# Predicting Paravalvular Regurgitation Following Transcatheter Valve Replacement: Utility of a Novel Method for Three-Dimensional Echocardiographic Measurements of the Aortic Annulus

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*Background:* Studies evaluating three-dimensional echocardiographic (3DE) annular sizing for balloon-expandable transcatheter aortic valve replacement (TAVR) are limited. In this study, a retrospective analysis of transesophageal echocardiographic images was performed to assess the feasibility of multiplanar measurements of annular dimensions by the novel off-label use of commercially available 3DE software and correlate annular sizing with severity of paravalvular regurgitation (PVR).

*Methods:* Intraprocedural transesophageal echocardiography was performed in 58 patients undergoing TAVR for severe, symptomatic aortic stenosis. Off-label use of commercially available software was used to measure transesophageal 3DE volumes. Pre-TAVR annular linear dimensions included two-dimensional echocardiographic sagittal diameter and 3DE measurements of minimal diameter, maximal diameter (MaxDiam), and the average or mean diameter. Three-dimensional echocardiographic average annular diameter derived from annular perimeter ($AveAnnDiam_P$) and average annular diameter derived from annular area ($AveAnnDiam_A$) were calculated. A cover index was calculated using each measurement. Short-axis PVR color jet areas were summed after deployment and at the end of study.

*Results:* Two-dimensional echocardiographic sagittal diameter was significantly smaller than 3DE MaxDiam ($P < .0001$) and $AveAnnDiam_P$ ($P = .017$), significantly larger than 3DE minimal diameter ($P < .0001$), and not significantly different from 3DE mean diameter ($P = .36$) and $AveAnnDiam_A$ ($P = .38$). There was a linear relationship between all 3DE annular measurements and immediate post-TAVR PVR area ($P \leq .0001$), with the largest $R^2$ value (0.48) for 3DE MaxDiam, 3DE $AveAnnDiam_P$, and 3DE $AveAnnDiam_A$. The largest areas under the curve to detect greater than mild PVR were for 3DE $AveAnnDiam_P$ cover index (0.772) and 3DE $AveAnnDiam_A$ cover index (0.769). Intraclass correlation coefficients for interobserver and intraobserver variability were high for 3DE $AveAnnDiam_P$ and 3DE $AveAnnDiam_A$ and lower for 3DE MaxDiam.

*Conclusions:* Using a novel approach to 3DE annular measurements, 3DE $AveAnnDiam_P$ and 3DE $AveAnnDiam_A$ can be reliably measured and correlate best with post-TAVR PVR area. New sizing algorithms with 3DE measurements should be developed. (J Am Soc Echocardiogr 2013;26:1043-52.)

*Keywords:* Transcatheter aortic valve replacement, Aortic stenosis, Paravalvular regurgitation

Although transcatheter aortic valve replacement (TAVR) has emerged as an alternative to surgical aortic valve replacement for patients with severe aortic stenosis who are at "high risk" or deemed inoperable,[1,2] recent studies have shown an association between postprocedural paravalvular regurgitation (PVR) and increased late mortality.[3-10] Some degree of PVR has been reported in 80% to 96% of patients undergoing TAVR.[1,11-14] In most cases, the degree of regurgitation is mild; however, moderate and severe aortic regurgitation are found in 7% to 24% of patients.[1,11-14] A small cover index or large annular size,[6,11,15,16] annular eccentricity,[6] the degree and distribution of leaflet calcifications,[17-21] and malpositioning of the valve[22-25] have all been identified as risk factors for PVR.[26] A recent meta-analysis confirmed that implantation depth, valve undersizing, and Agatston calcium score were the important predictors of PVR after TAVR.[27] Numerous studies have suggested that three-dimensional (3D) assessment of the aortic annulus using multislice computed tomography

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**Abbreviations**

**$AveAnnDiam_A$** = Average annular diameter derived from annular area

**$AveAnnDiam_P$** = Average annular diameter derived from annular perimeter

**ICC** = Intraclass correlation coefficient

**MaxDiam** = Maximal diameter

**MeanDiam** = Mean annular diameter

**MinDiam** = Minimal diameter

**PVR** = Paravalvular regurgitation

**SagDiam** = Sagittal diameter

**TAVR** = Transcatheter aortic valve replacement

**TEE** = Transesophageal echocardiographic

**3D** = Three-dimensional

**3DE** = Three-dimensional echocardiographic

**THV** = Transcatheter heart valve

**2DE** = Two-dimensional echocardiographic

can accurately assess the noncircular anatomy of the aortic annulus and improve annular sizing of the transcatheter heart valves (THVs) by measuring the perimeter or area of the annulus.[28-33] Three-dimensional transesophageal echocardiographic (TEE) imaging can also accurately measure the annular aortic annulus.[15,34-37] Both techniques rely primarily on direct planimetry of the annulus in the transverse plane, which has inherent limitations. The aims of this study were to evaluate the feasibility and reproducibility of real-time 3D measurements of the aortic annulus utilizing a novel off-label use of commercially available software and to use this method to predict PVR after the placement of a balloon-expandable THV.

