Quantitative Assessment of Mitral Regurgitation
Comparison Between Three-Dimensional Transesophageal Echocardiography and Magnetic Resonance Imaging

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Background—Quantification of mitral regurgitation severity with 2-dimensional (2D) imaging techniques remains challenging. The present study compared the accuracy of 2D transesophageal echocardiography (TEE) and 3-dimensional (3D) TEE for quantification of mitral regurgitation, using MRI as the reference method.

Methods and Results—Two-dimensional and 3D TEE and cardiac MRI were performed in 30 patients with mitral regurgitation. Mitral effective regurgitant orifice area (EROA) and regurgitant volume (Rvol) were estimated with 2D and 3D TEE. With 3D TEE, EROA was calculated using planimetry of the color Doppler flow from en face views and Rvol was derived by multiplying the EROA by the velocity time integral of the regurgitant jet. Finally, using MRI, mitral Rvol was quantified by subtracting the aortic flow volume from left ventricular stroke volume. Compared with 3D TEE, 2D TEE underestimated the EROA by a mean of 0.13 cm². In addition, 2D TEE underestimated the Rvol by 21.6% when compared with 3D TEE and by 21.3% when compared with MRI. In contrast, 3D TEE underestimated the Rvol by only 1.2% when compared with MRI. Finally, one third of the patients in grade 1 and ≥50% of the patients in grade 2 and 3, as assessed with 2D TEE, would have been upgraded to a more severe grade, based on the 3D TEE and MRI measurements.

Conclusions—Quantification of mitral EROA and Rvol with 3D TEE is feasible and accurate as compared with MRI and results in less underestimation of the Rvol as compared with 2D TEE. (Circ Cardiovasc Imaging. 2010;3:694-700.)

Key Words: mitral regurgitation ■ real-time 3-dimensional transesophageal echocardiography ■ MRI

The clinical relevance of quantitative assessment of mitral regurgitation has been demonstrated in several studies.¹ ² In patients with isolated, asymptomatic organic mitral regurgitation, the effective regurgitant orifice area (EROA) as assessed with echocardiographic Doppler techniques is one of the strongest determinants of long-term outcome.¹ In addition, EROA and regurgitant volume (Rvol) are independent predictors of excess mortality in asymptomatic and symptomatic patients with functional mitral regurgitation.³ In light of this evidence, current recommendations of the American Society of Echocardiography underscore the use of quantitative methods to grade mitral regurgitation, including the Rvol as a marker of volume overload and the EROA as a descriptor of lesion severity.³

Clinical Perspective on p 700
Quantitative evaluation of mitral regurgitation remains challenging. Two-dimensional (2D) color flow and Doppler echocardiography with the use of the proximal isovelocity surface area (PISA) method is the standard approach to estimate the EROA and Rvol. However, the presence of ellipsoid regurgitant orifices or the presence of eccentric regurgitant jets limits the accuracy of 2D echocardiographic PISA method to quantify mitral regurgitation.⁴ Recent advances in 3-dimensional (3D) echocardiography have allowed direct visualization and measurement of even highly asymmetrical EROA. Validation studies have demonstrated good correlation between EROA-3D echocardiography (EROA-3D) measurements and angiographic⁵ ⁶ and MRI measurements.⁷ ⁸ In addition, several recent studies using transthoracic echocardiography (TTE) have demonstrated less underestimation of EROA-3D compared with 2D vena contracta width (VCW-2D) and 2D PISA-derived measurements, suggesting improved accuracy in the estimation of mitral regurgitation severity.⁹ ⁴

The advent of a 3D fully sampled matrix array transesophageal echocardiography (TEE) probe allowing real-time acquisition of 3D images has constituted a step forward in the evaluation of patients with mitral regurgitation. The superb...
image quality obtained with real-time 3D TEE has led to an increasing implementation of this technique in the daily clinical practice to evaluate mitral valve anatomy and to localize the coaptation leaflet failure. More important, the improved visualization of the vena contracta with 3D TEE may result in more accurate quantitative evaluation of mitral regurgitation and, consequently, in an improved risk stratification of patients with mitral regurgitation. The present study aimed to compare the accuracy of 2D TEE and 3D TEE for quantification of the severity of mitral regurgitation, using MRI as method of reference.

