Understanding Imaging to Assess the Aortic Annulus for TAVR

A review of imaging for annulus size assessment for transcatheter aortic valve replacement.

BY PAUL T. VAITKUS, MD, MBA, AND MAYRA GUERRERO, MD

Transcatheter aortic valve replacement (TAVR) of stenotic aortic valves is now a well-established therapeutic modality with substantial supportive evidence from both pivotal prospective clinical trials[1] and real-world registries.[2] As with any first-generation technology, TAVR bears a number of imperfections that can result in important clinical issues, which in turn lead to substantial morbidity and mortality. Among these are aortic regurgitation, the need for pacemaker therapy, and rupture of the aortic annulus. We highlight these three complications because they have been the target of investigations into relationships between the implanted valves and aortic annular assessment by imaging.

Aortic insufficiency after TAVR is predominantly attributable to perivalvular leak (PVL) and uncommonly to central regurgitation through the valve orifice due to leaflet noncoaptation.[3] Moderate or greater PVL occurs in a substantial minority of patients and is associated with a significant reduction in long-term survival after TAVR.[2] Physiologically, superimposing the volume overload of acute aortic insufficiency onto a ventricle that has adapted over many years to a state of pressure overload could be detrimental, especially if the ventricle has also developed systolic dysfunction. Imaging studies have elucidated some of the factors that lead to nonapposition of the valve prosthesis to the surrounding annulus, and the resulting PVL, and point to immediate opportunities for improved preprocedural decision making and also identify elements that may lead to technological improvements in developing next-generation devices.

The key concept underlying the various issues we will review is matching the valve size to the patient's annulus. Currently, using FDA-approved devices in the United States, the decision is binary: to implant either a 23-mm-diameter or a 26-mm-diameter Sapien valve (Edwards Lifesciences, Irvine, CA). Larger-diameter valves are available internationally but are presently investigational in the United States. Manufacturer recommendations and current practice focus on choosing a valve with a slight oversizing of the nominal diameter versus the measured aortic annulus diameter.

DIFFERENCES AMONG IMAGING MODALITIES

The first, and consistent, observation that has emerged is different imaging modalities lead to different measured annular dimensions. In general, transthoracic echocardiography yields the smallest values, two-dimensional transesophageal echocardiography (TEE) yields larger values, three-dimensional TEE produces even higher measures, and tomographic modalities (most commonly CT and, to a comparable degree, magnetic resonance imaging) provide the largest measures. The magnitude of the difference between modalities in various reports has ranged from a very modest "mean delta" of 0.3 mm[4] to a much more substantial 2.7 mm.[5]

This general observation of the magnitude and directionality of differences between modalities, however, belies the fact that in an individual patient, the direction of the discordance can vary, and the magnitude can be clinically significant. This discordance is most evident when comparing two modalities according to the method of a Bland-Altman analysis, as shown in Figure 1. Although CT yielded diameter values larger than TEE by only an inconsequential 0.3 mm, inspection of the scatter of individual patients told a different story. Individual patients were as likely to have a larger or smaller diameter assessment by CT versus TEE and the magnitude of the difference was at times much more substantial and clinically relevant than the mean difference.

TABLE 1. MEASURES AND CRITERIA OF OVALNESS		
Measure	**Ovalness Criteria**	**Reference**
Dmax–Dmin	> 3-mm difference	Tops et al[6]
Ratio Dmax/Dmin	≥ 1.1 or ≥ 1.2	Buellesfeld et al[7] and Buzzatti et al[8]
EI = 1–(Dmin/Dmax)	> 0.1	Blanke et al[9]
ε = √[1–(b/a) 2].	Unspecified	Rixe et al[4]
Abbreviations: ε, eccentricity; EI, eccentricity index.		

