JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 76, NO. 9, 2020

PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Systematic Approach Toward Transcatheter Treatment of BAV Disease

One Size Does Not Fit All*

Saif Anwaruddin, MD, Nimesh Desai, MD, PHD

As the field of transcatheter valve repair/replacement takes hold and expands at a feverish pace, it remains imperative that we endeavor to preserve the exacting standards that led to its success. Transcatheter aortic valve replacement (TAVR) has revolutionized the care of patients with aortic stenosis. First-generation devices were predominantly used in higher-risk patients due to the requirement for surgical access and concerns about paravalvular leak and durability (1). Iterative advances in TAVR technology have enabled its routine use in a wider variety of patients with severe aortic stenosis, and recent trials have shown noninferiority to surgical aortic valve replacement (SAVR) in low-risk patients (2,3). However, randomized trials comparing TAVR with SAVR have excluded patients with bicuspid aortic valves and have predominantly enrolled older patients. Among patients under age 70 years who are undergoing surgical aortic valve replacement for stenosis, up to 50% are bicuspid variants (4). While bicuspid aortic valve stenosis represents another potential target for TAVR with emerging data touting its utility, we should not view this disease complex as simply a slight departure from the standard trileaflet degenerative aortic valve stenosis.

Several features of bicuspid valves raise concern when considering TAVR therapy for severe stenosis. At the annular level, bicuspid valves often have extremely large annuli that are too large for on-label use of current commercially available TAVR devices. The annulus of the bicuspid valve is also highly elliptical compared to trileaflet aortic valves, raising concern about paravalvular leaks at the commissures when placing valves designed to conform for more circular landing zones. The leaflets of the bicuspid valve often have severe, bulky calcification that frequently extends beyond the leaflet insertion and deep into the left ventricular outflow tract. Severe calcification of the aorto-mitral curtain may even extend several centimeters onto the anterior leaflet of the mitral valve in such cases. The majority of stenotic bicuspid valves have a fused raphe that is typically fibrotic and heavily calcified. Stiff fibrotic raphe tissue cannot reliably be pushed over to the aortic wall in the same way as a degenerated leaflet in a trileaflet valve, and in combination with severe bulky calcification may cause highly asymmetric valve expansion into the nonconjoined sinus. These features increase risk for both paravalvular leak and, more concerningly, annular rupture.

Concomitant aortopathy is also common among patients with bicuspid valves and may be related to embryological differences in the wall of the aorta and flow dynamic phenomena through the valve causing abnormal loading on the aortic wall. A total of 20% to 30% of patients with bicuspid aortic valves have significant aortopathy (5). Current guidelines recommend ascending aortic replacement with concomitant

