



Real-Time 3D Transesophageal Echocardiography for the Evaluation of Rheumatic Mitral Stenosis

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OBJECTIVES The aims of this study were: 1) to assess the feasibility and reliability of performing mitral valve area (MVA) measurements in patients with rheumatic mitral valve stenosis (RhMS) using real-time 3-dimensional transesophageal echocardiography (3DTEE) planimetry (MVA_{3D}); 2) to compare MVA_{3D} with conventional techniques: 2-dimensional (2D) planimetry (MVA_{2D}), pressure half-time (MVA_{PHT}), and continuity equation (MVA_{CON}); and 3) to evaluate the degree of mitral commissural fusion.

BACKGROUND 3DTEE is a novel technique that provides excellent image quality of the mitral valve. Real-time 3DTEE is a relatively recent enhancement of this technique. To date, there have been no feasibility studies investigating the utility of real-time 3DTEE in the assessment of RhMS.

METHODS Forty-three consecutive patients referred for echocardiographic evaluation of RhMS and suitability for percutaneous mitral valvuloplasty were assessed using 2D transthoracic echocardiography and real-time 3DTEE. MVA_{3D} , MVA_{2D} , MVA_{PHT} , MVA_{CON} , and the degree of commissural fusion were evaluated.

RESULTS MVA_{3D} assessment was possible in 41 patients (95%). MVA_{3D} measurements were significantly lower compared with MVA_{2D} (mean difference: -0.16 ± 0.22 ; $n = 25$, $p < 0.005$) and MVA_{PHT} (mean difference: -0.23 ± 0.28 cm²; $n = 39$, $p < 0.0001$) but marginally greater than MVA_{CON} (mean difference: 0.05 ± 0.22 cm²; $n = 24$, $p = 0.82$). MVA_{3D} demonstrated best agreement with MVA_{CON} (intraclass correlation coefficient [ICC] 0.83), followed by MVA_{2D} (ICC 0.79) and MVA_{PHT} (ICC 0.58). Interobserver and intraobserver agreement was excellent for MVA_{3D} , with ICCs of 0.93 and 0.96, respectively. Excellent commissural evaluation was possible in all patients using 3DTEE. Compared with 3DTEE, underestimation of the degree of commissural fusion using 2D transthoracic echocardiography was observed in 19%, with weak agreement between methods ($\kappa < 0.4$).

CONCLUSIONS MVA planimetry is feasible in the majority of patients with RhMS using 3DTEE, with excellent reproducibility, and compares favorably with established methods. Three-dimensional transesophageal echocardiography allows excellent assessment of commissural fusion. (J Am Coll Cardiol Img 2011;4:580–8) © 2011 by the American College of Cardiology Foundation

Echocardiography is the principal diagnostic tool for the evaluation and management of rheumatic mitral valve stenosis (RhMS). Among the most important aims of echocardiography is the assessment of the severity of RhMS by measuring the mitral valve area (MVA) and the selection of suitable patients for percutaneous mitral valvuloplasty (PTMV) (1).

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More recently, it has been suggested that real-time 3-dimensional (3D) echocardiography can overcome some of the known technical limitations posed by 2-dimensional (2D) echocardiography (2,3). Real-time 3D transthoracic echocardiography (3DTTE) has been shown to be highly reproducible and accurate for the measurement of MVA in RhMS (4-9). However, in clinical practice transthoracic image quality may compromise accurate assessment of the rheumatic mitral valve using 3D imaging (10).

The close proximity of the transducer to the mitral valve and the higher transmission frequencies used in real-time 3D transesophageal echocardiography (3DTEE) allow high resolution images of the mitral valve independent of the quality of transthoracic acoustic windows and may provide additional information to that obtained by 3DTTE (11,12). To date, there have been no feasibility studies investigating the utility of 3DTEE in the assessment of RhMS using the new matrix-array 3D probe, which permits real-time acquisition.

The aims of this study were: 1) to assess the feasibility and reliability of performing MVA measurements in patients with RhMS using 3DTEE planimetry (MVA_{3D}); 2) to compare MVA_{3D} with MVA obtained using conventional 2D techniques; and 3) to evaluate semiquantitatively the degree of mitral commissural fusion.

