Quantitation of Mitral Regurgitation Using the Systolic/Diastolic Pulmonary Venous Flow Velocity Ratio

CHRISTIAN SEILER, MD, FACC, BEAT C. AESCHBACHER, MD, BERNHARD MEIER, MD, FESC, FACC

Bern, Switzerland

Objectives. The purpose of this study was to test the hypothesis that pulmonary venous flow velocity ratios during systole and diastole in patients with mitral regurgitation (MR) correctly predict the quantitative degree of MR.

Background. Pulmonary venous flow velocity measurements have thus far been used only for the qualitative assessment of MR. Recent studies have evaluated this method using transesophageal echocardiography against semiquantitative references.

Methods. In 100 patients without aortic regurgitation or atrial fibrillation and with left ventricular (LV) ejection fraction >45%, MR was assessed by quantitative echocardiographic Doppler and color Doppler, providing forward and total LV stroke volume for the calculation of the mitral regurgitant fraction (RFstandard), the reference parameter, and also supplying mitral regurgitant orifice area (ROA) values and the RF by the flow convergence method (RFPISA [proximal isovelocity surface area]). Measurements of pulmonary venous flow velocity time integral values during systole to diastole (VTIs/VTId) were obtained and tested for their predictability of ROA, RFstandard and RFPISA.

Results. There was an inverse and significant correlation between VTIs/VTId and ROA, RFPISA and RFstandard, respectively: RFstandard = 49 − 20 VTIs/VTId, r = 0.77, p = 0.0001. A principal source of variability in the relation between VTIs/VTId and RFstandard was the presence of mitral valve prolapse as the cause of MR. Pulmonary venous flow reversal (VTIs/VTId <0) correctly identified severe MR with 52% sensitivity, 96% specificity and 80% positive and 87% negative predictive accuracy.

Conclusions. The VTIs/VTId ratio allows a moderately accurate assessment of the severity of MR.

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Quantitation of mitral regurgitation (MR) is a prerequisite to surgical decision making in patients with MR (1,2), but a recent study has shown that the best method of quantitative characterization remains uncertain (3). This is also reflected by the wide variety of methods used for the determination of MR, including the invasive left ventricular (LV) angiography/thermodilution technique (4), noninvasive Doppler flow methods such as color Doppler flow mapping of the regurgitant jet (5,6), vena contracta analysis of the regurgitant jet (7), analysis of the flow convergence zone proximal to the regurgitant orifice (8), examination of the power or amplitude of the received regurgitant jet flow velocity signal (9,10) and analysis of the momentum of the regurgitant jet (11). It has even been declared that there is no single effective method for the calculation of MR in an individual patient using echocardiographic Doppler (12). This notion may be challenged because the so-called quantitative Doppler method of total and forward (across the LV outflow tract) LV stroke volume (SVtot and SVfw) calculation has been demonstrated to be accurate compared with invasive methods, although it is tedious and time-consuming to perform (13).

Pulmonary venous flow velocity patterns have been used for the qualitative or semiquantitative estimation of MR (14). Systolic flow reversal in the pulmonary veins indicates severe MR with high diagnostic accuracy (Fig. 1). However, there are a number of other variables influencing either the systolic or diastolic part of pulmonary vein flow such as atrial compliance (changing with age), the presence of systolic dysfunction (with increased atrial pressure), atrial fibrillation and diastolic dysfunction (15–17). So far, pulmonary venous flow velocity spectra for the qualitative characterization of MR have been obtained exclusively by transesophageal Doppler echocardiography (TEE) (14,18,19). Yet in our experience, at least one of the pulmonary veins (usually the upper right) can be interrogated through the transthoracic approach in >90% of cases.

Consequently and because of the lack of an ideal, easy to apply gold standard for the quantitation of MR, the goal of this prospective study was to test the hypothesis that the ratio of pulmonary venous flow velocity during systole and diastole (Fig. 2) accurately predicts the regurgitant fraction (RF) in patients with pure MR.

