Clinical Situations Associated with Inappropriately Large Regurgitant Volumes in the Assessment of Mitral Regurgitation Severity Using the Proximal Flow Convergence Method in Patients with Chordae Rupture

Kyusup Lee, MD, Sang Yong Om, MD, Sun Hack Lee, MD, Jin Kyung Oh, MD, Hong-Kyung Park, RDCS, Yoon-Sil Choi, RDCS, Seung-Ah Lee, MD, Sahmin Lee, MD, Dae-Hee Kim, MD, Jong-Min Song, MD, Duk-Hyun Kang, MD, and Jae-Kwan Song, MD, PhD, Seoul, Republic of Korea

Background: Regurgitant volume (RVol) calculated using the proximal flow convergence method (proximal isovelocity surface area [PISA]) has been accepted as a key quantitative parameter for the diagnosis of and clinical decision-making with regard to severe mitral regurgitation (MR). However, a recent prospective study showed a significant overestimation of RVol by the echocardiographic PISA method compared with the MR volume measured using magnetic resonance imaging. We aimed to evaluate the frequency of overestimation of RVol by the PISA method and the clinical conditions that require a different quantitative method to correct the overestimation.

Methods: We retrospectively enrolled 166 consecutive patients with degenerative MR and chordae rupture, in whom RVol was measured using both the PISA and two-dimensional Doppler volumetric methods. The volumetric method was used to measure total stroke volume using the two-dimensional Simpson biplane method, and forward stroke volume was measured using pulsed Doppler tracing at the left ventricular (LV) outflow tract. RVol by the volumetric method was calculated using total stroke volume – forward stroke volume. Severe MR was defined as an RVol >60 mL.

Results: All patients had severe MR based on RVol by the PISA method, but 68 (41.1%) showed RVol by the volumetric method values of <60 mL, resulting in discordant results. The patients with discordant results were characterized by a higher prevalence of female sex, lower body surface area, smaller LV diastolic and systolic dimensions and volumes, smaller left atrial volume, smaller PISA angle, and lower frequency of flail leaflets (39.7% vs 62.2%, P = .004). Multivariate analysis revealed that LV end-diastolic volume (LVEDV) and PISA angle were independent factors, with the best cutoff LVEDV and PISA angle being 173 mL and 103°, respectively. During follow-up (median, 3.4 years; interquartile range, 2.0-4.8 years), mitral valve repair and replacement were performed in 103 and six patients, respectively. The 2-year mitral valve surgery-free survival rate was higher in the discordant group (51.8% ± 0.06% vs 31.2% ± 0.05%, P < .001).

Conclusions: Even in the patients with documented chordae rupture, the PISA method alone resulted in inappropriate overestimation of MR severity in a significant proportion of patients. Thus, an additive quantitative method is absolutely necessary in patients with a small LVEDV or narrow PISA angle. (J Am Soc Echocardiogr 2019; - - - - .)

Keywords: Mitral regurgitation, Doppler echocardiography, Proximal flow convergence method, Regurgitant volume

From the Division of Cardiology, Asan Medical Center Heart Institute, University of Ulsan College of Medicine, Seoul, Republic of Korea.

Conflicts of Interest: None.

Reprint requests: Jae-Kwan Song, MD, PhD, Professor of Medicine, Division of Cardiology, Asan Medical Center Heart Institute, University of Ulsan College of Medicine, Seoul, Republic of Korea (E-mail: jksong@amc.seoul.kr).

0894-7317/$36.00
Copyright 2019 by the American Society of Echocardiography.
https://doi.org/10.1016/j.echo.2019.08.020
Quantitative assessment of the severity of mitral regurgitation (MR) is critical for both diagnosis of severe MR and clinical decision-making on the optimal timing of surgical intervention.\(^1,2\) Quantitation using the proximal isovelocity surface area (PISA) in the flow convergence region during routine echocardiography has been established to calculate regurgitant volume (RVol\(_{\text{PISA}}\)) and effective regurgitant orifice area.\(^3,4\) Along with a high success rate of mitral valve repair surgery for MR due to myxomatous degeneration with better clinical outcomes, earlier surgical intervention in MR even in the absence of symptoms based on these indexes has been suggested, which reinforces the clinical importance of accurate assessment of MR severity. A recent prospective multicenter study compared RVol measurement by PISA and by magnetic resonance imaging (MRI) and reported that the PISA method tended to overestimate MR severity.\(^5\) The authors of that study concluded that MRI should be considered, especially when MR severity as assessed by echocardiography influences important clinical decisions such as the decision to undergo MR surgery. However, performing both echocardiography and MRI for assessment of MR severity in all patients is quite impractical. A more practical approach is to establish clinical conditions in which other imaging modalities in addition to multiple echocardiographic techniques are required for accurate assessment of MR severity.\(^6\) The purpose of this article was to evaluate the frequency of overestimation by RVol\(_{\text{PISA}}\), its impact on clinical outcomes, and the clinical conditions that require a different quantitative method to correct the overestimation.