METHODS

Patient population. Forty-three consecutive patients referred to our institution for echocardiographic assessment of RhMS and suitability for PTMV between May 2008 and October 2009 were studied. As is routine clinical practice at our institution for echocardiographic assessment before PTMV, all patients in addition to transthoracic echocardiography also underwent transesophageal echocardiography, primarily to exclude left atrial thrombi.

Echocardiographic examination. 2D ECHOCARDIOGRAPHY. Two-dimensional transthoracic echocardiography (2DTTE) used a commercial ultrasound system (S3-1 probe and iE33; Philips Medical Systems, Andover, MA). MVA using 2D planimetry (MVA_{2D}) was performed in a parasternal short-axis view. Gain was optimized to visualize the whole contour of the mitral valve orifice. The mitral valve orifice was magnified. Systematic scanning from the apex to the base of the left ventricle was performed to ensure that the mitral valve cross-sectional area was obtained at the leaflet tips. The image was paused during early diastole at the time of greatest mitral valve leaflet separation. Mean and peak transmitral gradients and the time-velocity integral were obtained by continuous-wave Doppler tracings through the mitral valve from the apical 4-chamber view. MVA using pressure half-time (MVA_{PHT}) was estimated using the formula $220/\text{pressure half-time}$ in the absence of no more than moderate aortic or mitral regurgitation (13). MVA using continuity equation (MVA_{CON}) was calculated using the formula $\text{time-velocity integral of the left ventricular outflow tract}/\text{time-velocity integral of the mitral valve} \times (\text{left ventricular outflow tract})^2 \times 0.785$ if there was less than moderate left-sided valve regurgitation (14). Left ventricular outflow tract measurements were made in the parasternal long-axis view. Three cardiac cycles for patients in sinus rhythm and 5 representative cycles for patients in atrial fibrillation were measured, and their results were averaged. Assessment of left ventricular size and function, right ventricular size and function, pulmonary artery systolic pressure, left atrial size and area, and the degree of mitral regurgitation severity were also made. The short-axis view of the mitral valve orifice was used to grade semiquantitatively the degree of fusion of the anterolateral (P1 and A1) and posteromedial commissures (P3 and A3) as minimal fusion, partial fusion, or complete fusion (15).

3DTEE. After providing informed consent, patients underwent 3DTEE under conscious sedation on the same day as 2DTTE. Acquisition was performed using a commercially available matrix-array transducer and echocardiographic unit (X7-2 t probe and iE33; Philips Medical Systems). The same ultrasound platform was used for both 2D and 3D acquisitions.

Conventional 2D transesophageal echocardiography was performed to assess valve morphology

ABBREVIATIONS AND ACRONYMS

ICC = intraclass correlation coefficient

MVA = mitral valve area

MVA_{CON} = mitral valve area by continuity equation

MVA_{PHT} = mitral valve area by pressure half-time

MVA_{3D} = mitral valve area by real-time 3-dimensional transesophageal echocardiographic planimetry

MVA_{2D} = mitral valve area by 2-dimensional planimetry

PTMV = percutaneous mitral valvuloplasty

RhMS = rheumatic mitral valve stenosis

3DTEE = real-time 3-dimensional transesophageal echocardiography

3DTTE = real-time 3-dimensional transthoracic echocardiography

2DTTE = 2-dimensional transthoracic echocardiography

and functional information. For 3DTEE image acquisition, the 2D image of the mitral valve in the bicommissural view was optimized, and then 3D “en face” views of the mitral valve were obtained in real time using the 3D zoom mode. By adjusting the mitral valve to the center of the screen, sector settings were optimized for image and color resolution.

MVA_{3D} was determined offline on an Xcelera workstation using dedicated Philips QLAB version 7.0 advanced quantification software (Philips Medical Systems). Gain and brightness settings were optimized offline to allow the best endocardial definition detection. Multiplanar reconstruction of the mitral valve orifice was used to identify the plane at which the mitral valve orifice was smallest (Fig. 1). First, the smallest orifice in the most perpendicular plane was determined. This plane was then steered systematically in small depths and angulations in 3D space to ensure that the truly smallest orifice was obtained. Planimetry was performed en face at the cross-sectional plane in early to mid diastole during its greatest diastolic opening (Fig. 2).