From the Department of Cardiology, University Hospital, Bern, Switzerland.
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Address for correspondence: Dr. Christian Seiler, University Hospital, Cardiology, Inselspital, Freiburgstrasse, Bern, Switzerland. E-mail: christian.seiler@insel.ch.
Abbreviations and Acronyms

LV = left ventricular  
MR = mitral regurgitation  
PISA = proximal isovelocity surface area  
RF = regurgitant fraction  
ROA = regurgitant orifice area  
RV = regurgitant volume  
SVfw and SVtot = forward and total stroke volume  
TEE = transesophageal echocardiography  
TTE = transthoracic echocardiography  
VTI/VTI,d = systolic/diastolic flow velocity time integral ratio

Methods

Patients. One hundred patients (age 62 ± 14 years, range 30 to 88; 58 men, 42 women) with pure MR ranging from minimal to severe were included in this prospective study. All of them underwent transthoracic Doppler echocardiography (TTE) (n = 80) or TTE and TEE (n = 20) depending on the clinical indication. The patients gave informed consent to participate in this study.

The inclusion criteria were 1) the presence of pure, isolated, at least mild MR or no regurgitation as determined by standard two-dimensional Doppler echocardiography, 2) an adequate measurement of the LV outflow tract in the parasternal long axis view, 3) the satisfactory determination of end-diastolic and end-systolic LV volumes in the apical four-chamber and two-chamber view, 4) the ability to measure flow convergence zone data at the regurgitant orifice in order to calculate the regurgitant orifice area (ROA) and the regurgitant volume (RV) according to the proximal isovelocity surface area (PISA) method (8), and 5) adequate pulmonary flow velocity signals obtained by TTE or TEE from one or more pulmonary veins. The exclusion criteria were 1) age <30 years, 2) an LV ejection fraction <45%, 3) the presence of atrial fibrillation or flutter, and 4) the presence of aortic regurgitation.

The study cohort was divided into four groups according to the mitral RF determined by echocardiographic LV planimetry (providing the SVtot) and by the echocardiographic Doppler-derived calculation of SVfw across the LV outflow tract. This method is subsequently called the quantitative echocardiographic Doppler (standard) method. The four study groups were “mild MR” (RF ≤20%; n = 31), “moderate MR” (RF >20% to 35%; n = 28), “moderately severe MR” (RF >35% to 50%; n = 18), and “severe MR” (RF >50%; n = 23).

Two-dimensional Doppler echocardiography. Patients underwent conventional two-dimensional echocardiography and Doppler examination using an Acuson XP-128 phased array system equipped with a 2.0-, 2.5- or 3.5-MHz transducer. LV measurements were obtained at end-systole and end-diastole and were performed according to the recommendations of the American Society of Echocardiography (leading edge method [20]). LV volume measurements were performed as recommended by the American Society of Echocardiography (21). Apical two- and four-chamber views were acquired. The LV volumes were calculated on-line. Trabeculations and papillary muscles were excluded from the endocardial border. LV end-diastolic and end-systolic volumes were computed using the biapical Simpson rule (summed disk method) (21). LV SVtot was calculated as the difference between end-diastolic and end-systolic LV volume. LV SVfw across the LV outflow tract was computed as the LV outflow tract cross-sectional area (from the parasternal long axis view) times the velocity time integral of the systolic outflow signal obtained by pulsed Doppler, with the sample volume positioned in the LV outflow tract. The RF determined by this quantitative echocardiographic Doppler standard method, that is, RFstandard was determined as follows:

$$RF_{\text{standard}} = \frac{(SV_{\text{tot}} - SV_{\text{fw}})}{SV_{\text{tot}}}$$

In all patients, MR was also quantitated using the flow convergence method (PISA method [8]), whereby the radius of the flow convergence zone at the regurgitant orifice was measured several times during systole. Determination of the aliasing velocity of the flow convergence zone, the maximum velocity within the regurgitant orifice and the flow velocity time integral of the regurgitant continuous wave Doppler spectrum allowed calculation of the mitral ROA and RV (8). RFPISA was then determined as follows:

$$RF_{\text{PISA}} = RV/SV_{\text{tot}}$$

Arterial blood pressure was recorded at the time when the flow convergence measurements were made.

