Peak Filling Rate Normalized to Mitral Stroke Volume: A New Doppler Echocardiographic Filling Index Validated by Radionuclide Angiographic Techniques

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The noninvasive measurement of left ventricular filling has relied predominantly on radionuclide-derived peak filling rate normalized to end-diastolic volume. Doppler echocardiography also has the ability to measure peak filling rate, but wide application of this technique has been limited by technical errors involved in quantitative echocardiographic determination of mitral anulus cross-sectional area and ventricular volumes.

For Doppler echocardiography, normalization of peak filling rate to mitral stroke volume rather than end-diastolic volume permits the derivation of a diastolic filling index that is relatively free of errors caused by geometric assumptions, diameter measurements, and sample volume positioning. This normalization process can be achieved by simply dividing early peak filling velocity by the time velocity integral of mitral inflow.

To validate this new Doppler echocardiographic filling index, Doppler echocardiographic and radionuclide-derived peak filling rate, both normalized to mitral stroke volume, were compared in 30 patients; there was an excellent correlation ($r = 0.91, \text{SEE} = 0.86$). This variable was not influenced by the position of the sample volume in relation to the mitral apparatus in contrast to early filling velocity, which increased 37%, and early/late filling (E/A) ratio, which increased 43% as the sample volume was moved from the anulus to the tips of the mitral leaflets. In a cohort of 22 normal patients, the mean peak filling rate normalized to mitral stroke volume (SV) was $5.25 \pm 1.47$ SV/s. The mean peak filling rate for a subgroup of eight normal patients aged 57 to 89 years (mean 71 ± 9) was $3.9 \pm 1$ SV/s.

In conclusion, normalization of peak filling rate to mitral stroke volume minimizes technical errors involved in measuring Doppler echocardiographic peak filling rate, in the same fashion that normalization to end-diastolic volume minimizes technical errors involved in radionuclide angiographic measurement of peak filling rate. For this reason, peak filling rate normalized to mitral stroke volume may provide a more reliable and reproducible method for assessing left ventricular filling. Further studies are required to assess the clinical relevance of this new index.

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With the realization that measurement of diastolic function provides important complementary information to traditional indexes of systolic function (1–4), increasing interest is being shown in the noninvasive measurement of left ventricular filling by Doppler echocardiography (5–7) and radionuclide angiography (8–12). The most extensively studied filling variable utilized by these techniques is peak filling rate, which has been demonstrated to be a useful index for evaluating diastolic function and for assessing the effect of therapeutic interventions (10–12).

By convention, radionuclide peak filling rate has been normalized to end-diastolic volume to derive a filling index that eliminates errors involved in converting counts to absolute volume. Doppler echocardiographic peak filling rate can be normalized to end-diastolic volume (5 6) or can be expressed in absolute volume (5.6). Both of these methods, however, have limitations. Expression of peak filling rate in absolute volume does not account for cardiac output and involves errors relating to measurement of the mitral anulus cross-sectional area (5–7). Normalization to end-diastolic volume propagates these errors because of further diameter measurements and geometric assumptions regard-
ing ventricular volumes (5). These inherent methodologic problems have resulted in difficulty in selecting the most appropriate Doppler echocardiographic method for the non-invasive measurement of peak filling rate and poor correlations when Doppler echocardiographic- and radionuclide-derived peak filling rate are compared (6).

To overcome these problems, we propose that Doppler echocardiographically derived peak filling rate should be normalized to mitral stroke volume. This normalization process overcomes a major technical obstacle by eliminating errors involved in diameter measurements and geometric assumptions and derives an index that takes into account the integrated diastolic mitral flow velocity. The purpose of this study was to validate a method for deriving Doppler echocardiographic peak filling rate normalized to mitral stroke volume and to examine the potential advantages of this normalization process for Doppler echocardiographic- and radionuclide-derived peak filling rate.

Methods

Study patients. The study group consisted of 30 consecutive patients undergoing routine equilibrium radionuclide angiography for assessment of cardiac function. Patients with aortic regurgitation and patients not in sinus rhythm were excluded. The mean age was 62 ± 12 years and mean radionuclide ejection fraction was 52 ± 18% (range 5 to 74).

The Doppler echocardiographic study was performed immediately before the radionuclide study in all patients. The clinical indications for the study were assessment of hypertension in 6 patients, ischemic heart disease in 12, cardiomyopathy in 2, adriamycin therapy in 4, pulmonary edema in 2, aortic stenosis in 1, arrhythmias in 2 and chronic renal failure in 1.

