A three-dimensional insight into the complexity of flow convergence in mitral regurgitation: adjunctive benefit of anatomic regurgitant orifice area

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Chandra S, Salgo IS, Sugeng L, Weinert L, Settlemier SH, Mor-Avi V, Lang RM. A three-dimensional insight into the complexity of flow convergence in mitral regurgitation: adjunctive benefit of anatomic regurgitant orifice area. Am J Physiol Heart Circ Physiol 301: H1015-H1024, 2011. First published June 17, 2011; doi:10.1152/ajpheart.00275.2011.—Mitral effective regurgitant orifice area (EROA) using the flow convergence (FC) method is used to quantify the severity of mitral regurgitation (MR). However, it is challenging and prone to interobserver variability in complex valvular pathology. We hypothesized that real-time three-dimensional (3D) transesophageal echocardiography (RT3D TEE) derived anatomic regurgitant orifice area (AROA) can be a reasonable adjunct, irrespective of valvular geometry. Our goals were to 1) determine the regurgitant orifice morphology and distance suitable for FC measurement using 3D computational flow dynamics and finite element analysis (FEA), and (2) to measure AROA from RT3D TEE and compare it with 2D FC derived EROA measurements. We studied 61 patients. EROA was calculated from 2D TEE images using the 2D-FC technique, and AROA was obtained from zoomed RT3DE TEE acquisitions using prototype software. 3D computational fluid dynamics by FEA were applied to 3D TEE images to determine the effects of mitral valve (MV) orifice geometry on FC pattern. 3D FEA analysis revealed that a central regurgitant orifice is suitable for FC measurements at an optimal distance from the orifice but complex MV orifice resulting in eccentric jets yielded nonaxisymmetric isovelocity contours close to the orifice where the assumptions underlying FC are problematic. EROA and AROA measurements correlated well (r = 0.81) with a nonsignificant bias. However, in patients with eccentric MR, the bias was larger than in central MR. Intermeasurement variability was higher for the 2D FC technique than for RT3DE-based measurements. With its superior reproducibility, 3D analysis of the AROA is a useful alternative to quantify MR when 2D FC measurements are challenging.

three-dimensional echocardiography; Doppler echocardiography; mitral valve; proximal isovelocity surface area

TWO- AND THREE-DIMENSIONAL (2D and 3D) echocardiography combined with Doppler interrogation plays a crucial role in the identification of the mechanisms, in the accurate quantification of the severity of mitral regurgitation (MR), and in the assessment of the suitability for repair. The severity of MR has been used to determine the progression of disease (9), identify patients at the highest mortality risk without surgical intervention, (8, 13, 14, 16, 20, 33), and guide the timing of surgery (4, 23, 32, 35). Effective regurgitant orifice area (EROA) based on 2D methods of flow convergence (FC) estimation is currently one of the standards used to assess the severity of MR.

Unlike 2D planimetry of mitral and aortic stenotic valves, planimetry of the regurgitant orifice area in patients with MR is not feasible because of the complex, nonplanar 3D geometry of the orifice. Consequently, indirect measurements are used to determine the EROA using Doppler measurements of the proximal FC (2, 10, 11, 25). The proximal FC method has been studied in computer simulation, empirically in the controlled environment of in vitro flow models, and is well validated in clinical studies. FC is based on the fluid dynamics theory postulating that flow converges to a finite orifice as a series of isovelocity shells with decreasing surface area and increasing velocities, wherein the flow rate at each isovelocity surface equals that at the regurgitant orifice (the principle of mass and momentum conservation). Volumetric flow rate itself can be calculated by multiplying the surface area of the concentric shell by the aliasing velocity (and hence the isovelocity value) for the hemispheric shell of radius r. However, this approach is predicated on the hypothetical hemispherical shape, which in reality may not be strictly hemispherical, thereby, causing underestimation or overestimation of the flow rate (24).

