Quantitative Doppler Assessment of Valvular Regurgitation

Maurice Enriquez-Sarano, MD; Kent R. Bailey, PhD;
James B. Seward, MD, FACC; A. Jamil Tajik, MD, FACC;
Mary J. Krohn, RDQS; and Janel M. Mays, RN, RDQS

Background. Quantitation of valvular regurgitation remains a challenge. The accuracy of quantitative Doppler is controversial, and its ability to measure regurgitant volume is unknown; therefore, it is not widely used.

Methods and Results. In 120 patients (20 without regurgitation, 19 with aortic regurgitation, and 81 with mitral regurgitation), the stroke volume through the mitral annulus and left ventricular outflow tract were measured using pulsed-wave Doppler concurrently with left ventricular stroke volume calculated using left ventricular volumes measured by two-dimensional echocardiography Simpson’s biapical method. Regurgitant volume and fraction were thus computed using Doppler or ventricular methods. In normal patients there were good correlations between Doppler and left ventricular measurements of stroke volume. Doppler regurgitant volume and fraction were 4.4±4.4 mL and 5.3±4.5%, respectively. In patients with aortic regurgitation, there were good correlations between Doppler and left ventricular measurements of stroke volume, regurgitant volume, and regurgitant fraction (r=0.97, r=0.95, and r=0.93, respectively; p<0.0001). In patients with mitral regurgitation, despite good correlations between Doppler and ventricular methods for stroke volume, regurgitant volume, and regurgitant fraction (r=0.94, r=0.93, and r=0.94, respectively; p<0.001), these variables were overestimated by Doppler. However, in the last 54 patients compared with the first 27, overestimation decreased significantly for regurgitant volume (5±10 mL versus 18±27 mL, p<0.05) and regurgitant fraction (3.3±6.7% versus 6.2±6.8%, p=0.05).

Conclusions. Quantitative Doppler can be performed in large numbers of patients in a clinical laboratory. Its potential limitation was identified as overestimation of mitral regurgitation, which is overcome with increased experience. Its achieved accuracy in mitral and aortic regurgitation allows measurement not only of regurgitant fraction but most importantly of regurgitant volume. (Circulation 1993;87:841-848)

KEY WORDS • aortic regurgitation • echocardiographic left ventricular volume • mitral regurgitation • regurgitant fraction

In the clinical decision-making process regarding regurgitant valvular lesions, accurate determination of the severity of the regurgitation is of major importance. Although the cardiac examination, the chest radiograph, and the electrocardiogram yield useful information, the risk of surgery warrants confirmation of severity by a complementary method. Angiography has played this role for years. However, it has been shown that the qualitative angiographic grading of aortic and mitral regurgitation (AR and MR) is often at variance with the quantitative indexes of regurgitation. Furthermore, although quantitative analysis of color flow Doppler is possible, weak correlations were found with regurgitant fraction, and eccentricity of the jet affects jet area at any regurgitant flow. These limitations of angiography and color flow Doppler explain the difficulties encountered even in semiquantitation of valvular regurgitations and emphasize the need for a reliable, reproducible noninvasive method for accurate quantitation of valvular regurgitation.

Although Doppler methods of quantification of regurgitations have been validated in single institutions and on small numbers of patients, these methods have not been widely used as a clinical tool and are even considered unreliable by some authors. To clarify this controversial issue, we undertook a prospective study to determine 1) the applicability and accuracy of quantitative Doppler, 2) the existence of a potentially correctable pitfall, and 3) the possibility of measuring the actual regurgitant volume.

Methods

We prospectively studied 120 patients between January and March 1991. This series represents the consecutive experience of the authors. Inclusion criteria were 1) the presence of pure, isolated, at least mild MR or AR or no regurgitation, as determined by standard two-dimensional echocardiography (2-DE) and Doppler color flow imaging and 2) an adequate measurement of the left ventricular outflow tract (LVOT), mitral annulus (MA), and left ventricle (LV). Among the 125

From the Division of Cardiovascular Diseases and Internal Medicine (M.E.S., J.B.S., A.J.T., M.J.K., J.M.M.) and the Section of Biostatistics (K.R.B.), Mayo Clinic and Mayo Foundation, Rochester, Minn.