To determine the normal range of values for peak filling rate normalized to mitral stroke volume and to assess the influence of age on this variable, we examined an additional 22 clinically normal patients (mean age 46 ± 21 years, range 18 to 89) with the use of two-dimensional Doppler echocardiography. Of the 22 normal patients, 12 were normal volunteers and 10 were outpatients referred for two-dimensional echocardiography. The clinical indications for the echocardiogram in the 10 outpatients were exclusion of mitral valve prolapse in 3, syncope in 2, assessment of valvular function in 3, presence of exclusion of endocarditis in 1 and presence of transient ischemic attack in 1. All of the patients had normal two-dimensional and Doppler echocardiograms. None of the normal patients had symptoms of dyspnea or angina.

Derivation of the formula for Doppler echocardiographic peak filling rate normalized to mitral stroke volume. Absolute peak filling rate (PFR) can be derived by multiplying early peak filling velocity (V) by mitral anulus cross-sectional area (CSA). i.e.,

\[ \text{PFR (mL/s)} = V \times \text{CSA} \times \text{TVI} \]

where TVI = time-velocity integral of mitral inflow. After cancellation of terms,

\[ \text{PFR (mL/s)} = \frac{V \times \text{CSA}}{\text{TVI}} \]

To derive peak filling rate normalized to mitral stroke volume, absolute peak filling rate is divided by mitral stroke volume (SV)

\[ \text{PFR (SV/s)} = \frac{V \times \text{CSA}}{\text{SV}} \]

where

\[ \text{SV} = \text{CSA} \times \int_{t1}^{t2} V \, dt \]

Because

\[ \text{TVI} = \frac{\int_{t1}^{t2} V \, dt}{\text{CSA}} \]

where TVI = time-velocity integral of mitral inflow. After cancellation of terms,

\[ \text{PFR (SV/s)} = \frac{V}{\text{TVI}} \times \text{CSA} \]

Doppler examination. The ultrasound examination was performed with a Hewlett-Packard (model 77020A) Doppler imaging system and was separately analyzed by an operator unaware of the radionuclide results. For Doppler measurement of peak filling rate an apical four chamber view was obtained. The sample volume was positioned at the level of the mitral anulus and aligned so that the angle between the ultrasound beam and the blood flow vector was as close to zero as possible. The mitral anulus diameter was measured at the insertion of the anterior and posterior mitral leaflets and cross-sectional area calculated assuming a circular shape of the anulus (13). The sample volume (5 mm in length) was positioned at the level of the mitral anulus and mitral inflow velocity curves were recorded on videotape at 100 mm/s. Velocity curves from 5 cycles were traced after the most intense portion of the velocity profile and the areas were determined by planimetry and averaged with use of an off-line computer system.

Peak filling rate was derived in absolute terms and was also normalized to mitral stroke volume for comparison with radionuclide angiography. Early peak filling velocity was identified as the maximal deflection in the velocity profile before the onset of atrial contraction (Fig. 1). Late peak filling velocity was defined as the maximal deflection after diastasis occurring in the second half of diastole. Absolute peak filling rate, in milliliters per second, was derived using equation 1. Peak filling rate normalized to mitral stroke volume was derived using equation 5. The ratio of early and
late peak filling velocity (E/A ratio) was derived by dividing early by late peak filling velocity.

To assess the influence of sample volume position on mitral inflow velocities, 10 patients (mean age 52 ± 22 years) with an echocardiographically normal mitral valve were examined. Five of these patients were normal, two had aortic stenosis, two had ischemic heart disease and one had concentric left ventricular hypertrophy. The sample volume was positioned at the plane of the mitral anulus and velocity curves recorded. The sample volume was then moved to the tips of the mitral leaflets and velocity curves again recorded. Peak filling rate normalized to mitral stroke volume, E/A ratio and early peak velocity were calculated from an average of five velocity profiles at the two different positions.

Radionuclide derivation of peak filling rate. Radionuclide angiography was performed on all patients with use of standard in vivo-in vitro red blood cell labeling techniques. Gated list mode studies were acquired on 15 patients and frame mode studies were acquired on the remaining 15. All studies were formatted at 16 frames per cardiac cycle: a previously validated time-dependent background subtraction method was used to derive the raw time-activity curve. The time-activity curve was smoothed and interpolated using truncated four harmonic Fourier series. This method has been compared with high temporal resolution acquisitions using the nuclear probe (14), and good correlations have been found with no differences in calculated peak filling rate seen when framing rates were increased from 16 to 64 frames per cardiac cycle. Peak filling rate was derived as the maximal change in counts in the first half of diastole and was normalized to both end-diastolic counts and stroke counts that are proportional to volume.

