Quantitation of mitral regurgitation by Doppler echocardiography

STEVEN BLUMLEIN, M.D., ALAIN BOUCHARD, M.D., NELSON B. SCHILLER, M.D., MICHAEL DAE, M.D., BENJAMIN F. BYRD III, M.D., THOMAS PORTS, M.D., AND ELIAS H. BOTVINICK, M.D.

ABSTRACT The evaluation and care of patients with mitral regurgitation would be facilitated by an easy, reproducible and noninvasive method that could quantitate the hemodynamic burden. In this study, we describe a new Doppler echocardiographic method that measures the regurgitant fraction and we compare it with angiographic and scintigraphic methods. A total of 27 patients with mitral regurgitation were evaluated by echocardiography and either cardiac catheterization or scintigraphy. With two-dimensional echocardiographic and diastolic and systolic volumes were measured to derive the left ventricular stroke volume (LVSV). The forward stroke volume (FSV) was obtained from the product of M mode-derived aortic valve area and ascending aortic flow velocity integral assessed by continuous-wave Doppler. Regurgitant fraction was calculated as follows: (LVSV - FSV)/LVSV. Comparisons showed that regurgitant fraction calculated by Doppler echocardiography correlated with regurgitant fraction determined by both cardiac catheterization (r = .82) and by scintigraphy (r = .89). There was, however, an important interobserver variability within each method: 10%, 13%, and 11% for Doppler echocardiography, angiography, and scintigraphy, respectively. In conclusion, Doppler echocardiography can be used to quantitate mitral regurgitation. Serial noninvasive determinations of regurgitant fraction may be useful in the evaluation of therapy and in the follow-up of patients with mitral insufficiency.


MITRAL REGURGITATION is a common valvular lesion often leading to excessive ventricular dilatation and dysfunction, and the timing of surgical intervention is frequently difficult and controversial.1-3 In such patients, a major determinant of myocardial size and function is the severity of regurgitation. An accurate noninvasive method for its quantitation would be desirable.

The development of ultrasonic Doppler techniques has permitted noninvasive analysis of the dynamics of intracardiac flow.4,5 By means of pulsed Doppler echocardiography, valvar regurgitation can be identified6-8 with great sensitivity and specificity.9-16 Although the degree of regurgitation can be estimated qualitatively by Doppler mapping of the regurgitant flow in the left atrium, both overestimation and underestimation occur frequently.9,16

At the present time, optimal determination of the severity of valvular regurgitation requires angiographic quantitation of regurgitant flow. This is based on a comparison of left ventricular stroke volume, determined by biplane angiography, and forward flow, determined by the Fick or indicator dilution technique. In this report we describe the application of a new noninvasive Doppler echocardiographic method for quantitation of mitral regurgitation. The method compares the left ventricular stroke volume, obtained from biplane two-dimensional echocardiograms, with forward stroke volume, determined from the integral of the blood flow velocity in the ascending aorta obtained by continuous-wave Doppler and aortic valve area obtained by M mode echocardiography. The volume of regurgitation expressed as regurgitant fraction was compared with that measured at angiography and by the scintigraphic method.

Methods

Patient selection. From September 1983 through February 1985, 12 consecutive patients referred for evaluation of mitral
regurgitation were examined within a 24 hr period by both echocardiographic and scintigraphic methods. In the same period, 18 consecutive patients who were found to have mitral regurgitation at cardiac catheterization were studied in our Doppler/echocardiography laboratory before the institution of medical or surgical therapy. Two patients were excluded because of technically poor left ventricular angiograms and one patient had both scintigraphic and angiographic studies. The final study group consisted of 27 patients (17 women and 10 men, ages 23 to 72 years) with the following diagnoses: mitral valve prolapse, congestive cardiomyopathy, ischemic heart disease, bacterial endocarditis, and prosthetic valve dysfunction. Three patients were in atrial fibrillation and the rest were in normal sinus rhythm. During the same period, 24 controls (eight women and 16 men, ages 25 to 78 years) investigated invasively for suspected coronary disease and who were free of mitral regurgitation were similarly studied in our laboratory within 24 hr of catheterization. Patients with aortic or subaortic valvular abnormalities were excluded from the study. These included patients with aortic stenosis or sclerosis, subaortic stenosis, and prosthetic aortic valves. Patients with aortic regurgitation alone were not excluded.

