Pulsed Doppler Echocardiographic Measurement of Beat-to-beat Changes in Stroke Volume in Dogs

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SUMMARY Measurement of stroke volume by pulsed Doppler echocardiography has not been validated against a reference method in vivo. We compared Doppler systolic frequency shift integrals with electromagnetic flowmeter stroke volume in seven open-chest dogs. A pulsed Doppler echocardiographic transducer was held on the aortic arch with the sample volume in the ascending aorta. Stroke volume was varied by epinephrine or pentobarbital infusions, fluid administration or inferior vena caval constriction. Linear regression analysis of stroke volume vs Doppler systolic frequency shift integrals revealed strong correlations and intercepts close to zero ($r = 0.74–0.996, p < 0.001$). Minor changes in transducer position did not influence Doppler frequency shift integrals substantially. Therefore, pulsed Doppler echocardiography served as an excellent measurement of stroke volume changes in this model. However, serious limitations are presented that may limit its clinical application.

STROKE VOLUME can be measured reliably by invasive techniques such as indicator dilution and left ventriculography. However, because these techniques are associated with some morbidity and are not practical for serial measurements, there is great interest for a reliable and reproducible noninvasive method of cardiac output determination.

Ultrasound and radioisotopic techniques have been investigated for this purpose. M-mode echocardiography uses left ventricular internal dimensions to derive volume parameters used to calculate stroke volume, so it is unreliable because of its geometric assumptions, especially if abnormalities of the left ventricle are present.1 Echocardiographic methods using valvular motion to estimate cardiac output have not been fully validated.2 Moreover, with this technique, adequate studies may not be obtained in all patients. Radionuclide angiography provides a measure of stroke volume by ventriculographic volume determinations.3 However, absolute quantification is unreliable and for serial determinations over days, repeated injections of radioisotopes are necessary. Alternatively, the measurement of blood velocity by Doppler techniques as a noninvasive indicator of stroke volume have the advantages of simplicity and independence of cardiac geometric assumptions. Doppler shifted ultrasonic waves can provide direct information on aortic blood velocity and flow can be derived by $F = VxA$, where $F =$ volume flow, $V =$ average velocity across the vessel lumen and $A =$ vessel cross-sectional area.

As aortic vessel area changes minimally over a wide range of systolic pressures,4 5 the area under the Doppler frequency shift curve in systole (systolic frequency shift integral) as an index of velocity is a measure of stroke volume. Early experience with continuous-wave Doppler techniques6 7 and more recently with pulsed Doppler echocardiography8 9 has demonstrated some clinical usefulness for these techniques. However, as serious limitations difficult to evaluate in clinical trials have become evident,10 11 we investigated the use of a commercially available pulsed Doppler echocardiographic instrument in a dog model to compare Doppler flow profiles with those obtained from an electromagnetic flowmeter in the aortic root.

Methods

Seven mongrel dogs that weighed 10–25 kg were anesthetized with pentobarbital, 30 mg/kg i.v., intubated and ventilated at a tidal volume of 700 ml with supplemental oxygen (30–50%) at a rate appropriate to body weight. In each dog left thoracotomy and pericardectomy were performed and an electromagnetic flowmeter (Carolina Instruments) previously calibrated with blood and saline using a piece of aorta in vitro was placed on the ascending aorta above the aortic valve. Care was taken to ensure a stable fit without constricting the vessel lumen despite a wide range of aortic pressures. Zero check of the electromagnetic flowmeter was performed by brief mechanical occlusion of the aorta. A catheter was placed in the descending aorta via the femoral artery to monitor aortic pressure. The Doppler transducer of an ATL 500A pulsed Doppler echocardiogram (Advanced Technology Laboratories, Seattle, Washington) was manually held on the aortic arch, the sample volume was directed into the region of the ascending aorta encircled by the electromagnetic flowmeter and analog frequency shift curves were obtained.

