Stroke Volume Calculated from the Mitral Valve Echogram in Patients With and Without Ventricular Dyssynergy

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SUMMARY A formula was derived for calculating mitral valve stroke volume (MVSV) using the rate of mitral valve (MV) opening (DE slope on the MV echogram), the vertical distance between the mitral leaflet echoes early in diastole (EE), the electrocardiographic PR interval and heart rate. The formula was tested prospectively on 80 consecutive patients from whom 95 simultaneous MV echograms and either thermodilution (45) or Fick (50) cardiac outputs were obtained. Sixteen patients were normal; 54 had coronary artery disease; three had cardiomyopathy; and seven had nonrheumatic mitral regurgitation (MR). Linear regression for stroke volume was \( r = 0.90, \text{SEE} \pm 6 \), and for cardiac output \( r = 0.83, \text{SEE} \pm 0.5 \) liter for the 73 patients without MR. The presence or absence of ventricular dyssynergy did not alter statistical findings. MVS consistently overestimated forward stroke volume for the seven patients with MR. This study shows that the MV echogram provides an accurate, widely applicable method for calculating MVSV.

MITRAL VALVE LEAFLET MOTION has been shown to be affected by valve stenosis and prolapse, left ventricular compliance, diastolic pressure, heart rate, and cardiac rhythm. Recordings of the volume of blood flow across the mitral valve in animal studies closely resemble the pattern of mitral valve motion seen echocardiographically. This similarity in motion suggests that the mitral valve echogram reflects blood flow across the valve.

The purpose of this study was to develop and test a clinically applicable method for calculating stroke volume based on information readily available from mitral valve echograms.

Materials and Methods

Patients

Three groups of patients (total number = 96) were included in this study, and 120 cardiac output determinations were made. The first group (A) was the subject of a pilot study and was comprised of 16 patients with coronary artery disease. Twenty-five simultaneous mitral valve echograms and thermodilution cardiac outputs (TDCOs) were performed while the Group A patients were in a coronary care unit. Groups B and C were prospective study groups. Group B represented 30 consecutive patients in a coronary care unit from whom 45 simultaneous mitral echograms and TDCOs were performed. Group C included 50 consecutive patients undergoing cardiac catheterization, including coronary cineangiography and left ventriculography studies, from whom mitral echograms were recorded simultaneously with a Fick cardiac output determination.

Pilot Study: Group A

One technically good mitral valve echogram was selected for each TDCO. In selecting a mitral valve echogram we looked for an echogram in which the DE slope appeared as a continuous echo; tips of both leaflets (EE) were well-defined; and the beat was neither preceded nor followed by a premature complex. The echogram was manually traced on a digital tabloid and entered into a Tektronic graphic terminal. A DEC System 10 program was developed to collect the digital coordinates from the tabloid. The coor-
Dordinate system was translated and rotated; a smoothing spline was applied and scaling was normalized for computer enhancement of the data. Computer analysis included determination of: 1) the area enclosed by echoes from the mitral valve, 2) average vertical diameter of the mitral echogram, 3) time-dependent slopes and 4) time intervals. Figure 1 shows a computer printout of data derived from a manually traced mitral valve echogram. While the early diastolic points on the mitral valve are usually labelled E, F and F', computer data acquisition necessitated the letter F not being used twice. Therefore, the letters, E, K and F were used to represent E, F and F', respectively. Twenty-one variables were included for analysis. Thirteen variables were derived directly from the mitral echogram and eight additional variables were manually entered (2) or computed (6) (appendix A).

**Data Analysis Procedure to Determine How Stroke Volume and the Mitral Valve Echogram Are Related**

Linear regression analyses were performed on the data from the pilot study using a standard statistical package. We looked for interrelationships between variables by considering the multiple correlation and the partial correlation coefficients. Using two mitral valve variables (EE, DE) and two electrocardiographic variables (HR, PR), a formula was derived from the pilot study for calculating stroke volume.

**Prospective Studies**

*Echo Determination of Stroke Volume*

Variables used to determine mitral valve stroke volume (MVSV) are illustrated in figure 2. The mitral variable EE represented the maximum vertical separation between the anterior and posterior mitral valve leaflets which occurred during early diastole. The EE was measured from the outermost point of the anterior leaflet to the outermost point of the posterior leaflet, and this distance was expressed in millimeters. The mitral variable DE represented a time-dependent slope, with point D the point at which the anterior and posterior leaflets first separated in early diastole, and point E the maximum excursion of the anterior mitral valve leaflet following the early diastolic opening. The most rapid slope of the echo between points D and E was measured and expressed in mm/sec.