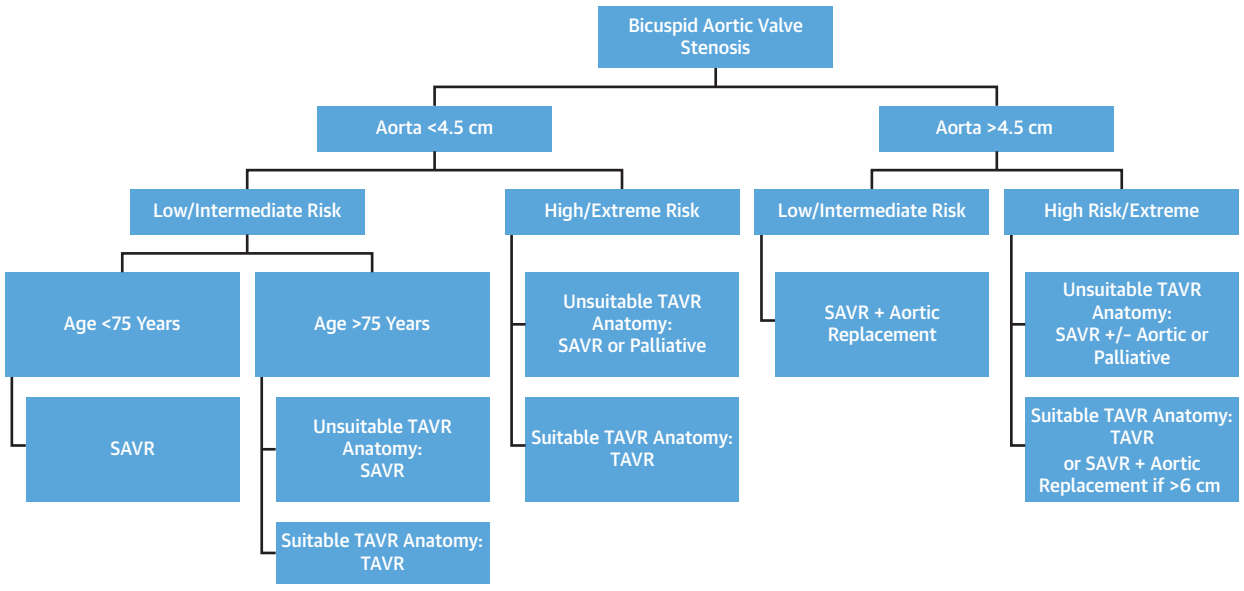
*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania. Dr. Anwaruddin has served as a consultant for Edwards Lifesciences and V Wave; has served on the advisory board of Medtronic; and has received speaking fees from Siemens. Dr. Desai has served as a speaker and consultant for Gore and Medtronic.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC* author instructions page.

ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2020.07.019

FIGURE 1 Decision Pathway for Bicuspid Aortic Stenosis



Unsuitable anatomy for transcatheter aortic valve replacement (TAVR): 1) the presence of excessively large annulus; 2) bulky leaflet, raphe, or left ventricular outflow tract calcification; or 3) the presence of >1 raphe or fused commissure. SAVR = surgical aortic valve replacement.

SAVR at 4.5 cm and between 5 and 5.5 cm for ascending aortic aneurysm without a primary valve indication (6,7). In addition to the late risk for aortic complications, aneurysmal dilatation of the root or ascending aorta may complicate TAVR placement due to eccentric dilation of the noncoronary sinus causing significant angulation and a very horizontal valve plane.

SEE PAGE 1018

In the study by Yoon et al. (8) in this issue of the *Journal*, from the voluntary International Bicuspid Aortic Valve Stenosis Registry, we gain further insight into the impact of the various anatomic features on outcomes of TAVR in bicuspid valve patients (8). This study is unique in that it is a large multicenter collaboration with a central core laboratory adjudication of the pre-procedural anatomy as opposed to site-reported data seen in other registry reports. This study elevates the role for computed tomography angiography imaging in delineating anatomical subsets within the bicuspid aortic valve cohort that may be associated with less favorable characteristics for TAVR. The study also confirms that in patients with bicuspid aortic valve stenosis who were deemed anatomically appropriate for TAVR, calcified raphe or excess leaflet calcium are associated with significantly worse procedural and 1-year outcomes. The prognosis of the combination of these anatomic risk factors was particularly poor.

Unfortunately, this combination of factors is quite common in patients undergoing surgical valve replacement for bicuspid stenosis, and studies of TAVR in patients with bicuspid valves remain highly selected and not generally representative of the overall scope of bicuspid valve disease and aortopathy. In a recent publication from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy registry by Makkar et al. (9), the overall proportion of bicuspid valve patients in the registry was only 3%. By comparison, in relatively contemporary large U.S. Food and Drug Administration investigational device exemption trials of surgical valves performed before the approval of TAVR for low- or intermediate-risk patients, consistently about 30% of patients had bicuspid aortic valves (10,11). As aortopathy patients were excluded from these studies, the overall aortic valve replacement population includes an even larger proportion of patients undergoing aortic valve replacement with concomitant aortic replacement.