The Doppler principle states that the frequency of a beam of ultrasound incident on a moving object will be shifted proportionally to the velocity of that object...
as given by the equation
\[ \Delta F = \frac{2F_0 \cos \theta}{C}, \]
rearranging to
\[ V = \frac{\Delta FC}{2F_0 \cos \theta}, \]
where \( \Delta F \) = frequency shift, \( \cos \theta = \) cosine of angle of incidence of sound on moving object, \( F_0 \) = frequency of transmitted sound, \( C \) = velocity of sound in medium and \( V \) = velocity of reflecting object. Cosine \( \theta \) can be assumed to be 1 \( (\pm 6\%) \) if the angle of incidence is kept within 20° of zero (fig. 1).

Net analog output from the Doppler, electromagnetic flowmeter signal and ECG were fed into an Electronics for Medicine or Irex strip-chart recorder for hard-copy reproduction at a paper speed of 50 mm/sec. The Doppler frequency shift curves were finely tuned using echocardiographic control and beam alignment manipulation until they resembled typical flow curves from the ascending aorta (fig. 2). Once this procedure was completed no controls were changed, but the transducer was removed and replaced frequently over the course of a study.

To produce variability in blood flow, different interventions were used. Stroke volume was varied by volume infusion with normal saline solution at 200-ml increments, infusion of epinephrine (2 mg in 500 ml of normal saline), rapid pentobarbital infusions (5–10 ml/kg) and graded inferior vena caval constriction. Two to 3 minutes were allowed to elapse between each intervention for stabilization of stroke volume, at which time electromagnetic flowmeter, Doppler and electrocardiographic signals were recorded for at least 30 seconds. An average of 9.2 consecutive beats was analyzed for each intervention. The area under each electromagnetic flow curve and Doppler systolic frequency shift curve was obtained using a SAC Graf pen on line with a PDP 1170 computer. Intraobserver variability in area determination was less than 5%. Stroke volumes and peak velocities were computed from the electromagnetic flowmeter curves. Peak excursion of the Doppler curve was measured from the zero frequency shift line in diastole to the peak of the systolic curve.

Results

Data Analysis

The Doppler systolic frequency shift integral for each beat was plotted against the electromagnetic flowmeter stroke volume in all seven dogs and linear regression analysis performed. The standard deviation of Doppler systolic frequency shift integral on electromagnetic stroke volume was used to assess the reproducibility of Doppler measurements. Because many clinically available techniques of stroke volume analysis are derived from averages of cardiac output determination, mean Doppler frequency shift integral was similarly plotted against mean electromagnetic stroke volume per intervention and linear regression analysis performed.

Uncalibrated controls are adjusted to obtain frequency shift curves from each dog, so data from each dog are individually analyzed, with no comparisons made between dogs.

The data from all experiments are shown in figure 3 and the results are summarized in table 1.

**Figure 1.** Schematic representation of the ultrasonic beam from the pulsed Doppler echocardiographic transducer incident on moving red blood cells. Note that changes in the angle of incidence (\( \theta \)) can markedly affect the value of \( \cos \theta \) used in the calculation of frequency shifts. If \( \theta \) is kept close to 0°, there is little variation in \( \cos \theta \).
Dog 1

Six interventions were performed and 60 beats analyzed (10 beats per intervention). Stroke volume ranged from 7–28 ml and the correlation with Doppler frequency shift integral was 0.89 ($p < 0.001$). Peak velocity was consistently less than 110 cm/sec at all stroke volumes. The correlation between mean stroke volume and mean Doppler frequency shift integral between interventions was 0.96 ($p < 0.01$).

Dog 2

Twelve interventions were performed and 9.1 consecutive beats per intervention analyzed. Stroke volume varied from 3–30 ml; the Doppler vs stroke volume correlation was 0.96 ($p < 0.001$). Peak velocity by electromagnetic flowmeter was as high as 163 cm/sec for the higher stroke volumes. Mean Doppler frequency shift integral and mean stroke volume per intervention demonstrated an $r$ value of 0.97 ($p < 0.001$).

Dog 3

Fifteen interventions were performed and 139 beats analyzed as above. Stroke volume varied from 2–28 ml, with peak velocities ranging from 15–81 cm/sec. The correlation between Doppler and stroke volume was 0.95 ($p < 0.001$). Mean Doppler vs mean stroke volume per intervention showed an $r$ value of 0.96 ($p < 0.001$).