Schwammenthal et al. (30) demonstrated in 2D the prolate and oblate ellipsoidal shape of the isovelocity shells distal and proximal to the orifice, respectively, challenging the arbitrary assumption that shells are always hemispherical. They also demonstrated that an optimal isovelocity zone computed mathematically can significantly improve the accuracy of the FC method. Those isovelocity shells in general are less hemispherical and more ellipsoidal in shape irrespective of valvular geometry but retain axisymmetry in the optimal isovelocity zone. Therefore, FC or proximal isovelocity surface area (PISA) is most applicable in the optimal isovelocity zone, where axisymmetry is preserved (i.e., when a symmetry line can be defined in the central axis). A formula for the appropriate hemi-ellipsoidal surface area should be used instead of hemispherical surface area. Unfortunately, this concept crucial to FC calculation is difficult to apply reliably in certain settings, especially complex noncircular orifices (1). In more complex flow convergence phenomena, there is loss of axisymmetry, thereby, challenging the standard operating assumptions. Ultimately, it is important to distinguish those jets where PISA can be performed reliably and those where calculations should be supplemented.

We, therefore, hypothesized that 1) the use of 3D echocardiography combined with 3D computational flow dynamics and finite element analysis (FEA) would further elucidate the challenges in PISA measurement by demonstrating when an asymmetric PISA zone is present, and 2) matrix transesophageal echocardiography (mTTE) could be used to quantify the anatomic regurgitant orifice area (AROA) in 3D space providing an adjunctive means to assess severity of MR, especially in...
patients with noncircular, nonplanar orifices where FC is not likely to be reliable. Our aims were to 1) to demonstrate by FEA the geometric limitations of hydraulic calculations of the EROA, 2) to quantify AROA in patients with varying degrees of severity of MR, 3) to compare AROA values to 2D FC measurements of EROA, and 4) to compare the reproducibility of these two techniques.

MATERIALS AND METHODS

Patients. Seventy-seven consecutive patients with mild to severe MR undergoing clinically indicated TEE between 2008 and 2010 were studied using iE33 imaging system (Philips Healthcare, Andover, MA) with the matrix array transducer (X7–2t). Exclusion criteria were as follows: poor quality 3D images, precluding analysis (n = 6), presence of prostatic valves and/or post-MV repair (n = 6), and poorly visualized FC (n = 4). The remaining 61 patients comprised the main study group (age 59 ± 10 years, 36 males) in which 38 patients had eccentric MR jets from flail or prolapsing leaflets as a result of degenerative or ischemic MV disease and 23 had central MR jets from functional MR (Table 1). Additionally, to test the ability of the new quantitative method to define the integrity of the coaptation zone, we studied 20 patients with no MR on color flow Doppler during their TEE. The study received approval from the Institutional Review Board, and every patient signed an informed consent before enrollment.

Imaging. The clinical portion of the 2D TEE exam was performed according to standard protocol. For FC imaging, a narrow color flow sector and minimal depth were used to maximize image resolution; images were obtained in a magnified four-chamber view. Proximal FC zone was optimized by shifting the baseline of color Doppler aliasing velocity, as previously described (37). The radial distance r between the aliasing contour (red/blue interface) and the valve plane was measured during midsystole. Systematically, additional multiple radial measurements were made by shifting the baseline of the color Doppler scale from a low to high velocity (at a Nyquist limit of 20 to 60 cm/s) on a random subset of patients (central jet: n = 10; eccentric jet: n = 9). The system was adjusted to provide maximal continuous wave Doppler alignment between the ultrasound beam and the axial direction of flow. After the clinically indicated study was completed, real-time three-dimensional echocardiographic (RT3DE) imaging of the MV was performed. Initially, gain settings were optimized to minimize visible dropouts in the MV, which was confirmed by uninterupted coaptation in patients without MR on 2D TEE. Similar gain settings and medium line density were subsequently used in all patients with MR, resulting in measurable orifices. Narrow-angled acquisition mode was used, allowing RT3DE imaging of a pyramidal volume of ~30° × 60° without the need for ECG gating. Multiple zoomed RT3DE images of the MV were then acquired during a single cardiac cycle resulting in mean frame rates of 9 ± 3 Hz, which were similar in both groups of patients with MR. Care was taken to include the entire MV apparatus in the scan volume. The acquisition of the 3D data set took ~3–5 min per study.