Address for reprints: Maurice Enriquez-Sarano, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

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patients fulfilling criterion 1, in whom quantitative Doppler was attempted, five were excluded for criterion 2 (inadequate measurements of MA \([n=4]\) or LV \([n=1]\)), leaving a final study group of 120 patients. The mean age was 59±15 years; 62 patients were men and 58 were women. The patients were divided into three groups: group 1, patients without regurgitation: This group contained 20 patients, all of whom were in sinus rhythm; group 2, AR: This group contained 19 patients, and 18 were in sinus rhythm; group 3, MR: This group contained 81 patients, and 69 were in sinus rhythm.

**Doppler and Two-dimensional Echocardiographic Examination**

Doppler and 2-DE were performed using a Hewlett-Packard or an Acuson phased-array system equipped with a 2.5-MHz transducer. The diameter of the LVOT at the aortic annulus (inner edge) was measured in the parasternal long-axis view. The apical window was used to record the pulsed-wave velocities at the LVOT and at the MA and to measure the diameter of the MA. The technique was applied as previously described (Figure 1).\(^{10,15}\) The diameter of the MA (inner edge) was measured at the base of the leaflets at the time of maximal valvular opening. The Doppler spectral display was digitized on the brightest line (modal velocity) for the MA, and the black/white interface for the LVOT\(^{16}\) and the time velocity integral was computed. At least three measurements of each variable were averaged (six in patients in atrial fibrillation). Cross-sectional areas of the MA and the LVOT were calculated using the \(\pi r^2\)
formula, assuming a circular shape. The MA and LVOT stroke volumes were obtained by multiplying the cross-sectional area by the respective time–velocity integral. The regurgitant volume (RV) by Doppler was calculated as

$$RV\ (\text{Doppler}) = |MA\ SV - LVOT\ SV|$$  \hspace{1cm} (1)

The regurgitant fraction (RF) by Doppler was calculated as

$$RF\ (\text{Doppler}) = \frac{RV\ (\text{Doppler})}{LV\ SV\ (AR)} $$  \hspace{1cm} (2)

$$RF\ (\text{Doppler}) = \frac{RV\ (\text{Doppler})}{MA\ SV\ (MR)} $$  \hspace{1cm} (3)

$$RF\ (\text{Doppler}) = \frac{RV\ (\text{Doppler})}{\text{larger of LVOT or MA SV}} $$  \hspace{1cm} (4)

for patients without regurgitation

Quantitative Two-dimensional Echocardiography

LV volume measurements were performed as recommended by the American Society of Echocardiography (Figure 2).\textsuperscript{17} Apical two- and four-chamber views were obtained just after Doppler examination was completed. The ventricular volumes were computed off-line without prior knowledge of the Doppler results. Trabeculations and papillary muscles were excluded from the endocardial border. The LV end-diastolic and end-systolic volumes were computed using the biapical Simpson rule (method of disks)\textsuperscript{17}; their difference represents the LV stroke volume. Quantification of regurgitation using left ventricular volumes was modified from Blumlein et al\textsuperscript{11} and used Doppler to measure the forward stroke volume (non-regurgitant valve):

$$RV\ (2-DE) = |LV\ SV - \text{forward SV}| $$  \hspace{1cm} (5)

$$RF\ (2-DE) = \frac{RV\ (2-DE)}{LV\ SV} $$  \hspace{1cm} (6)

Interobserver Variations

In 19 patients, interobserver variation was assessed by obtaining the same quantitative Doppler measurements using a blinded second observer.

Statistics

Values are expressed as mean±1 SD. Group differences were assessed by Student's \(t\) test or ANOVA when more than two groups were involved. Paired data were compared using paired \(t\) tests. Comparisons between two methods were performed in two ways.
First, linear regression was used to judge linear association, and the standard error of the estimate (SEE) was reported to describe the closeness of the linear relation. Although calculation of regurgitant volume and regurgitant fraction involved subtracting the same quantity (stroke volume of the nonregurgitant orifice) from both the 2-DE and Doppler total stroke volume, we had to estimate linear correlations separately for stroke volume, regurgitant volume, and regurgitant fraction because the nonzero variance of the stroke volume of the nonregurgitant orifice contributed to the correlations between the two methods for regurgitant volume and regurgitant fraction.