Methods

Study Population and Protocols

The study population consisted of 30 patients who were clinically referred for a TEE and cardiac MRI for assessment of mitral regurgitation. Patients with irregular heart rhythm (including atrial fibrillation), a history of mitral valve replacement, significant aortic or tricuspid valve regurgitation, or absolute contraindications to TEE or MRI were excluded. The standard MRI protocol was applied to assess left ventricular (LV) size, LV function, and aortic flow. The MRI study was performed on the same day as TEE. The standard volumetric and flow measurements were subsequently used for quantification of mitral regurgitation. The severity of mitral regurgitation on TEE was quantified from 2D and 3D color Doppler data sets and compared, using MRI as a reference. Functional mitral regurgitation was defined on TEE as leaflet tethering and incomplete leaflet coaptation in the presence of normal mitral valve anatomy and regional or global LV remodeling, whereas organic mitral regurgitation was a result of intrinsic valve lesions.

Two-Dimensional and 3D TEE Data Acquisition and Analysis

Transesophageal echocardiography was performed using the iE33 ultrasound imaging system (Philips Medical Systems, Andover, Mass) equipped with the fully sampled matrix-array TEE transducer (X7-2t) capable of displaying both 2D and live 3D images. Complete 2D, color, pulsed, and continuous wave Doppler images were obtained for assessment of cardiac structures and function. Mitral regurgitation severity was determined quantitatively from the 4-chamber views obtained at mid esophageal level with 0° tilt.

Figure 1. Three-dimensional echocardiography for assessment of EROA. A, The 3D color Doppler data set is manually cropped using the plane perpendicular to the jet direction until the narrowest cross-sectional area of the jet is reached. B, In an en face view, the EROA-3D is measured by manual planimetry of the color Doppler signal. An example of an asymmetrical EROA-3D elongated along the leaflet coaptation line is provided, for which the hemispherical convergence method using geometric assumptions may not be applicable.

Figure 1. Three-dimensional echocardiography for assessment of EROA. A, The 3D color Doppler data set is manually cropped using the plane perpendicular to the jet direction until the narrowest cross-sectional area of the jet is reached. B, In an en face view, the EROA-3D is measured by manual planimetry of the color Doppler signal. An example of an asymmetrical EROA-3D elongated along the leaflet coaptation line is provided, for which the hemispherical convergence method using geometric assumptions may not be applicable.

MRI Data Acquisition and Analysis

Data acquisition was performed on a 1.5-T Gyroscan ACS-NT/Intera MRI scanner (Philips Medical Systems, Eindhoven, The Nether-
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epicardial and endocardial borders. LV stroke volume was on the short-axis series using MASS analytic software (Medis, 2016). To determine mitral valve Rvol by MRI (Rvol-MRI), aortic flow volume was subtracted from LV stroke volume. LV stroke volume was subtracted from LV stroke volume. LV stroke volume was obtained by subtracting LV end-systolic volume from LV end-diastolic volume. In addition, aortic flow was obtained using phase-contrast velocity maps. Multislice spin-echo images oriented in the coronal plane were obtained to identify the orientation and course of the aortic arch. At a position 2 to 5 cm above the aortic valve, where the aorta was nearly parallel to the caudal cranial axis of the patient, a velocity map was acquired in the axial orientation using velocity-encoded cine MRI as described previously. Retrospective gating was applied to acquire images evenly spaced over a complete cardiac cycle, resulting in 20 cardiac phases. By semiautomatic drawing of regions of interest over the appropriate flow areas, phase-contrast velocity maps were acquired, integrated over time, and subtracted using FLOW analytic software (Medis). To determine mitral valve Rvol by MRI (Rvol-MRI), aortic flow volume was subtracted from LV stroke volume.