Image analysis. Images were reviewed and analyzed offline on an Xcelera workstation (Philips Healthcare). For any regurgrant orifice resulting in either central or eccentric jet, flow in the proximal FC zone was calculated by using previously described methodology (5, 24, 37). In the presence of multiple MR jets, PISA measurements were attempted on both jets, which was feasible usually in the largest visualized jet.

The 3D analysis of maximal AROA was performed using custom software (MVQ, QLAB; Philips Healthcare) by two investigators blinded to the results of the 2D TEE images and to each other’s measurements. To improve the visualization of MV leaflets, pyramidal data sets acquired in the zoom mode were cropped along designated x-y-z axes or using a manually positioned arbitrary cropping plane. The midsystolic frame was selected for analysis, and gain settings were optimized in the 50-dB range. Initially, a long-axis view of the mitral apparatus was used to determine anterior, posterior, anterolateral, and posteromedial annular coordinates. The annulus was manually initialized by defining annular points in multiple planes rotated around the axis perpendicular to the mitral annular plane (Fig. 1A). The annulus was then segmented to identify leaflet geometry and coaptation points by manually tracing the leaflets in multiple parallel long-axis planes spanning the annulus from commissure to commissure (Fig. 1B), resulting in a 3D coaptation zone (Fig. 1C). The leaflets were traced from their insertion point in the annulus to the leaflet tip. In patients with MR, this resulted in an area of leaflet mal-coaptation visualized as an interruption in the computer-generated coaptation zone (Fig. 2B), yielding a 3D regurgitant orifice, which was then automatically measured in 3D space. This interrupted coaptation zone as well as the reconstructed annulus was displayed as a color-coded 3D-rendered surface representing a topographical map of the mitral apparatus (Fig. 2C, bottom). This display provided a detailed view of the leaflets and the interruptions in the coaptation zone. Since the orifice boundary is not necessarily planar, AROA was defined as the minimal 3D surface area and was computed numerically by solving an approximation to the “stretched membrane” using a fourth-order partial differential biharmonic equation. In cases of multiple regurgrant orifices, AROA was calculated automatically as the sum of areas of individual orifices. Image analysis took up to 6 min per study after the initial learning curve (starting with 10 to 15 min per study).

Computational fluid dynamics simulation. We modeled flow convergence by solving the Navier-Stokes fluid mechanics equation in 3D space using the finite element analysis technique. A Newtonian fluid model of blood with a viscosity of 4 centiPoise was used (28). Using a commercial finite element analysis system (CFDesign; Blue Ridge Numerics, Charlottesville, VA) to mesh the geometry and solve the partial differential equations of fluid motion, we characterized the geometry of the flow convergence zones in 3D of the actual patients’ valves. This finite element analysis system has been used to model steady and unsteady flows, and its use have been verified on steady and transient flow conditions. It is a highly robust solver and was run

<table>
<thead>
<tr>
<th>Gender (male)</th>
<th>Eccentric MR (n = 38)</th>
<th>Central MR (n = 23)</th>
<th>No MR (n = 20)</th>
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<tr>
<td>Age, yr</td>
<td>54 ± 10</td>
<td>56 ± 7</td>
<td>58 ± 12</td>
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<tr>
<td>LV EDV, ml</td>
<td>161 ± 23</td>
<td>243 ± 42</td>
<td>150 ± 56</td>
</tr>
<tr>
<td>LV ESV, ml</td>
<td>69 ± 10</td>
<td>158 ± 23</td>
<td>61 ± 15</td>
</tr>
<tr>
<td>EF, %</td>
<td>56 ± 8</td>
<td>35 ± 5</td>
<td>59 ± 11</td>
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<tr>
<td>Etiology of MR, %</td>
<td></td>
<td></td>
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<tr>
<td>Flail</td>
<td>23</td>
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<td>N/A</td>
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<td>N/A</td>
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<td>N/A</td>
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<td>N/A</td>
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<td>Rheumatic</td>
<td>N/A</td>
<td>3</td>
<td>N/A</td>
</tr>
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</table>