Statistics. Mean values and SD of data groups are reported. Paired t tests were used to assess significant differences (<0.05) between filling variables measured at the mitral anulus compared with the leaflet tips. Linear regression performed with a least squares method was used to assess comparisons between data groups. A t test was used to compare the regression lines of the list mode and frame mode studies. The t value was calculated as the difference of the regression slopes divided by the standard error of the difference of the regression slopes.

Results

Comparison between Doppler and radionuclide peak filling rate (Table 1). Mean Doppler peak filling rate data normalized to mitral stroke volume for the group of 30 patients was 4.43 ± 2.04 (range 2.27 to 10.05). When Doppler and radionuclide peak filling rate normalized to mitral stroke volume were compared (Fig. 2), the correlation was excellent (r = 0.91, SEE = 0.88) with the line of identity virtually coincident with the regression line (y = 1.01x - 0.04). When frame mode and list mode acquisitions reformatted with beat rejection were separately analyzed, the correlation between Doppler peak filling rate (SV/s) and radionuclide peak filling rate (SV/s) was r = 0.90, SEE = 1.08 for the list mode acquisitions and r = 0.92, SEE = 0.68 for the frame mode acquisitions. There was no significant difference between the slopes of the regression lines for the two correlations.

There was a poor correlation between radionuclide peak filling rate normalized to end-diastolic volume and radionuclide peak filling rate normalized to mitral stroke volume (r = 0.25) (Fig. 3). Two patients had a high filling rate when the rate was normalized to mitral stroke volume but an abnormally low peak filling rate when it was normalized to end-diastolic volume. Both of these patients had reduced left ventricular function associated with mitral regurgitation. When nuclear peak filling rate normalized to end-diastolic volume was compared with absolute Doppler peak filling rate expressed in milliliters per second, there was no correlation (r = 0.07).