**METHODS**

**Study Populations**

The clinical data of patients with MR who were \(\geq 18\) years of age and referred for echocardiographic evaluation at Asan Medical Center in South Korea from November 2006 to June 2016 were retrospectively reviewed. For enrollment in this study, patients had to meet all of the following inclusion criteria: (1) RVol able to be calculated by both the conventional PISA and two-dimensional (2D) Doppler volumetric methods, (2) MR due to myxomatous degeneration and chordae rupture, and (3) chronic severe MR (RVol \(>60\) mL by either method). Patients with atrial fibrillation, regional wall motion abnormality due to coronary artery disease, infective endocarditis, functional MR, acute MR, or aortic valvular dysfunction were excluded. This retrospective study was approved by the institutional review board, and informed consent was waived owing to the noninvasive procedure and retrospective nature of the study.

**Echocardiography**

Comprehensive 2D and Doppler echocardiographic examinations were performed in all patients. We followed the standards and techniques recommended by the American Society of Echocardiography.\(^3,4\) The PISA was determined by measuring the proximal flow convergence by lowering the imaging depth and reducing the Nyquist limit at midsystole (Figure 1). Various views were used for optimal visualization of the PISA. Baseline shift was used to adjust the aliasing velocity to approximately 40 cm/sec. RVol by the PISA method was calculated as an effective orifice area by the PISA multiplied by the MR velocity-time integral in accordance with the current guidelines. The regurgitant velocity-time integral was determined by tracing the contour of the regurgitant jet obtained by continuous-wave Doppler imaging. The geometric convergence angle was determined to be the minimum angle between two sides of the proximal flow field obtained from two or more views.\(^3,8\) Angle correction was not used for routine RVol calculation.

The quantitative 2D Doppler volumetric method (Figure 2) was also used to calculate RVol.\(^9\) End-diastolic and end-systolic left ventricular (LV) volumes were measured using the biplane Simpson method, and the difference between the two volumes was used to calculate the total stroke volume. The LV outflow diameter was measured at the parasternal long-axis view, and pulsed Doppler tracing at the apical views was used to obtain the flow velocity signal at the outflow tract. Forward stroke volume was calculated by multiplication of the outflow tract area and the velocity-time integral of the flow signal. RVol by the quantitative 2D Doppler volumetric method was calculated using the difference between total stroke volume and forward stroke volume (RVol\(_{\text{volumetry}}\)). Patients with RVol \(<30\) mL were classified as the mild MR group, and those with RVol between 30 and 60 mL as the moderate MR group.

**Reproducibility**

To determine the intraobserver and interobserver reproducibility, we examined 14 randomly selected patients at a different time point (\(\geq 1\) month). Two experienced observers were blinded and assessed MR severity repeatedly by measuring RVol using both the PISA and quantitative 2D Doppler volumetric methods. The agreement of MR volume between the methods was compared using the intraclass correlation coefficient.