Heart rate was expressed in beats/min and was derived by dividing the number 60 by the electrocardiographic R-R interval in seconds. The PR interval was measured as the distance in seconds from the onset of the electrocardiographic P wave to the onset of the electrocardiographic Q wave. When the PR interval could not be accurately identified on the echogram, the interval was measured from a simultaneous lead II rhythm strip recording.

In the prospective studies, a minimum of five mitral valve echograms recorded during the cardiac output study were used for calculating MVSV. Determination of which mitral valve echogram would be measured was based on the technical quality of the echogram. Only echograms in which the DE slope appeared as a continuous echo and the tips of both mitral leaflets were well-defined (EE) were considered for measurement. The number of mitral valve complexes used for analysis depended on the regularity of both the cardiac rhythm and the configuration of the mitral valve echogram. When variation in the electrocardiographic R-R interval was less than the equivalent of 10 beats/min, a total of five mitral echograms were measured and averaged. A mitral echogram and its corresponding electrocardiogram was selected between minutes 1 and 1½, 1½ and 2, 2 and 2½, 2½ and 3, 3 and 3½ of the four-minute study. When the variation in the R-R interval was more than the equivalent of 10 beats/min, as in marked sinus
arrhythmia or atrial fibrillation, 10 consecutive complexes between minutes 2 and 3 were measured and average values for each variable were used to calculate stroke volume. When premature complexes were evident, a total of 10 echograms were measured and averaged (fig. 3). Five of the 10 echograms were selected from between minutes 1 and 3½, as previously described. The other five were consecutive complexes which were selected to include the arrhythmia. Values for all 10 complexes were used to calculate the mean for each variable. The calculated number for MVSV was rounded to the nearest whole number. All echocardiographic calculations of stroke volume were made without knowledge of thermodilution or Fick cardiac output results.

Statistical Analysis: Prospective Groups

The Student t test was used to test for any significant difference between group means for stroke volume and cardiac output as determined by echocardiography and thermodilution or Fick. Stroke volume and cardiac output data were also compared using the Mann-Whitney U test, Kolmogorov-Smirnov test and linear regression analyses.

Cardiac Outputs

Cardiac output determinations obtained by the thermodilution technique were made using Swan-Ganz catheters and an Edwards TDCO computer model 9510. Pulmonary artery pressures were recorded on a Honeywell #1858 recorder with medium gain amplifier modules. All Fick cardiac output studies were carried out before angiographic studies. Venous samples were obtained from either the right ventricle or pulmonary artery. Arterial samples were obtained from the thoracic aorta via the right femoral artery. Expired air was collected in a Douglas bag and the quantity of air inspired was measured using a Tissot spirometer. Expired air was collected for four minutes while simultaneously recording a lead II rhythm strip and mitral valve echograms. Venous and arterial blood were simultaneously sampled for one minute beginning at two and one-half minutes and ending at three and one-half minutes into the four-minute period.

Left Ventriculograms

Left ventriculography was performed before selective coronary arteriography. Left ventriculograms were routinely recorded in the right anterior oblique position. The ventriculogram was divided into five segments as follows: anterobasal, anterolateral, apical, diaphragmatic and posterobasal. Dyssnergy was considered to be present when at least one of the five segments did not move normally during systole. For patients studied in a coronary care unit, the presence of dyssnergy was based on the presence of echocardiographic wall motion abnormalities. We recognize that echocardiography and right anterior oblique left ventriculography are not always in agreement as to the presence of dyssnergy.

Murmurs

Cardiac auscultation was performed on all patients in order to detect mitral regurgitation. A holosystolic murmur was considered to represent mitral insufficiency when the murmur was loudest at the apex and radiated to the axilla, and/or regurgitant flow from the left ventricle to left atrium was evident on left ventriculography in the absence of premature ventricular complexes.