Quantitation of regurgitation

Scintigraphy. Equilibrium blood pool scintigrams were acquired on a standard, 37 phototube Searle Pho-gamma 5 scintillation camera with a linear, all-purpose 20 degree slant-hole collimator and processed on a PDP 11/40 minicomputer. Patients were imaged in the anterior, "best septal" left anterior oblique, and 70 degree left anterior oblique projections. Data were acquired in 28 frames and displayed in a 64 × 64 matrix, interpolated to a 128 × 128 format, smoothed, and viewed on a high-quality De Anza display with 256 gray shades. In each study, phase-amplitude analysis was performed, with the fundamental Fourier harmonic applied to the first 25 frames of the blood pool study according to our standard method. Briefly, amplitude images from the "best septal" left anterior oblique projection were used to determine the ratio of left ventricular amplitude to right ventricular amplitude. This ratio was corrected for the intrinsic underestimation of right ventricular amplitude caused by overlap of the right atrium. The difference between the exposed areas of the right atrium from the anterior projection, where overlap is minimal, and the "best septal" left anterior oblique projection was determined and multiplied by the mean amplitude (amplitude/pixel) of the right atrium in the same "best septal" projection. This value is then added to the original right ventricular amplitude to get the new corrected value (figure 1). The left ventricular stroke counts (LVSC) were expressed as a percentage of the right ventricular stroke counts (RVSC) and termed the "regurgitant index" (i.e., LVSC/RVSC). The regurgitant fraction (percentage of stroke volume moving retrograde through the mitral valve) was calculated as follows:

\[
\text{regurgitant fraction} = \frac{\text{regurgitant index} - 1}{\text{regurgitant index}}
\]

The method applied has been shown in a prior study to have very low intraobserver and interobserver variability while correcting for atrial overlap. This correction yields an index close to unity in patients without regurgitation.

Catheterization. At cardiac catheterization cardiac outputs were measured with a pulmonary arterial catheter by the thermodilution technique. The cardiac output was taken as the mean of three determinations that varied by less than 10%. The forward stroke volume (FSV) was obtained by dividing this cardiac output by the heart rate. With a No. 8F Cordis pigtail catheter advanced percutaneously into the left ventricle, biplane ventriculography (30 degrees right anterior oblique and 60 degrees left anterior oblique) was performed with meglumine diatrizoate (Renografin 76). The angiographic stroke volume (SV) was measured with a light-pen system using biplane Simpson's rule. Sinus beats were always used except in patients in atrial fibrillation when at least five cardiac cycles were averaged. Subjects with atrial fibrillation who were included in this study had a slow and relatively regular rate, so that beat-to-beat variations in volume would be expected to be minimal. The mitral valvular regurgitant flow was determined by relating mean left ventricular stroke volume calculated from the angiograms to mean forward flow per beat determined by the thermodilution method. The regurgitant fraction was calculated as follows:

\[
\text{regurgitant fraction}_{\text{cath}} = \frac{\text{SV} - \text{FSV}}{\text{SV}}
\]

Echocardiography. Two-dimensional echocardiograms were recorded with commercially available phased-array two-dimensional echocardiographs using a variety of standard transducers. During all recordings a simultaneous electrocardiogram and second left intercostal space phonocardiogram were displayed. One gating signal was affixed to the peak of the R wave to mark end-diastole and a second to the first component of the second heart sound to mark end-systole. When the phonocardiogram was unsuitable for gating, the end of the T wave was used as a marker for end-systole. Field-by-field analysis fixed the exact identity of end-systole by using the field just before mitral opening. Almost all echocardiographic recordings produced for later off-line analysis were acquired in a "flip-flop" mode. That is, only two frames were acquired for analysis from each beat, end-diastole and end-systole. Before a segment was recorded for later analysis, the chamber to be recorded was "maximized" by the technician. This process consisted of small increments.
and the volume of the aortic valve was recorded. When the walls of the aorta appeared to move in a parallel fashion, a recording was made from which the distance between the aortic leaflets was measured at the tip of the valve from the trailing edge of the right coronary cusp to the leading edge of the noncoronary cusp (figure 2). The aortic orifice is roughly circular during that period and its area is computed from the M mode measurements as: (AVA = \pi \times AVd^2/4), where AVA = aortic valve area and AVd = aortic valve diameter. All recordings were acquired with the patient in a steep left recumbency during suspended respiration.