**Statistical Analyses**

An RVol \(>60\) mL was used to define severe MR. Patients whose RVol\(_{\text{PISA}}\) and RVol\(_{\text{volumetry}}\) were \(>60\) mL were classified as the concordant group, whereas those whose RVol measured by only one method to be \(>60\) mL were classified as the discordant group. Continuous variables were presented as mean ± SD or median (range), and categorical variables were described as numbers (percentages). The independent \(t\) test and Pearson \(\chi^2\) test (or Fisher’s exact test) were used to compare the two groups for continuous and categorical variables, respectively. Linear regression analysis was performed to evaluate the linear relationship between the RVols by the two methods. A Bland-Altman plot was generated to evaluate the agreement between the methods. Logistic regression models were used to identify factors associated with the discordant classification of severe MR using RVol\(_{\text{PISA}}\) and RVol\(_{\text{volumetry}}\). Variables with unadjusted \(P < .1\) in the univariate analyses were included in the multivariate logistic regression analysis. The receiver-operating characteristic (ROC) curve analyses were performed to assess the optimal cutoff values of the echocardiographic

---

**Abbreviations**

- **2D** = Two-dimensional
- **LV** = Left ventricular, ventricle
- **LVEDV** = Left ventricular end-diastolic volume
- **MR** = Mitral regurgitation
- **MRI** = Magnetic resonance imaging
- **PISA** = Proximal isovelocity surface area
- **ROC** = Receiver-operating characteristic
- **RVol** = Regurgitant volume

---

\(18\) years of age
parameters independently associated with discordant classification. Kaplan-Meier survival curves with a log-rank test were used to compare the development of clinical events (surgical treatment) between the two groups (concordant vs discordant group) during follow-up (median, 3.4 years; interquartile range, 2.0-4.8 years). Statistical analysis was performed using the Statistical Package for Social Sciences version 21 (SPSS, Chicago, IL). All tests were two-sided, and a $P < .05$ was considered significant.

HIGHLIGHTS

- Discrepancy in mitral regurgitation (MR) severity assessment often occurs.
- The proximal isovelocity surface area (PISA) method overestimates MR volume.
- The overestimation is associated with a small left ventricular volume or narrow PISA angle.
- Additional techniques are necessary for accurate assessment of MR severity.

RESULTS

In this study, 166 patients with degenerative severe MR (mean age, 53.6 ± 13.7 years; 115 men [69.3%]) were included, and both RVol_PISA and RVol_volumetry were calculated (Figure 3). A modest positive correlation was observed between RVol_PISA and RVol_volumetry ($Y = 0.337X + 24.023$, $r = 0.535$, $P < .001$; Figure 3, left panel). RVol_PISA was significantly larger than RVol_volumetry, and the difference between the two measurements increased progressively with an increase in RVol ($Y = 0.584X + 7.184$, $r = 0.494$, $P < .001$; Figure 3, right panel). All the patients showed an RVol_PISA >60 mL, but RVol_volumetry was ≤60 mL in 68 patients (41.1%), resulting in a discordant classification (Figure 3, left panel). The patients with discordant classification between RVol_PISA and RVol_volumetry were characterized by a smaller body surface area ($1.68 ± 0.2$ vs $1.78 ± 0.2$ cm$^2$, $P = .001$), lower body weight ($62.9 ± 11.5$ vs $67.9 ± 11.0$ kg, $P = .005$), shorter height ($162.8 ± 8.6$ vs $168.5 ± 8.2$ cm, $P < .001$), and higher prevalence of female patients (47.1% vs 19.4%, $P < .001$; Table 1). The discordant group also showed smaller left atrial volume, LV dimensions and volumes, and PISA radius and angle and lower frequency of flail leaflets.

Figure 1 Representative images showing how to measure the radius and angle of the proximal flow convergence region. The eccentric MR flow was observed in two-chamber view (shown in A). In the magnified view of color Doppler flow mapping, chordae rupture was well demonstrated after removing Doppler signal (arrow in B) and the center of proximal flow convergence could be easily determined using this 2D image. Measurement of the radius and angle can be more easily done by using side-by-side demonstration of both 2D and color Doppler images (C and D). LA, Left atrium.
Figure 2  Representative images showing the calculation of RVol using the proximal flow convergence method and volumetry in patients with concordant (A-D, left panels) and discordant classifications (E-H, right panels). EDV, End-diastolic volume; FSV, forward stroke volume; TSV, total stroke volume; TVI, time-velocity integral.
Figure 3 Correlation between RVol measurement using the PISA and volumetric methods (left) demonstrated with a Bland-Altman plot (right).