Echocardiograms

All echocardiograms were recorded with a Smith-Kline echograph having a repetition rate of 1,000 pulses/sec and utilizing a single element 2.25 mHz transducer, 12 mm or 13 mm in diameter and collimated to 7.5 cm. A simultaneous electrocardiographic lead II was recorded on each tracing. Echoes from the mitral valve were recorded from the third or fourth intercostal space, with the transducer perpendicular to the chest wall. In this study, an adequate echocardiogram was considered one in which both leaflets of the mitral valve were recorded. Mitral echograms were recorded at paper speeds of 25 and 50 mm/sec, and 0.2 second time lines were recorded on all tracings.

Results

Pilot Study: Group A

Cardiac Outputs and Heart Rates

TDCO ranged from 3.4 l/min–6.4 l/min, with a mean of 4.93 l/min for the 25 measurements. Cardiac indices ranged from 1.92 l/min/m² to 3.05 l/min/m²,
with a mean of 2.51 l/min/m². Nine of the 16 patients from whom the 25 outputs were measured had a cardiac index of < 2.5 l/min/m². Heart rates ranged from 52–118 beats/min (mean 77). Four of the 25 outputs (16%) were obtained with heart rates ≥ 100, and four (16%) were obtained with heart rates < 60 beats/min. Heart rate was derived from the RR interval present on the mitral echogram. Thermodilution stroke volume (TDSV) was derived by dividing cardiac output by heart rate and was expressed in cubic centimeters. TDSV ranged from 34–96 cm³, with both a mean and median of 67 cm³.

**Digitized Mitral Echograms**

Appendix A shows group data for the 25 digitized mitral echograms, along with the correlation coefficient between each of the 21 variables and TDSV. TDSV was highly correlated with heart rate ($r = -0.85$), total time the valve was open ($r = 0.80$) and area enclosed by the mitral echoes ($r = 0.72$). The partial correlation coefficients showed that the total time the valve was open was also related to both heart rate (fig. 4) and to area enclosed by the mitral echoes. In addition, area enclosed by the mitral echoes correlated with EE divided by heart rate (EE/HR; $r = 0.85$). EE/HR alone correlated with stroke volume with an $r$ value of 0.83. The PR interval had a correlation coefficient ≥ 0.50 to the mitral EE, AA, and average diameter even though the correlation coefficient to stroke volume was only $r = 0.23$. The rate of mitral opening (DE slope) showed some correlation ($r = 0.40$) to cardiac output. Considering the interrelationships of these variables, a formula was derived for calculating stroke volume from variables readily measured by hand from tracings of mitral valve echograms (fig. 2).

The formula for calculating MVSV is:

$$\text{MVSV} = \left( \frac{\text{EE (mm)}}{\text{HR (beats/min)}} \right) + \text{PR (sec)} + 100 + \frac{2 \times \text{DE (mm/sec)}}{\text{HR (beats/min)}}$$

**MVSV vs TDSV**

For the 25 studies, stroke volume calculated from the mitral valve echogram averaged 66.2 cm³ ($\text{SD} \pm 13.3$). Stroke volume calculated from TDSV averaged 67.2 cm³ ($\text{SD} \pm 17.4$). Linear regression showed a correlation coefficient of 0.88 ($\text{SEE} \pm 10$).

**Prospective Studies**

Data from 80 consecutive patients on whom 95 simultaneous mitral echograms and either thermodilution (45) or Fick (50) cardiac outputs were performed were included for analysis. Data from five additional studies (five patients) were not included due to inadequate echograms, and 11 studies (seven patients) were not included due to technical difficulties in obtaining the cardiac outputs. Six patients had more than one TDCO study. Repeat studies were separated by at least 12 hours and were performed for clinical purposes.

Seventy-three of the 80 prospective patients had no clinical or angiographic evidence for mitral regurgitation. Linear regression for stroke volume was $r = 0.90$, $\text{SEE} \pm 6$, and for cardiac output $r = 0.83$, $\text{SEE} \pm 0.5$ for these 73 patients. The presence or absence of ventricular dyssnergy did not alter statistical findings. MVSV consistently overestimated forward stroke volume for the seven patients with mitral regurgitation.

**Group B: CCU Patients**

Initial data analysis was based on 35 TDCO measurements from 26 patients. Four additional patients had mitral insufficiency murmurs at the time of the studies; data from these cases are presented later.