Influence of sample volume position on filling variables (Table 2). As the sample volume was moved from the mitral anulus to the leaflet tips, there was no significant change in peak filling rate normalized to mitral stroke volume. There was, however, a 43% increase in E/A ratio and a 37% increase in early peak velocity. The time-velocity integral frequently increases as the sample volume is moved from the mitral anulus to the tips of the mitral leaflets despite a constant stroke volume because the cross-sectional area at the tips is less than that at the anulus. This finding would be troublesome only if the time-velocity integral at the leaflet tips were multiplied by mitral anulus cross-sectional area, which could occur if the operator was unaware of sample volume movement that may be caused by respiratory movement. On the equipment used, the operator had frequent
Table I. Individual Values for Filling Variables in 30 Patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>Age (yr)</th>
<th>DOP SV</th>
<th>RNA SV</th>
<th>RNA EDV</th>
<th>EF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cardiomyopathy</td>
<td>51</td>
<td>9.50</td>
<td>11.20</td>
<td>0.56</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Pre-adriamycin</td>
<td>36</td>
<td>5.31</td>
<td>6.74</td>
<td>4.85</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>Pre-adriamycin</td>
<td>47</td>
<td>6.34</td>
<td>4.98</td>
<td>2.74</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>CAD, stable</td>
<td>76</td>
<td>2.70</td>
<td>4.04</td>
<td>1.01</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>Hypertension</td>
<td>50</td>
<td>6.10</td>
<td>4.48</td>
<td>1.79</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>Renal failure</td>
<td>50</td>
<td>10.05</td>
<td>9.79</td>
<td>1.86</td>
<td>19</td>
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<tr>
<td>7</td>
<td>Arrhythmia</td>
<td>59</td>
<td>5.78</td>
<td>5.61</td>
<td>2.47</td>
<td>44</td>
</tr>
<tr>
<td>8</td>
<td>Angina</td>
<td>69</td>
<td>3.43</td>
<td>4.27</td>
<td>1.11</td>
<td>26</td>
</tr>
<tr>
<td>9</td>
<td>Unstable angina</td>
<td>52</td>
<td>4.30</td>
<td>4.79</td>
<td>2.49</td>
<td>52</td>
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<tr>
<td>10</td>
<td>CHF</td>
<td>83</td>
<td>2.50</td>
<td>2.20</td>
<td>1.23</td>
<td>56</td>
</tr>
<tr>
<td>11</td>
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<td>4.53</td>
<td>2.04</td>
<td>45</td>
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<tr>
<td>12</td>
<td>Hypertension</td>
<td>57</td>
<td>3.20</td>
<td>3.05</td>
<td>2.26</td>
<td>74</td>
</tr>
<tr>
<td>13</td>
<td>Pre-adriamycin</td>
<td>56</td>
<td>4.59</td>
<td>3.40</td>
<td>2.21</td>
<td>65</td>
</tr>
<tr>
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<td>4.11</td>
<td>1.56</td>
<td>38</td>
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<tr>
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<td>4.70</td>
<td>4.58</td>
<td>2.98</td>
<td>65</td>
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<tr>
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<td>3.64</td>
<td>2.15</td>
<td>59</td>
</tr>
<tr>
<td>17</td>
<td>Post CABG ischemia</td>
<td>52</td>
<td>7.10</td>
<td>7.24</td>
<td>3.08</td>
<td>55</td>
</tr>
<tr>
<td>18</td>
<td>Ischemic hrt dse</td>
<td>77</td>
<td>5.20</td>
<td>5.83</td>
<td>3.09</td>
<td>53</td>
</tr>
<tr>
<td>19</td>
<td>Non-Q wave MI</td>
<td>78</td>
<td>3.50</td>
<td>2.23</td>
<td>0.87</td>
<td>39</td>
</tr>
<tr>
<td>20</td>
<td>Aortic stenosis</td>
<td>71</td>
<td>2.27</td>
<td>1.52</td>
<td>1.89</td>
<td>73</td>
</tr>
<tr>
<td>21</td>
<td>Arrhythmia</td>
<td>59</td>
<td>3.40</td>
<td>3.80</td>
<td>2.66</td>
<td>70</td>
</tr>
<tr>
<td>22</td>
<td>Hypertension</td>
<td>74</td>
<td>3.75</td>
<td>3.37</td>
<td>1.65</td>
<td>49</td>
</tr>
<tr>
<td>23</td>
<td>Hypertension</td>
<td>65</td>
<td>2.85</td>
<td>2.68</td>
<td>2.09</td>
<td>78</td>
</tr>
<tr>
<td>24</td>
<td>Pre-adriamycin</td>
<td>43</td>
<td>6.92</td>
<td>6.74</td>
<td>3.91</td>
<td>58</td>
</tr>
<tr>
<td>25</td>
<td>Hypertension</td>
<td>65</td>
<td>2.95</td>
<td>3.37</td>
<td>2.36</td>
<td>70</td>
</tr>
<tr>
<td>26</td>
<td>Hypertension</td>
<td>65</td>
<td>3.76</td>
<td>3.00</td>
<td>1.70</td>
<td>57</td>
</tr>
<tr>
<td>27</td>
<td>Angina</td>
<td>69</td>
<td>5.23</td>
<td>5.05</td>
<td>2.88</td>
<td>57</td>
</tr>
<tr>
<td>28</td>
<td>Unstable angina</td>
<td>68</td>
<td>3.63</td>
<td>4.78</td>
<td>3.06</td>
<td>64</td>
</tr>
<tr>
<td>29</td>
<td>CAD, stable</td>
<td>63</td>
<td>3.03</td>
<td>3.26</td>
<td>2.25</td>
<td>69</td>
</tr>
<tr>
<td>30</td>
<td>Cardiomyopathy</td>
<td>66</td>
<td>3.06</td>
<td>2.70</td>
<td>0.57</td>
<td>21</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; DOP SV = Doppler peak filling rate normalized to mitral stroke volume; EF = ejection fraction; MI = myocardial infarction; Pulm = pulmonary; RNA EDV = radionuclide peak filling rate normalized to end-diastolic volume; RNA SV = radionuclide peak filling rate normalized to stroke volume.

Image updates (every 5 cycles) of sample position while the Doppler signal was being acquired.

Relation between age and peak filling rate normalized to mitral stroke volume. The mean peak filling rate normalized to mitral stroke volumes for the group of normal subjects was 5.25 ± 1.47 SV/s. As previously reported with other filling variables (15,16), there was a linear relation between peak filling rate normalized to mitral stroke volume and age (r = -0.72, y = -0.05x + 7.6, SEE = 1.1 SV/s) (Fig. 4). The mean peak filling rate for 14 patients aged 18 to 45 years...

Figure 2. Relation between Doppler echocardiographic- and radionuclide-derived peak filling rate (PFR) normalized to mitral stroke volume.