MVA_{3D} measurements were compared with MVA_{2D} , MVA_{PHT} , and MVA_{CON} . All values used in the final analysis were obtained independently, blinded to the results of the other MVA measurements. For interobserver and intraobserver variability, images of 15 randomly selected patients were

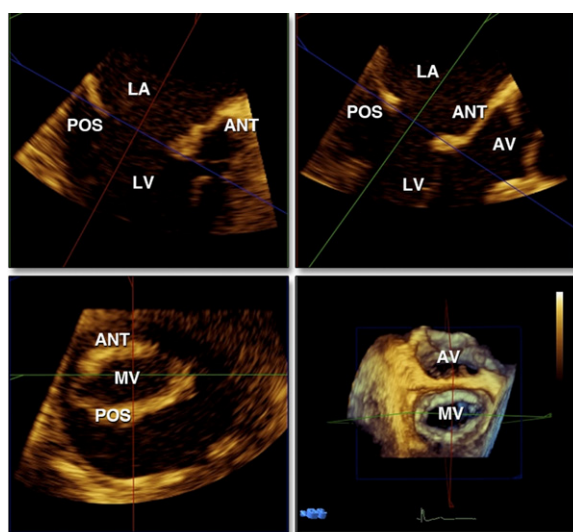


Figure 1. Multiplanar Reconstruction of MV Orifice Showing Orthogonal Imaging Planes at the Tips of the MV Leaflets

ANT = anterior mitral leaflet; AV = aortic valve; LA = left atrium; LV = left ventricle; MV = mitral valve; POS = posterior mitral leaflet.

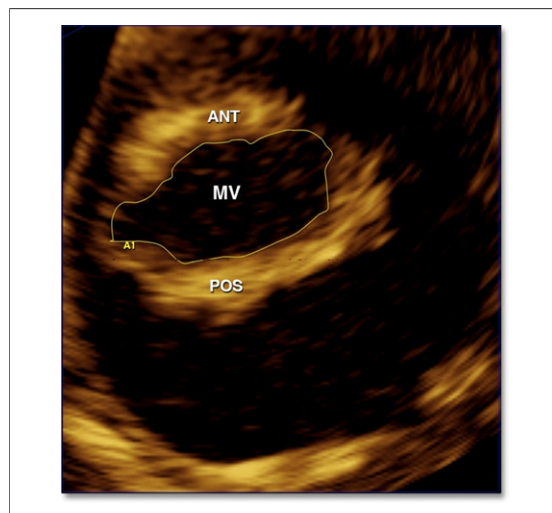


Figure 2. Three-Dimensional Planimetry of the MVA Traced at the MV Leaflet Tips Using the Short-Axis View Determined After Multiplanar Reconstruction

ANT = anterior mitral leaflet; MV = mitral valve; MVA = mitral valve area; POS = posterior mitral leaflet.

repeated at different times by 2 independent observers. The same images were also analyzed on a different day by 1 of these observers.

Similar to 2DTTE, the degree of commissural fusion was assessed semiquantitatively. 3D en face views of the mitral valve were used to assess the commissures from the left atrial, left ventricular, and lateral views.

Statistical analysis. Continuous variables are expressed as mean \pm SD. MVA values obtained by 2D and 3D echocardiography were compared using Student *t* tests. Qualitative data are expressed as an absolute number (percentage). Statistical analysis of the association of variables was performed using Pearson correlation coefficients. Interobserver and intraobserver reproducibility was evaluated using intraclass correlation coefficients (ICC) or kappa statistics (StatsDirect statistical software; StatsDirect Ltd., Altrincham, United Kingdom). Intermethod agreement was evaluated using the Bland-Altman method. Statistical significance was defined as $p < 0.05$.