Dog 4

Five interventions were performed in dog 4, and 43 beats were analyzed (8.6 per intervention). In this series of experiments, the stroke volume varied from 3–23 ml, with peak velocities of 16–87 cm/sec. The correlation coefficient between beat-to-beat Doppler frequency shift integral and stroke volume was 0.74 ($p < 0.001$). Mean Doppler vs mean stroke volume per intervention showed an $r$ value of 0.83 (NS).

Dog 5

Nine interventions were performed and 81 beats analyzed. The stroke volume ranged from 3–21 ml, with peak velocities of 17–53 cm/sec. The correlation between Doppler and stroke volume was 0.80 ($p < 0.001$). The mean data from each intervention show an $r$ value of 0.81 ($p < 0.01$).

Dog 6

Twelve interventions were performed in these experiments and 121 beats analyzed (10.1 per intervention). Stroke volume varied from 1–16 ml, with peak velocities of 7–85 cm/sec. The correlation coefficient of Doppler vs stroke volume was 0.87 ($p < 0.001$).
The mean data between interventions showed an $r$ value of 0.85 ($p < 0.001$).

**Dog 7**

Ten interventions were performed, with 83 beats analyzed (8.3 beats per intervention). Stroke volume and peak velocity ranged from 1-11 ml and 7-26 cm/sec, respectively. The correlation between Doppler frequency shift integral and stroke volume was 0.95 ($p < 0.001$). Mean data between interventions showed an $r$ value of 0.96 ($p < 0.001$).

**Table 1. Electromagnetic Flowmeter and Pulsed Doppler Measurements for All Seven Dogs**

<table>
<thead>
<tr>
<th>Dog</th>
<th>No. of interventions</th>
<th>Mean no. of beats per intervention</th>
<th>SV</th>
<th>SFSI</th>
<th>SV vs SFSI</th>
<th>PV</th>
<th>MSV</th>
<th>MSFSI</th>
<th>MSV vs MSFSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>10.0</td>
<td>10</td>
<td>0.311-0.669</td>
<td>0.89†</td>
<td>0.047</td>
<td>52-138</td>
<td>12-24</td>
<td>0.401-0.613</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>9.1</td>
<td>20</td>
<td>0.107-0.655</td>
<td>0.96†</td>
<td>0.051</td>
<td>25-263</td>
<td>4-28</td>
<td>0.162-0.668</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>9.3</td>
<td>28</td>
<td>0.042-0.771</td>
<td>0.95†</td>
<td>0.054</td>
<td>15-81</td>
<td>4-22</td>
<td>0.082-0.524</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>8.6</td>
<td>22</td>
<td>0.101-0.947</td>
<td>0.74†</td>
<td>0.173</td>
<td>16-87</td>
<td>4-17</td>
<td>0.240-0.756</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>9.0</td>
<td>28</td>
<td>0.176-0.748</td>
<td>0.80†</td>
<td>0.084</td>
<td>17-53</td>
<td>5-16</td>
<td>0.253-0.639</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>10.1</td>
<td>16</td>
<td>0.015-0.189</td>
<td>0.87†</td>
<td>0.030</td>
<td>7-85</td>
<td>3-14</td>
<td>0.056-0.223</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>8.3</td>
<td>11</td>
<td>0.044-0.485</td>
<td>0.95†</td>
<td>0.038</td>
<td>7-26</td>
<td>3-10</td>
<td>0.115-0.446</td>
</tr>
</tbody>
</table>

* $p < 0.01$.
† $p < 0.001$.
‡ Range of values for all interventions.

