Valvular Heart Disease

Three-Dimensional Echocardiography Compared With Computed Tomography to Determine Mitral Annulus Size Before Transcatheter Mitral Valve Implantation

George J. Mak, MD; Philipp Blanke, MD; Kevin Ong, MD; Christopher Naoum, MBBS; Christopher R. Thompson, MD; John G. Webb, MD; Robert Moss, MBBS; Robert Boone, MD; Jian Ye, MD; Anson Cheung, MD; Brad Munt, MD; Jonathon Leipsic, MD; Jasmine Grewal, MD

Background—Previously, through the use of computed tomography (CT), it has been proposed that D-shaped versus saddle-shaped mitral annulus (MA) segmentation is more biomechanically appropriate to determine transcatheter mitral valve implantation size and eligibility.

Methods and Results—Forty-one patients with severe mitral regurgitation being considered for transcatheter mitral valve implantation who had undergone cardiac CT and 3-dimensional transesophageal echocardiography (3D-TEE) were retrospectively evaluated. A standardized segmentation protocol for the D-shaped MA was developed using Philips Q-Laboratory mitral valve quantification software. MA dimensions were compared using Spearman’s rank correlation and Bland–Altman analysis. Inter- and intraobserver agreement was quantified by intraclass correlation coefficient and Bland–Altman analysis. Mean age was 77±14 years; 71% male (n=29); mitral regurgitation pathogenesis was functional in 54% (n=22) and myxomatous in 46% (n=19). Mean MA area and circumference by 3D-TEE and CT were 11.3±2.7 versus 11.4±3.0 (P=0.67) and 124.1±15.6 versus 123.9±15.5 (P=0.79), respectively, with excellent correlation between modalities (r=0.84 and r=0.86; P<0.0001) and no systematic bias (−0.20±1.8 cm² [−3.7 cm²; 3.3 cm²], 0.37±9 mm [−18.0 mm; 17.27 mm]). Mean septal-to-lateral and inter-trigone distances by 3D-TEE and CT were 33.2±4.7 versus 32.5±4.4 (P=0.24) and 31.7±3.5 versus 32.6±3.6 (P=0.06), respectively, with good correlation (r=0.69 and r=0.71; P<0.0001) and no systematic bias (0.77±3.8 mm [−6.7 mm; 8.2 mm], −1.5±3.1 mm [−4.6 mm; 7.6 mm]). There was excellent intra- and interobserver agreement according to intraclass correlation coefficients >0.90 for all parameters.

Conclusions—Similar to cardiac CT, 3D-TEE allows for D-shaped MA segmentation with no systematic difference in MA dimensions between modalities. This study supports the utilization of 3D-TEE as a complementary tool to CT assessment of the D-shaped MA to determine transcatheter mitral valve implantation size. (Circ Cardiovasc Imaging. 2016;9:e004176. DOI: 10.1161/CIRCIMAGING.115.004176.)

Key Words: computed tomography • 3D echocardiography • mitral valve annulus • percutaneous valve implantation • TMVI • TMVR • transcatheter

Transcatheter mitral valve implantation (TMVI) is currently being investigated as a potential treatment option for patients with mitral regurgitation (MR) whose surgical risk is considered prohibitive because of advanced age and comorbidities. Similar to transcatheter aortic valve implantation, determination of anatomic eligibility and valve sizing is contingent on preprocedural imaging. It is well established that the mitral annulus (MA) contour is nonplanar and saddle-shaped with 2 peaks; a posterior peak formed by the insertion of the posterior mitral valve leaflet and an anterior peak which extends to the level of the aortic valve and annulus. The nadirs of the MA are located close to the fibrous trigones. For anatomic quantification, this 3-dimensional contour can be projected onto a 2-dimensional plane using the method of least squares planes, as automatically used by postprocessing platforms. However, the anterior horn of the saddle-shaped contour projects onto the left ventricular outflow tract. With regard to TMVI planning, it has recently been suggested that the anterior horn of the saddle-shaped annulus should be omitted by truncating the saddle-shaped contour along a virtual line connecting both fibrous trigones, yielding a D-shaped more planar contour, with the so-called trigone-to-trigone line forming the flat portion of the D (Figure 1). It is thought that the D-shaped approach is a better representation of the cross-sectional area of current TMVs under investigation.
including the Tiara\textsuperscript{10} and Tendyne valves.\textsuperscript{11} Additionally, a TMVI encroaching beyond the intertrigonal line would likely result in left ventricular outflow tract obstruction.