**Heart rate and rhythm**

Heart rate varied from 60–129 beats/min, with an average of 91 and a median of 90 beats/min. One patient was studied while in atrial fibrillation, one while being paced with a temporary pacemaker, and four while either ventricular (3) or atrial (1) premature complexes were occurring.

**MVSV vs TDSV**

Table 1 lists data pertaining to the 35 cardiac output and stroke volume determinations both by thermodilution and mitral valve techniques. When TDCOs were corrected for body size, cardiac indices ranged from 1.52 l/min/m²–3.18 l/min/m². Ten of the 26 patients had indices < 2.5 l/min/m². There was no statistical difference in MVSV vs TDSV (fig. 5).
mitral valve cardiac output (MVCO) vs TDCO when data were compared using either the Student t test, the Mann-Whitney U test or the Kolmogorov-Smirnov test.

**Group C: Cardiac Catheterization Patients**

Group data for the 47 patients in this analysis are presented in table 2. Three additional patients had ventriculographic and clinical evidence of mitral insufficiency. Data from these three patients are presented later. Sixteen of the 47 patients had no angiographic evidence of myocardial or coronary artery disease. Twenty-eight patients had significant (≥ 75%) narrowing of at least one of the three major coronary arteries. Three patients were diagnosed as having cardiomyopathy. For the group of 47 patients, there was no statistical difference between MVSV and Fick stroke volume or between MVCO and Fick cardiac output when data were compared using either the Student t test, the Mann-Whitney U test or the Kolmogorov-Smirnov test.

**Normals**

The 16 patients without objective evidence of cardiac disease were considered normal. All 16 had normal contraction patterns on the left ventriculograms. All 16 patients were in sinus rhythm with heart rates ranging from 56-116 beats/min (mean 79, median 75 beats/min). Fick stroke volume ranged from 40-116 cm³ (mean = 80.8 cm³, SD ± 17.5). Stroke volume calculated from the mitral valve ranged from 53-107 cm³ (mean = 79.8 cm³, SD ± 14.5). Linear regression for stroke volumes showed a correlation coefficient of 0.95 (SEE ± 6) (fig. 6). Fick cardiac output ranged from 4.64 to 8.47 l/min (mean = 6.23, SD ± 0.96 l). Cardiac output calculated from the mitral valve ranged from 5.12-7.1 l/min (mean = 6.14, SD ± 0.64 l). Linear regression analysis showed $r = 0.81$ (SEE ± 0.6 l).

### Table 1. Group B Data for 35 Cardiac Output and Stroke Volume Determinations Both by Thermodilution and Mitral Valve Techniques in the Coronary Care Unit

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>60-129</td>
<td>91</td>
<td>90</td>
<td>16.6</td>
</tr>
<tr>
<td>TDSV (cc)</td>
<td>24-83</td>
<td>56</td>
<td>60</td>
<td>14.06</td>
</tr>
<tr>
<td>MVSV</td>
<td>23-84</td>
<td>57</td>
<td>60</td>
<td>14.47</td>
</tr>
<tr>
<td>TDCO (l/min)</td>
<td>2.70-6.30</td>
<td>4.92</td>
<td>5.10</td>
<td>0.80</td>
</tr>
<tr>
<td>MVCO</td>
<td>2.55-6.19</td>
<td>4.99</td>
<td>5.10</td>
<td>0.78</td>
</tr>
<tr>
<td>EE (mm)</td>
<td>0-40</td>
<td>30</td>
<td>32</td>
<td>8.2</td>
</tr>
<tr>
<td>DE (mm/sec)</td>
<td>0-565</td>
<td>287</td>
<td>305</td>
<td>108.4</td>
</tr>
<tr>
<td>PR (sec)</td>
<td>0-0.26</td>
<td>0.16</td>
<td>0.16</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Zero values for EE and DE represent instances in which the MV ephogram only revealed value opening following atrial contraction. Zero PR intervals represent cases in which atrial fibrillation, temporary (RV) pacemaker, or PVCs were present.

**Abbreviations:** TDSV = thermodilution stroke volume; MVSV = mitral valve stroke volume; TDCO = thermodilution cardiac output; MVCO = mitral valve cardiac output.