Statistical Analysis
Continuous data are presented as mean±SD. Categorical data are presented as absolute numbers or percentages. The Student t test and Mann–Whitney U test were used to compare 2 groups of unpaired data of gaussian and nongaussian distribution, respectively. Linear regression analysis (Pearson correlation) for continuous variables was performed to evaluate the relation between VCW-2D and 2D PISA-derived measurements. The Kendall τ-b test for categorical variables was used to evaluate the relation between the etiology of mitral regurgitation and direction of mitral regurgitation jet. Bland-Altman plots were used to evaluate differences in Rvol and EROA assessments by 2D TEE, 3D TEE, and MRI. The mean differences and limits of agreement are reported. The percentage of underestimation or overestimation by 2D and 3D TEE versus MRI was calculated as the mean of the percentage difference observed in each of the studied patients. The interobserver and intraobserver reproducibility of the EROA-3D measurements were evaluated in the 30 study patients. To test the intraobserver reproducibility, 1 experienced observer repeated the measurements at 2 different time points. To evaluate the interobserver reproducibility, a second experienced observer blinded to the measurements of the observer 1 performed the measurements at a different time point. The intraclass correlation coefficients were calculated and the mean bias, and 95% limits of agreement were calculated with Bland-Altman analysis. Good correlation was defined as intraclass correlation coefficient >0.8. All statistical analyses were performed using SPSS for Windows (SPSS Inc, Chicago, Ill), version 16. A probability value <0.05 was considered to be statistically significant.

Results
The study population consisted of 20 men and 10 women (mean age, 63.3±11.6 years). Table 1 describes the clinical characteristics of the patients. Functional mitral regurgitation was present in 16 (53.3%) patients and organic mitral regurgitation in 14 (46.7%) patients, with mitral valve prolapse in 12 (30.0%) patients, infective endocarditis in 1 (3.3%) patient, and chordal rupture in 1 (3.3%) patient. Mitral regurgitation was directed anteriorly in 11 (36.7%) patients and posteriorly in 2 (6.7%) patients. Central or eccentric mitral regurgitant jets were observed in 17 (57%) and 13 (43%) patients, respectively. Mean LV end-diastolic volume and end-systolic volume as measured with MRI were 257.9±88.1 mL and 117.1±64.6 mL, respectively. Mean LV ejection fraction was 56.1±15.0%.

Vena Contracta, Mitral Valve Effective Regurgitant Orifice Area, and Regurgitant Volume
The mean VCW-2D of the mitral regurgitant jet was 5.71±2.58 mm. There was a significant although modest correlation between VCW-2D and EROA-2D (r=0.624; P<0.001) and Rvol-2D (r=0.655; P<0.001). The mean EROA-2D was 0.35±0.34 cm² and EROA-3D was 0.47±0.37 cm². Two-
dimensional TEE underestimated the EROA by a mean of 0.13 cm² (95% limits of agreement, 0.55 cm²; 0.29 cm²) without significant trend. The mean Rvol-2D was 53.2 ± 35.3 mL/beat, Rvol-3D was 63.2 ± 41.3 mL/beat, and Rvol-MRI was 65.1 ± 42.7 mL/beat. The mean differences in the Rvol between 2D TEE, 3D TEE, and MRI are described in Figure 3. Two-dimensional TEE underestimated the Rvol by 21.6% when compared with 3D TEE and by 21.3% when compared with MRI. In addition, 3D TEE underestimated the Rvol by 1.2% when compared with MRI.

The intraobserver reproducibility and interobserver reproducibility for the EROA-3D measurements were evaluated in the 30 study patients using Bland-Altman and intraclass correlation coefficient analyses. There was a good intraobserver reproducibility (mean difference, 0.011 ± 0.16 cm²; intraclass correlation coefficient, 0.98) as well as interobserver reproducibility (mean difference, −0.013 ± 0.14 cm²; intraclass correlation coefficient, 0.98).