Recently, the feasibility and reproducibility of the D-shaped mitral annular assessment has been demonstrated using cardiac computed tomography (CT) data sets.\textsuperscript{6} Advances in 3-dimensional transesophageal echocardiography (3D-TEE) have also enabled the measurement of various MA parameters.\textsuperscript{12} However, there are currently no data on the utility of 3D-TEE in analyzing the MA using the D-shaped approach. Therefore, the objectives of this study were to investigate the feasibility and reproducibility of D-shaped MA segmentation using 3D-TEE volume data sets and to compare measurements to cardiac CT in patients with moderate or severe MR being evaluated for potential TMVI.

Methods

Study Population

This retrospective study consisted of consecutive patients with severe MR determined by transthoracic echocardiography, who were subsequently evaluated for potential TMVI between December 2012 and December 2014 at St Paul’s Hospital, Vancouver, BC. Patients were eligible for inclusion if they had undergone both cardiac CT and 3D-TEE imaging with acquisition of data sets. Exclusion criteria included the following: (1) existing aortic or mitral valve prosthesis; (2) history of atrial fibrillation; (3) previous cardiac surgery; (4) complex congenital heart disease; and (5) severe mitral annular calcification preventing clear visualization of the entire mitral valve annulus. The study protocol was approved by the Institutional Research Ethics Board with a waiver for informed consent.

Image Data Acquisition and Mitral Annular Assessment

Cardiac CT

Contrast-enhanced cardiac CT examinations were performed using a 64-slice Discovery HD 750 high-definition or volume CT scanner (GE Healthcare, Milwaukee, WI) with an estimated temporal resolution of 165 ms.

The method for segmentation and assessment of the D-shaped MA with cardiac CT has been previously described.\textsuperscript{6} Briefly, mid to late diastolic image reconstructions with the least artifact identified were used for MA segmentation. The MA was tracked by manually placing 16 seeding points for cubic spline interpolation along the insertion of the posterior mitral valve leaflet and along the contour of the anterior peak comprising the fibrous aorto-mitral continuity by step-wise rotation of a long-axis view aligned to the left ventricular long axis. The lateral and medial fibrous trigones were then manually identified. The initially segmented saddle-shaped annulus was truncated along a virtual line connecting both trigones, referred to as trigone–trigone (TT) distance. Annular area was computed for the D-shaped component as an area projected onto the least-squares plane fitted to the 3D annular contour as described previously.\textsuperscript{6} Total annular circumference was defined as the sum of the TT distance and the 2D circumference of the posterior aspect of the D-shaped annulus. The septal–lateral (SL) distance was defined as the projected distance from the TT line to the posterior peak (Figure 2). CT and 3D-TEE studies were all performed within 3 months of each other.

Echocardiography

TEE image acquisition was performed using an X7-2t transducer and iE33 xMATRIX echocardiography system (Phillips Ultrasound, Phillips Medical Systems, Bothell, Washington). A comprehensive TEE examination was performed in accordance with American Society of Echocardiography guidelines.\textsuperscript{13,14} MR severity was graded according to recommendations by Zoghbi et al.\textsuperscript{15} Three-dimensional images of the MV were acquired with a focused wide sector zoom mode, ensuring inclusion of the aortic valve and the entire MA throughout the cardiac cycle in a single beat. Offline assessment of 3D data sets was performed using Philips Q-Laboratory 8.0 mitral valve quantification (MVQ) software. The analysis was performed by an independent, blinded investigator (Dr Mak), and the results were used to compare the 3D-TEE and cardiac CT measurements.

Analysis was initiated by using the standard MVQ protocol for assessing MA dimensions with a subsequent modified segmentation to specifically assess the D-shaped annulus (Figure 3). This can be performed using either Q-Laboratory 8.0 or 9.0 MVQ software. This modified segmentation was extrapolated from CT methodology as previously described.\textsuperscript{6} Using MVQ, 3 orthogonal imaging planes were displayed and subsequently manipulated to optimize visualization of the endocardium and entire MA. The mid to late diastolic frame where the MA was largest, image resolution greatest, and the entire annulus well visualized was selected. The mid to late diastolic phase was chosen for echocardiographic annular assessment because it is in line with the phase used for CT annular assessment. The orthogonal planes were adjusted to optimize visualization of the MA hinge points. Four segmentation points were initially placed along the MA in an antero-lateral, postero-medial, anterior, and posterior location. Subsequently, with the 3 orthogonally oriented viewing planes locked, 7 rotational planes were created along the long axis, allowing for placement of 14 additional segmentation points along the MA. Based on the total of 18 seeding points, a cubic spline interpolation contour was formed. Accurate positioning of the seeding points was achieved by simultaneous observation in all 3 planes.