### Table 2. Group Data for 47 Subjects Having Cardiac Catheterization and Cardiac Output Studies

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>52-116</td>
<td>76</td>
<td>75</td>
<td>13.9</td>
</tr>
<tr>
<td>Fick SV (cc)</td>
<td>35-139</td>
<td>78</td>
<td>63</td>
<td>22.0</td>
</tr>
<tr>
<td>MVSV</td>
<td>45-119</td>
<td>75</td>
<td>78</td>
<td>14.9</td>
</tr>
<tr>
<td>Fick CO (l/min)</td>
<td>2.76-9.69</td>
<td>5.86</td>
<td>5.68</td>
<td>1.22</td>
</tr>
<tr>
<td>MVCO</td>
<td>3.56-7.28</td>
<td>5.64</td>
<td>5.51</td>
<td>0.79</td>
</tr>
<tr>
<td>EE (mm)</td>
<td>18-45</td>
<td>34</td>
<td>34</td>
<td>5.28</td>
</tr>
<tr>
<td>DE (mm/sec)</td>
<td>99-1000</td>
<td>396</td>
<td>377</td>
<td>153</td>
</tr>
<tr>
<td>PR (sec)</td>
<td>0.14-0.22</td>
<td>0.19</td>
<td>0.19</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Abbreviations:** SV = stroke volume; MVSV = mitral valve stroke volume; CO = cardiac output; MVCO = mitral valve cardiac output.

**Figure 5.** Thermodilution stroke volume (TDSV) compared to mitral valve stroke volume (MVSV) for 35 cardiac output determinations from 26 coronary care unit (CCU) patients. Open circles represent repeat output determinations while patients were in the CCU.

**Figure 6.** Fick stroke volume (SV) compared to calculated mitral valve stroke volume (MVSV) for 16 patients with normal left ventriculograms and no angiographic evidence for coronary artery disease.
Coronary Artery Disease — Myopathy

Twenty-seven of the 31 patients with either coronary artery disease or cardiomyopathy had abnormal ventriculograms. In the absence of premature ventricular complexes, 25 patients had dyssynergy of contraction recorded on the left ventriculogram, two showed generalized hypokinesis, and in four patients the contraction pattern was completely normal. All patients were in sinus rhythm with heart rates ranging from 52–103 (mean = 76, median = 78) beats/min. Fick stroke volume ranged from 35–139 cm³ (mean = 76.3, SD ± 21.4). Stroke volume calculated from the mitral valve ranged from 45–119 cm³ (mean = 73, SD ± 15.0). Linear regression showed r = 0.82 (SEE ± 12) (fig. 7). Fick cardiac output ranged from 2.76–9.69 l/min (mean = 5.65 l/min, SD ± 1.3 l/min). Cardiac output calculated from the mitral valve ranged from 3.56–7.28 (mean = 5.40, SD 0.75 l). Linear regression analysis showed r = 0.79 (SEE ± 0.8 l). There were two patients in whom the clinical status and left ventriculograms were inconsistent with the stroke volumes derived from the Fick outputs. Had these two patients been omitted from the study, the correlation coefficient for stroke volume would have increased to r = 0.90 SEE ± 7, and the correlation coefficient for cardiac output would have increased to r = 0.85 (SEE ± 0.5 l).

Mitral Insufficiency: Patients from Groups B and C

Seven of the 80 patients in this study had mitral insufficiency. Four patients were in the coronary care unit and had 10 thermodilution outputs performed. Three patients had cardiac catheterization which included cardiac output measurement by the Fick method. MVSV ranged from 34–78 cm³ (mean 55.4, median 53), while forward stroke as measured by thermodilution or Fick ranged from 13–74 cm³ (mean 36.5, median 53). MVCO ranged from 4.58–6.04 l/min, while forward cardiac output ranged from 1.86–5.23 l/min. Stroke volume and cardiac output determinations calculated from the mitral valve echograms were significantly (P < 0.001) greater than those values obtained by Fick or thermodilution methods (fig. 8).

Discussion

Results of this study indicate that the mitral valve echogram provides an accurate, widely applicable method for calculating MVSV. In the presence of an anatomically normal mitral valve, stroke volume and cardiac output can be calculated from the mitral valve echogram with an accuracy equivalent to that obtained by either Fick or thermodilution techniques.