**Mitral Valve Regurgitation Severity Grade**

Based on Rvol-2D, 6 (20%) patients had grade 1, 7 (23%) patients had grade 2, 6 (20%) patients had grade 3, and 11 (37%) patients had grade 4 mitral regurgitation. Based on VCW-2D, 3 (10%) patients had grade 1, 20 (63%) patients had grade 2 or 3, and 8 (27%) patients had grade 4 mitral regurgitation. Compared with Rvol-2D, VCW-2D underestimated the severity of mitral regurgitation by 1 grade in 5 (17%) patients. On the other hand, 4 (14%) patients were classified as having more severe mitral regurgitation by 1 grade using VCW-2D, compared with Rvol-2D. Compared with 3D TEE and MRI, mitral regurgitation severity using Rvol-2D was underestimated in 9 (30%) patients and overestimated in 1 (3.4%) patient. More specifically, 2 (33%) patients in grade 1, 4 (57%) patients in grade 2, and 3 (50%) patients in grade 3 by Rvol-2D would be upgraded to a higher mitral regurgitation grade by quantifying mitral Rvol with 3D TEE and MRI. Figure 4 shows the number of the patients classified into the same versus different mitral regurgitation severity grades after applying the currently used Rvol-2D mitral regurgitation grading criteria to all 3 imaging techniques. Similar results were seen with VCW-2D, where 9 (30%) patients graded as having moderate (grade 2 to 3) mitral regurgitation would be upgraded to severe (grade 4) regurgitation with 3D TEE, whereas the same upgrade would apply to 8 (27%) patients if MRI was used. On the other hand, 2 (7%) patients had their severity of mitral regurgitation underestimated by at least 1 grade by VCW-2D, when compared with 3D TEE and MRI.

**Etiology and Direction of Mitral Regurgitation**

There was a significant although only modest correlation between the etiology and direction of the mitral regurgitation jet (r=0.605, P<0.001). Two (13%) patients with functional mitral regurgitation had eccentric regurgitant jets, whereas 4 (29%) patients with organic mitral regurgitation had central regurgitant jets. Compared with both 3D TEE and MRI, there

<table>
<thead>
<tr>
<th>Table 1. Clinical Characteristics of the Patients</th>
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<tr>
<td>Variable</td>
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<tr>
<td>Age, y</td>
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<tr>
<td>Male/female, %</td>
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<td>New York Heart Association class, %</td>
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<td>I</td>
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<td>II</td>
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<td>III</td>
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<td>Medical history, %</td>
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<tr>
<td>Coronary artery disease</td>
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<td>Hypertension</td>
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<td>Diabetes mellitus</td>
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<td>Hyperlipidemia</td>
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<td>Medications, %</td>
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<tr>
<td>β-blockers</td>
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<tr>
<td>ACEI/ARB-II</td>
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<td>Calcium channel blockers</td>
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<td>Diuretics</td>
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<td>Spironolactone</td>
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<td>Anticoagulation</td>
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ACEI indicates angiotensin-converting enzyme inhibitor; ARB-II, angiotensin receptor blocker-II.
Accurate quantitative assessment of mitral regurgitation has been shown to be crucial in risk stratification and clinical practice. Versus 3D TEE

Quantification of Mitral Regurgitation Using 2D and 3D TEE

The main findings of the study include (1) 2D TEE underestimates the mitral valve EROA and Rvol compared with 3D TEE and MRI; (2) compared with 3D TEE and MRI, 2D TEE underestimated the Rvol significantly more in the eccentric than in the central mitral regurgitation; and (3) using the current grading system for the severity of mitral regurgitation based on Rvol-2D, one third of the patients in grade 1 and over half of the patients in grade 2 and 3 would have been upgraded into a more severe grade based on the 3D TEE and MRI measurements.

Table 2. Etiology and Direction of Mitral Regurgitation: Comparison Between 2D TEE, 3D TEE, and MRI

<table>
<thead>
<tr>
<th></th>
<th>Mean Difference in Rvol, mL/beat</th>
<th>Central Jet (n=17)</th>
<th>Eccentric Jet (n=13)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D TEE vs 3D TEE</td>
<td>−12.45±9.0</td>
<td>−4.3±6.9</td>
<td>−17.5±25.9</td>
<td>0.020</td>
</tr>
<tr>
<td>2D TEE vs MRI</td>
<td>−8.0±6.56</td>
<td>−5.8±10.1</td>
<td>−20.9±20.5</td>
<td>0.040</td>
</tr>
<tr>
<td>3D TEE vs MRI</td>
<td>−4.5±8.1</td>
<td>−1.5±5.3</td>
<td>−3.4±11.3</td>
<td>0.950</td>
</tr>
</tbody>
</table>