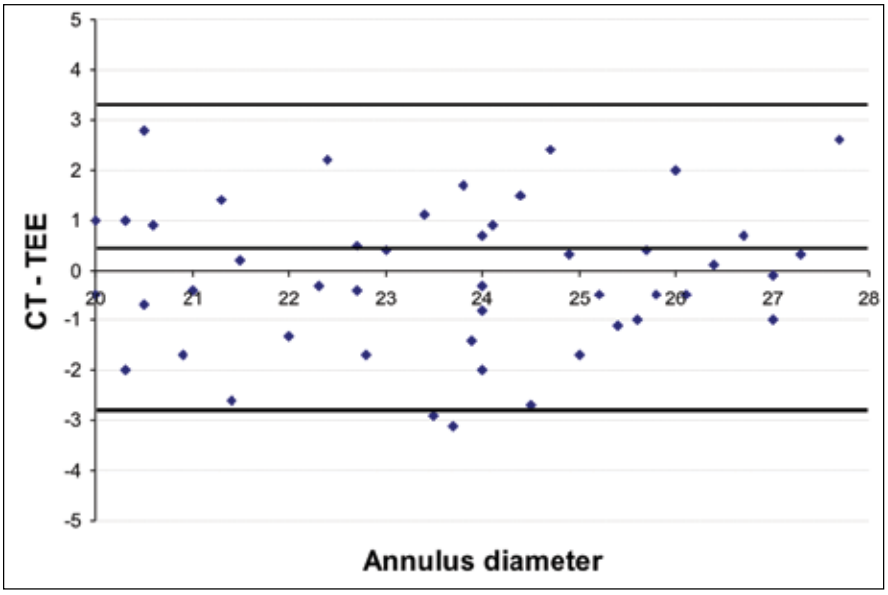

Figure 1. A hypothetical Bland-Altman analysis of multidetector CT and TEE in assessing aortic annular size based on multiple published examples. The x-axis plots the mean value of the two modalities (which simplistically can be taken to represent the "true value"), whereas the difference between the two modalities is plotted on the y-axis. The bold horizontal line at 0.3 mm represents the average difference between the two modalities.

GEOMETRIC AND TECHNICAL ISSUES: WHAT IS THE DIAMETER?

In most patients, the annulus is not perfectly round and is oval or oblong to some degree. Prior to the development of TAVR, the roundness or ovalness of the anatomic aortic annulus was not clinically relevant. Although surgically implanted aortic valve prostheses were round, a surgeon manually sewing in a valve under direct visual guidance ensured a perfect fit into even the most oblong-shaped annulus.

Varying frequencies and degrees of ovalness have been reported in the literature, partly as an artifact of different approaches and thresholds of expressing this asymmetry (Table 1).[4,6-9] The increasing complexity of these indices has contributed only marginally to the main lessons learned.

First, the degree of ovalness (asymmetry) has not been a significant predictor of PVL. Measurements of absolute diameter and/or annular perimeter or area have been more useful in predicting and making decisions, as will be discussed later. The relevance of ovalness, however, comes into play when considering which measure of diameter to rely upon in decision making.

At first glance, the possibility that ovalness or asymmetry may lead to nonapposition of the implanted valve to the annulus appears plausible. The device is mounted on a blimp-shaped balloon that has a circular cross-section. Therefore, a circular device is being implanted into an oblong receptacle. Conceivably, such an exercise could result in nonapposition in the larger diameter of the oblong. That this does not necessarily occur could be attributed to several possible mechanisms: (1) the deploying balloon conforms to the oblong annulus during inflation, and thus the implanted valve conforms perfectly to the oblong shape; (2) the balloon deploys the valve to its full dimension in the widest diameter but remains constrained in the minimum diameter; or (3) the circular deploying balloon forces the annulus into a more circular configuration. The first mechanism is unlikely. The balloon's compliance is limited and, therefore, so is its ability cross-sectionally to take on an oblong shape during inflation in vivo in patients with aortic stenosis. Although such a question could be addressed ex vivo in laboratory models, the degree to which this occurs in vivo cannot be pragmatically answered with current imaging technologies. The second and third possibilities are supported by observations from imaging after TAVR.[9,10] In early postprocedural imaging, none of the implanted prostheses examined by CT had been expanded to their nominal area