A mathematical model was developed, using basic fluid dynamic equations and simplified geometric assumptions regarding the mitral valve, which supports our echocardiographic equation for calculating MVSV. A first order approximation of flow through the mitral valve was obtained mathematically using the variables EE, DE, PR and the time the mitral valve is open (appendix B). Mathematically, the EE term represents the diameter of the mitral valve, DE represents the rapidity with which the flow field develops and PR represents volume of the atrial contribution. The two mitral valve leaflets were assumed to be of equal length and to remain rigid and symmetric throughout diastole. The leaflets were also assumed to be passive elements and to exert no influence on the developing flow field. These geometric assumptions, together with the principles of conservation of momentum and mass, allowed us to derive the interrelationship of echocardiographic variables EE and DE with respect to mitral flow. Conservation of momentum was used to relate the development of velocity in a flow field to an applied pressure gradient. Conservation of mass was used to relate development
of motion of the mitral valve leaflets to the developing velocity during diastole.

Experimental studies have shown that the normal mitral valve starts to open with the onset of blood flow across the valve,\textsuperscript{11,12} that a flow wave occurs with atrial contraction,\textsuperscript{11} and that cessation of flow occurs with valve closure.\textsuperscript{19} We found in this study that the total time the mitral valve was open was inversely related to heart rate; therefore, in the clinical application of the equation, heart rate was used to represent time during which flow occurred. Use of heart rate expressed as beats/min enabled a less complicated formula to be used for calculating mitral valve flow.

The importance of atrial systole for ventricular filling depends on the time and vigor with which atrial systole occurs and on the completeness with which the ventricle has already filled at the time of the systole.\textsuperscript{16} Timing of atrial systole has been shown to affect the vigor of atrial contraction.\textsuperscript{15} Nolan et al.\textsuperscript{11} have reported that progressive shortening of the PR interval in calves resulted in a progressive decrease in the amount of mitral flow, and that the loss of atrial contraction during junctional rhythm was accompanied by a decrease in aortic flow. The PR term in our mathematical equation represents volume of flow occurring with atrial contraction and is based on an assumed incremental pressure gradient across the mitral valve which begins at the beginning of the electrocardiographic P wave and ends at the Q wave. While 11 of the 73 patients in this study have PR intervals between 0.21 and 0.26 second, prolonged PR intervals may not always be accompanied by increments in pressure or volume. Because the mitral valve may close with atrial relaxation, a sufficiently long PR interval would be associated with a lower average pressure gradient and therefore error and overestimation of stroke volume could occur with our equation. Also, if atrial systole should occur during ventricular systole, such a long PR interval could actually be accompanied by a decreased cardiac output.\textsuperscript{17} Coronary artery disease was the primary underlying pathology present in our study group. In other disease states, such as systemic hypertension or aortic stenosis, the left ventricular filling pattern may differ due to change in compliance, and therefore the PR interval would not be the only determinant of atrial volume contribution as implied in our equation. In patients with atrial disease, the PR interval could overestimate flow if the vigor of the atrial contraction was decreased.

We cannot definitively explain why the values derived by the mitral valve technique are numerically equal to cubic centimeters derived by thermodilution or Fick cardiac outputs. This is explained mathematically by assuming that the coefficient of the mitral EE measurement has units of ml/mm, the coefficient of the PR measurement has units of ml/sec, and that the coefficient of the mitral DE measurement has units of ml/sec/mm.

Determination of the best method of calculating mitral valve flow from so many measurements required extensive correlations and regression analyses. Our goal was to derive measurements which would be made easily and reliably reproduced. This is one reason EE was measured from the outermost mitral valve echoes and why the PR interval was used for atrial flow instead of the width of the A wave on the mitral echogram. Ideally, we would have preferred using fewer variables and/or a simpler equation, but we could not. For example, although heart rate and area enclosed by the mitral leaflets were each related to stroke volume, the correlations were associated with large standard errors. The variable EE/HR versus stroke volume had an r value of 0.83 in the pilot study, but the correlation was later found to be good only for low stroke volumes and in the absence of arrhythmias. Although the correlation of PR interval to stroke volume was low, this variable proved valuable in the equation because its correlation was statistically independent of EE and heart rate. The variable DE was selected on the assumption that it would reflect velocity of blood flow and also be independent of valve diameter. These variables were selected and combined with the goal of determining stroke volume accurately over a wide range of outputs with minimum error for any given patient.