RESULTS

Feasibility. MVA_{3D} assessment was possible in 41 patients (95%). In 2 patients (5%), excess calcification precluded adequate image quality and MVA_{3D} determination. MVA_{CON} assessment was performed in 26 patients (60%). In 13 patients (30%), MVA_{CON} was not performed, because of significant mitral or aortic regurgitation. In 4 patients (9%), insufficient data were

available. MVA_{2D} assessment was possible in 27 patients (63%). In 10 patients (23%), image quality was inadequate. In 6 patients (14%), short-axis views of the mitral valve were deemed technically insufficient for MVA_{2D} assessment, because they were obtained at the incorrect level of the mitral valve leaflets. MVA_{PHT} was determined in 41 patients (95%). In 2 patients (5%), MVA_{PHT} could not be assessed, because of significant mitral or aortic regurgitation.

Population. Forty-three consecutive patients with RhMS constituted our study group. The mean age of the study population was 61 ± 16 years, 74% were women, and 58% were in atrial fibrillation. Left ventricular function was normal in 91%. Mitral stenosis was the predominant valvular lesion in all patients. Twelve patients had at least moderate mitral regurgitation. One patient had moderate to severe aortic stenosis. One patient had moderate to severe aortic regurgitation. The mean gradient across the mitral valve was 10 ± 5 mm Hg. Clinical and echocardiographic characteristics of the population are summarized in Table 1.

Assessment of MVA. MVA_{3D} measurements were significantly lower compared with MVA_{2D} (mean difference: -0.16 ± 0.22 ; $n = 25$, $p < 0.005$) and MVA_{PHT} (mean difference: -0.23 ± 0.28 cm²; $n = 39$, $p < 0.0001$) but marginally greater than MVA_{CON} (mean difference: 0.05 ± 0.22 cm²; $n = 24$, $p = 0.82$), but this was not significant.

Agreement between MVA_{3D} and conventional methods. MVA_{3D} demonstrated the best agreement with MVA_{CON} (95% limits of agreement: -0.38 to 0.47 ; ICC 0.83), followed by MVA_{2D} (95% limits of agreement: -0.6 to 0.27 ; ICC 0.79). Agreement was less good with MVA_{PHT} (95% limits of agreement: -0.77 to 0.31 ; ICC 0.58). Agreement between methods is summarized in Table 2. Bland-Altman plots and correlations comparing paired observations between methods are shown in Figures 3A to 3F.

Intraobserver and interobserver variability. Interobserver and intraobserver agreement was excellent for MVA_{3D} , with ICCs of 0.93 and 0.96, respectively. Bland-Altman plots and correlation are presented in Figures 4A to 4D.

Commissural anatomy. Commissural evaluation was possible in all patients using 3DTEE. In comparison, 2DTTE commissural evaluation was possible in only 32 patients (78%), because of suboptimal image quality in the remainder. Assessment of commissural fusion with 2DTTE showed minimal fusion in 33%, partial fusion in 52%, and complete fusion in 15%. In contrast, using 3DTEE, minimal fusion was observed in 17%, partial fusion in 57%, and complete

Table 1. Clinical and Echocardiographic Characteristics

Women/men	32/11
Age (yrs)	61 ± 16
AF	25 (58)
LV function	
Normal	39 (91)
Impaired	4 (9)
LA area (cm ²)	33 ± 7
SPAP (mm Hg)	50 ± 18
Transmitral gradient (mm Hg)	10 ± 5
Mitral regurgitation grade moderate or greater	12 (29)
Aortic regurgitation greater than moderate	1 (2)
Aortic stenosis greater than moderate	1 (2)

Data are expressed as mean \pm SD or as n (%).
 AF = atrial fibrillation; LA = left atrial; LV = left ventricular; SPAP = systolic pulmonary artery pressure.

fusion in 26% (Fig. 5). Agreement between methods was weak ($\kappa = 0.34$, 54% agreement), and a lower degree of commissural fusion using 2DTTE was observed in 19%. A lower degree of commissural fusion was equally seen for posteromedial and anterolateral commissures, with poor agreement for both ($\kappa < 0.4$). Examples of commissural fusion are shown in Figures 6A to 6F and Online Videos 1, 2, 3, 4, 5, and 6. The degree of commissural fusion for individual patients measured by 2DTTE and 3DTEE is shown in Tables 3 and 4. Patients with minimal fusion of both commissures had the largest MVAs, whereas patients with complete fusion of both commissures had the smallest MVAs (Table 5).