The other approach used was based on the method of Bland and Altman\textsuperscript{18} in which the difference between the two measurements was plotted and regressed against their average. To construct upper and lower limits to the relation of difference to the average, an extension of the Bland and Altman approach was used, using the residuals from the regression.

Statistical significance was represented by a probability value of $p \leq 0.05$.

### Results

Quantitative Doppler and LV measurements are summarized in Tables 1 and 2, respectively. The comparisons between the three groups show that the increased flow through the regurgitant mitral and aortic orifice is accomplished primarily by increase in the diameter of the orifice and less by increase in velocities. To host the regurgitant volume, there is an increase in ventricular volumes.

#### Patients Without Regurgitation

There was a highly significant correlation between the stroke volume computed for the MA and the LVOT ($r=0.94$, $p<0.001$, SEE=5.4 mL). Although the difference was small, the calculated stroke volume was significantly larger through the MA than through the LVOT ($p<0.01$) (Figure 3).

There was no significant difference and a significant correlation between ventricular and MA stroke volumes ($r=0.94$, SEE=5.3 mL, $p<0.001$) and also between ventricular and LVOT stroke volumes ($r=0.96$, SEE=3.9 mL, $p<0.001$) (Figure 4). The calculated regurgitant volumes and fractions by the Doppler (Table 1) and ventricular (Table 2) methods were small and not significantly different.

### Aortic Regurgitation (19 Patients)

There was an excellent correlation between the LV (2-DE) and LVOT stroke volumes ($r=0.97$, $p<0.001$) and no significant difference between their values. Results regarding the regurgitant volume and regurgitant fraction are shown in the upper part of Table 3. No significant difference and strong correlations (Figure 5) were found between the Doppler and ventricular (2-DE) methods. No systematic trend of overestimation or underestimation was found.

### Mitral Regurgitation (81 Patients)

There was a significant correlation between the MA stroke volume and the LV (2-DE) stroke volume

![Figure 3. Scatterplot of the difference between mitral annulus (MA) and left ventricular outflow tract (LVOT) stroke volume (SV) on the y-axis and the mean of MA and LVOT stroke volume on the x-axis in patients without regurgitation. The horizontal solid line represents the mean difference; shaded area represents 95% confidence interval. The horizontal dashed line represents the ideal zero difference between MA SV and LVOT SV. Points above this line correspond to a larger MA SV than LVOT SV, and points below this line correspond to a smaller MA SV than LVOT SV. This scatterplot shows clearly the mild but significant overestimation of SV calculated at the mitral orifice compared with the LVOT.](image-url)
Correlation
left
line
volumeandfraction. There
FIGURE 4. Panel A: Correlation between the mitral annulus (y-axis) and quantitative two-dimensional echocardiography left ventricular (x-axis) stroke volume in patients without regurgitation. Dashed line represents the identity line; solid line is the regression line; shaded area represents 1 SEE. Panel B: Correlation between ventricular stroke volume (y-axis) and left ventricular outflow tract stroke volume (aortic, x-axis). The presentation is the same as in panel A.

\( r = 0.94, p < 0.001 \). However, the MA stroke volume was mildly overestimated compared with the LV stroke volume (119 versus 109 mL, \( p < 0.0001 \)). With regard to the regurgitant volume and fraction (lower part of Table 3), there were strong correlations between the Doppler and the ventricular (2-DE) methods (Figure 6), yet Doppler significantly overestimated both regurgitant volume and fraction. There was a systematic trend of more overestimation by Doppler of regurgitant volume, with increasing values of this variable. There was no such systematic trend with regard to regurgitant fraction.

However, these results are strongly influenced by the phase of our experience (Table 4). From the first 27 patients to the last 54 patients, overestimation of regurgitant volume decreased from 18±27 mL to 5±10 mL (\( p < 0.05 \)), overestimation of regurgitant fraction decreased from 6.2±6.8\% to 3.3±6.7\% (\( p = 0.05 \)), and the trend of larger overestimation with larger regurgitant volume disappeared (Figure 7).