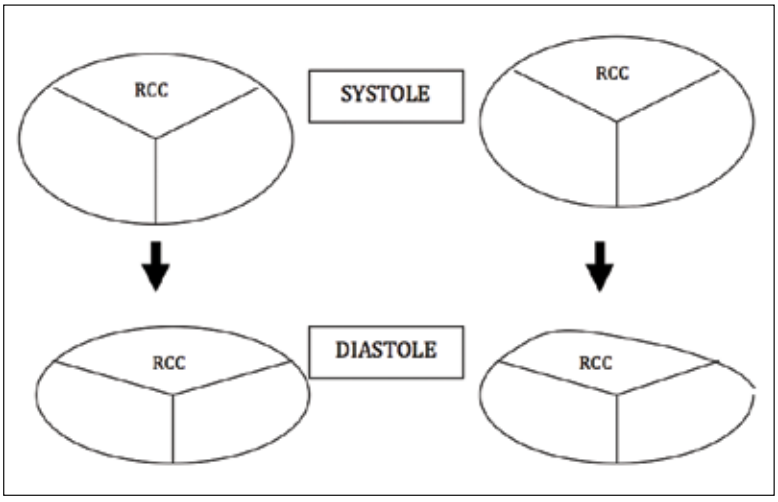

Figure 2. The already elliptoid annulus (top images) during systole undergoes further shortening in the Dmin during diastole (bottom images), which can either be "smooth" and "elliptoid" (left column) or irregular and asymmetric (right column).

size.[9] Thus, the native annulus is constraining the shape of the valve stent frame. Later observations (> 1 year) offer a very different view that the prostheses are fully expanded.[10] On the other hand, in the majority of patients, the shape of the annulus after implantation was circular at both early and late imaging,[9,10] suggesting that the annulus was, in turn, reshaped by the balloon and valve.

The greater relevance of the ovalness of the annulus is that it begs the question: how do we measure the "diameter" of the annulus and adapt the measurements into decision making? That the term *diameter* is used in the singular incorrectly implies that the annulus has a single definable diameter, when in reality, an oblong object has an infinite set of diameters. The first, and simplest, measures of diameter are the maximum (Dmax) and minimum (Dmin) within the oblong. An "average" diameter (Da) may then be derived by two different approaches. The first is to simply average the Dmax and Dmin. A somewhat more rigorous approach is to directly measure the entire two-dimensional area of the oblong and then derive an average diameter by a calculation based on geometry, $Da = 2 * \sqrt{(area)/\pi}$. Finally, one may measure diameters with reference to the anatomic landmarks of the three aortic leaflets, using the diameter from the center of the base of each cusp to the corresponding opposing commissure (ie, between the other two cusps).[11] This latter approach has been used mostly in research and not clinical decision making.

An important principle in imaging-based diameter assessment is to use the correct imaging plane. Reliance on standard anatomic planes of imaging (ie, frontal, sagittal, and transverse) invariably presented off-axis slices through the aortic valve and thus has been supplanted. With the ability to rotate tomographic images in all three dimensions, the relevant plane in which to assess the annulus is in the specific plane corresponding to the basal attachments of the three cusps.

Finally, it has now been described that the annulus changes shape during the cardiac cycle. The annulus undergoes compression during diastole in a manner that may be smoothly elliptoid or entirely nonuniform, but the overall result can be best described as a shortening of the Dmin (Figure 2).[3,11] The Dmin in question corresponds anatomically to the diameter from the center of the right coronary cusp to the commissure between the left and noncoronary cusps. If the overarching goal of accurately assessing the annulus is to prevent PVL, adopting the systolic measure would seem most appropriate,[11] but in reality, the differences between systole and diastole are usually inconsequential.[6]

CLINICAL CORRELATES

Efforts to define which of the myriad of measures are most clinically useful have examined the issue from three different angles. First, some studies analyzed how frequently reliance on one modality versus another modality would have led to different valve size decisions. The results are predictable and not particularly useful. Modalities that provide larger diameter estimates will lead to a corresponding increase in valve size selection. However, this exercise lacked meaningful insight into which decision (whether in favor of the smaller or larger prosthesis) would have been clinically superior. The second approach relied on retrospective analyses to determine which technology and parameter had the best predictive power for PVL. A number of rigorously conducted studies produced the consistent finding that CT outperforms any form of echocardiography.[3,12]