DISCUSSION

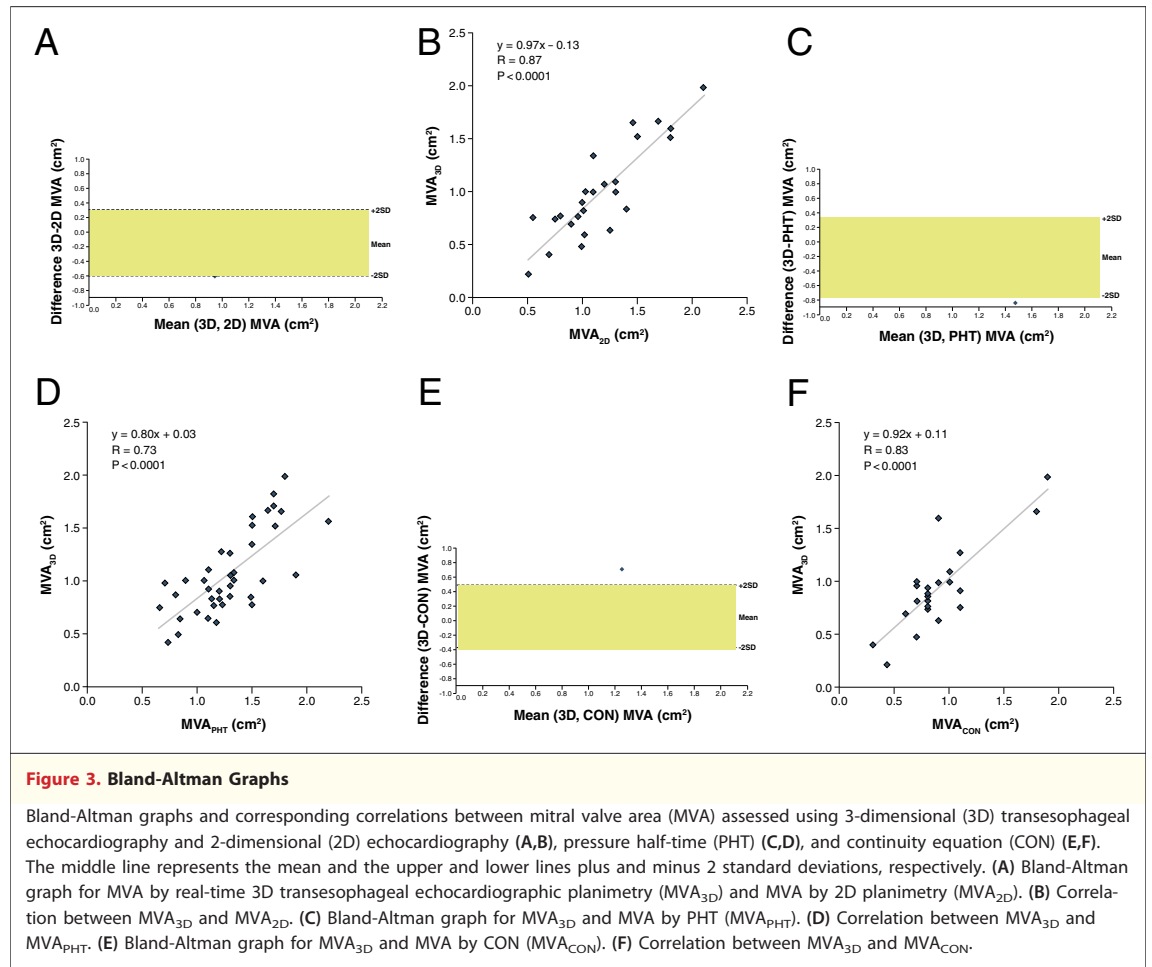
Findings. The present study is the first to evaluate the reliability and feasibility of 3DTEE technology for MVA measurements and the assessment of commissural fusion in patients with moderate to severe RhMS. The main findings were that 3DTEE: 1) provides excellent images of the mitral valve leaflets in the majority of patients; 2) permits accurate MVA planimetry in 95% of patients, with low interobserver