Discussion

The main findings of the study include (1) 2D TEE underestimates the mitral valve EROA and Rvol compared with 3D TEE and MRI; (2) compared with 3D TEE and MRI, 2D TEE underestimated the Rvol significantly more in the eccentric than in the central mitral regurgitation; and (3) using the current grading system for the severity of mitral regurgitation based on Rvol-2D, one third of the patients in grade 1 and over half of the patients in grade 2 and 3 would have been upgraded into a more severe grade based on the 3D TEE and MRI measurements.

Quantification of Mitral Regurgitation Using 2D Versus 3D TEE

Accurate quantitative assessment of mitral regurgitation has been shown to be crucial in risk stratification and clinical treatment of patients with mitral regurgitation.1,2 Currently, the PISA method with 2D echocardiography is one of the most commonly used quantitative methods to grade mitral regurgitation severity, providing information on lesion severity (EROA) and volume overload (Rvol).3 However, the accuracy of the PISA method to quantify EROA and Rvol may be limited by the presence of hemi-elliptical shape of the flow convergence region or by the presence of eccentric regurgitant jets.18 Differences of EROA asymmetry among different etiologies of mitral regurgitation have been demonstrated, with a noncircular shape observed in the majority of the patients.4,9,19 In particular, the patients with functional mitral regurgitation often show typical elongation of EROA along the semilunar-shaped line of incomplete mitral leaflet closure caused by leaflet tethering.4 On the other hand, a broad spectrum of irregularly shaped EROA is often found in patients with organic mitral valve disease.6,7,20 Considering the ability of 3D color Doppler echocardiography to directly image the EROA without the assumption of rotational symmetry, this technique may be more accurate than 2D echocardiography for quantification of mitral regurgitation. Several in vitro and in vivo studies have compared the accuracy of 2D and 3D color Doppler techniques to quantify mitral regurgitant volume against reference methods (flowmeter standard and MRI).6,21–23 Three-dimensional color Doppler echocardiography resulted in less regurgitant volume underestimation for all orifice shapes tested compared with the 2D flow-convergence method.6,21–23 Similar results were obtained in clinical studies in which the assumption of a hemispherical shape of the regurgitant orifice by 2D echocardiography significantly underestimated the flow rate by 35% to 44%,9,22,24,25 Accordingly, the use of formulas that assume a hemi-elliptical shape of the flow convergence region even in circular orifices have been proposed to improve the accuracy of the PISA method in mitral regurgitation quantification,9 although this may further increase the complexity of the measurements. In addition, the PISA method is less reliable in eccentric than central regurgitation, as demonstrated in the present study.3,6 Similarly to PISA measurements, disagreement in the assessment of the severity of mitral regurgitation was also observed between VCW-2D and 3D TEE and MRI. Moreover, disagreement was observed between the 2D TEE techniques themselves (VCW-2D and Rvol-2D). This could be related to some of the limitations of VCW-2D technique, including the small values of the width of the vena contracta, with small errors potentially leading to a large percent error and misclassification of the severity of regurgitation.3 A relatively large number (43%) of our patient population had eccentric mitral regurgitation, which further limited the assessment of its severity because of a potential for underestimation of the mitral regurgitation jet area on color Doppler or because of incomplete continuous wave Doppler signal potentially affecting the density of the mitral regurgitant jet. Some of these limitations may be resolved by direct en face visualization of the vena contracta area. In this regard, real-time
3D echocardiography has provided meaningful insights into the quantitative assessment of mitral regurgitation.\textsuperscript{4,6,26} Real-time 3D echocardiography permits direct visualization of the vena contracta. With the use of multiplanar reformattting planes, the exact cross-sectional view of the regurgitant orifice can be obtained. Several studies have demonstrated the superior accuracy of real-time 3D echocardiography over 2D echocardiography to assess the EROA.\textsuperscript{4,26,27} For example, in 57 patients with significant mitral regurgitation of different etiologies, Kahlert et al\textsuperscript{4} demonstrated good correlation between the direct measurement of the vena contracta with real-time 3D TTE and the measurement of EROA by hemi-elliptic PISA method. In contrast, in noncircular regions, the hemispheric PISA method resulted in significant underestimation of the EROA.\textsuperscript{4} Similarly, in a recent series including 64 patients with functional mitral regurgitation, 2D echocardiography significantly underestimated the EROA as compared with real-time 3D TTE, with a mean difference ranging between 0.06 to 0.10 cm\textsuperscript{2} (P<0.001).\textsuperscript{26} The present study confirms and extends previous findings by demonstrating the superior accuracy of real-time 3D TEE over 2D TEE in the quantitative evaluation of mitral regurgitation. The 2D TEE PISA method significantly underestimated the EROA as compared with real-time 3D TEE. This resulted in up to half of the patients being classified into the lower mitral regurgitation severity grade by 2D TEE. In addition, compared with 3D TEE, the underestimation of EROA and Rvol by 2D TEE was more pronounced in the eccentric jets than in the central regurgitant jets.\textsuperscript{26} On the other hand, no differences were observed in underestimation of the mitral regurgitation severity in different etiologies of mitral regurgitation. This could be related to the fact that there was only a modest correlation between the etiology and direction of mitral regurgitation in our study. This finding further highlights the usefulness of 3D imaging to directly visualize the EROA in any given mitral regurgitant jet by allowing free orientation of the imaging planes.