Color Doppler imaging of MR. Qualitative assessment of MR was performed using color Doppler imaging through an apical window, as described previously (22). Visual estimates of four degrees of MR (mild, moderate, moderately severe and severe) were acquired on-line, and comprised factors such as...
late systolic atrial filling. VTI_s/VTI_d in centimeters per second times
signal comprises two peaks, one related to the early and a second to the
pressure signal; ECG

Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mild MR (RF &gt;0–20%)</th>
<th>Moderate MR (RF &gt;20–35%)</th>
<th>Moderately Severe MR (RF &gt;35–50%)</th>
<th>Severe MR (RF &gt;50%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>63 ± 16</td>
<td>62 ± 13</td>
<td>62 ± 18</td>
<td>61 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>18 (58%)</td>
<td>14 (50%)</td>
<td>9 (50%)</td>
<td>16 (70%)</td>
<td>NS</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.76 ± 0.2</td>
<td>1.84 ± 0.2</td>
<td>1.72 ± 0.2</td>
<td>1.82 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>132 ± 25</td>
<td>123 ± 20</td>
<td>133 ± 21</td>
<td>123 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>77 ± 11</td>
<td>73 ± 12</td>
<td>76 ± 12</td>
<td>70 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>71 ± 18</td>
<td>70 ± 21</td>
<td>84 ± 20</td>
<td>74 ± 17</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>2 (6%)</td>
<td>2 (7%)</td>
<td>6 (33%)*</td>
<td>10 (43%)*</td>
<td>0.0006</td>
</tr>
<tr>
<td>LV diastolic dysfunction</td>
<td>14 (45%)</td>
<td>11 (39%)</td>
<td>5 (28%)</td>
<td>6 (26%)</td>
<td>NS</td>
</tr>
<tr>
<td>TEE</td>
<td>6 (19%)</td>
<td>3 (11%)</td>
<td>3 (18%)</td>
<td>10 (34%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*p < 0.01 versus mild and moderate mitral regurgitation (MR). Data presented are mean value ± SD or number (%) of patients. LV = left ventricular; RF = regurgitant fraction; TEE = transesophageal echocardiography.
Echocardiographic data. Table 2 shows that there was a tendency to larger end-diastolic LV cavity sizes with increasing severity of MR, although the respective differences were statistically different only between patients with severe and those with mild MR. The same trend to larger cavity sizes with more severe MR was found for the left atrium. The LV mass index tended to be larger in patients with severe MR than in those with mild and moderate MR (Table 2), a finding related to the larger cavity sizes in patients with more severe MR and not to different LV wall thicknesses. There was no significant difference in maximal systolic pressure gradients across an insufficient tricuspid valve among the study groups.

Doppler echocardiographic data for the assessment of MR. The comparison between the two quantitative methods for the assessment of MR used in this study, the quantitative echocardiographic Doppler standard method and the PISA method, revealed a good and statistically significant agreement (Fig. 3), although the RFstandard values were slightly underestimated by the PISA method (SEE = 10.6%). The data presented in Table 3 indicate that mild to moderate degrees of MR were overestimated by color Doppler imaging in most cases, whereas the more severe MR was most often assessed correctly. All values of PISA-derived RVs and ROAs differed significantly among the study groups.

Figure 3. A, Comparison between mitral RF determined by the flow convergence method (PISA method, RF\textsubscript{PISA}; horizontal axis) and RF calculated by quantitative echocardiographic Doppler (RF\textsubscript{standard}; vertical axis). There was a significant correlation between those parameters. B, Analysis of the average between the RF\textsubscript{PISA} and RF\textsubscript{standard} values (horizontal axis) and the deviation of RF\textsubscript{PISA} from the average (vertical axis).