Table 1 Comparison of clinical variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (N = 166)</th>
<th>Discordant group (n = 68)</th>
<th>Concordant group (n = 98)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>53.6 ± 13.7</td>
<td>55.5 ± 14.9</td>
<td>52.3 ± 12.6</td>
<td>.13</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>115 (69.3)</td>
<td>36 (52.9)</td>
<td>79 (80.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.8 ± 3.2</td>
<td>23.6 ± 3.2</td>
<td>23.9 ± 3.1</td>
<td>.64</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.74 ± 0.2</td>
<td>1.68 ± 0.2</td>
<td>1.78 ± 0.2</td>
<td>.001</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>65.9 ± 11.5</td>
<td>62.9 ± 11.5</td>
<td>67.9 ± 11.0</td>
<td>.005</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.2 ± 8.8</td>
<td>162.8 ± 8.6</td>
<td>168.5 ± 8.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>63 (38.0)</td>
<td>27 (39.7)</td>
<td>36 (36.7)</td>
<td>.70</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>8 (4.8)</td>
<td>3 (4.4)</td>
<td>5 (5.1)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>15 (9.0)</td>
<td>6 (8.8)</td>
<td>9 (9.2)</td>
<td>.94</td>
</tr>
<tr>
<td><strong>Echocardiographic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV EF, %</td>
<td>67.2 ± 7.5</td>
<td>64.9 ± 9.2</td>
<td>68.8 ± 5.6</td>
<td>.002</td>
</tr>
<tr>
<td>LAVI, mL/m² (IQR)</td>
<td>64 (52, 86)</td>
<td>56 (46, 72)</td>
<td>70 (56, 92)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LVIDd, mm</td>
<td>50.0 ± 6.0</td>
<td>57.1 ± 5.7</td>
<td>61.1 ± 5.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LVIDs, mm</td>
<td>36.9 ± 5.8</td>
<td>35.3 ± 6.2</td>
<td>38.0 ± 5.2</td>
<td>.003</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>189 ± 52</td>
<td>150 ± 35</td>
<td>216 ± 45</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>62 ± 25</td>
<td>54 ± 26</td>
<td>68 ± 22</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ERO area, cm²</td>
<td>0.94 ± 0.45</td>
<td>0.76 ± 0.35</td>
<td>1.07 ± 0.47</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PISA radius, mm</td>
<td>13.4 ± 2.9</td>
<td>12.1 ± 2.4</td>
<td>14.3 ± 2.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PISA angle, degrees</td>
<td>101 ± 26</td>
<td>87 ± 20</td>
<td>111 ± 25</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>RVol, mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By PISA method</td>
<td>114 ± 44</td>
<td>126 ± 53</td>
<td>106 ± 35</td>
<td>.008</td>
</tr>
<tr>
<td>By volumetric method</td>
<td>71 ± 36</td>
<td>38 ± 15</td>
<td>94 ± 27</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Flail motion, n (%)</td>
<td>88 (53.0)</td>
<td>27 (39.7)</td>
<td>61 (62.2)</td>
<td>.004</td>
</tr>
<tr>
<td>Multisegment prolapse, n (%)</td>
<td>46 (27.7)</td>
<td>18 (26.5)</td>
<td>28 (28.8)</td>
<td>.77</td>
</tr>
</tbody>
</table>

*EF, Ejection fraction; ERO, effective regurgitant orifice; IQR, interquartile range; LAVI, left atrial volume index; LVESV, left ventricular end-systolic volume; LVIDd, left ventricular internal dimension-diastolic; LVIDs, left ventricular internal dimension-systolic. 

*Between the discordant and concordant groups.
A multivariate analysis was performed to evaluate the clinical variables associated with the discordant classification. After adjustment for body surface area, sex, and presence of flail mitral valve, the discordance was independently associated with smaller LV end-diastolic volume (LVEDV; odds ratio [OR], 0.96; 95% CI, 0.95-0.97; \( P < .001 \)) and narrower PISA angle (OR, 0.96; 95% CI, 0.94-0.98; \( P < .001 \); Table 2). In the ROC curve analysis (Figure 4), LVEDV (0.889; 95% CI, 0.838-0.940) showed a larger area under the curve than the PISA angle (0.766; 95% CI, 0.695-0.837). The best cutoff LVEDV and PISA angle were 173 mL and 103°, respectively.