Quantification of Mitral Regurgitation Using 3D TEE Versus MRI

The majority of the studies comparing different methods to quantify mitral regurgitation have relied on echocardiographic techniques, and only few have evaluated the accuracy of 3D echocardiography to estimate mitral Rvol using MRI as the reference method.\textsuperscript{8,22,26} MRI measures directly flow through an area of interest, whereas conventional 2D PISA method resulted in significant underestimation of the EROA.\textsuperscript{4} For example, in 57 patients with significant mitral regurgitation by live three-dimensional transthoracic echocardiography, prospective studies to determine the importance of 3D data for the clinical outcome may be needed.

Study Limitations

In the present study, quantification of mitral regurgitation based on 2D TEE data was performed only with the PISA method. The inclusion of other methods such as volumetric quantification could help define the accuracy of this methodology to quantify mitral regurgitation severity using MRI as the reference method.

Conclusion

The present study demonstrated that 3D TEE is feasible and is more accurate in the quantitative assessment of both functional and organic mitral regurgitation when compared with 2D TEE. Given the potential strengths of 3D echocardiography, prospective studies to determine the importance of the 3D data for the clinical outcome may be needed.

Disclosures

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References

Quantification of the severity of mitral valve regurgitation by measuring regurgitant volume (Rvol) and effective regurgitant orifice area (EROA) is recommended in current clinical practice. The accuracy of 2-dimensional (2D) echocardiographic methods to quantify these parameters is significantly lower than 3-dimensional (3D) echocardiography or MRI. Eccentric regurgitant jets or ellipsoid regurgitant orifices are important determinants of the accuracy of 2D imaging techniques. The advent of a 3D fully sampled matrix array transesophageal echocardiography (TEE) probe allows real-time acquisition of 3D images and direct visualization and measurement of highly asymmetric EROA. The present study compared the accuracy of 2D TEE and 3D TEE for quantification of the severity of mitral regurgitation using MRI as method of reference. Compared with 3D TEE, 2D TEE underestimated the EROA by a mean of 0.13 cm². In addition, 2D TEE underestimated the Rvol by 21.6% when compared with 3D TEE and by 21.3% when compared with MRI. In contrast, 3D TEE underestimated the Rvol by only 1.2% when compared with MRI. Finally, one third of the patients in grade 1 and ≥50% of the patients in grade 2 and 3, as assessed with 2D TEE, would have been upgraded to a more severe grade, based on the 3D TEE and MRI measurements. Faced with the prognostic implications of mitral valve regurgitation, implementation of 3D TEE in the routine clinical practice may provide more accurate quantification of the severity of the regurgitant lesion and improve the clinical decision-making of these patients.
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