Each two-dimensional echocardiogram was measured by one of two investigators or by both using a microprocessor-controlled light-pen digitizing system previously described.\(^{21}\) In brief, the ventricular endocardial outline at both systole and diastole was traced so as to cover the endocardial inner border with the computer-generated line (figure 3A). Surface irregularities were smoothed and dropout gaps bridged. In no case did the traced outline extend beyond the border of the fan-shaped video display (i.e., no extrapolations were made). Papillary muscles were treated as part of the cavitary contents and not as a portion of the myocardial wall. In patients with normal sinus rhythm, an average of three measurements was taken; in patients with atrial fibrillation, an average of six measurements at different RR intervals was taken.

**Doppler.** Doppler aortic blood flow velocity measurements were made with a spectrum analyzer–based, Doppler velocimeter (Irex Corp.). Flow velocity patterns and an electrocardiographic tracing were displayed in real time at a 50 mm/sec sweep speed and recorded on glossy black-on-white electrostatic paper also at the same speed. Blood flow through the aortic valve was studied with a 2.25 MHZ independent Pedoff transducer positioned sequentially at the apex with the patient in a steep left lateral decubitus position, at the suprasternal notch with the patient in the dorsal decubitus position, and in the second or third right parasternal space with the patient in a steep right recumbency. Continuous-wave Doppler was used and the transducer was angulated until Doppler flow velocity signals were obtained. The maximum velocity was identified by listening to the audio signal from the Doppler velocimeter and

**FIGURE 3A.** Representative apical two- and four-chamber views (systole on the right) of a patient with mitral regurgitation. Those images were planimetered with a light pen system and the computer derived left ventricular stroke volume was 138 ml.
by noting the peak velocity from the tracing visualized on the oscilloscope screen. The velocity signals from the three positions were compared and the position that gave the maximum velocity was used in all calculations. The area under the flow velocity curve or flow velocity integral was electronically planimetered with a light-pen system. The smooth outer edge was outlined excluding spikes from the tracing. Each measurement was calibrated for 1 m/sec (vertical axis) and for 1 sec (horizontal axis). In patients with normal sinus rhythm, an average of three maximal velocities was taken. In patients with rhythm disturbances the average of 10 consecutive, well-defined velocities was taken. The flow velocity integral has units of length and represents the distance that a column of blood moves through the aortic valve during systole. The forward stroke volume (FSV_Dop) is calculated by taking the product of this distance with the aortic valve area (figure 2 and figure 3B).

**Regurgitant fraction.** The mitral valvular regurgitant fraction was determined by relating the mean left ventricular stroke volume calculated from the two-dimensional echocardiograms (LVSV_ECHO) to the mean forward stroke volume determined by continuous-wave Doppler of aortic velocity and M mode of aortic valve area (FSV_Dop):

\[
\text{regurgitant fraction} = \frac{\text{LVSV}_{\text{ECHO}} - \text{FSV}_{\text{Dop}}}{\text{LVSV}_{\text{ECHO}}}
\]

**FIGURE 3B.** M mode aortic valve and the continuous-wave Doppler velocity tracing (open arrow) from the same patient. The aortic valve area \((4.15 \text{ cm}^2)\) times the velocity integral \((16.38 \text{ cm})\) resulted in a forward stroke volume of 68 ml. The calculated regurgitant fraction was then 51% \([(138 - 68)/138]\).

**Data analysis.** Aortic valve measurements, planimetry of the Doppler signal, and the echocardiographic volume measurements were made independently. The catheterization and the scintigraphic data were compiled separately by different observers from unpaired samples so that all data acquisition was done in a blinded fashion. The regurgitant fraction determined by echocardiography/Doppler was compared with the regurgitant fraction obtained by scintigraphy or cardiac catheterization by linear regression analysis. To evaluate the scatter between Doppler and catheterization stroke volume and regurgitant fraction and between Doppler and scintigraphic regurgitant fraction, the mean and standard deviation of paired differences between individual measurements were calculated and expressed as absolute values (milliliters for stroke volume and percent for regurgitant fraction).