**Interobserver Variations**

The correlations between the values obtained by the two observers were: MA stroke volume, \( r = 0.98, p < 0.0001, \text{SEE}=13 \text{ mL} \); LVOT stroke volume, \( r = 0.95, p < 0.0001, \text{SEE}=9 \text{ mL} \); regurgitant volume (Doppler), \( r = 0.96, p < 0.0001, \text{SEE}=17 \text{ mL} \); and regurgitant fraction (Doppler), \( r = 0.97, p < 0.0001, \text{SEE}=6\% \).

**Discussion**

Our prospective series shows that a large number of patients can be routinely studied by quantitative Doppler methods to determine the severity of valvular regurgitation.

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**Table 3. Measurements of Regurgitant Volume and Regurgitant Fraction**

<table>
<thead>
<tr>
<th></th>
<th>Doppler method</th>
<th>Ventricular method</th>
<th>( p^* )</th>
<th>( r )</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic regurgitation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RV (mL)</td>
<td>52±37</td>
<td>51±36</td>
<td>NS</td>
<td>0.95</td>
<td>12</td>
</tr>
<tr>
<td>RF (%)</td>
<td>35±17</td>
<td>35±17</td>
<td>NS</td>
<td>0.93</td>
<td>6</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>RV (mL)</td>
<td>51±49</td>
<td>41±40</td>
<td>0.0001</td>
<td>0.93</td>
<td>18</td>
</tr>
<tr>
<td>RF (%)</td>
<td>37±19</td>
<td>32±19</td>
<td>0.0001</td>
<td>0.94</td>
<td>7</td>
</tr>
</tbody>
</table>

\( r \), coefficient of correlation between the two methods; SEE, standard error of the estimate; RV, regurgitant volume; RF, regurgitant fraction.

* Applies to paired \( t \) test between Doppler and ventricular methods.
Patients Without Regurgitation

The results from patients without regurgitation show minimal discrepancy between stroke volume computed using the LVOT, the MA, or the LV. This discrepancy does not preclude the use of the method, as has been advocated by others. A small amount of calculated false regurgitation was found—less than by angiography—and even less than in the initial series published with quantitative Doppler, probably because of the consistent use of the method in large numbers of patients. These results and those previously published show that Doppler flow—volume calculations through a nonregurgitant orifice can be used confidently to determine forward stroke volume and cardiac output.

Aortic Regurgitation

Excellent correlations were found for the measurements of total stroke volume and regurgitant volume and fraction calculated independently by the quantitative 2-DE method and the Doppler method in patients with AR. These results confirm the previously published data based on a small number of patients and should prompt more frequent use of the quantitative Doppler method as a clinical tool in AR.

Mitrail Regurgitation

In patients with MR, our study identified the pitfall of quantitative Doppler as overestimation of the MA stroke volume compared with LV stroke volume and thus, overestimation of MR severity. Calculation of the regurgitant fraction partially corrects this overestima-

![Figure 6](image1.png)

**FIGURE 6.** Panel A: Correlation for calculated regurgitant volume between Doppler (y-axis) and quantitative two-dimensional echocardiography (ventricle, x-axis) in patients with mitral regurgitation. Dashed line is the identity line; solid line is the regression line; shaded area represents 1 SEE. Panel B: Correlation for calculated regurgitant fraction between Doppler (y-axis) and quantitative two-dimensional echocardiography (ventricle, x-axis). Dashed line is the identity line; solid line is the regression line; shaded area represents 1 SEE.

![Figure 7](image2.png)

**FIGURE 7.** Scatterplot of the difference between Doppler and quantitative two-dimensional echocardiography (ventricle) regurgitant volume on the y-axis and the mean of those two regurgitant volumes on the x-axis. Panel A: The first 27 patients with mitral regurgitation. Panel B: The last 54 patients with mitral regurgitation. Shaded area represents 95% confidence interval; the solid line in the middle of this zone represents the regression line. Dashed line represents the ideal zero difference. These two scatterplots show clearly the decreasing overestimation in the last part of our experience, with disappearance of the systematic trend toward larger overestimation for a higher regurgitant volume by Doppler echocardiography.