Figure 3. Relation between radionuclide-derived peak filling rate (PFR) normalized to end-diastolic volume (EDV) and radionuclide peak filling rate normalized to mitral stroke volume (SV).
Table 2. Filling Indexes as Measured at the Mitral Anulus and at the Leaflet Tips in 30 Patients

<table>
<thead>
<tr>
<th>Index</th>
<th>Anulus</th>
<th>Leaflet Tips</th>
<th>% Change</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPV</td>
<td>43 ± 14</td>
<td>58 ± 15</td>
<td>37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.2 ± 0.75</td>
<td>1.72 ± 1.12</td>
<td>43</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>PFR (SV/s)</td>
<td>5.09 ± 1.6</td>
<td>5.11 ± 1.6</td>
<td>1</td>
<td>n</td>
</tr>
</tbody>
</table>

E/A ratio = peak early to late filling velocity ratio; EPV = early peak filling velocity (cm/s); PFR = peak filling rate normalized to mitral stroke volume; SV = stroke volume.

(mean 32 ± 8) was 6.0 ± 1.2 SV/s and the mean peak filling rate for 8 patients aged 57 to 89 years (mean 71 ± 9) was 3.9 ± 1 SV/s.

Discussion

Radionuclide angiography has become an accepted standard for the noninvasive diagnosis of left ventricular filling abnormalities because of its reproducibility and ability to identify patients with abnormal diastolic filling (1.2,8-12). Doppler echocardiography can also be used to assess left ventricular filling (5-7) and has potential advantages over radionuclide angiography in that it can readily measure heat to beat filling, can more accurately measure the atrial contribution to left ventricular filling, can be performed without radiation exposure at a lower cost and allows serial measurements of peak filling rate over days and weeks. The measurement of peak filling rate by Doppler echocardiography, however, has been limited by technical problems relating to mitral anulus cross-sectional area measurement (6) and difficulty with normalization requirements.

Advantages of normalizing peak filling rate to mitral stroke volume. Normalization to mitral stroke volume allows the derivation of a Doppler echocardiographic peak filling index that is calculated entirely from mitral inflow velocity and is therefore independent of diameter measurements and geometric assumptions. Because mitral inflow velocities are highly reliable and reproducible (13), this ability overcomes a previous major technical obstacle and allows a more reliable Doppler assessment of peak filling rate. Alignment of the ultrasound beam parallel to the presumed blood flow vector is also not critical because early peak velocity and time-velocity integral are equally influenced by alignment errors, thus leaving the ratio unaffected. The ease of comparison with radionuclide techniques is another advantage of this method in that it allows both practical comparison between Doppler echocardiographic- and radionuclide-derived peak filling rate and serial measurement of peak filling rate by either of these two commonly used techniques. Retrospective derivation of radionuclide peak filling rate normalized to mitral stroke volume can be calculated by simply dividing peak filling rate normalized to end-diastolic volume by the ejection fraction.

The independence of this index from sample volume position is another strength of our proposed normalization method. Errors in measuring Doppler echocardiographic peak filling rate may inadvertently occur because of respiratory movement and movement of the heart in relation to the sample volume during the cardiac cycle. As the sample volume is moved from the anulus to the tips of the mitral leaflets, an increase in velocity is often seen. This increase would result in an erroneously high absolute peak filling rate if multiplied by the mitral anulus cross-sectional area. We have shown that peak filling rate normalized to mitral stroke volume is not affected by sample volume position, whereas a 37% increase is seen in early peak velocity and a 43% increase occurs in E/A ratio as the sample volume is moved from the anulus to the leaflet tips. Although the E/A ratio shares some of the advantages that accrue to peak filling rate normalized to mitral stroke volume, it is markedly influenced by heart rate (17) and sample volume positioning (18).

Another major benefit of this technique is that it derives a filling index that accounts for cardiac output independent of end-diastolic volume, an advantage that is equally pertinent to radionuclide techniques. Hammermeister and Warbasse (19) showed that in a normal population there was a close linear correlation between absolute peak filling rate (ml/s) and both stroke volume (r = 0.95) and end-diastolic volume (r = 0.92). Our study also showed that the values of the majority of patients with heart disease fell above the normal regression line when absolute peak filling rate was compared with both end-diastolic volume and stroke volume, indicating that normalization to either of these variables was equally effective in identifying patients with heart disease. Normalization to end-diastolic volume has been employed in many centers out of convention rather than for reasons based on rigorous examination of its advantages over other normalization techniques. Indeed, normalization to end-diastolic volume may mask early filling behavior in patients with mitral regurgitation or cardiomyopathy, in which end-diastolic volume may be markedly increased. In these patients, peak filling rate normalized to end-diastolic volume may be below normal despite normal or high absolute peak filling rate.
filling. In this setting it may be physiologically more appropriate for filling to occur at a rate commensurate with mitral stroke volume rather than end-diastolic volume.

