JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 11, NO. 17, 2018

PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Optimizing Valve Sizing in Balloon-Expandable Transcatheter Aortic Valve Replacement*

Amar Krishnaswamy, MD, Samir R. Kapadia, MD

Transcatheter aortic valve replacement (TAVR) is a mature technology for the treatment of patients with severe aortic stenosis. However, despite excellent trial and "real-world" results, operators and investigators continue to find ways to improve. One such opportunity is to more precisely size the limited selection of valves specifically for each patient. On the basis of the clinical data and experience thus far, it is clear that some degree of valve "oversizing" in comparison to the measured annulus size is necessary for an optimal valve result with little or no paravalvular aortic regurgitation (PAR) (1). On the other hand, too generous a degree of oversizing increases the risk of complications, including pacemaker implantation, coronary obstruction, annular trauma/rupture, and leaflet thrombosis (2–4). To further minimize these complications, operators must take in to consideration, not only the degree of oversizing, but also the specific characteristics of the aortic root, including quantity and distribution of left ventricular outflow tract calcification, size of the sinuses and sinotubular junction, and depth of valve implantation. However, undersizing too aggressively may promote leaflet degeneration and failure (5). In routine practice, interventional cardiologists and cardiac surgeons have taken to underexpanding a larger valve or overexpanding a smaller valve as they see fit to walk the line between annular trauma and paravalvular regurgitation.

SEE PAGE 1696

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

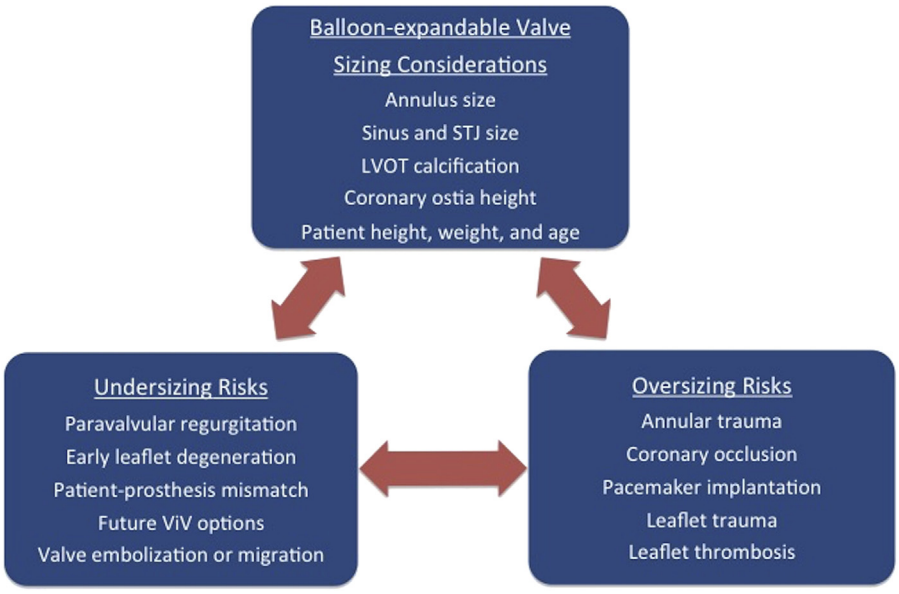
From the Division of Interventional Cardiology, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

It is in this arena that the papers in this issue of *JACC: Cardiovascular Interventions*, by Sathananthan et al. (6) and Huchet et al. (7) seek to introduce some objective data. Using systematic overexpansion of the SAPIEN-3 (S3) series of valves (Edwards Lifesciences, Irvine, California), Sathananthan et al. (6) analyzed gross valve morphology and hydrodynamic function. After overexpansion, they found that all valves had restricted leaflets; there was worse hydrodynamic function, with regurgitation noted for the over-expanded 23- and 26-mm valves, but not for the 29-mm valves; and the 26-mm valves demonstrated leaflet disruption. Further, compliant balloon post-dilation (as used for the 29-mm valves) resulted in asymmetric valve frame expansion (inflow and outflow > mid-valve), whereas non-compliant balloon dilation (for the 23- and 26-mm valves) resulted in symmetrical dilation. Huchet et al. (7) studied 6 valves, which they expanded and found that although nominally deployed valves demonstrated only mild stretching lesions, those dilated modestly (+1.5 ml) and significantly (+3.0 ml) demonstrated more leaflet stretching and some leaflet tearing. How can we place the benchtop findings of these 2 studies together and in clinical context?