Association between pulmonary venous flow velocity measurements and MR. VTI\textsubscript{P}/VTI\textsubscript{d} ratios differed significantly among all study groups (Table 3). Figure 4 illustrates that there was an inverse curvilinear, significant relation between the VTI\textsubscript{P}/VTI\textsubscript{d} ratio and the ROA of the mitral valve. This relation was improved by normalizing ROA for body surface area: ROA/m\textsuperscript{2} = 0.48 − 0.52 VTI\textsubscript{P}/VTI\textsubscript{d} + 0.1(VTI\textsubscript{P}/VTI\textsubscript{d})\textsuperscript{2}; r = 0.70, p = 0.0001. An inverse, linear relation was observed between the VTI\textsubscript{P}/VTI\textsubscript{d} ratio and the RF (i.e., RF\textsubscript{PISA}; Fig. 5). There was a slight tendency toward a closer correlation between those parameters if the pulmonary venous flow velocity signals were obtained using TEE instead of TTE (Fig. 5, filled symbols; TEE-derived RF\textsubscript{PISA} = 59 − 26 VTI\textsubscript{P}/VTI\textsubscript{d}, r = 0.82). The linear regression equation for the correlation be-

Table 2. Echocardiographic Data

<table>
<thead>
<tr>
<th></th>
<th>Mild MR (RF &gt;0–20%)</th>
<th>Moderate MR (RF &gt;20–35%)</th>
<th>Moderately Severe MR (RF &gt;35–50%)</th>
<th>Severe MR (RF &gt;50%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-diastolic LV diameter (mm)</td>
<td>49 ± 8</td>
<td>51 ± 9</td>
<td>56 ± 8</td>
<td>57 ± 5*</td>
<td>0.0005</td>
</tr>
<tr>
<td>End-systolic LV diameter (mm)</td>
<td>32 ± 8</td>
<td>35 ± 9</td>
<td>39 ± 9</td>
<td>37 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>Septal wall thickness, ED (mm)</td>
<td>13 ± 3</td>
<td>12 ± 3</td>
<td>12 ± 2</td>
<td>13 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Posterior wall thickness, ED (mm)</td>
<td>11 ± 2</td>
<td>11 ± 3</td>
<td>11 ± 2</td>
<td>12 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Left atrium (mm)</td>
<td>40 ± 7</td>
<td>43 ± 5</td>
<td>46 ± 9</td>
<td>52 ± 8†</td>
<td>0.0001</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>63 ± 10</td>
<td>59 ± 14</td>
<td>59 ± 15</td>
<td>63 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass index (g/m\textsuperscript{2})</td>
<td>135 ± 49</td>
<td>124 ± 40</td>
<td>141 ± 37</td>
<td>162 ± 39</td>
<td>0.04</td>
</tr>
<tr>
<td>Systolic ΔP\textsubscript{max} RA-RV (mm Hg)</td>
<td>30 ± 8</td>
<td>38 ± 11</td>
<td>35 ± 13</td>
<td>36 ± 13</td>
<td>NS</td>
</tr>
</tbody>
</table>

*p < 0.05 versus mild mitral regurgitation (MR). †p < 0.05 versus mild and moderate mitral regurgitation. Data presented are mean value ± SD. ΔP\textsubscript{max} = maximal pressure gradient; ED = end-diastolic; RA = right atrium; RV = right ventricle; other abbreviations as in Table 1.
between TEE-derived and TTE-derived VTls/VTId (n = 20) was as follows: TEE-derived VTls/VTId = 0.93 TTE-derived VTls/VTId + 0.03; r = 0.91, p = 0.0001. The regression equation for the calculation of echocardiographic Doppler–derived RF values was RFstandard = 49 – 20 VTls/VTId; r = 0.77, p = 0.0001.