Clinical Limitations

Both theoretically and clinically, the validity of this formula for calculating forward stroke volume depends on the integrity of the valve itself. Based on the mathematical model, error would result when either gross anatomical alterations are present (i.e., stenosis or prolapse), when a force is imposed on the developing flow field (i.e., decreased compliance, mitral stenosis, aortic insufficiency), or when atrial systolic pressure gradients exceed normal limits.

References

10. DeMaria AN, Lies JE, King JF, Miller RR, Amsterdam EA, Mason DT: Echographic assessment of atrial transport, mitral movement, and ventricular performance following electro-

APPENDIX A. Pilot Study Group Data for 25 Digitized Mitral Valve Echograms

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Mean</th>
<th>sd</th>
<th>Correlation coefficient (r) to thermodilution stroke volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Average diameter (cm)</td>
<td>0.83–2.47</td>
<td>1.52</td>
<td>0.30</td>
<td>0.19</td>
</tr>
<tr>
<td>2. Area (cm-sec)</td>
<td>0.27–1.25</td>
<td>0.77</td>
<td>0.26</td>
<td>0.72</td>
</tr>
<tr>
<td>3. PR (sec)</td>
<td>0.12–0.29</td>
<td>0.16</td>
<td>0.03</td>
<td>0.22</td>
</tr>
<tr>
<td>4. RR (sec)</td>
<td>0.51–1.16</td>
<td>0.82</td>
<td>0.18</td>
<td>0.85</td>
</tr>
<tr>
<td>5. R-open (sec)</td>
<td>0.23–0.84</td>
<td>0.35</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>6. Total time open (sec)</td>
<td>0.28–0.86</td>
<td>0.52</td>
<td>0.16</td>
<td>0.80</td>
</tr>
<tr>
<td>7. A-C (sec)</td>
<td>0.06–0.16</td>
<td>0.10</td>
<td>0.02</td>
<td>0.18</td>
</tr>
<tr>
<td>8. EE (mm)</td>
<td>24–39</td>
<td>33.1</td>
<td>4.0</td>
<td>0.38 (*0.58)</td>
</tr>
<tr>
<td>9. AA (mm)</td>
<td>16–41</td>
<td>28.7</td>
<td>4.4</td>
<td>0.42</td>
</tr>
<tr>
<td>10. DE slope (mm/sec)</td>
<td>80–200</td>
<td>181</td>
<td>51</td>
<td>−0.44 (*+0.40)</td>
</tr>
<tr>
<td>11. EF (EF') slope (mm/sec)</td>
<td>40–222</td>
<td>112</td>
<td>45</td>
<td>0.16</td>
</tr>
<tr>
<td>12. EF (EF') slope (mm/sec)</td>
<td>56–282</td>
<td>145</td>
<td>54</td>
<td>0.41</td>
</tr>
<tr>
<td>13. AC slope (mm/sec)</td>
<td>100–310</td>
<td>188</td>
<td>49</td>
<td>−0.12</td>
</tr>
<tr>
<td>14. Body surface area (m²)</td>
<td>1.71–2.19</td>
<td>1.95</td>
<td>0.16</td>
<td>0.46</td>
</tr>
<tr>
<td>15. Cardiac output (l/min)</td>
<td>3.4–6.4</td>
<td>4.93</td>
<td>0.75</td>
<td>0.58</td>
</tr>
<tr>
<td>16. Heart rate (beats/min)</td>
<td>51–118</td>
<td>77</td>
<td>18.5</td>
<td>−0.85</td>
</tr>
<tr>
<td>17. Stroke volume (cc)</td>
<td>34–96</td>
<td>67</td>
<td>17.5</td>
<td>1.0</td>
</tr>
<tr>
<td>18. EE/HR (mm/HR)</td>
<td>0.21–0.66</td>
<td>0.45</td>
<td>0.12</td>
<td>0.83</td>
</tr>
<tr>
<td>19. DE/HR [(mm/sec)/HR]</td>
<td>1.23–3.93</td>
<td>2.4</td>
<td>0.72</td>
<td>0.21</td>
</tr>
<tr>
<td>20. Area/HR [(cm/sec)/HR]</td>
<td>0.002–0.021</td>
<td>0.011</td>
<td>0.006</td>
<td>0.78</td>
</tr>
<tr>
<td>21. EF/HR [(mm/sec)/HR]</td>
<td>0.47–2.85</td>
<td>1.5</td>
<td>0.58</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Patients with mitral insufficiency omitted.