Data are means ± SD; n = no. of patients. MR, mitral regurgitation; LV EDV and ESV, left ventricular end diastolic and systolic volume, respectively; EF, ejection fraction; N/A, not applicable.
on an 8 core workstation before its use on our patient’s data set to verify numerical stability.

Graphic verification. To determine whether the FC shells are truly axisymmetric, we developed a tool in MATLAB (The MathWorks, Natick, MA) to test the symmetry of the hemisphere: a histogram, demonstrating the distribution of the radii measured at different points on the shell (Fig. 3). It is a tool that tests the sphericity assumption, whereby the larger the standard distribution on the histogram, the greater the likelihood that the sphericity assumption does not apply.

Intertechnique comparisons. Volumetric AROA measurements were compared with the 2D FC values using linear regression and Bland-Altman analyses. These comparisons were performed for the entire group of 61 patients with MR and, separately, for the subgroups with central and eccentric MR jets.

Reproducibility analysis. For both techniques, reproducibility was assessed in 2 separate groups of 10 patients each with central and eccentric MR jets. Intraobserver variability was assessed using repeated measurements performed by the same observer a month later, while interobserver variability was evaluated by repeating the analysis by a second independent observer, blinded to the results of all prior measurements. Variability was defined as the absolute difference between repeated measurements expressed as a percentage of their mean.

RESULTS

Table 1 lists the clinical and demographic characteristics of the patients in the study group. In all 20 patients with normal MV and no MR, the prototype 3D volumetric analysis method allowed successful rendering of an uninterrupted coaptation zone (Fig. 1C).

A theoretical calculation of a 3D FC isovelocity contour in the computational fluid dynamic finite element model (Fig. 3) showed that the histograms of the distribution of the radii measured at different points on the isovelocity shells depict the degree of its symmetry. In a true 3D FC hemisphere model, there was complete or near complete uniformity of the radii, yielding a single sharp peak in the histogram with no dispersion. In contrast, when the radii measurements varied considerably on the same contour, yielding a wider distribution in the histogram, a more prolate or oblate shape of the shell was observed, leading to under- or overestimation of the surface area.

The computational flow dynamics and finite element analysis of actual patients’ data confirmed that a planar, central regurgitant orifice permits clinically useful FC measurements, provided that the radius is measured at an optimal distance from the orifice. We also found that in the setting of a noncircular regurgitant orifice (Fig. 4A), the analysis near the orifice depicted a multidirectional, distorted, and split flow pattern (Fig. 4B). The isovelocity contours proximal to the orifice were flattened and nonhemispherical (Fig. 4C), and its lack of axisymmetry was confirmed by wide distribution of the contour’s radii (Fig. 4E). In contrast, when analysis was performed on a more distant isovelocity contour, it showed less sphericity distortion (Fig. 4D), and the histogram of radii showed a single peak with minimal spread (Fig. 4F), as predicted by the theoretical calculation (Fig. 3). Furthermore, we found that a more complex orifice caused by overlapping leaflets results in isovelocity contours with no axisymmetry at any distance.

In the example of a patient with central MR shown in Fig. 2, the FC demonstrated a single central MR jet (Fig. 2A), sec-
ondary to annular dilatation, which was confirmed visually by the centrally located orifice in the 3D image and quantitatively by the volumetric analysis of AROA (Fig. 2C). In this patient, the hydraulic and mechanical measurements of the orifice area were similar (EROA = 0.32; AROA = 0.37 cm²).