Abbreviations: SV = electromagnetic flowmeter determined stroke volume; SFSI = pulsed Doppler systolic frequency shift integral; PV = electromagnetic flowmeter determined peak velocity; MSV = mean of electromagnetic flowmeter determined stroke volumes per intervention; MSFI = mean of pulsed echo Doppler systolic frequency shift integrals per intervention.
Discussion

Our study demonstrates that under controlled experimental conditions, pulsed Doppler echocardiography can provide a sensitive and reproducible measure of beat-to-beat stroke volume changes. The sensitivity of this method is demonstrated by the linear Doppler response to minimal changes in stroke volume and the reproducibility by the small standard error of the estimate (fig. 3, table 1). Absolute quantification of blood velocity was not possible because the uncalibrated echocardiographic controls of the pulsed echo Doppler influence zero crossing detection of frequency shifts. However, by holding these controls constant in a given study, changes in frequency shift are a linear representation of changes in velocity. An in vitro method of pulsed Doppler calibration has been developed using a nonpulsatile water tank that may provide a paradigm for absolute quantitation of pulsatile blood velocity in vivo.

Other methods of pulsed Doppler calibration using water tank models with blood substitutes or direct in vivo measurement of blood volume per unit time should be considered.

The ability to range gate pulsed Doppler is a major advantage over continuous-wave Doppler, and frequency shifts from a 2 × 4 mm sample volume can be assessed while excluding those from extraneous objects or vessels (i.e., pulmonary artery). The pulse repetition rate, however, limits the maximal blood velocity that can be detected, which is 164 cm/sec, with pulse repetition rates used in this and most human studies. Colocausis et al. showed in animal experiments that peak velocity is linearly related to stroke volume except at higher cardiac outputs, where stroke volume is augmented by a prolongation of ejection while peak velocity plateaus. In our study, peak velocity as measured by electromagnetic flowmeter did not exceed 155 cm/sec (fig. 4). In addition, because peak velocities in the ascending aorta in humans are well under 120 cm/sec over wide ranges of cardiac outputs, the limit to peak velocity determination imposed by pulsing the echo beam was not of practical significance in our study, nor should it be a factor in clinical use.

Doppler frequency shift integrals underestimated the true stroke volume in some interventions. The data points from two interventions in dog 2 (fig. 3B, open triangles) and from one intervention in dog 4 (fig. 3D, open circles) lie to the right, but parallel to those of other interventions. This variability in Doppler frequency shift integral for a given stroke volume would make clinical prediction of stroke volume from Doppler analysis unreliable. However, qualitative analysis of Doppler frequency shift curves from these interventions show considerable systolic irregularity and low-frequency diastolic activity, as shown in figure 5, compared with those in figure 2. As the audio profile was harsh, multiple reflectors traveling at different velocities were probably present in the sample volume during these measurements. Such diversification of velocity, and therefore of frequency shift, can be produced by systolic turbulence. However, low-frequency signals are seen in diastole, indicating low-

![Figure 4](link)

**Figure 4.** Stroke volume vs peak blood velocity as measured by electromagnetic flowmeter from a representative dog. Note the tendency for peak velocity to plateau at higher stroke volumes.

![Figure 5](link)

**Figure 5.** Doppler frequency shift curves showing systolic and diastolic irregularities that may influence frequency shift quantitation by zero crossing meter analysis.
velocity movement in the sample volume, which are usually due to moving tissue interfaces or motion of the transducer relative to reflectors. If these low-frequency signals were present in systole, they would significantly interfere with frequency shift analysis, and thus, with systolic blood velocity determination using zero crossing meter analysis. High-frequency components may "ride" on lower frequencies (fig. 6) and if these high frequencies are of relatively low amplitude they will not cross the baseline and will escape detection.11 By excluding from analysis Doppler curves that manifest low-frequency contamination (open triangles and circles in figure 3), the correlation between mean Doppler systolic frequency shift integral and mean electromagnetic flowmeter stroke volume in dog 4 becomes 0.9 (p < 0.025) and scatter of Doppler measurements is further reduced both in dogs 2 and 4. In human studies, the distance from the suprasternal notch to the ascending aorta and intervening structures18 that absorb and reflect ultrasound necessitates using higher gain settings, which may aggravate this problem with extraneous high-amplitude, low-frequency sounds.