**Observer variability.** To determine the intraobserver and interobserver variability in the measurement of regurgitant fraction by Doppler echocardiography, a random sample of eight studies was reanalyzed by the same observer and 11 studies by a second observer, both blinded to the result of the former analysis and the result of the cardiac catheterization or scintigraphy. To test interobserver variability within the angiographic and the scintigraphic methods, all measurements were repeated by a second observer. This variability was expressed as the standard deviation of the difference in the paired measurements.

**Results**

Figure 2 illustrates how regurgitant fraction is derived from the Doppler and echocardiographic data of a patient with mitral regurgitation.

Tables 1 and 2 list the data obtained for each of the patients studied. The differences between the mean heart rate and mean systolic blood pressure during the echocardiographic and the scintigraphic examination were not statistically significant: 76 ± 20 vs 80 ± 22 beats/min for heart rate and 115 ± 13 vs 118 ± 24 mm Hg for blood pressure. However, during the cardiac catheterization, the mean heart rate and systolic blood pressure were higher than those during the echocardiographic examination: 88 ± 19 vs 79 ± 19 beats/min (p < .025) for heart rate and 135 ± 25 vs 129 ± 20 mm Hg (p < .025) for systolic blood pressure.

Figure 4 illustrates the echocardiographic measurements of the left ventricular end-diastolic volume, end-systolic volume, and stroke volume plotted against those measured by angiography. There was poor correlation between stroke volume measured by echocardiography and angiography \((r = .48, \text{ SEE } = 19 \text{ ml})\). The mean echocardiographic stroke volume was 94 ml (range 52 to 125) and the mean angiographic stroke volume was 104 ml (range 44 to 180). Overall, when compared with angiography, two-dimensional echocardiography underestimated left ventricular end-diastolic volume by 18 ± 31 ml and left ventricular stroke volume by 10 ± 27 ml.

Figure 5 illustrates the correlation between forward stroke volume measured by Doppler and by thermodilution \((r = .88, \text{ SEE } = 10 \text{ ml})\). The mean forward...
**TABLE 1**
Clinical features and echocardiographic/Doppler measurements in patients who had undergone cardiac catheterization

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>2D Echo</th>
<th>Doppler</th>
<th>Angiography</th>
<th>Thermodilution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LVEDV (CC)</td>
<td>SV (CC)</td>
<td>FSV (CC) RF</td>
<td>LVEDV (CC)</td>
</tr>
<tr>
<td>1</td>
<td>28</td>
<td>F</td>
<td>RHD, MR, CHF</td>
<td>180</td>
<td>111</td>
<td>51</td>
<td>220</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>M</td>
<td>MVP, SBE, MR, CHF</td>
<td>191</td>
<td>125</td>
<td>24</td>
<td>239</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>F</td>
<td>RHD, MR, CHF</td>
<td>137</td>
<td>76</td>
<td>29</td>
<td>156</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>M</td>
<td>RHD, MS, MR, CHF</td>
<td>168</td>
<td>86</td>
<td>61</td>
<td>191</td>
</tr>
<tr>
<td>5</td>
<td>39</td>
<td>M</td>
<td>IHD, CHF, MR</td>
<td>234</td>
<td>98</td>
<td>81</td>
<td>256</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>M</td>
<td>CM, MR</td>
<td>69</td>
<td>52</td>
<td>34</td>
<td>113</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>M</td>
<td>IHD, MR, TR, PR, An</td>
<td>303</td>
<td>116</td>
<td>62</td>
<td>318</td>
</tr>
<tr>
<td>8</td>
<td>72</td>
<td>F</td>
<td>MS, MR, TR</td>
<td>88</td>
<td>64</td>
<td>72</td>
<td>159</td>
</tr>
<tr>
<td>9</td>
<td>51</td>
<td>F</td>
<td>RHD, MS, MR</td>
<td>177</td>
<td>124</td>
<td>63</td>
<td>122</td>
</tr>
<tr>
<td>10</td>
<td>56</td>
<td>F</td>
<td>RHD, MS, MR</td>
<td>175</td>
<td>124</td>
<td>63</td>
<td>122</td>
</tr>
<tr>
<td>11</td>
<td>32</td>
<td>M</td>
<td>PVD</td>
<td>111</td>
<td>73</td>
<td>68</td>
<td>151</td>
</tr>
<tr>
<td>12</td>
<td>60</td>
<td>F</td>
<td>RHD, MS, MR</td>
<td>210</td>
<td>89</td>
<td>15</td>
<td>266</td>
</tr>
<tr>
<td>13</td>
<td>23</td>
<td>F</td>
<td>RHD, MS, MR, TR</td>
<td>166</td>
<td>111</td>
<td>73</td>
<td>187</td>
</tr>
<tr>
<td>14</td>
<td>34</td>
<td>F</td>
<td>RHD, MR</td>
<td>101</td>
<td>60</td>
<td>38</td>
<td>57</td>
</tr>
<tr>
<td>15</td>
<td>40</td>
<td>F</td>
<td>RHD, MR</td>
<td>170</td>
<td>81</td>
<td>38</td>
<td>201</td>
</tr>
<tr>
<td>16</td>
<td>42</td>
<td>M</td>
<td>RHD, MS, MR</td>
<td>164</td>
<td>104</td>
<td>67</td>
<td>193</td>
</tr>
</tbody>
</table>