Next is the question of which pre-TAVR parameters most reliably predict post-TAVR PVL. Of the numerous ways in which to quantitatively assess the annulus, several closely related parameters have been reported to significantly predict PVL—one was the Dmax.[8] The larger the Dmax, the more likely the occurrence of PVL. Of somewhat greater sophistication was an observation that a mismatch between the area-derived estimated diameter of the annulus and the nominal diameter of the selected valve was a significant predictor.[3] Finally, a mismatch between the measured annular area and the

"nominal" valve area was perhaps the most potent predictor of PVL.[8,12]

A large German registry provided another telling insight in that many German centers relied primarily or exclusively on echocardiography for decision making, whereas others primarily used CT.[2] Of 426 cases in which decision making was echocardiography based, 88 (36%) developed clinically significant PVL as compared to only 28 of 243 patients (12%) in whom decision making was CT based. As with all nonrandomized observational studies, we need to be mindful of a potential selection bias. Perhaps sites that did not utilize CT scanning may have been less proficient in TAVR techniques.

Although the focus of this review has thus far been the relationship between annular assessment and post-TAVR PVL, data exist on other post-TAVI complications. If there were no countervailing issues, the decision on which valve size to select could be simple: take the largest assessment of diameter or area by any technology and choose the next biggest valve. Or, if in doubt, just reach for the biggest valve on the shelf.

But there is another issue of concern: whether oversizing the valve contributes to other undesirable or dangerous complications, such as the need for permanent pacemaker implantation due to injury to the conduction system or causing annular rupture with its high attendant mortality. To date, available data suggest that annular sizing decisions do not contribute to conduction problems with the Sapien valve,[8] but there are suggestions that valve oversizing contributes to annular rupture.[9] Although the latter observations are based on a very limited number of cases (and it is fortunate that this complication is sufficiently rare to preclude large case series), the correlation is sufficiently compelling to make anyone unlikely to test this hypothesis prospectively. Indiscriminate oversizing of valve prostheses is best avoided.

OPPORTUNITIES FOR INNOVATION

Currently, TAVR exists in a state comparable to coronary stenting circa 1993. Randomized controlled trials had established the evidence for regulatory approval and clinical adoption of an important new technology. Accumulating real-world clinical experience then identified the limitations and new iatrogenic diseases associated with the technology. Before stents, there was no stent thrombosis. Before TAVR, there was no TAVR-related PVL. As stents evolved both incrementally and sometimes by paradigm-changing leaps, so too will TAVR. The observations about post-TAVR PVL and the geometric issues of the annulus and the adjoining left ventricular outflow tract and aortic root suggest potential future design improvements.

We suggest that the solution to PVL probably does not lie in better assessment of the annulus or in expecting the valvular ring of the prosthesis to better conform to the ovoid annulus. To distort the ring on which the prosthetic leaflets are mounted would likely invite noncoaptation of the leaflets and lead to central aortic regurgitation.

One technological solution to the valve-annulus mismatch issue could be in the form of an external belt of expandable material ringing the valve that could react when in contact with fluid (ie, blood) and fill the perivalvular space, abolishing PVL. This approach has been adopted in several next-generation devices. Alternatively, instead of seeking a perfect fit at the level of the annulus, a new design could focus on allowing greater expansibility of the metal frame and fabric skirt either superior and/or inferior to the valvular ring. The dimensions of the left ventricular outflow tract and aortic root are consistently larger than those of the annulus.[7]

Until such engineering advances are further developed, the lessons learned thus far place us in a better position to maximize the power of existing imaging technologies to minimize valve-annulus mismatch and the risks of PVL. ■

Paul T. Vaitkus, MD, MBA, is a fellow in the Structural Heart Disease Interventional Fellowship Program, Division of Cardiovascular Medicine, Henry Ford Hospital in Detroit, Michigan. He has disclosed that he has no financial interests related to this article.

Mayra Guerrero, MD, is Director of the Structural Heart Disease Fellowship Program, Division of Cardiovascular Medicine, Henry Ford Hospital in Detroit, Michigan. She has disclosed that she has no financial interests related to this article. Dr. Guerrero may be reached at (313) 916-2382; mguerre1@hfhs.org.

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