## METHODS

### Patients and Procedure

Data from 58 (nonconsecutive) patients treated between May 2007 and November 2011 with Edwards SAPIEN THVs (Edwards Lifesciences, Irvine, CA) as part of the Placement of Aortic Transcatheter Valves and Placement of Aortic Transcatheter Valves 2 trials were retrospectively analyzed. After implantation of the THV, reballooning or postdilatation of the implanted valve was performed at the discretion of the operator, typically on the basis of the assessment of PVR severity.

### Echocardiographic Data

All TEE studies were performed using an iE33 xMATRIX system using the X7-2t TEE transducer (Philips Medical Systems, Andover, MA). Intraprocedural two-dimensional echocardiographic (2DE) and 3D echocardiographic (3DE) images were selected for evaluation. Two-dimensional echocardiographic sagittal diameter (SagDiam) measurements were made from the long-axis view of the aorta, with biplane imaging used to ensure that the largest diameter was measured (Figure 1). Frequently, a lower TEE window was required to avoid acoustic shadowing of the anterior annulus by the bulky calcified aortic cusps.

Color Doppler short-axis imaging of the region just apical to the proximal edge of the THV was used for the evaluation of PVR (Figure 2). Simultaneous multiplane imaging was used to enable consistent imaging of this plane using the long-axis view (120°–140°) as the primary plane with the orthogonal short-axis view placed in the left ventricular outflow tract just beneath the skirt of the THV. The short-axis areas of the jets were measured and the sum of the jet areas was used as the total PVR area. Central regurgitation resulting from malcoaptation of leaflets created by the guidewire was distinguished from PVR by locating the catheter on real-time images and correlating it with the associated color Doppler signal, changing wire position to better identify the regurgitant jet, or removing the wire completely.

From the long-axis two-dimensional TEE views of aortic valve, user-defined 3D TEE volumes of the aortic valve complex were acquired (single-beat acquisition). Commercially available software (QLAB MVQ version 8.1; Philips Medical Systems) was used to measure the aortic annulus using the following protocol (Figure 3, Video 1; available at www.onlinejase.com):

1. A short-axis view of the annulus is positioned in the "blue" plane using a double oblique technique.
2. A frame in early systole is selected.
3. The orthogonal long-axis green and red planes are then centered on the annulus in the blue (short-axis) plane.
4. In the green and then the red planes, the blue plane is then positioned at the most caudal attachments of the aortic valve leaflets (hinge points).
5. The orthogonal planes are repeatedly rotated in the blue plane, and the level of the annulus is confirmed in the green and red planes.
6. Once the level and location of the annulus have been confirmed, the green and red planes are returned to position on the blue plane that will bisect the minimal diameter (MinDiam) and maximal diameter (MaxDiam), respectively.
7. A pair of orthogonal points on the annulus is chosen. The MVQ package automatically approximates the annulus using these four points.
8. Using an eight-slice protocol, the annular plane is confirmed for eight pairs of orthogonal segments in the green and red planes.
9. The annular measurement must exclude ectopic calcifications, with the points measured outside the calcifications so as not to underestimate the annular area. In some cases, real-time imaging may help distinguish side-lobe and reverberation artifacts from real structures.

Using this protocol, the following annular measurements were made: MinDiam, MaxDiam, perimeter, and area. From these measurements, the following pre-TAVR annular calculations were made:

- Mean annular diameter (MeanDiam) = (MinDiam + MaxDiam)/2
- Average annular diameter derived from annular perimeter ($AveAnnDiam_P$) = perimeter/$\pi$
- Average annular diameter derived from annular area ($AveAnnDiam_A$) = $(\text{area}/\pi)^{1/2} \times 2$
- Eccentricity index = (MaxDiam − MinDiam)/MaxDiam

Undersizing the THV relative to the annular size has been identified in numerous studies to be the cause of PVR.[8,11,38] Using the formula for cover index[11] as 100 × [(THV diameter − TEE annular diameter)/THV diameter], cover indexes were calculated using the following TEE annular diameters 2DE SagDiam, 3DE MinDiam, 3DE MaxDiam, 3DE MeanDiam, 3DE $AveAnnDiam_P$, and 3DE $AveAnnDiam_A$.

### Statistical Analysis

All analyses were performed using SPSS version 19.0 (IBM, Armonk, NY). $P$ values < .05 were considered statistically significant, and all $P$ values are two sided. Categorical variables were compared using $\chi^2$ or Fisher's exact tests and are expressed as percentages. Chi-square tests were used to calculate trend $P$ values. Continuous variables were compared using unpaired Student's $t$ tests and are expressed as mean ± SD. For comparisons of the effect of postdilatation on PVR, patients were divided into two groups: those who received postdilatation and those who did not. Postdilatation was performed in cases in which PVR as determined by transesophageal echocardiography immediately after THV implantation was qualitatively more than mild, as determined by