LVEDV = left ventricular end-diastolic volume; SV = stroke volume; FSV = forward stroke volume; RF = regurgitant fraction; RHD = rheumatic heart disease; CHF = congestive heart failure; MR = mitral regurgitation; MVP = mitral valve prolapse; SBE = subacute bacterial endocarditis; MS = mitral stenosis; IHD = ischemic heart disease; CM = cardiomyopathy (idiopathic); TR = tricuspid regurgitation; PR = pulmonic regurgitation; An = LV aneurysm; PVD = prosthetic valve dysfunction.

Patients in atrial fibrillation.

stroke volume was 51 ± 20 ml (range 15 to 81) by Doppler and 55 ± 22 ml (range 27 to 94) (p = NS) by thermodilution. The largest discrepancy between forward stroke volumes measured by these two methods was 18 ml. When compared with thermodilution, forward stroke volume measured by Doppler was under-estimated by a mean of 4 ± 10 ml. In the 24 control patients, the correlation coefficient and SEE between Doppler (FSV\textsubscript{Dop}) and thermodilution stroke volume (FSV\textsubscript{id}) were .94 and 9 ml, respectively, and the equation for the regression line was FSV\textsubscript{Dop} = .87 \times FSV\textsubscript{id} + 13.2. The mean Doppler stroke volume was slightly

**TABLE 2**
Clinical features and echocardiographic/Doppler measurements in patients who had undergone scintigraphy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>CHF</th>
<th>2D Echo</th>
<th>Doppler</th>
<th>Scintigraphy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LVEDV (CC)</td>
<td>SV (CC)</td>
<td>FSV (CC) RF</td>
</tr>
<tr>
<td>1</td>
<td>40</td>
<td>F</td>
<td>RHD, MR</td>
<td>170</td>
<td>81</td>
<td>38</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>M</td>
<td>IHD, MR</td>
<td>150</td>
<td>88</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>M</td>
<td>CM*, CHF, MR</td>
<td>229</td>
<td>69</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>F</td>
<td>CM*, MR</td>
<td>113</td>
<td>65</td>
<td>49</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>F</td>
<td>RHD, MS, MR, TR</td>
<td>166</td>
<td>111</td>
<td>73</td>
</tr>
<tr>
<td>6</td>
<td>59</td>
<td>M</td>
<td>CHF, MR, Ch</td>
<td>127</td>
<td>97</td>
<td>39</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>M</td>
<td>CM, MR</td>
<td>296</td>
<td>81</td>
<td>49</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>F</td>
<td>RHD, MS, MR</td>
<td>140</td>
<td>103</td>
<td>57</td>
</tr>
<tr>
<td>9</td>
<td>66</td>
<td>F</td>
<td>MR, RHD</td>
<td>117</td>
<td>87</td>
<td>53</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>F</td>
<td>IHD, CHF, MR</td>
<td>200</td>
<td>90</td>
<td>47</td>
</tr>
<tr>
<td>11</td>
<td>56</td>
<td>F</td>
<td>RHD, MC, MS, MR, TR, IHD</td>
<td>175</td>
<td>124</td>
<td>63</td>
</tr>
<tr>
<td>12</td>
<td>68</td>
<td>F</td>
<td>Ch</td>
<td>234</td>
<td>171</td>
<td>42</td>
</tr>
</tbody>
</table>