Abbreviations: Area = area enclosed by mitral echoes; R-open = time from preceding electrocardiographic R wave to initial opening (mitral D point) of mitral valve; HR = heart rate in beats/min; sd = standard deviation.

APPENDIX B. Flow through the mitral valve can be calculated using:

\[ Q = \beta U A dt \]

when \( Q \) is flow, \( U \) is velocity, \( A \) is the cross sectional area normal to the flow field and \( t \) is time the valve is open. The velocity and cross-sectional area can be defined using conservation of momentum and mass according to

\[
\begin{align*}
(i) & \quad \frac{\partial A}{\partial t} = -\frac{\partial UA}{\partial X} \\
(ii) & \quad \frac{\partial U}{\partial t} + U \frac{\partial U}{\partial X} = -\frac{\partial P}{\partial X} / \rho
\end{align*}
\]

where \( P \) is pressure and \( \rho \) is specific density. Intrinsic in these equations are the assumptions that no external body forces are applied, that flow is incompressible, axisymmetric and that viscosity is negligible. The geometry of the mitral valve at varying intervals of diastole is shown in the following figure:

at zero time (mitral D) | early diastole (mitral EE)

The cross sectional area is given by

\[ A = \pi \left( \frac{EE}{2} - M_o (t) X \right)^2 \]

where \( \frac{EE}{2} \) is the maximum mitral valve diameter, \( M_o (t) \) is the slope of the mitral valve leaflets \( (L) \) at any point in time \( (t) \) and \( X \) is the distance through the mitral valve. To a first order approximation the flow through the mitral valve can be given by
\[ Q = Q_0 + \frac{\partial Q}{\partial EE} EE + \frac{\partial Q}{\partial DE} DE + \frac{\partial Q}{\partial PR} PR + E (EE^2, DE^2, PR^2) \]

where the error term (E) is the higher order influences. The coefficients in this equation are the sensitivity of flow with respect to the independent variables EE, DE and PR.

Using this mathematical model, one can determine these sensitivities as follows:

\[ \frac{\partial Q}{\partial EE} = 2\pi (\bar{u} EE - L\bar{u}m) t \]

where \( \bar{u}m = \frac{1}{t} \int_0^t U (L,t) M_0 (t) dt \)

\[ \bar{u} = \frac{1}{t} \int_0^t U (L,t) dt \]

\[ \frac{\partial Q}{\partial DE} = 2\pi t (\bar{u} EE - L\bar{u}m) (2\alpha_1 t DE + \frac{EE}{DE}) \]

where \( tDE \) is the time from initial opening to first maximum deflection. The sensitivity with respect to PR required added assumptions regarding atrial systole. It is reasonable to assume that the atrial contribution is an additive pressure gradient during atrial systole,

\[ \frac{\partial P}{\partial X} = \begin{cases} \frac{\partial P_0}{\partial X}, & 0 \leq \xi \leq t - Pr \\ \frac{\partial P_0}{\partial X} + \frac{\partial P_0 (t)}{\partial X} t - PR \leq \xi \leq t. \end{cases} \]

From the momentum equation this will increase the velocity by some amount \((\Delta U)\). Flow through the mitral valve will be:

\[ Q = \int_0^{t PH} U dt + \int_{t PH}^t (U + \Delta U) dt \]

therefore

\[ Q = Q' + \Delta UA PR \]

where \( \Delta UA \) is the average flow per unit time imposed by atrial systole and \( Q' \) is the flow through the mitral without atrial systole.

Summarizing then to a first order approximation, the regression equation as derived from the mathematical considerations should have the form,

\[ Q = a' + a'EE + a'DE + a'PR \]

where \( a' \), \( a'_EE \) and \( a'_DE \) are the sensitivities as derived.

The time factor \( t \) is the time that the mitral valve is open. We have shown this to be inversely proportional to heart rate (fig. 4).

The model presented depends on the integrity of the mitral valve and the inherent assumptions associated with first order approximations, geometry considerations and validity of the assumptions regarding flow.
Stroke volume calculated from the mitral valve echogram in patients with and without ventricular dyssynergy.
S Rasmussen, B C Corya, H Feigenbaum, M J Black, D E Lovelace, J F Phillips, R J Noble and S B Knoebel

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