Table 2. Agreement Between Different Methods and MVA_{3D}

Method	n	Mean $\Delta \pm$ SD (cm ²)	p Value*	Limits of Agreement (cm ²)	ICC
MVA_{2D}	25	-0.16 ± 0.22	<0.005	-0.6 to 0.27	0.79
MVA_{PHT}	39	-0.23 ± 0.28	<0.0001	-0.77 to 0.31	0.58
MVA_{CON}	24	0.05 ± 0.22	0.82	-0.38 to 0.47	0.83

*Paired t test compare with MVA_{3D} .

ICC = intraclass correlation coefficient; mean Δ = mean difference compared with MVA_{3D} ; MVA = mitral valve area; MVA_{CON} = mitral valve area using continuity equation; MVA_{PHT} = mitral valve area using pressure half-time; MVA_{3D} = planimetry of mitral valve area using real-time 3-dimensional transesophageal echocardiography; MVA_{2D} = planimetry of mitral valve area using 2-dimensional echocardiography.



and intraobserver variability; and 3) demonstrates detailed assessments of commissural fusion in all patients. **MVA measurements.** MVA measurements play a major role in the management of RhMS. Methods that provide sufficient accuracy and low variability are therefore desirable. MVA assessments by planimetric methods are recommended as reference standards, because they are relatively unaffected by hemodynamic changes (16).

In the present study, MVA_{3D} measurements were lower than MVA_{PHT} and MVA_{2D} measurements but provided similar values to MVA_{CON} . Similar observations have been made by previous studies using 3DTTE (4,7,8). It is well known that MVA_{PHT} can be affected by several hemodynamic factors. In our study, both undiagnosed diastolic dysfunction and the high proportion of patients in atrial fibrillation (60%) may have affected the accuracy of MVA_{PHT} . MVA_{3D} measurements showed the best correlation and agreement with the ones obtained by MVA_{CON} . Similar observations were made by Chu *et al.* (17) during the assessment of MVA in calcific mitral stenosis using

3DTTE. 3DTEE may provide lower values for MVA compared with MVA_{2D} because of inferior lateral resolution. However, other investigators have demonstrated that MVA measured with 3DTTE, which has an inferior lateral resolution compared with 3DTEE, show superior accuracy compared with traditional 2D and Doppler methods when compared with MVA derived from Gorlin formula used as the gold standard.

MVA_{2D} assessment was possible in only 63% of patients, which is lower than reported in published research. One explanation may be that more than 20% of the patient cohort was older than 75 years of age and had very severe mitral stenosis. MVA_{2D} is technically challenging and requires technical expertise, especially in the elderly with severe mitral stenosis, in whom there are often poor acoustic windows and the mitral valve is frequently distorted and heavily calcified (16).

The geometry and complex structure of the mitral valve in RhMS make it difficult to determine the correct MVA with 2D echocardiography. Importantly, controlled sectioning of the mitral valve funnel orifice in a second plane is not possible. This may lead