Previous comparisons of Doppler echocardiographic filling variables. Doppler echocardiographic-derived filling variables have previously been validated against invasive and noninvasive techniques. Rokey et al. (5) found good correlations between absolute peak filling rate and peak filling rate normalized to end-diastolic volume when two-dimensional echocardiography was compared with Doppler echocardiography. Despite these good results they suggested that the main limitation in assessing filling rate by Doppler echocardiography was related to the determination of mitral annulus cross-sectional area and end-diastolic volume by two-dimensional echocardiography. This opinion was confirmed by Friedman et al. (6), who compared Doppler echocardiography and radionuclide angiography and found good correlations between Doppler filling variables that were independent of diameter measurements, but a poor correlation between Doppler and radionuclide peak filling rates normalized to end-diastolic volume. By comparing Doppler echocardiography and radionuclide angiography, Spirito et al. (7) also found good correlation between filling ratios and diastolic filling periods when the isovolumetric filling period was included in the Doppler echocardiographic measurement. They did not, however, compare any measure of absolute or normalized peak filling rate and suggested that because of errors involved in quantitative echocardiographic determination of mitral annulus cross-sectional area and ventricular volumes, peak filling rate normalized to end-diastolic volume would be of limited clinical value.

Study limitations. The primary aim of this study was to validate a Doppler echocardiographic method for deriving peak filling rate normalized to mitral stroke volume and to assess potential advantages of this normalization process for Doppler echocardiography and radionuclide angiography. We did not attempt to assess the efficacy of peak filling rate normalized to mitral stroke volume in identifying patients with diastolic dysfunction or to compare this normalization with indexes of diastolic function. Clearly, further studies are required to address these questions and to compare the relative benefits of normalization to mitral stroke volume and to end-diastolic volume. We also recognize that any measure of peak filling rate will predominantly reflect the atrioventricular pressure gradient and therefore will be influenced by left ventricular loading conditions, left atrial compliance and other factors (20).

The assumption of a constant mitral annulus area during diastole may introduce a small error into the calculation of peak filling rate normalized to mitral stroke volume. Ormiston et al. (21) demonstrated an increase of approximately 12% in mitral cross-sectional area from early to late diastole. This error would be minimized, however, if the average mitral annulus cross-sectional area during diastole equaled the cross-sectional area at early peak filling velocity. It appears from the data of Ormiston et al. that this may indeed be the case. Furthermore, the excellent correlation between Doppler peak filling rate and peak filling rate measured using a radionuclide technique (which does not share the assumption of a constant mitral annulus area) implies that there is no significant error in this assumption.

To assess a normal range of values for this filling index, we have examined only a small group of normal subjects; further studies would be required to accurately define an age-corrected lower limit of normal. We also cannot exclude that some of these older "normal" patients had ischemic heart disease despite lack of symptoms.

References

14. Lee FA, Fetterman R, Zuez BL, Wackers FJTh. Rapid radionuclide-
derived systolic and diastolic cardiac function using cycle-dependent
background correction and Fourier analysis. IEEE Comput Cardiol

15. Kou LC, Quinones MA, Rokey R, Santor M, Ahnader EG, Zoghbi WA.
Quantitation of atrial contribution to left ventricular filling by pulsed
Doppler echocardiography and the effect of age in normal and diseased

contribution to left ventricular inflow with aging as assessed by intracardiac

17. Herzog CA, Elsperger J, Manoles M, Murakami M, Asinger R. Effect of
atrial pacing on left ventricular diastolic filling measured by pulsed
Doppler echocardiography (abstract). J Am Coll Cardiol 1987;9:197A.

18. Driscoll N, Smith MD, Wisenbaugh T, Friedman B, Kwan DL,
DeMaria AN. Influence of sampling site upon the ratio of atrial to early
diastolic trans-mitral flow velocities by Doppler (abstract). J Am Coll Cardiol
1987;9:16A.

19. Hummermeister K, Warhause J. The rate of change of left ventricular
volume in man. II. Diastolic events in health and disease. Circulation
1974;49:739-47.

20. Ichida Y, Mesner J, Tsuchioka K, et al. Left ventricular filling dynamics:
influence of left ventricular relaxation and left atrial pressure. Circulation