When considering the patient, the decision pathway for choosing TAVR or SAVR for bicuspid stenosis should include the presence of aortopathy,

patient surgical risk, patient age as long-term durability of TAVR is still uncertain, and the presence of high-risk anatomic features for TAVR (**Figure 1**). These higher-risk anatomic features include the presence of excessively large annulus, bulky leaflet, raphe, or left ventricular outflow tract calcification; or the presence of >1 raphe or fused commissure. Among patients with aortopathy (aortic diameter >4.5 cm), the prognostic benefits of surgery to address the aneurysm should not be denied to the patient unless they are at high risk for surgery and have favorable TAVR anatomy. Even in such situations, the presence of a large (>6 cm) aneurysm, which carries a >10% per year rupture rate, may still warrant a higher-risk surgical intervention (12).

Among patients without aortopathy, patients who are lower risk and younger should undergo SAVR, whereas TAVR is appropriate in lower-risk, older (age >75 years) patients without high-risk anatomic features. Among higher-risk bicuspid patients without aortopathy, TAVR in the presence of suitable anatomy is the preferred option. When TAVR is not feasible due to anatomy, either high-risk surgery or medical palliation may be appropriate.

As evidence and technology continue to advance, the broader use of TAVR in a larger proportion of bicuspid patients may eventually be appropriate. Critical issues regarding balloon-expandable versus self-expanding valves and appropriate sizing techniques tailored to particular patient anatomy still need to be better understood, and long-term outcomes of TAVR in bicuspid patients warrant careful further study. Randomized trials of SAVR versus TAVR in bicuspid patients could potentially address some of the concerns; however, they will be limited by very narrow inclusion criteria and are not generalizable to the broader population of patients with bicuspid aortic valve stenosis. Until then, we need to provide those with bicuspid aortic stenosis a thorough evaluation of both anatomic and clinical factors at play and offer individualized and comprehensive treatment that provides the best outcome over the long term.

ADDRESS FOR CORRESPONDENCE: Dr. Saif Anwaruddin, Transcatheter Valve Program, Hospital of the University of Pennsylvania, Perelman School of Medicine at the University of Pennsylvania, South Tower, 11-106, 3400 Civic Center Boulevard, Philadelphia, Pennsylvania 19104. E-mail: Saif.Anwaruddin@pennmedicine.upenn.edu. Twitter: @PennMedicine.

REFERENCES

1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

2. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695–705.

3. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019;380:1706–15.

4. 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.

5. Michelena HI, Della Corte A, Prakash SK, Milewicz DM, Evangelista A, Enriquez-Sarano M. Bicuspid aortic valve aortopathy in adults: incidence, etiology, and clinical significance. Int J Cardiol 2015;201:400–7.

6. Borger MA, Fedak PWM, Stephens EH, et al. The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve-related aortopathy: full online-only version. J Thorac Cardiovasc Surg 2018;156:e41–74.

7. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine [published correction appears in J Am Coll Cardiol 2013;62:1039–40]. J Am Coll Cardiol 2010;55:e27–129.

8. Yoon S-H, Kim W-K, Dhoble A, et al. Bicuspid aortic valve morphology and outcomes after transcatheter aortic valve replacement. J Am Coll Cardiol 2020;76:1018–30.

9. Makkar RR, Yoon SH, Leon MB, et al. Association between transcatheter aortic valve replacement for bicuspid vs tricuspid aortic stenosis and mortality or stroke. JAMA 2019;321:2193–202.

10. Bavaria JE, Desai ND, Cheung A, et al. The St Jude Medical Trifecta aortic pericardial valve: results from a global, multicenter, prospective clinical study. J Thorac Cardiovasc Surg 2014;147:590–7.

11. Puskas JD, Bavaria JE, Svensson LG, et al. The COMMENCE trial: 2-year outcomes with an aortic bioprosthesis with RESILIA tissue. Eur J Cardiothorac Surg 2017;52:432–9.

12. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002;74:S1877–98.

KEY WORDS aortic stenosis, bicuspid aortic valve, transcatheter aortic valve implantation