The influence of preload and heart rate on Doppler echocardiographic indexes of left ventricular performance: comparison with invasive indexes in an experimental preparation

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ABSTRACT We evaluated the ability of Doppler echocardiography to assess left ventricular performance in six open-chest dogs studied under various conditions. Intravenous infusions of nitroglycerin were used to vary preload, atrial pacing was used to control heart rate, and changes in inotropic state were induced by two different doses of dobutamine (5 and 10 μg/kg/min iv) and by administration of propranolol (1 mg/kg iv). Left ventricular anterior wall myocardial segment length was used as an index of preload. Maximum aortic blood flow, peak acceleration of aortic blood flow, and dP/dt were measured with an electromagnetic flow probe around the ascending aorta and a high-fidelity pressure transducer in the left ventricle. A continuous-wave Doppler transducer applied to the aortic arch was used to measure peak aortic blood velocity, mean acceleration, time to peak velocity, and the systolic velocity integral. The differences between mean values obtained under different inotropic conditions were significant at the p < .01 level for peak velocity and at the p < .05 level for mean acceleration. Within a given animal, Doppler measurements of peak velocity correlated very closely with maximum aortic flow (r = .96), maximum acceleration of aortic flow (r = .95), and with maximum dP/dt (r = .92). Mean acceleration measured by Doppler echocardiography also correlated very closely with conventional indexes, but was subject to greater interobserver variability. Doppler measurements of time to peak and the systolic velocity integral correlated less well with conventional hemodynamic indexes. In conclusion, Doppler measurements of peak aortic blood velocity and mean acceleration offer an effective means to noninvasively assess short-term changes in left ventricular performance under conditions of varying preload, heart rate, and inotropic state.


THE ASSESSMENT of left ventricular performance is of key importance in determining the presence and prognosis of many forms of heart disease, and in monitoring the effectiveness of therapeutic interventions. Conventional invasive techniques are limited by high cost, the risk to the patient of complications, and technical difficulties in assessing performance during dynamic states such as exercise. These limitations become particularly important in the context of the serial determinations required to monitor the course of disease or response to therapy.

The potential use of measurements of aortic blood acceleration and peak velocity as indexes of ventricular performance in patients with heart disease was suggested by Rushmer1 more than 20 years ago. Since then, invasive studies have demonstrated the sensitivity of maximum acceleration of aortic blood flow (dQ/dt) to depressed ventricular function caused by coronary occlusion,2 acute myocardial infarction,3 and the administration of propranolol.4 The development of Doppler echocardiography now offers a reliable method with which to measure aortic blood flow velocity and acceleration noninvasively.5–8 Clinical studies have suggested its use in the management of critically ill patients,9 and in the identification of left ventricular dysfunction in patients during exercise.10,11

Validation of Doppler echocardiography as a useful tool in assessment of ventricular performance depends on the demonstration of the sensitivity of Doppler measurements to changes in contractility, and on an appre-
cation of the degree to which these measurements are influenced by preload, afterload, and heart rate. The current study was undertaken to define the relationship between Doppler echocardiographic measurements related to the ascending aortic blood velocity and the more conventional indexes left ventricular dP/dt, maximum aortic blood flow (Q\text{max}), and maximum dQ/dt under varying conditions of preload, heart rate, and inotropic state.

Methods

Six mongrel dogs weighing 23.6 to 33.0 kg were screened for parasites, fasted overnight, and anesthetized with intravenous administration of an \( \alpha \)-chloralose and urethane solution. The dogs were then intubated and ventilated by a volume respirator (Harvard Apparatus Co.) with the use of air enriched with oxygen (5 liters/min), and a thoracotomy was performed in the left fifth intercostal space of each. Polyvinyl catheters (Tygon Microbore Tubing, 0.05 inch inside diameter; Norton Plastics) were introduced into the right atrium via the internal thoracic vein, into the left atrium through a purse-string suture, and into a femoral artery, and were connected to fluid-filled Statham P23Db pressure transducers (Statham Instrument Co.), with the zero pressure reference point at mid right atrial level. A micromanometer-tipped catheter (Millar Instruments) was advanced to the ascending aorta via the internal thoracic artery for measurement of aortic blood pressure. An electromagnetic flow probe (Howell Instrument Co.) was placed around the ascending aorta and blood flow was measured with a Narcomatic flowmeter (Model RT-500, Narco Biosystems). A micromanometer (Konigsberg Instruments) was inserted into the left ventricle through an apical stab wound and secured with a purse-string suture. Two sonomicrometer crystals (Vermitron Piezoelectric Division, PZT5A, flat and cylinder) were inserted into the anterior left ventricular free wall at midmyocardial level perpendicular to the long axis of the heart, and the distance between them was measured (Hartley Multichannel Flow-Dimension System) as an index of preload. Pacing wires were sutured to the left atrium, and a hydraulic occluder was placed on the descending thoracic aorta to allow maintenance of aortic blood pressure if needed. The electrocardiogram was monitored throughout, and arterial blood gases were measured at intervals of 1 hr and were maintained in the normal range.