![Figure 1. Saddle-shaped (A) versus D-shaped (B) mitral annulus.](http://circimaging.ahajournals.org/)

Figure 1. Saddle-shaped (A) versus D-shaped (B) mitral annulus.
Adhering to the previously described definition of the D-shaped annulus, the anterior margin of the annulus was defined by a virtual line connecting the lateral and medial trigones (representing the TT distance) rather than the initially traced MA contour following the fibrous intervalvular continuity. Thus, the TT line excluded the anterior horn of the MA. The medial and lateral trigones were identified using both the short-axis and long-axis planes. The trigones were identified by panning through the short-axis plane to obtain the most precise lateral and medial points where the anterior leaflet attached to the fibrous skeleton of the heart representing the site of inflection of the anterior and posterior mitral valve. Although rotating through the long-axis view, the areas where the anterior mitral leaflet insertion separates from the aortomitral junction were also noted as being at or close to the points representing the trigones. The D-shaped annulus was achieved by truncating the saddle-shaped annulus at the TT distance, whereas the posterior peak and TT distance remained unchanged (Figure 4). To accomplish this, the points marking the initial anterior margin of the annulus are brought into line with the points making up the straight line connecting the trigones. The TT line should not be manipulated. This change should be reviewed by rotating through the long-axis planes to ensure that the annular points line up with the TT points. This step is necessary to ensure that the annular measurements reported by the program are those of the D-shaped annulus and not the saddle-shaped annulus. After finalizing the segmentation, MVQ automatically derived the following 2-dimensional MA parameters projected onto the least squares plane: area, circumference, TT distance, and SL diameter (Figure 5). This entire analysis could be completed within 5 minutes by an experienced operator, which provides added value in an operating room setting. The approach to D-shaped mitral annular assessment is outlined in Movie in the Data Supplement.

**Statistical Analysis**

Categorical variables were summarized using frequencies and percentages. Continuous variables were summarized using mean ± standard deviation. Paired Student’s t tests were used to test for significant differences between continuous variables. The relationship between 3D-TEE and cardiac CT measured annular dimensions was evaluated using Pearson correlation coefficient. Bland–Altman analysis was performed to assess mean difference and limits of agreement between the 2 imaging modalities. Inter- and intraobserver agreement were each quantified with both intraclass correlation coefficient with 95% confidence intervals and Bland–Altman limits of agreement. A P value <0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS version 21.0 for Windows (SPSS, Chicago, IL).

**Results**

Of 42 consecutive patients undergoing diagnostic evaluation for potential TMVI with 3D-TEE and cardiac CT data sets, 41 patients were enrolled in this analysis. One patient was excluded because the 3D-TEE data did not include the entire mitral valve annulus. The mean age of the study population was 77±14 years, with 71% males (n=29). The MR pathogenesis was secondary in 54% (n=22) of patients and primary (all myxomatous) in the remaining 46% (n=19) of patients. Severe MR was present in 88% (n=36), with the remaining patients having moderate regurgitation. These latter patients were referred on the basis of severe MR, but our TMVI work-up revealed MR in the moderate range, and hence, TMVI was not performed in these patients. The left ventricular end diastolic and end systolic diameters by cardiac CT assessment were 59±11 and 44±14 mm, respectively.

The D-shaped MA dimensions determined by cardiac CT were mean area 11.4±3.0 cm²; mean circumference 123.9±15.5 mm; mean TT distance 32.6±3.6 mm, and mean SL distance 32.5±4.4 mm. The 3D-TEE-derived D-shaped MA dimensions were mean area 11.3±2.7 cm²; mean...
circumference 124.1±15.6 mm; mean TT distance 31.7±3.5 mm, and mean SL distance 33.2±4.7 mm. There were no significant differences between the cardiac CT MA measurements versus the 3D-TEE MA measurements (Table 1). 3D-TEE-derived annular dimensions were significantly larger in the myxomatous valve disease group versus the functional MR group (Table 2).

The correlations between cardiac CT and 3D-TEE mitral annular measurements were excellent for area (r=0.84; P<0.0001) and circumference (r=0.86; P<0.0001), whereas moderate correlations were found for TT distance (r=0.71; P<0.0001) and SL distance (r=0.69; P<0.0001; Figures 6–9).