Another finding in our data that requires further comment is the apparent overestimation of stroke volume by Doppler systolic frequency shift integral at very low stroke volumes (fig. 3B, open squares). These squares represent data points from four different interventions restricting preload and resulting in clinical shock. Similar findings have been reported comparing continuous-wave Doppler measures of stroke volume against thermodilution cardiac output.12 As we could directly visualize transducer alignment relative to flow, we would speculate that changes in aortic diameter or velocity profile at low stroke volume cause this overestimation of stroke volume. Concurrent measurement of aortic area and blood velocity with combined two dimensional pulsed Doppler instrumentation would eliminate the need for the perhaps unwarranted assumption of constant aortic area at these extremes of cardiac output. This question, as well as the nature of the velocity profile across the aortic lumen at varying flow rates, requires further study.

Our data demonstrate the usefulness of pulsed Doppler techniques to measure stroke volume changes. The use of Fourier analysis to provide a more precise measure of all frequency shifts within the sample volume17 and two-dimensional pulsed Doppler echocardiographic systems18 are innovations that may make pulsed Doppler echocardiography a practical quantitative measure of beat-to-beat stroke volume in man.

References

Determination of Left Ventricular Volume in Children: Echocardiographic and Angiographic Comparisons

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SUMMARY  Left ventricular volumes and ejection fraction were calculated from the M-mode and two-dimensional echocardiograms and cineangiograms in 20 children, ages 2 months to 18 years. The cube and corrected cube methods were used to calculate volumes from the M-mode recordings. Ventricular volumes were measured from two-dimensional echocardiograms using the apical long-axis and apical four-chamber views. Endocardial outlines were traced from the televised images with a light pen and analyzed by a microcomputer. With a single-plane area-length method, the end-diastolic volume, end-systolic volume, stroke volume, and ejection fraction were calculated for each left ventricular view. The ventricular volumes and ejection fraction were computed by biplane area-length and Simpson’s rule methods from the combined recorded outlines of the two left ventricular views. The volumes and ejection fraction determined by echocardiography were compared with those determined from cineangiograms recorded 24 hours after the echocardiographic studies. In general, the correlation coefficients were better for the two-dimensional than the M-mode technique. Two-dimensional echocardiography was a good predictor of the angiographic end-diastolic volume but overestimated slightly the angiographic end-systolic volume. For ejection fraction, the best correlation with angiography was achieved by the two-dimensional echocardiographic techniques, especially the biplane area-length method ($r = 0.82$) and the apical, long-axis, single-plane area-length method ($r = 0.77$). Two-dimensional echocardiography is more accurate than M-mode echocardiography for predicting angiographic left ventricular volume and function in pediatric patients.

LEFT VENTRICULAR volume determination is useful in children with congenital heart disease for evaluating left ventricular function, intracardiac and extracardiac shunts, and pulmonary blood flow in patients with aortopulmonary transposition. The standard method for evaluating left ventricular volume is an invasive technique that uses ventricular outlines traced from cineangiograms. An accurate, noninvasive technique for determining left ventricular volume and ejection fraction in children has not been established. Measurements of ventricular volume and ejection fraction by M-mode echocardiography may be compromised by segmental dysfunction or paradoxical septal motion. In studies in adults, two-dimensional echocardiography is more accurate than M-mode echocardiography for estimating ventricular volume and ejection fraction. We compared ventricular volumes and ejection fraction derived from several M-mode and two-dimensional echocardiographic methods to those derived from cineangiography to determine the most accurate noninvasive technique for predicting these variables in children.

Methods

We calculated the end-systolic volume, end-diastolic volume, stroke volume and ejection fraction from the M-mode and two-dimensional echocardiograms obtained from 20 consecutive patients who had left ventricular angiograms suitable for analysis. Their ages ranged from 2 months to 18 years, body surface area ranged from 0.24–1.86 m² and weight ranged from 3.54–70 kg (table 1). The echocardiograms were recorded in the 24 hours before cardiac catheterization and were evaluated before calculating left ventricular volumes from the angiograms.

The ventricular angiograms were considered satisfactory for biplane volume analysis only if there were three consecutive, opacified sinus beats. The third beat was used for volume analysis. Three investigators manually traced the left ventricle from posteroanterior and lateral angiograms and averaged...
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Circulation. 1980;62:542-548
doi: 10.1161/01.CIR.62.3.542

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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