The test accuracies of normal (VTls/VTId >1), mildly blunted (VTls/VTId >0.5 to 1), blunted (VTls/VTId = 0 to 0.5) and reversed (VTls/VTId <0) pulmonary venous flow velocity ratios for different degrees of MR according to RFstandard are shown in Table 4. The test accuracy of any systolic pulmonary venous flow reversal (i.e., not only net flow reversal during the entire systole) for severe MR was 56% sensitivity, 91% specificity, 65% positive predictive accuracy and 88% negative predictive accuracy.

### Discussion

This prospective study of 100 patients with pure MR found that the quantitative characterization of pulmonary venous flow patterns using TEE or TTE, or both, allows the prediction of echocardiographic Doppler–derived mitral RF with moderate accuracy.

### Methods for the quantitation of MR

Although angiography is a clinically useful and well accepted semiquantitative technique, it is invasive and can cause discomfort to patients. Therefore, echocardiography is often used as a non-invasive alternative for the quantification of MR. In this study, the authors utilized the flow convergence method to quantify the pulmonary venous flow patterns.

### Figure 4

**Correlation between VTls/VTId (horizontal axis) and mitral ROA determined by the flow convergence method (vertical axis). The thick vertical line indicates the limit between systolic anterograde (>0) and retrograde pulmonary vein flow.**

\[ y = 0.5 - 0.5x + 0.13x^2 \]

\[ r = 0.65, p = 0.0001 \]

### Figure 5

**Correlation between VTls/VTId (horizontal axis) and mitral RF determined by the flow convergence method (vertical axis). The thick vertical line indicates the limit between systolic anterograde (>0) and retrograde pulmonary vein flow. Open triangles indicate patients who underwent TTE, solid triangles those who underwent TEE. Upright triangles indicate patients without mitral valve prolapse (MVP), reversed triangles those with MVP.**

\[ y = 55 - 26x \]

\[ r = 0.82, p = 0.0001 \]
approach in the assessment of MR, it cannot be considered a reference method. Qualitative angiographic grading of MR has been demonstrated to vary often be at variance with the quantitative indexes of MR (24). Studies using "quantitative" angiography have reported up to 40% of RF computed in normal subjects (25) and 0% RF in patients with documented significant MR (24,25). Similarly, there are numerous problems and pitfalls inherent in the noninvasive, echocardiographic Doppler–based methods for the assessment of MR, such as the reported underestimation of RF using color Doppler in patients with eccentric MR jets or MR jets due to ischemic heart disease (5). The sound theory behind the flow convergence (PISA) method, a procedure widely used for the quantitation of MR, is affected by several error-producing discrepancies, namely the noncircular orifice of the regurgitant hole; the nonhemispheric, often blunted, proximal flow convergence region; the nonflat surface of the mitral valve plane; and eccentric MR jet directions (26). The theoretically very elegant method of the jet momentum analysis (11) is actually almost unemployable because the receiving chamber of the MR jet is not unlimited in space but has discrete, often narrow, boundaries that render the analysis of the color Doppler jet impractical. The amplitude-weighted mean MR jet velocity method, a nonvolumetric spectral Doppler method, mandates a special, not widely available, data processing software; it is not applicable in the presence of pulmonary vein flow patterns that was weaker than the RF to pulmonary vein flow reversal as characteristic for severe MR (14,18,19). At variance with those studies, our investigation did not use just one qualitative grading reference method (i.e., 1+ to 4+ angiographic degrees of MR) but rather two quantitative references. From our perspective, it is methodologically problematic to use a qualitative reference to evaluate a quantitative method. The study of a larger number of patients than in previous reports to determine the validity of pulmonary vein flow patterns for the estimation of MR is overdue because the influence of other variables on the dependence of pulmonary vein flow and MR can be estimated only in this way. In addition to the earlier mentioned qualitative association of the previous studies, the present study reveals a continuous, inverse relation between an index of the systolic to diastolic pulmonary vein flow and the RF. However, this association is not strong because of the covarying effect of factors other than MR altering pulmonary venous flow patterns (see later).

The ROA of the mitral valve, the parameter regarded as the most fundamental measure for the severity of the regurgitation, showed a curvilinear relation to pulmonary venous flow patterns that was weaker than the RF to pulmonary vein flow velocity association. Most likely, body size is a covariable that influences the ROA in addition to the degree of MR.