The mean difference±SD (3D-TEE-CT) and limits of agreement between 3D TEE and CT measurements of MA parameters were area :=−0.20±1.8 cm² (−3.7 cm²; 3.3 cm²; P=0.51); circumference= −0.37±9 mm [−18.0 mm; 17.27 mm]; P=0.79); TT distance =−1.5±3.1 mm (−4.6 mm; 7.6 mm; P=0.04); and SL distance =0.77±3.8 mm (−6.7 mm; 8.2 mm; P=0.23; Figures 6–9). For intraobserver analyses, intraclass correlation coefficient was 0.96 (0.94–0.97) for area, 0.98 (0.96–0.99) for circumference, 0.90 (0.76–0.92) for TT distance, and 0.97 (0.95–0.99) for SL distance. For interobserver analyses, the intraclass correlation coefficient was 0.95 (0.91–0.99) for area, 0.89 (0.62–0.97) for

**Figure 3.** A standardized algorithm for measuring the D-shaped mitral annulus using Philips Q-laboratory 8.0 mitral valve quantification software (MVQ). This analysis can also be performed using Philips Q-Laboratory 9.0 MVQ software. (1) Once the image is optimized by adjusting gain and magnification settings, a mid to late diastolic frame is selected, and the orthogonal planes are adjusted so that the mitral annular hinge points are well visualized (A). (2) Four segmentation points along mitral annulus are selected (B). MVQ requires selection of a nadir and aortic valve point to proceed with the analysis; however, these are not required for the final analysis. (3) The program generates 14 additional segmentation points along the mitral annulus in 7 rotational planes along the long axis. These points are then manually positioned to outline the contour of the mitral annulus (C). (4) To generate the virtual line connecting both trigones, 4 contiguous points are manipulated to represent a straight line along the anterior flat portion of the D-shaped annulus to form the virtual TT line (C, red arrow). The 2 outermost points are placed at the fibrous trigones (D). The inner 2 points are aligned with the outer points placed to form a straight line (E and F). To facilitate the manual creation of a straight line, the commissure segmentation tool can be used to resemble a straight line, which is then used to align the annular segmentation points.

The correlations between cardiac CT and 3D-TEE mitral annular measurements were excellent for area (r=0.84; P<0.0001) and circumference (r=0.86; P<0.0001), whereas moderate correlations were found for TT distance (r=0.71; P<0.0001) and SL distance (r=0.69; P<0.0001; Figures 6–9).
circumference, 0.94 (0.77–0.98) for TT distance, and 0.96 (0.85–0.98) for SL distance. Limits of agreement for inter and intraobserver variability are shown in Table 3.

Discussion

3D-TEE has been used extensively for MA assessment\(^\text{13,16-22}\), however, its utility in assessing the proposed D-shaped MA,
particularly in the context of TMVI, has not been studied to date. Therefore, we developed a practical and reproducible protocol using commercially available software (Philips Q-Laboratory MVQ) to evaluate the D-shaped MA. Using this novel protocol, we demonstrated that the 3D-TEE MA measurements were clinically comparable with those acquired from cardiac CT. Importantly, 3D-TEE assessment of the D-shaped MA was highly reproducible with excellent inter and intraobserver variability.

Currently, the majority of TMVI assessments rely on CT mitral annular measurements. The feasibility of measuring the D-shaped annulus by cardiac CT was recently documented in patients with severe functional MR undergoing assessment for TMVI.6 Although CT is generally well tolerated, certain limitations exist that need to be considered (Table 4).23,24 Therefore, it is imperative to have an alternative imaging strategy such as 3D-TEE which has become increasingly available in many institutions. Previous studies have demonstrated excellent correlation between 3D-TEE and CT measurements of the aortic annulus,25,26 but this has not been verified for MA dimensions. Despite extensive literature describing the saddle-shaped annulus on 3D-TEE, our study is the first to report a 3D-TEE method that analyzes the MA as a D-shaped structure, an analysis which may be more relevant to TMVI sizing. Our study shows that 3D-TEE assessment is a feasible adjunct or alternative to cardiac CT sizing of the D-shaped MA and merits further study.