<table>
<thead>
<tr>
<th>Table 4. Learning Curve in Mitrail Regurgitation</th>
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<tbody>
<tr>
<td>First 27 patients</td>
</tr>
<tr>
<td>Doppler (MA) 2-DE (LV)</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
</tr>
<tr>
<td>RV (mL)</td>
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<tr>
<td>RF (%)</td>
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<tr>
<td>Overestimation of RV (mL)</td>
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<tr>
<td>Overestimation of RF (%)</td>
</tr>
</tbody>
</table>

MA, mitral annulus; 2-DE, two-dimensional echocardiography; LV, left ventricle; RV, regurgitant volume; RF, regurgitant fraction.
tion because the same overestimated value is present in the numerator and denominator. However, averaged overestimation represents 10 mL per beat of regurgitant volume (or 24% of its value) or 5% of regurgitant fraction (or 16% of its value). This fact probably accounts for a general reluctance to use this method.

The asymmetrical shape of the MA\textsuperscript{20} is an unlikely explanation of the overestimation because in MR the annulus becomes more circular,\textsuperscript{15} and autopsy and four-chamber measurement of MA are very close.\textsuperscript{21}

Doppler MA velocity measurement is probably responsible for the overestimation not only because the flow profile is not flat\textsuperscript{22} but also because of the funnel shape of the mitral valve with increasing velocities from the base to the tip of the leaflets.\textsuperscript{23} An overestimated time–velocity integral results mainly from an improper positioning of the Doppler sample volume. Meticulous positioning of the sample volume at the MA was the key technical factor in the improved accuracy of Doppler in the late phase of our experience.

Many techniques and corrections have been used for mitral stroke volume measurement,\textsuperscript{24–29} but the MA method is simple and accurate after the initial learning phase, allowing quantitative Doppler to be used, in experienced hands, as a clinical tool in MR.

**Regurgitant Volume**

For MR and AR, the regurgitant fraction should be calculated as was recommended earlier.\textsuperscript{10,11} However, the achieved accuracy of Doppler volumetric flow measurements also allows calculation of the regurgitant volume, which is an important variable in assessment of severity of valvular regurgitation.\textsuperscript{30} Its accessibility has not been underscored as well as that of the regurgitant fraction,\textsuperscript{30,11} yet it should provide a better understanding of the pathophysiology of these lesions by noninvasive methods.

**Cross-indexing**

Because of their clinical impact, the data provided by quantitative Doppler echocardiography can be substantiated by 2-DE LV volume measurements,\textsuperscript{31} as was independently done in this series. Other methods of assessment of regurgitation severity\textsuperscript{32–34} are under clinical investigation and could in the future be incorporated into a comprehensive, quantitative assessment of regurgitation severity in the same ultrasound examination to draw sound conclusions and avoid unnecessary “confirmatory angiography.”

**Use of Echocardiographic LV Volumes**

Should we have chosen LV angiography rather than 2-DE LV volume computation as a reference? Limitations of quantitative angiography were demonstrated in previous studies: up to 40% of regurgitant fraction calculated in normal subjects\textsuperscript{19} and 0% regurgitant fraction in patients with documented significant regurgitation.\textsuperscript{35} Thus, although angiography is a clinically useful and well-accepted semiquantitative approach, it cannot be considered as a reference method. In addition, regurgitation severity can vary with several hemodynamic factors.\textsuperscript{30,35} To assess the accuracy of Doppler, it is imperative to measure simultaneously the total LV stroke volume, making 2-DE the ideal method for this purpose. Underestimation of LV volumes by 2-DE has been reported compared with angiography\textsuperscript{36} but was not confirmed with other techniques.\textsuperscript{57–59} Moreover, LVOT stroke volume, which is widely accepted for the measurement of cardiac output\textsuperscript{15,16,40} and aortic valve area,\textsuperscript{41,42} also shows excellent correlations to LV (2-DE) stroke volume. Therefore, we consider the use of 2-DE as an appropriate reference standard in this study and not a limitation.

**Conclusions**

Our study demonstrates that quantitative Doppler assessment of valvular regurgitation can be performed in large numbers of patients in a clinical laboratory. Our data identified the pitfall of quantitative Doppler as overestimation of MR. However, with increased experience, this overestimation became minimal, warranting the use of quantitative Doppler as a clinical tool for the assessment of severity of valvular regurgitations. The most important finding of the present study is that quantitative Doppler can provide not only the regurgitant fraction but also the actual regurgitant volume, which should provide important insight into the clinical understanding of valvular regurgitations.

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