RI = regurgitant index; U = uncorrected; C = corrected for right atrium; CM* = cardiomyopathy (Adriamycin); Ch = ruptured chordae tendineae; MC = mitral commissurotomy; other abbreviations as in table 1.
higher than the stroke volume calculated by thermodilution: 81 ± 26 ml (range 30 to 137) vs 77 ± 28 ml (range 30 to 148) (p = NS).

The correlation coefficient between regurgitant fraction measured by Doppler echocardiography and angiography was .82 (figure 6, A). The mean regurgitant fraction by Doppler echocardiography was 44 ± 24%, slightly lower than the angiographic regurgitant fraction (mean 47 ± 19%) (p = NS). The correlation coefficient between Doppler echocardiographic and scintigraphic regurgitant fraction was .89 and the SEE was 9%. The regression equation is shown in figure 6, B. The mean regurgitant fraction was 39 ± 19% by echocardiography/Doppler and 38 ± 16% (p = NS) by scintigraphy. In three patients with ejection fractions of less than 40% as determined by scintigraphy, there was good agreement between Doppler and scintigraphic regurgitant fraction (See table 2). Two patients had tricuspid regurgitation detected by Doppler (patients 5 and 11). Patient 5 had also cardiac catheterization that revealed a regurgitant fraction of 48% and correlated better with scintigraphic (52%) than with Doppler regurgitant fraction (34%).

Among the 24 control subjects who had Doppler examination and cardiac catheterization, 14 had twodimensional echocardiographic studies. Comparing the stroke volume obtained by echocardiography and Doppler, seven patients had a mean calculated regurgitant fraction of 5% (range 1% to 10%). The average calculated regurgitant fraction for the group was 2.5 ± 5%.

Observer variability. The standard deviation of the difference in the paired measurements of regurgitation for each method is listed in table 3. For the Doppler/echocardiographic method, the largest discrepancy of regurgitant fraction measured by the same observer and by two observers was 12% and 19%, respectively. The largest interobserver differences for the scintigraphic and angiographic methods were 28% and 33%, respectively.

Discussion

Doppler echocardiography potentially has a prime role in the diagnosis and the follow-up of patients with mitral regurgitation because it is a safe, noninvasive, and reproducible method of evaluating changes in both ventricular volume and ventricular function. Since the severity of regurgitation is an important determinant of prognosis in patients with aortic and probably mitral insufficiency, quantitation of regurgitant fraction

Vol. 74, No. 2, August 1986
FIGURE 6. Correlation between the regurgitant fraction (RF) calculated by echocardiography/Doppler and cardiac catheterization (A) and between echocardiography/Doppler and scintigraphy (B). There is a significant SEE between each comparison. Note also the tendency of echocardiography/Doppler for underestimating regurgitant fraction.

would be a useful addition to the volume criteria used in the follow-up of these patients.

However, the severity of valvular insufficiency is difficult to assess. Most of the ultrasonic studies have used pulsed Doppler to assess the regurgitant lesion qualitatively compared with ventriculography. Using a rating of mild, moderate, and severe, Pearlman et al.\textsuperscript{16} classified correctly by pulsed Doppler approximately 50% of patients with moderate regurgitation. Abbasi et al.,\textsuperscript{9} using a 0 to 4 + scale to describe severity of mitral regurgitation, found agreement between pulsed Doppler and ventriculography in 14 of 21 patients (66%).