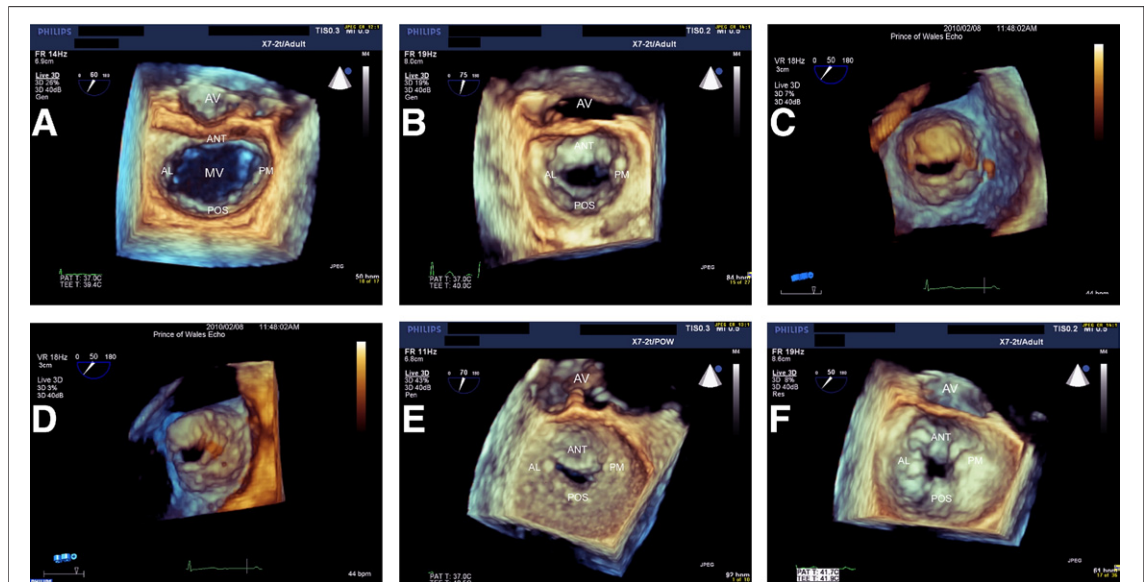


Figure 6. Images Displaying Different Views of the MV Commissure Using 3DTEE

(A) Normal MV with normal commissures. (B) Partial fusion of both anterolateral commissure (AL) and posteromedial commissure (PM) viewed from the left atrium. (C) Partial fusion of both AL and PM viewed from the left ventricle. (D) Partial fusion of both AL and PM viewed from the left ventricle from the side. (E) Partial fusion of AL and complete fusion of PM. (F) Complete fusion of both AL and PM. ANT = anterior mitral leaflet; AV = aortic valve; MV = mitral valve; POS = posterior mitral leaflet.

achieved a mean frame rate of >18 Hz and were able to acquire consistently high-quality real-time 3D images of the mitral valve. This allowed real-time, en face evaluation of the mitral valve apparatus from multiple angles, providing detailed visualization of the mitral valve leaflets, subvalvular structures, and commissures. 3DTEE was particularly useful for the MVA assessment of eccentric mitral valve orifices and the characterization of shape and distribution of the mitral valve orifice.

MVA measurements could not be performed in 2 patients with very severe RhMS ($MVA \leq 0.5$ cm²) and extensive calcification. This led to overgaining of the 3D and multiplanar images, which precluded MVA assessment in these patients, because the mitral valve orifice was not sufficiently delineated. It is important to note that MVA_{2D} assessment was possible in these patients.

Commissural assessment. The detailed visualization of the mitral valve commissures in RhMS with

3DTEE constitutes a major advantage over 2D echocardiographic methods. 3DTEE provided detailed morphological evaluation and accurate assessment of commissural fusion in all patients. In contrast, commissural assessment was possible in only 60% using 2DTTE. In accordance with previous studies, the degree of commissural fusion was underestimated with 2DTTE in 19% of patients compared with 3DTEE (9).

The mitral valve commissures traverse several different 2D planes and thus are ideally suited to be visualized by 3DTEE. This can be readily appreciated by viewing the commissures from the atrial, ventricular, and lateral perspective (Figs. 6A to 6F).

Commissural calcification is an important predictor of outcome after PTMV (23). Commissural calcification is not always easily visualized by 3DTEE, as current 3D images represent a 3D surface rendition of the mitral valve. In surgical

Table 3. Commissural Fusion Using 2DTTE

2D	Posteromedial Commissure		
	Minimal	Partial	Complete
Anterolateral Commissure			
Minimal	2	5	1
Partial	5	11	1
Complete	6	0	1

Data are expressed as number of patients.
2DTEE = 2-dimensional transesophageal echocardiography.

