results are uniformly poor, being much worse than those for TAVI post-SAVR. In a meta-analysis of 10 studies with 1,690 SAVR post-TAVI patients, 30-day mortality (16.7%) was more than twice as high as the STS Predicted Risk of Mortality and was independent of endocarditis[10]. One of the reasons for the excess mortality was necessary concomitant procedures, the most common being aortic repair in 29% of patients[10]. SAVR is particularly challenging

post-insertion of a self-expanding TAVI device because of aortic ingrowth that occurs into the high-riding stent frame, the high aortotomy required, and the resulting challenging surgical exposure. Future transcatheter coronary access is also known to be more challenging in patients receiving self-expanding TAVI devices.

In summary, multiple reasons support the use of SAVR as the initial intervention of choice in young BAV patients. TAVI should not be performed in such patients, unless within the confines of a properly designed randomised controlled trial.

Conflict of interest statement

M. Borger declares that his hospital receives speakers' honoraria and/or consulting fees on his behalf from Edwards Lifesciences, Medtronic, Abbott and Artivion.

References

1. Abdel-Wahab M, Landt M, Neumann FJ, Massberg S, Frerker C, Kurz T, Kaur J, Toelg R, Sachse S, Jochheim D, Schäfer U, El-Mawardy M, Robinson DR, Richardt G; CHOICE Investigators. 5-Year Outcomes After TAVR With Balloon-Expandable Versus Self-Expanding Valves: Results From the CHOICE Randomized Clinical Trial. *JACC Cardiovasc Interv.* 2020;13:1071-82.

2. Shibayama K, Harada K, Berdejo J, Tanaka J, Mihara H, Itabashi Y, Shiota T. Comparison of aortic root geometry with bicuspid versus tricuspid aortic valve: real-time three-dimensional transesophageal echocardiographic study. *J Am Soc Echocardiogr.* 2014;27:1143-52.

3. Blackman D, Gabbieri D, Del Blanco BG, Kempfert J, Laine M, Mascherbauer J, Parma R, Tchétché D. Expert Consensus on Sizing and Positioning of SAPIEN 3/Ultra in Bicuspid Aortic Valves. *Cardiol Ther.* 2021;10:277-88.

4. Williams MR, Jilaihawi H, Makkar R, O'Neill WW, Guyton R, Malaisrie SC, Brown DL, Blanke P, Leipsic JA, Pibarot P, Hahn RT, Leon MB, Cohen DJ, Bax JJ, Kodali SK, Mack MJ, Lu M, Webb JG. The PARTNER 3 Bicuspid Registry for Transcatheter Aortic Valve Replacement in Low-Surgical-Risk Patients. *JACC Cardiovasc Interv.* 2022;15:523-32.

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. 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, Sádaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention.* 2022;17:e1126-96.

7. Kanjanahattakij N, Horn B, Vutthikraivit W, Biso SM, Ziccardi MR, Lu MLR, Rattanawong P. Comparing outcomes after transcatheter aortic valve replacement in patients with stenotic bicuspid and tricuspid aortic valve: A systematic review and meta-analysis. *Clin Cardiol.* 2018;41:896-902.

8. Çelik M, Milojevic M, Durko AP, Oei FBS, Bogers AJJC, Mahtab EAF. Differences in baseline characteristics and outcomes of bicuspid and tricuspid aortic valves in surgical aortic valve replacement. *Eur J Cardiothorac Surg.* 2021;59:1191-9.

9. Borger MA, Fedak PWM, Stephens EH, Gleason TG, Girdauskas E, Ikonomidis JS, Khoynezhad A, Siu SC, Verma S, Hope MD, Cameron DE, Hammer DF, Coselli JS, Moon MR, Sundt TM, Barker AJ, Markl M, Della Corte A, Michelena HI, Elefteriades JA. The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve-related aortopathy: Executive summary. *J Thorac Cardiovasc Surg.* 2018;156:473-80.

10. Yokoyama Y, Kuno T, Zaid S, Kaneko T, Takagi H, Tang GHL, Fukuhara S. Surgical explantation of transcatheter aortic bioprosthesis: A systematic review and meta-analysis. *JTCVS Open*. 2021;8:207-27.