Figure 5A shows a patient with severe bilateral prolapse with overlapping MV leaflets, resulting in an eccentric MR jet with distorted geometry of the FC. The measurements of the regurgitant orifice were discordant despite attempt at optimization of isovelocity contours (EROA = 0.33 cm² at aliasing velocity of 35 cm/s vs. EROA = 0.28 cm² at aliasing velocity of 44 cm/s vs. AROA = 0.43 cm²). Figure 5B shows an example of a patient with Barlow’s disease, in whom 2D color-Doppler shows two separate regurgitant jets (left), originating from two separate orifices clearly visualized in the 3D images (middle). The 3D volumetric measurement of AROA reflected the contribution of both orifices, which is not possible to obtain with 2D FC technique. In this case, the intertechnique ROA measurements were discordant as well (EROA = 0.19 cm²; AROA = 0.31 cm²).

In the group of 61 patients with MR, FC measurement of EROA ranged from 0.07 to 0.98 cm² (mean: 0.41 ± 0.20 cm²), whereas 3D volumetric measurements of AROA resulted in a range of 0.10 to 0.96 cm² (mean: 0.47 ± 0.21 cm²). AROA and EROA measurements correlated well (r = 0.80) with a small positive bias (0.06 cm²; Fig. 6, left). In the 38 patients with eccentric MR, FC measurements of EROA ranged from 0.10 to 0.90 cm² (mean: 0.47 ± 0.21 cm²), while in the 23 patients with central MR, they ranged from 0.07 to 0.56 cm² (mean: 0.31 ± 0.14 cm²). 3D measurements of AROA resulted in a range of 0.14 to 0.96 cm² (mean: 0.54 ± 0.21 cm²) in the patients with eccentric MR, and from 0.10 to 0.66 cm² (mean: 0.36 ± 0.16 cm²) in the patients with central MR. AROA and EROA measurements correlated better in patients with central vs. eccentric MR (r = 0.87 and r = 0.73, respectively). Biases were larger in the eccentric compared with the central MR group (0.07 and 0.05 cm², respectively), and the limits of agreement were twice as wide in patients with eccentric MR (Fig. 6, middle and right).

Table 2 summarizes the severity of MR as classified by different parameters (including EROA and AROA) using criteria defined in the current American Society of Echocardiography guidelines (37). As data in Table 2 show, there was wide variability in the definition of severity of MR using different conventional parameters. Of note, seven more patients were classified as having severe MR by using AROA compared with EROA (38 vs. 26% of the cohort): EROA underestimated severity in five eccentric and two central MR cases. Interestingly, in the 10 patients with the largest discrepancy between 2D and 3D measurements (r = 0.6) of their regurgitant orifice, all had eccentric MR jets; 7 had anterior leaflet prolapse, and 4 had multiple jets. In the latter four patients with multiple jets, mean EROA was 0.25 cm² (range: 0.19 to 0.37 cm²) and AROA 0.36 cm² (range: 0.27 to 0.43 cm²). Optimization of the velocity profile was performed in a subset of patients with central and eccentric MR jets. Measure-
ments obtained from FC contours distant from the orifice (>0.70 cm) correlated better with the AROA measurements compared with those performed closer to the regurgitant orifice ($r = 0.92$ vs. $r = 0.75$; $P < 0.05$). Additionally, radial measurements on elongated contours with higher longitudinal vs. transverse radial measurements (mean ratio: 1.73) yielded lower correlation ($r = 0.77$). In patients with eccentric MR jets, with severely overlapping leaflets and distorted orifice geometry apparent on 3D images, velocity contour optimization did not show a significant difference when EROA measurements were performed at varying radial distance ($r = 0.69$ proximal, $r = 0.73$ mid, and 0.77 distal).