In this study, we determined the mitral regurgitant fraction with a new Doppler method of measuring forward stroke volume. A continuous-wave Doppler beam is passed through the aortic valve from different positions and the tracing with maximum velocity is used for calculating the stroke volume. Because the maximal velocity occurs at the narrowest portion of the left ventricular outflow tract, we used the diameter of the aortic valve opening to calculate the forward stroke volume (patients with irregular aortic valve orifices in systole must be excluded for this method to be valid). In other work we have documented the accuracy of this technique compared with thermodilution.\textsuperscript{23} In the 16 patients with mitral regurgitation evaluated by cardiac catheterization, the correlation coefficient between Doppler and thermodilution forward stroke volume was .88 (SEE = 10 ml) with minimal underestimation by Doppler (mean of 4 ± 10 ml). In our controls, however, there was a better agreement between stroke volume obtained by Doppler and that determined by thermodilution. This may be attributed to the temporal delay allowed between the two studies in patients with mitral regurgitation. The possibility of bias is very unlikely because each measurement (Doppler, echocardiographic, and thermodilution stroke volume) was analyzed by different observers without knowledge of the results of the other tests.

The left ventricular stroke volume (forward plus regurgitant volume) obtained by two-dimensional echocardiography correlated poorly with that obtained by angiography (r = .48) (figure 4). An explanation for this may be that for both methods the stroke volume was calculated from the diastolic and systolic volumes; it was not measured directly. The inherent errors in measuring these volumes are compounded when the systolic is subtracted from the diastolic volume. The major error resides in the calculation of left ventricular end-diastolic volumes. Because it is more difficult to outline the endocardium in diastole, the measured left ventricular end-diastolic volume is underestimated (mean of 18 ± 31 ml in this study). If we subtracted

<table>
<thead>
<tr>
<th>Method</th>
<th>Standard deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler echocardiography</td>
<td></td>
</tr>
<tr>
<td>Intraobserver</td>
<td>8</td>
</tr>
<tr>
<td>Interobserver</td>
<td>10</td>
</tr>
<tr>
<td>Angiography</td>
<td></td>
</tr>
<tr>
<td>Interobserver</td>
<td>13</td>
</tr>
<tr>
<td>Scintigraphy</td>
<td></td>
</tr>
<tr>
<td>Interobserver</td>
<td>11</td>
</tr>
</tbody>
</table>
from this volume a more accurate left ventricular systolic volume, the resulting stroke volume would be underestimated. In this study, the mean underestimation was 10 ± 27 ml and in one case it was as high as 55 ml. Significant underestimations of left ventricular stroke volume (>30 ml) occurred in five patients (table 1; patients 2, 3, 6, 9, and 8) and can be explained by the underestimation of the left ventricular end-diastolic volume by two-dimensional echocardiography. The first four patients had very severe mitral regurgitation with very small forward stroke volume; therefore the underestimation of left ventricular stroke volume did not influence significantly the calculation of regurgitant fraction. Patient 8 had an L-shaped left ventricle, which explained the underestimation of left ventricular stroke volume and echocardiographic regurgitant fraction. In one case (patient 10), the left ventricular stroke volume and regurgitant fraction were significantly lower at cardiac catheterization. This may be due in part to differences in heart rate and systolic blood pressures between the two studies: 64 and 110 mm Hg during the noninvasive examination and 106 and 100 mm Hg during cardiac catheterization.

In this study, the mean forward stroke volume and left ventricular stroke volume were underestimated when compared with catheterization data (echocardiography by a mean 10 ± 27 ml and Doppler by a mean 4 ± 10 ml) and the resulting regurgitant fraction was underestimated by a mean of 2 ± 14%. This difference is not significant if one considers the interobserver variability related to each method (Doppler echocardiography and cardiac catheterization).

Cardiac catheterization is not without problems, since the difference between total left ventricular stroke volume from biplane angiograms and forward stroke volume by the Fick or indicator dilution method is often off by ± 20%. However, we preferred to compare regurgitant fraction26 instead of using the 0 to 4+ scale of severity because the latter is too subjective and also can be influenced by technical problems such as inadequate mixing of blood and contrast material in the ventricle, catheter position, premature ventricular contractions, diastolic regurgitation, and chamber size.