Table 4. Commissural Fusion Using 3DTEE

3D	Posteromedial Commissure		
	Minimal	Partial	Complete
Anterolateral Commissure			
Minimal	2	3	0
Partial	4	18	4
Complete	4	2	6

Data are expressed as number of patients.
3DTEE = 3-dimensional transesophageal echocardiography.

specimens, mitral valve calcification is often found to be endothelialized rather than located on the surface of the commissures. 3D is good at demonstrating protruding bulk, while 2D imaging, which is cross-sectional, permits better characterization of the calcification. This highlights how 2D and 3D methods are complementary.

Assessment of commissural morphology has been shown to provide additional predictive value above other components of mitral valve anatomy in patients considered for PTMV (23–27). Preliminary studies have indicated that morphological assessment of the rheumatic mitral valve before PTMV using 3D echocardiography may be more accurate and reliable than 2D methods (6,15). Splitting of the commissures is the principal mechanism that leads to increased MVA and hemodynamic improvement after PTMV. PTMV is therefore unlikely to increase MVA if commissural fusion is minimal or if the commissures are rigid because of presence of calcium (28). The improved visualization of the commissures with 3D echocardiography may thus be superior to conventional 2D techniques in predicting outcomes after PTMV.

Limitations of 3DTEE. The 3D zoom mode used to image the mitral valve results in relatively low frame rates (usually <20 Hz), and as a result, image motion is not smooth, and fine structures such as chordae tendineae are not as well visualized (21,29). Patients with very heavily calcified valves tend to have a greater incidence of tissue dropout, and the lack of adequate border definition can adversely affect the accuracy of planimetry measurements. However, this can be overcome by appropriate gain and threshold settings before 3D image acquisition (29).

Current 3D analysis software allows planimetry of the mitral valve orifice only in a single carefully selected plane. In some patients, the mitral orifice may be curvilinear and is not optimally represented by a single plane.

Clinical implications. Its semi-invasive nature makes 3DTEE less practical for the widespread assessment of patients with RhMS. However, in patients with severe RhMS considered for PTMV, transesophageal echocardiography is a prerequisite to exclude the presence of atrial thrombi. In these patients, 3DTEE can provide useful supplementary information regarding mitral valve anatomy and suitability for PTMV compared with 2D transesophageal echocardiography.

Study limitations. The lack of a gold standard as a reference standard did not allow any final conclu-

Table 5. MVA_{3D} (cm²) and Degree of Commissural Fusion by 3DTEE

MVA (cm ²)	Posteromedial Commissure			
	Anterolateral Commissure	Minimal	Partial	Complete
Minimal		1.74 ± 0.11	1.05 ± 0.29	—
Partial		1.58 ± 0.3	1.04 ± 0.4	1.06 ± 0.37
Complete		0.89 ± 0.14	0.97 ± 0.15	0.48 ± 0.18

Data are expressed as mean ± SD.
 MVA_{3D} = planimetry of mitral valve area using real-time 3-dimensional transesophageal echocardiography.

sions about the relative accuracy of 3DTEE compared with established methods for the assessment of MVA. The choice of an absolute gold standard for MVA assessment in RhMS is controversial (30). MVA measured using Gorlin formula is invasive and has several technical limitations and therefore was not included in this study.

It would have been preferable to compare the relative benefits of 3DTEE over 3DTTE. However, the primary aim of this study was to assess the feasibility of MVA and commissural assessment in RhMS using 3DTEE.

CONCLUSIONS

3DTEE allows excellent visualization of the MV orifice and leaflets in RhMS and provides important complementary information to 2D TEE. Assessment of MVA and commissural morphology is feasible in most patients with RhMS using 3DTEE. 3DTEE estimation of MVA offers excellent reproducibility and compares favorably with established 2DE methods. 3DTEE provided detailed assessment of the degree of commissural fusion in all patients. Future studies are needed to clarify if assessment of the mitral valve using 3DTEE translates into improved patient selection and outcome after PTMV.

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Key Words: mitral stenosis ■ mitral valve ■ rheumatic heart disease ■ 3DTEE ■ 3DTTE.

APPENDIX

For supplementary videos and their legends, please see the online version of this article.