Table 3 summarizes the results of the reproducibility analysis in the two subgroups of patients with central and eccentric MR jets. First, as expected, in both groups, for both techniques, the interobserver variability was higher than the intraobserver variability. Secondly, the reproducibility of the 2D FC measurements was lower (higher variability) than that of the volumetric AROA. In addition, the reproducibility was lower in the eccentric compared with central MR group, as reflected by higher variability in the former group.

**DISCUSSION**

PISA has been demonstrated to reliably measure severity of regurgitation, when axisymmetry of the isovelocity contours is preserved. However, in clinical practice, there is considerable uncertainty regarding when to utilize FC technique (3). Our study elucidated the 3D mechanisms behind the high variability in the classification of severity of MR, which has clinical implications when determining the timing of surgery. We showed that preservation of the axisymmetry of the FC zone is preferable to measure MR severity by FC more consistently. The 3D finite element analysis demonstrated that when the regurgitant orifice deviates from being a planar, circular source (to a complex, elongated slit for example), it becomes difficult to apply FC methodology, especially near the orifice (1). The 3D AROA method described in our study may be used as an adjunctive means of determining MR severity, when the conventional 2D PISA is not compliant with its symmetry assumptions. 3D measurement of AROA is feasible even in patients with complex MV pathology, including those with flail, overlapping leaflets and eccentric jets.

**Limitations of flow convergence.** From our 3D computational fluid dynamics model, we found that as the regurgitant orifice gets larger but remains circular, the convergence zones become oblate spheroidal (flattened) near the orifice and prolate ellipsoidal (elongated) far from the orifice consistent with the findings of Schwammenthal et al. (30). Therefore, the near-hemispherical shell must first be identified before measuring PISA radius, which at times is difficult to perform. It is known from 3D studies (17, 22) that the orifice is often not circular but frequently hemiellipsoidal or even irregularly shaped. It is known from previous studies (26, 36) that the application of the PISA method for estimation of severity of MR is feasible in an optimal isovelocity zone. Additionally, we know that there is greater intermeasurement variability with FC.
technique (3), exacerbated when PISA calculation involves contours close to a complex orifice (oblate spheroid), since the FC zone becomes less symmetric near the orifice. Such altered morphology of the orifice is likely to lead to either under- or overestimation of EROA (6, 12, 15, 21, 27), as evidenced by the greater discrepancy between the 3D and FC measurements in patients with eccentric MR jets. FC analysis described previously (30) demonstrated reduced accuracy of MR severity evaluation compared with catheterization, when applied clinically to patients with MV prolapse who likely had complex, nonplanar, noncircular regurgitant orifices and where the assumptions regarding jet orientation, planarity of the orifice and leaflets, and, therefore, the symmetry of hemispherical isovelocity profiles break down (7, 29–31, 34, 36). Therefore, it appears that determining the complexity of the mitral regurgitant orifice is paramount to ascertaining the applicability of the PISA method.

**Interpretation of results.** When the regurgitant orifice is not a point source, but rather flat and circular, the PISA isovelocity shells change their contour from flat to hemispherical to elongated, while remaining axially symmetric as the distance from the orifice increases. Our 3D computations corroborated that in the vicinity of the orifice, the true isovelocity contour flattens. A proximal isovelocity contour may not necessarily represent a true hemispherical hydraulic isovelocity surface but one in which the velocity at a fixed distance from the orifice progressively increases, as the Doppler angle $\theta$ decreases, with an inverse relation between the velocity and $\cos \theta$ (12). In such a case, the hemispherical assumption will underestimate the true isovelocity surface area, even if the flow convergence shape in the periphery of the orifice is hemispherical. This occurs because measurements are performed close to the orifice where the shape of the convergent flow has already started to flatten.

While the results of this study cannot definitively prove that AROA is the correct and true value, because there is no gold-standard reference technique to do so, our findings indicate that it is a better measure of severity of MR than other conventional methods. We found that AROA measurements correlated with the 2D FC values, but the correlation was higher in patients with central MR jets with no overlapping leaflets, likely due to the more circular nature of the orifice, which is in keeping with the findings of a recent study by Altiok et al. (1). This is especially true when isovelocity contours could be optimized resulting in axisymmetric FC.
zones consistently distal to the orifice. Also, the reproducibility of the AROA method was higher compared with 2D FC measurements. In patients with complex regurgitant orifice geometry with overlapping leaflets and eccentric MR jets, detection of a spherical isovelocity contour was more difficult by both 3D FEA and by 2D techniques.