Covariables influencing pulmonary venous flow. The earlier mentioned association holds true even when more crude means are used to obtain pulmonary vein flow velocity spectra (i.e., TTE). It is also correct in patients with conditions presumably influencing the systolic/diastolic pulmonary venous flow velocity ratios such as a younger age (between 30 and 40 years; probably with increased atrial compliance) and LV diastolic as well as mild systolic dysfunction. Figure 5 illustrates that most of the deviation from the exact association among pulmonary vein flow ratios and MR is related to the presence of mitral valve prolapse. The excentricity of the MR jet in the presence of posterior (medial-anterior direction) or anterior leaflet (lateral-posterior direction) mitral valve prolapse likely

<table>
<thead>
<tr>
<th>Normal PV Ratio</th>
<th>Mildly Blunted PV Ratio</th>
<th>Blunted PV Ratio</th>
<th>Reversed PV Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTI1/VTId &gt;1</td>
<td>(VTI1/VTId &gt;0.5–1</td>
<td>(VTI1/VTId = 0–0.5</td>
<td>(VTI1/VTId &lt;0</td>
</tr>
<tr>
<td>predicts RF &gt;0–20%</td>
<td>predicts RF &gt;20–35%</td>
<td>predicts RF &gt;35–50%</td>
<td>predicts RF &gt;50%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>84%</td>
<td>57%</td>
<td>33%</td>
</tr>
<tr>
<td>Specificity</td>
<td>84%</td>
<td>81%</td>
<td>85%</td>
</tr>
<tr>
<td>Positive predict.</td>
<td>70%</td>
<td>53%</td>
<td>33%</td>
</tr>
<tr>
<td>Negative predict.</td>
<td>92%</td>
<td>83%</td>
<td>85%</td>
</tr>
<tr>
<td>Total accuracy</td>
<td>84%</td>
<td>74%</td>
<td>76%</td>
</tr>
</tbody>
</table>

PV = pulmonary vein; RF = mitral regurgitant fraction; VTId = pulmonary venous flow velocity time integral during diastole (cm); VTI = pulmonary venous flow velocity time integral during systole (cm).
caused an over- or underestimation, respectively, with regard to the right upper pulmonary vein, (i.e., the prevalent measurement site used in this study). Unexpectedly, the use of TEE for pulmonary venous flow assessment did not improve the association between the RF and systolic/diastolic flow velocity ratio, suggesting that the application of TTE was not a limitation to our study. Young age and systolic or diastolic dysfunction did not appear to be associated with the scattering of the relation between pulmonary vein flow velocity ratios and mitral RF (data not shown), most likely because they did not occur often in the entire study group.

In the case of the PISA reference method, an additional factor causing variation in the predictability of mitral RF by pulmonary vein flow characterization is the increasing overestimation of RF in higher degrees of MR by the PISA method (Fig. 3), which may be related to factors such as underestimation of the peak regurgitant flow velocity in cases of eccentric jet directions. Problems with the correct detection of MR flow velocity spectra using the PISA method can be circumvented by the use of an empirically determined constant that reflects the maximal/time integrated velocity ratio of the MR jet (28).

Clinical implications. In patients without atrial fibrillation and with an LV ejection fraction > 45%, assessment of pulmonary vein flow velocities should be used more often for the characterization of MR. Measurement of pulmonary vein flow velocities can also be readily performed using TTE, which provides semiquantitative velocities can also be readily performed using TTE, which provides semiquantitative 1-velocities can also be readily performed using TTE, which..., VTI

VTI

VTId ratio of the MR jet (28).

circumvented by the use of an empirically determined ratio of the vena contracta [see comments]. Circulation 1997;95:636–42.


Conclusions. The VTI/VTId ratio allows a moderately accurate assessment of the severity of MR. However, it cannot replace the quantification of MR using quantitative Doppler echocardiographic methods.

References


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