During follow-up (median, 3.4 years; interquartile range, 2.0-4.8), 75 patients (76.5%) in the concordant group underwent mitral valve surgery (mitral valve repair \( n = 73 \) and replacement \( n = 2 \)), whereas 34 patients (50.0%) in the discordant group underwent surgery (repair \( n = 30 \) and replacement \( n = 4 \)). The 2-year mitral valve surgery-free survival rate was higher in the discordant group (52.8% 6 0.06% vs 31.2% 6 0.05%, \( P < .001 \); Figure 5).

**DISCUSSION**

Our study demonstrated only a modest agreement between RVol_PISA and RVol_volumetry in the quantitative assessment of MR severity in patients with degenerative or primary MR. RVol_PISA was significantly higher than RVol_volumetry, resulting in a discordant classification of severe MR in a significant proportion (up to 41%) of patients with documented chordae rupture. Small LVEDV and narrow PISA angle were associated with the discordant classification of severe MR. As the patients with discordant classification showed a higher MR surgery-free survival rate, repeated RVol measurement using different echocardiographic techniques in addition to the PISA method should be considered in patients with lower cutoff LVEDV or PISA angle.

Echocardiography is the most commonly used method for determining MR severity, and the PISA method has been successfully introduced into routine clinical practice and remains as the most popular technique for quantitative assessment of MR severity.\(^{1,2}\) Effective regurgitant orifice area and RVol by the PISA method are two key indexes used for the classification of MR severity.\(^{10}\) Along with the progressive increase in the success rate of MR repair surgery in patients with primary myxomatous degenerative MR, earlier surgical intervention in asymptomatic patients with severe MR has been suggested, igniting a controversy.\(^{11,12}\) RVol 60 mL, although calibrated and established using LV angiography >20 years ago,\(^{10}\) is currently being used to define severe MR. The PISA method, probably the most widely used quantitative method for MR assessment, is based on hydrodynamics and is expected to work best over a relatively small hole with an infinitely wide proximal flow convergence region.\(^{13,14}\) Unfortunately, the human left heart and mitral valve do not provide the ideal conditions for the application of the PISA principle, which includes many limitations that eventually diminish the accuracy of quantitative assessment of MR severity. The current guidelines for quantification of MR severity recommend an integrated approach using multiple echocardiographic techniques but do not specify clinical situations in which a different approach is necessary to reconcile potential inconsistency or discordant classification.

A prospective multicenter study using both the PISA method and cardiac MRI demonstrated that RVol_PISA overestimated MR
severity and led to a substantial discordance, with 34% of patients with severe MR based on RVol_PISA having only mild MR according to MRI. Moreover, RVol_PISA showed no correlation with postsurgical LV remodeling, whereas RVol by MRI showed a strong correlation with postsurgical LV remodeling. These observations suggest that cardiac MRI may be more accurate than the PISA method for assessing MR severity, and clinical decision-making on the timing of surgery based on RVol_PISA alone in patients with MR may be inappropriate. Thus, it is important to determine clinical situations associated with potential overestimation of MR severity by the conventional PISA method for which an additional quantitative approach including MRI may be useful.

Progressive enlargement of the left-sided cardiac chambers is an expected morphologic change associated with volume overload in MR. Indexes of volumetric changes in the LV or left atrium have been reported to be useful to predict the postoperative clinical course; thus, LV systolic dimension and LV ejection fraction have been used to determine the optimal timing of intervention in the current practice guidelines.

However, these indexes do not adequately represent the severity of valvular regurgitation, and a more sophisticated study using cardiac MRI confirmed that LVEDV shows better correlation with RVol than other indexes such as LV end-systolic volume or LV end-diastolic dimensions. Tight coupling between RVol and LVEDV in patients with chronic, isolated MR has been reported, and postsurgical remodeling was used as a representative index of MR severity before surgery. RVol is an instantaneous measure, whereas LVEDV is a longer-term and better measure representing the long-term average of MR severity. In our study, LVEDV was independently associated with the discordant classification of severe MR and thus is an important and useful index to consider in the application of different imaging techniques for accurate assessment of MR severity. Our observation that patients with LVEDV smaller than a certain cutoff value (173 mL) had a high probability of overestimation of MR severity by the PISA method also supports the idea of a strong correlation between RVol and LVEDV in patients with chronic MR.