Volumetric quantification of AROA resulted in a positive bias, with slightly larger orifice areas compared with EROA. This probably reflects the physical differences between the two methods. The potential advantage of the AROA technique is that it directly measures the true anatomic orifice in 3D, whereas the FC method is not only subject to orifice geometry and flow but also relies on the quantification of the narrowest flow emerging from the orifice, which is expected to be smaller by the coefficient of contraction (5). In contrast, the 3D measurements of AROA can be expected to be less affected by these constraints and thus be less prone to intermeasurement variability even in degenerative MV disease with eccentric regurgitant jets (3).

Fig. 5. A: patient with severe bileaflet prolapse and overlapping leaflets, depicting the difficulty in the quantification of flow convergence in the presence of severely distorted valvular geometry. Overlapping leaflets result in a complex 3D shape of the regurgitant orifice noted in the color-coded 3D-rendered surface and distorted flow convergence (FC) geometry, causing considerable discrepancy between FC and 3D volumetric measurements of anatomic EROA because of invalid PISA geometric assumptions. B: patient with Barlow’s disease and multisegmental prolapse. Two separate regurgitant jets are depicted (left). Individual orifices are noted in 3D (middle, arrows) and the color-coded 3D-rendered surface (right).

Not surprisingly, the largest intermethod discrepancy was seen in patients with eccentric jets resulting from multisegmental prolapse, especially involving the anterior mitral valve leaflet, highlighting the difficulties with PISA radius measurements in these patients. Additionally, the FC model demonstrated that the convergence hemisphere may be asymmetric or incomplete if the flow is constrained by leaflets or ventricular wall, requiring corrections (24), which can lead to errors and variability in measurements. Importantly, we found that the 3D analysis, unlike the FC method, is able to take into account the individual contributions of multiple jets (19).

Alternative 3D techniques. Theoretically, the use of 3D PISA measurements might overcome the challenges posed by 2D FC technique. However, 3D PISA measurements are likely to share the same limitation of the angle or geometric effect as the 2D methods (21). Indeed, accounting for the effects of MV geometry, issues with proximal flattening in Doppler-derived isovelocity area calculations in vivo remains the obstacle to the wide use of 3D techniques to directly measure PISA. PISA calculations by other 3D techniques, which have assumed a priori a valid geometric shape for the true isovelocity contours, have not been independent of geometric assumptions. Several hemiellipsoidal models have been tested in experimental settings, but these are subject to assumptions about the hemiellipsoidal nature of the contours, which is not necessarily the case in distorted MV geometry (18). Therefore, irrespective of dimensionality, the geometry of the orifice is fundamental to application of the PISA technique.

In a previous study (5), 3D planimetry of the regurgitant orifice area was applied to a single cut-plane extracted from 3D-reconstructed multiplane TEE data sets, demonstrating high correlation with FC measurements but with a negative bias. These results could be explained by the underestimation of the complexity of the 3D geometry of the regurgitant orifice. In contrast, true 3D measurements of AROA take into account the nonplanar nature of the regurgitant orifice resulting in larger areas. In addition, measurements reported in the study (5) could have been confounded by poor image quality, resulting from multiple image acquisition, 3D reconstruction, and misalignment. In contrast, we used zoomed 3D mTEE images acquired during a single beat to eliminate stitch artifacts.
Limitations. One of the limitations of this study is the lack of a “gold standard” reference technique for the measurement of the regurgitant orifice area in humans. However, a true “gold standard” technique that would provide accurate measurements in any MV regurgitant orifice geometry does not exist. With the advantages of high spatial resolution and real-time acquisition, mTEE may become an additional method for quantification of AROA in cases of distorted MV geometry. While at the current phase of development, this analysis relies on manual tracing in multiple planes and is time consuming, a larger degree of automation is expected to further reduce analysis time as well as intermeasurement variability. Since it is known that FC varies throughout systole, it is important to measure the PISA radius at its maximal length (4, 35). Even though all PISA and 3D data sets were acquired at midsystole, our study was limited by the lack of exact phasic correlation between 2D and 3D methods. Also, while it is known that preload and afterload affect the coapting forces and thereby the EROA measurements, the effects of loading conditions on AROA quantification remain to be tested in future studies.