The limited published case series of SAPIEN-3 valve overexpansion are for implantation of the 29-mm valve in patients with an annulus larger than what is recommended by the manufacturer. Tang et al. (8) recently demonstrated the feasibility of implanting the 29-mm valve in 69 patients with an average annulus area of 7.23 cm^2. Although 30% of the patients required only nominal fill volume, 70% were overfilled or post-dilated with between an additional 1 and 5 ml. The results were reasonable, with moderate aortic regurgitation (AR) seen in 4% of patients and none with severe AR, and no cases of annular trauma. Similarly, Mathur et al. (9) provided

ISSN 1936-8798/$36.00
https://doi.org/10.1016/j.jcin.2018.07.025

FIGURE 1 **Considerations for Balloon-Expandable Valve Sizing**



LVOT = left ventricular outflow tract; STJ = sinotubular junction; ViV = valve-in-valve.

their experience of 3 patients with an average annulus of 7.76 cm^2. Although no patients had moderate AR, they dilated more aggressively with 2 patients treated with nominal volume + 4 ml and 1 treated with nominal volume + 5 ml. Although the short-term results of these trials are encouraging with regard to procedural success and safety, the series are limited to 30-day outcomes. Whether the bench testing demonstrated by the current papers would imply a longer-term clinical valve deterioration and dysfunction is therefore unclear. Further, as prior series have suggested, a higher risk of leaflet thrombosis for the 29-mm valve than the others, whether an even greater risk exists for an oversized 29-mm valve is also a theoretic consideration (4).

In the Sathananthan et al. study (6), hydrodynamic function was adversely affected by overexpansion in the 23- and 26-mm valves, but not in the 29-mm valves. This may be encouraging from a clinical perspective because the most common reported situation for overexpansion is for those patients with a larger than 29-mm S3 annulus as in the clinical series in the preceding text. On the other hand, the limited evaluation by Huchet et al. (7) does also suggest a risk of leaflet damage of overexpansion. Taken together, in patients with a smaller annulus that is "in-between" sizes, these findings raise the question whether underexpansion is a better option to avoid leaflet trauma/overstretching or whether this also causes disordered leaflet function (i.e., better to implant an underfilled/underexpanded 26-mm valve instead of an overfilled/overexpanded 23-mm valve). In this regard, Barbanti et al. (10) analyzed a series of 47 patients who underwent balloon-expandable TAVR implantation (94% with the SAPIEN-XT device) that was purposely underfilled by ~10% volume (due to expected oversizing >20%) in comparison to 87 patients with nominal deployment. More than mild AR was seen in only 1 underfilled patient (vs. 6 patients in the control group; p = NS), and only 10.6% of patients in the underfilled group required post-dilation (3 with nominal volume and 2 with still underfilled balloons). Importantly, there was no difference in valve gradients between the 2 groups, though the underfilled group did demonstrate greater eccentricity of the valve stent on subsequent computed tomography scan at the inflow and mid-valve segments. Interestingly in this regard, modeling experiments have suggested that stent eccentricity and leaflet redundancy (as seen in underexpanded valves) result in greater leaflet stress and could portend reduced valve durability (5).

The applicability of the oversized/underexpanded SAPIEN XT valve choice (in the era when ~10%

oversizing was planned) shown in the preceding text to the current era of S3 valve use is unclear. Blanke et al. (11) have commented that such oversizing may be unnecessary on the basis of the design features of the current-generation valve. In their analysis of 835 patients undergoing S3 implantation as part of the PARTNER II (Placement of AoRTic TraNscathetER Valves) trial, they report "acceptable" rates of mild/moderate PAR (11.8%) and moderate PAR (2.8%) with only 0% to 5% oversizing, suggesting that choosing the smaller valve in borderline sizing situations could be reasonable. Although this is reflected in the conclusion statements of the paper and its accompanying editorial, it is interesting to note that when patients were treated with >10% oversizing, only 3.9% had mild/moderate PAR and 0.3% had moderate PAR. Because we know that moderate PAR (and even mild) can be detrimental to symptom resolution and long-term survival, continuing to oversize with careful attention to root characteristics and adverse features is likely still a wise endeavor.

The current studies are well written and well presented, though they have some specific limitations in addition to their small size. It is impossible to know from the current analyses whether the leaflet disruption that was noted is the result of use of the noncompliant balloon, inherent to the act of post-dilation itself, or the result of valve overexpansion. These points are important to understand, because it could be that simply deploying the valve at a higher fill volume (rather than post-dilation), or using a compliant balloon, could be a safer approach. Furthermore, it is clear that a non-negligible degree of valve-stent recoil occurs in vivo, perhaps thereby reducing the degree of overexpansion seen in vitro and therefore leaflet malfunction; this also by definition could not be addressed by the current studies (12). Additionally, the leaflet/stent morphology and hydrodynamic consequences of purposeful valve underexpansion would be important to understand as a necessary corollary to the data presented herein.