Cardiac CT has been shown to be highly reproducible in analyzing the D-shaped MA.6 Likewise, we also demonstrated excellent intraobserver and interobserver agreement of D-shaped mitral annular measurements using 3D-TEE. Although dedicated echo postprocessing software is currently unavailable to evaluate the D-shaped MA, a modified protocol using Philips Q-laboratory MVQ software provided a suitable platform for assessment. MVQ is preferred over 3DQ software, which is also widely available as part of Phillips’ Q-laboratory package. 3DQ does not allow for...
Mak et al D-Shaped Mitral Annulus in Transcatheter Implants

a precise point by point marking of the MA in the long-axis plane rather only a direct perimeter trace in the short-axis view. Other annular measurements are also made directly onto the short-axis view not taking into account the true non-planar configuration.

3D echocardiography can underestimate measurements compared with other imaging modalities, such as CT and magnetic resonance imaging. This may be due in part to sub-optimal lateral resolution in the coronal plane of 3D echocardiography, which reduces the ability to discriminate the blood/tissue interface. Nonetheless, this study demonstrated good agreement between MA dimensions derived by 3D-TEE and CT. The temporal resolution of the 3D TEE single beat 3D zoom acquisition was comparable to CT (6–9 Hz versus 7 Hz), making similar measurements possible between both modalities. Precise identification of the trigones on 3D-TEE images was challenging, and we attempted to mitigate the issue by actively panning through the short- and long-axis planes. Hence, this issue likely accounts for the weaker correlations and lower levels of agreement for TT distance compared with area and diameter. It is also of interest that the SL diameter demonstrated a lower correlation and level of agreement between modalities. This may be because of where the level of the TT line is drawn which ultimately influences the SL distance.

Limitations
The study was limited by a relatively small sample size and retrospective design. As a result, valve sizing was not prospectively performed. Although it is known that MA calcification could affect up to one third of cases and bring about difficulty in delineating the posterior annular contour in cardiac CT studies, this limitation also affects 3D echo assessment of the valve. It also must be emphasized that the D-shaped annulus pertains to current investigative mitral valve devices designed to be deployed at the level of the MA. It is likely that this concept will not be as relevant for nonannular TMVs should they be developed in the future.

Conclusions
In conclusion, this study demonstrates that 3D echocardiographic assessment of the D-shaped MA is comparable to cardiac CT. The use of commercially available analytic software with a standardized protocol allows an observer to provide an accurate and highly reproducible assessment of the

Figure 7. Regression analysis and Bland–Altman plot: annular circumference. A, Comparison of circumference as measured by cardiac computed tomography (CT) and 3-dimensional transesophageal echocardiography (3D-TEE). B, Agreement statistic for circumference as measured by cardiac CT and 3D-TEE.

Figure 8. Regression analysis and Bland–Altman plot: annular TT distance. A, Comparison of TT distance as measured by cardiac computed tomography (CT) and 3-dimensional transesophageal echocardiography (3D-TEE). B, Agreement statistic for TT distance as measured by cardiac CT and 3D-TEE.
of CT in certain clinical scenarios for the preprocedural planning of TMVR.

Disclosures
Drs Leipsic, Cheung, and Blank are consultants to Edwards Lifesciences and Neovasc Inc. Dr Webb is a consultant to Edwards Lifesciences. Drs Leipsic and Blank provide CT core laboratory services for Edwards Lifesciences, Neovasc Inc. and Tendyne Holdings Inc.

References
D-Shaped Mitral Annulus in Transcatheter Implants

CLINICAL PERSPECTIVE

The D-shaped mitral annulus (MA) has been shown in previous computed tomography studies to be more biomechanically appropriate than the saddle-shaped MA for sizing transcatheter mitral valve implants. This study compares 3-dimensional transesophageal echocardiography and cardiac computed tomography in assessing the D-shaped MA in patients with moderate to severe mitral regurgitation undergoing evaluation for transcatheter mitral valve implants. By using commercially available Philips Q-Laboratory mitral quantification software, a standardized protocol for the D-shaped MA was developed. Three-dimensional transesophageal echocardiography data in the study demonstrate no systematic difference when compared with cardiac computed tomography in sizing the D-shaped MA. Inter- and intraobserver agreement was excellent. Pending further validation, 3-dimensional transesophageal echocardiography could potentially be used as a complementary tool to cardiac computed tomography in assessing the D-shaped MA. Furthermore, by using the proposed protocol, the assessment of the MA can be rapidly made in clinical settings, such as an operating room, in determining transcatheter mitral valve implant size and eligibility.
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SUPPLEMENTAL MATERIAL

Video 1 Legend

Video animation of the step by step algorithm used for measuring the D-shaped mitral annulus using Phillips Q-laboratory mitral valve quantification software as described in the manuscript.