Because of these problems, we decided to study patients undergoing scintigraphic determination of mitral regurgitant fraction. The correlation coefficient between Doppler echocardiographic and scintigraphic regurgitant fraction was .89 (SEE = 9%). The largest discrepancy between the two studies was 18%. The effect of tricuspid regurgitation on the scintigraphic calculation of mitral regurgitant fraction cannot be inferred from this study because we had only two patients with tricuspid insufficiency. However, one would predict that scintigraphy would underestimate or calculate a negative LVS/RVS ratio in the case of severe tricuspid regurgitation. Furthermore, in this study, low ejection fraction did not influence the correlation between Doppler and scintigraphic regurgitant fraction.

Our ultrasonic studies were performed before medical therapy was altered or changes in the clinical status occurred. In most patients heart rate and blood pressure did not vary significantly between the studies, and in only one case it was of sufficient magnitude to alter the regurgitant fraction. Most of the variability in measuring regurgitant fraction is attributed to the method of ventricular volume calculation. Some of the variability can also be attributed to measurement of forward stroke volume. The intraobserver and interobserver variability in measuring regurgitant fraction by Doppler echocardiography was 8% and 10%, respectively, which is comparable to the variability of angiographic (13%) and scintigraphic methods (11%). The calculation of regurgitant fraction by Doppler echocardiography is relatively simple and can be easily done within 10 min.

The study population should be representative of the mitral regurgitation population in general. No patients were excluded from analysis on the basis of poor-quality echocardiograms, and our population included patients with a wide range of left ventricular end-diastolic dimensions (159 to 309 ml by angiography) and regurgitant fractions (13% to 78% by cardiac catheterization). Few patients with atrial fibrillation and moderate ventricular response were studied. Although we feel confident that the calculation of regurgitant fraction by Doppler echocardiography is relatively accurate and reproducible in patients with controlled ventricular response, additional studies are needed to validate this method in patients with atrial fibrillation.

The quantitation of regurgitant fraction does not discriminate well between control subjects and patients with mild mitral regurgitation. In this study group, the maximal calculated regurgitant fraction in the normal controls was 10%; however, in our clinical experience, regurgitant fractions up to 20% can be calculated in patients with absence of mitral regurgitation on pulsed Doppler. When such a situation arises clinically, it is easy to use range-gated pulsed Doppler with the sample volume just proximal to the mitral valve to check qualitatively for the presence of mitral regurgitation. Sorensen et al.25 found a mean regurgitant fraction of 1 ± 11% by scintigraphy in 20 control patients and a
mean regurgitant fraction of $7 \pm 17\%$ (angiographic/ Fick output or dye-dilution) in 10 normal subjects who underwent cardiac catheterization. Therefore, one should not consider regurgitant fraction as an isolated or independent evaluation of mitral regurgitation but rather as a useful addition to other means of assessment (clinical findings, pulsed Doppler or contrast angiography, and other complementary tools of quantitation).

The major limitation of this method is the exclusion of patients with aortic stenosis or sclerosis, aortic valve protheses, or subaortic stenosis. These patients either have an aortic valve diameter difficult to measure or have a disturbance of flow that would overestimate forward stroke volume. These conditions, however, do not preclude qualitative assessment by pulsed Doppler or scintigraphic evaluation. In patients with aortic regurgitation, it is not possible to quantitate the mitral regurgitant fraction by catheterization or scintigraphy. However, if the aortic valve behaves normally in systole, then quantitation of mitral regurgitation with our Doppler echocardiographic method is possible.

Clinical implications. Patients with moderate and severe mitral regurgitation should be followed carefully. The prognosis of these patients is probably related to the amount of regurgitation and the ventricular “tolerance” to it. Calculation of regurgitant fraction may prove to be useful in the timing of surgery in a certain group of patients who have not yet reached critical ventricular volume dilatation and decreased ventricular function. Determination of regurgitant fraction may also be helpful in evaluating the therapeutic effect of a drug regimen. These objectives can be best fulfilled by a noninvasive method that can serially and reproducibly assess regurgitant fraction, ventricular volumes, and ejection fraction. Our study demonstrates that Doppler echocardiography is capable of quantitatively evaluating these patients with mitral regurgitation.

References

Quantitation of mitral regurgitation by Doppler echocardiography.
S Blumlein, A Bouchard, N B Schiller, M Dae, B F Byrd, 3rd, T Ports and E H Botvinick

Circulation. 1986;74:306-314
doi: 10.1161/01.CIR.74.2.306

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/74/2/306

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/