Another limitation of RT3DE TEE in its current phase of development is its relative low frame rates. Even with the lower frame rates of 3D echo, the technique demonstrated good correlation when PISA symmetry assumptions were respected. Moreover, AROA measurements are gain, as well as line density and frame rate, dependent. First, in our experience, at the time of image acquisition, it is preferable to slightly over gain the image to ensure visualization of all pertinent structures. To determine the significance of gain during quantitative analysis, we studied several patients with variable gains (30 dB) and found that AROA was larger and in nonphysiologic range, when the gain was decreased, resulting in dropout artifacts, and conversely, when the gain was increased, the

Table 2. Summary of the severity of MR as classified by different parameters using criteria defined in the current ASE guidelines

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measured Range</th>
<th>Defined as Severe</th>
<th>Severe (n)</th>
<th>Mild to Moderate (n)</th>
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<tr>
<td>E-wave velocity</td>
<td>0.79–1.45 m/s</td>
<td>&gt;1.2 m/s</td>
<td>25</td>
<td>36</td>
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<td>Pulmonary venous flow reversal</td>
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<td>Left atrial volume</td>
<td>23–77 ml/m²</td>
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<td>&gt;0.39 cm²</td>
<td>23</td>
<td>38</td>
</tr>
</tbody>
</table>

American Society of Echocardiography (ASE) guidelines as described in Ref. 37. n = No. of patients. EROA, effective regurgitant orifice area; AROA, anatomic regurgitant orifice area.

Table 3. Reproducibility of EROA using the 2D FC technique and 3D analysis of AROA in two subgroups of patients with central and eccentric MR

<table>
<thead>
<tr>
<th></th>
<th>Central MR</th>
<th>Eccentric MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interobserver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D FC</td>
<td>15 ± 7</td>
<td>19 ± 15</td>
</tr>
<tr>
<td>3D EROA</td>
<td>11 ± 6</td>
<td>15 ± 12</td>
</tr>
<tr>
<td>Intraobserver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D FC</td>
<td>13 ± 8</td>
<td>16 ± 11</td>
</tr>
<tr>
<td>3D EROA</td>
<td>9 ± 5</td>
<td>13 ± 6</td>
</tr>
</tbody>
</table>

Data are means ± SD; n = 10 patients each. Inter- and intraobserver variability is shown in percent of the mean of the corresponding pair of repeated measurements. 2D and 3D, two- and three-dimensional.
FLOW CONVERGENCE IN MITRAL REGURGITATION

AROA measurements decreased into nonezero ranges in patients where all signs indicated presence of severe MR. However, minor gain adjustments necessary to optimize the accuracy of leaflet tracing were found to have very little effect on the results of repeated analyses performed by blinded observers. In addition, line density and frame rate were not significantly different between the two groups of patients and therefore did not affect our findings.

In summary, 3D computational flow dynamics and finite element analysis tools demonstrated the complexity involved in hydraulic calculations of the EROA in both simple and complex MV orifices. PISA calculation is more applicable in central vs. eccentric orifices. Attention towards symmetry of isovelocity contours is crucial and arbitrary or preset baseline velocity settings are problematic. 3D AROA measurements may provide a reasonable alternative to determine the severity of MR when such a determination is challenging using the conventional methodology.

REFERENCES