What are the take-home points (**Figure 1**)? In our clinical practice, we have been more cognizant of root morphology/sizing and fill volumes due to multiple factors. The understanding that the S3 platform generally requires less oversizing than previous generations provides more leeway to forego some of the nominal fill volume without sacrificing results and optimizing safety. Additionally, as we perform nearly all TAVR procedures using Sentinel cerebral embolic protection (Claret Medical, Santa Rosa, California), we feel more comfortable that post-dilation, if necessary, may have less neurological event risk (13). Although the current data point to a more "symmetrical" dilation of the valve stent using a noncompliant balloon, we generally use the delivery balloon for post-dilation so that we better understand the degree to which we are increasing the size. On the other hand, for the valve-in-valve (ViV) application, we routinely use the noncompliant balloon at high pressure in order to optimize hemodynamics and ViV expansion (14). Although it is entirely conjectural, we also tend to use an underexpanded larger valve for "in-between" sizing cases with the hope of optimizing the hemodynamics of future ViV placement, especially for younger patients who have a greater likelihood of surviving to the index valve degeneration, as long as there are no particularly adverse root characteristics for annular trauma. Lastly, although they are admittedly small series, the clinical data provided earlier in the text for application of the 29-mm S3 valve to patients with an annulus size beyond the "labeled indication" implies that this is a reasonable option for patients with symptomatic aortic stenosis who cannot be treated safely by traditional means.

ADDRESS FOR CORRESPONDENCE: Dr. Amar Krishnaswamy, Division of Interventional Cardiology, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, 9500 Euclid Avenue, Desk J2-3, Cleveland, Ohio 44195. E-mail: krishna2@ccf.org.

REFERENCES

1. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. J Am Coll Cardiol 2013;61:1585–95.

2. Khalique OK, Hahn RT, Gada H, et al. Quantity and location of aortic valve complex calcification predicts severity and location of paravalvular regurgitation and frequency of post-dilation after balloon-expandable transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2014;7:885–94.

3. Husser O, Pellegrini C, Kessler T, et al. Predictors of permanent pacemaker implantations and new-onset conduction abnormalities with the SAPIEN 3 balloon-expandable transcatheter heart valve. J Am Coll Cardiol Intv 2016;9:244–54.

4. Hansson NC, Grove EL, Andersen HR, et al. Transcatheter aortic valve thrombosis: incidence, predisposing factors, and clinical implications. J Am Coll Cardiol 2016;68:2059–69.

5. Martin C, Sun W. Transcatheter valve underexpansion limits leaflet durability: implications for valve-in-valve procedures. Ann Biomed Eng 2017;45:394–404.

6. Sathananthan J, Sellers S, Barlow A, et al. Overexpansion of the SAPIEN 3 transcatheter heart valve: an ex vivo bench study. J Am Coll Cardiol Intv 2018;11:1696–705.

7. Huchet F, Guerin P, Letocart V, Manigold T, Jordana F. Morphological and biomechanical consequences of post-dilatation following transcatheter aortic valve replacement: a pilot study. J Am Coll Cardiol Intv 2018. In press.

8. Tang G, Syed Z, George I, et al. Transcatheter aortic valve replacement with extremely large annuli greater than 683 mm2 using Edwards Sapien 3 valve: a multicenter experience. J Am Coll Cardiol 2017;70:B126.

9. Mathur M, McCabe JM, Aldea G, Pal J, Don CW. Overexpansion of the 29 mm SAPIEN 3 transcatheter heart valve in patients with large aortic annuli (area > 683 mm(2)): a case series. Catheter Cardiovasc Interv 2018;91:1149–56.

10. Barbanti M, Leipsic J, Binder R, et al. Underexpansion and ad hoc post-dilation in selected patients undergoing balloon-expandable transcatheter aortic valve replacement. J Am Coll Cardiol 2014;63:976–81.

11. Blanke P, Pibarot P, Hahn R, et al. Computed tomography-based oversizing degrees and incidence of paravalvular regurgitation of a new generation transcatheter heart valve. J Am Coll Cardiol Intv 2017;10:810–20.

12. Garg A, Parashar A, Agarwal S, et al. Comparison of acute elastic recoil between the SAPIEN-XT and SAPIEN valves in transfemoral-transcatheter aortic valve replacement. Catheter Cardiovasc Interv 2015;85:490–6.

13. Kapadia SR, Kodali S, Makkar R, et al. Protection against cerebral embolism during transcatheter aortic valve replacement. J Am Coll Cardiol 2017;69:367–77.

14. Patel JS, Krishnaswamy A, White J, et al. Optimizing hemodynamics of transcatheter aortic valve-in-valve implantation in 19-mm surgical aortic prostheses. Catheter Cardiovasc Interv 2017 Dec 11 [E-pub ahead of print].

KEY WORDS balloon-expandable valve-sizing, post-dilation, TAVR