The basic assumption for the application of the PISA technique is that isovelocity contours should be hemispheric in shape when inviscid fluid converges at a point-like orifice in a planar surface. As the regurgitant orifice in clinical practice is not point-like but rather a finite orifice, PISA contours lose their hemispheric shape and flatten out as they approach such a finite orifice, which may result in underestimation of RVol. Fortunately, this underestimation is approximately equal to the ratio of the contour velocity to the orifice velocity, and if the aliasing velocity between 5% and 10% of the orifice area is chosen, this underestimation is not clinically significant. In addition to the complex morphology of the regurgitant orifice and the temporal variation of the MR systolic jet through the orifice, proximal flow constraint especially in patients with eccentric MR is another limitation in applying the PISA method under the assumption of a hemispheric proximal flow contour for round orifices in a planar surface. However, the proximal constraint of the flow field precluding the full hemispheric spread of the isovelocity contours develops frequently in patients with myxomatous prolapse or degenerative changes characterized by an eccentric MR jet. These patients with a proximal constraint of flow field were reported to show a significant overestimation of MR severity. Thus, angle correction has been recommended but is not routinely accepted in daily practice.

Better clinical outcomes in patients with discordant classification need further explanation. Although neither angle correction of the PISA angle nor RVol by volumetry was routinely reported, the frequency of mitral valve surgery was significantly lower in patients with discordant classification. The fact that a lower percentage of those with discordant RVol had MV surgery suggests that the MR was not as severe in these patients. We believe that this finding repre- sents the current clinical practice pattern for assessment of MR severity and decision-making for timing of surgical intervention, in which attending physicians already have adopted an integrative approach for diagnosis of severe MR, as they believe that no single parameter can determine MR severity.

LIMITATIONS

Our study has several limitations. As in many clinical studies of MR, the absence of a gold standard for estimation of LV volumes and RVol is critical. Thus, the discordant classification observed in our study may be due to the falsely small LV volumes or RVol measured using the volumetry method. The traditional echocardiographic volumetry method for the calculation of total stroke volume requires accurate measurement of mitral annular dimension and flow velocity across the annulus, which demands a high level of operator skill and is not a routine in most institutions. In our study, we used a simple and routine biplane echocardiographic method, which also has several limitations including geometric assumptions for quantification of LV size and LV outflow tract and is reported to underestimate LV volume. Thus, the RVol_volumetry in our study may be due to the falsely small LV volumes or RVol measured using the volumetry method. The traditional echocardiographic volumetry method for the calculation of total stroke volume requires accurate measurement of mitral annular dimension and flow velocity across the annulus, which demands a high level of operator skill and is not a routine in most institutions. In our study, we used a simple and routine biplane echocardiographic method, which also has several limitations including geometric assumptions for quantification of LV size and LV outflow tract and is reported to underestimate LV volume. Thus, the RVol_volumetry in our study may underestimate MR severity, and further investigation is necessary to evaluate the appropriateness of the cutoff LVEDV and PISA angle we provided in our study. However, the biplane Simpson method using 2D echocardiography is one of the accepted methods for quantitative Doppler assessment of valvular regurgitation. Thus, we believe that this limitation does not mitigate our main message that LVEDV and PISA angle should be considered in the quantitative assessment of MR severity using the PISA method. Our subjects are characterized by a
rather homogeneous MR etiology with prolapse or flail mitral valve; thus, the cutoff LVEDV and PISA angle cannot be directly applied in patients with different MR etiologies.

As pointed out clearly in the recently published guideline, integration of multiple parameters is absolutely necessary for the ideal evaluation of MR severity because all methods have intrinsic limitations and lack precision. Thus, it would be unfair to draw the conclusion that our findings are against the idea that the echo-Doppler technique remains the main clinical tool for assessment and clinical decision-making of patients with MR. As selected patients with severe MR and chordae rupture were included in this study, the discordant results of the PISA method may be overestimated: inclusion of patients with a wide clinical spectrum in terms of MR severity and mechanism is expected to yield different results.

**CONCLUSION**

In patients with primary myxomatous MR and chordae rupture, RVol_PISA alone is associated with overestimation of the quantitative assessment of MR severity in patients with a small LVEDV and narrow PISA angle, and additional techniques are necessary for accurate assessment of MR severity. Further investigations using a gold standard measurement of LV volumes are necessary to determine the best cutoff LVEDV and PISA angle in this selected group of patients.

**REFERENCES**