All hemodynamic measurements were made under steady-state conditions with mechanical ventilation for 15 to 30 sec suspended to eliminate respiratory variation. Hemodynamic data were recorded on an analog FM tape recorder (A. R. Vetter Co.) and on an eight-channel strip-chart recorder (Gould Model 2800). Ten second data files were subsequently transferred to a digital computer (DEC LSI 11/23) and sequential interactive programs were used to calculate Q\text{max}, maximum dQ/dt, and maximum left ventricular dP/dt. Simultaneously with the collection of hemodynamic data, Doppler measurements of blood velocity were obtained in the continuous mode with a dedicated nonimaging Doppler transducer (Pedof) with a 2 MHz carrier frequency (Irex IIIB, Johnson & Johnson), and recorded on a strip-chart recorder at a paper speed of 50 mm/sec. The transducer was hand held and applied to the aortic arch. The ultrasonic beam was oriented parallel to ascending aortic blood flow, guided by audio and graphic signals to obtain maximal Doppler shift with velocity envelopes having distinct borders. Doppler measurements of peak blood velocity (PV), time to peak velocity (TTP), and mean acceleration (A = PV/TTP) were made for 6 consecutive beats (figure 1) and averaged. The systolic veloc-

**FIGURE 1.** A representative recording of the electrocardiogram, analog Doppler signal, and Doppler velocity envelope, illustrating the method of Doppler measurement. Velocity calibration = 1 m/sec. ET = ejection time. Mean acceleration was calculated as PV/TTP.

ity integral (SVI) was calculated as the product of mean velocity and ejection time, and was determined for a single representative beat. Doppler measurements were made by two observers and the data were averaged.

With the animals in the baseline contractile state, measurements were obtained before the administration of drugs, both at resting heart rate and with rapid atrial pacing (resting heart rate + 40 beats/min). The infusion of nitroglycerin was begun at 100 \( \mu \)g/min iv, and was increased to 200 \( \mu \)g/min if necessary to produce a greater than 2.5% decrease in end-diastolic myocardial segment length. Measurements were then obtained in dogs in sinus rhythm and during rapid atrial pacing. A simultaneous infusion of dobutamine was begun, and data were collected at infusion rates of 5 and at 10 \( \mu \)g/kg/min with the animals in sinus rhythm. The infusion of nitroglycerin was then discontinued, allowing segment length to increase. Measurements were then made sequentially at 10 \( \mu \)g/kg/min and 5 \( \mu \)g/kg/min dobutamine and in the control state, with and without rapid atrial pacing. Finally, propranolol was administered (1 mg/kg iv) and data were collected in dogs in sinus rhythm and, if tolerated, during rapid atrial pacing. Data were collected after a steady state had been maintained for at least 5 min. Data files in which pulsus alternans occurred were excluded from analysis.

For each animal studied, the values for each index of contractility obtained in each inotropic state were averaged. These within-animal means were themselves averaged to give equal weight to each animal, and the differences between states were
The expected changes in the ejection time and TTP were also present, but were less obvious. Changes in mean acceleration and the SVI were for the most part reflective of changes in the PV.

The mean values of all index measurements in all animals calculated for each inotropic state are presented in table 1, with comparisons by paired t tests of values obtained in adjacent inotropic states. Differences in the values of PV obtained with alterations in contractility were significant at the p < .01 level, and those for acceleration were significant at the p < .05 level. Changes in TTP and SVI in dogs in different inotropic states varied.

The relationships between each of the Doppler-derived indexes of ventricular function and the conventional invasively derived indexes are presented in table 2, and the specific correlation between PV and Q_max is illustrated in figure 3. PV was found to correlate very closely with Q_max (r = .96), with dQ/dt (r = .95), and with dP/dt (r = .92). Mean acceleration correlated best with dQ/dt (r = .92), but also correlated closely with Q_max and with dP/dt (r = .90 and .91, respectively). The correlations of the SVI with the conventional indexes were less significant. The poorest correlations were between TTP and the invasive indexes. When the regression analysis of Doppler vs invasive indexes was repeated after adjustment for the effect of heart rate and variations in preload, the resulting correlation coefficients were essentially unchanged from those obtained before adjustment.

The analysis of interobserver variability is summarized in figure 4. The measurement of PV was associated with the least interobserver variability, with a mean difference between observers of only 3.7%. Differences between observers were most problematic in

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**FIGURE 2.** Doppler recordings and simultaneous electrocardiogram taken from a representative animal in the control state, during the infusion of dobutamine (10 μg/kg/min iv), and after administration of propranolol (1 mg/kg iv).
TABLE 1
Mean ± SD values for each index under each inotropic condition

<table>
<thead>
<tr>
<th></th>
<th>Doppler indexes</th>
<th>Invasive indexes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PV (m/sec)</td>
<td>Acceleration (m/sec²)</td>
</tr>
<tr>
<td>Control vs</td>
<td>1.55 ± 0.34</td>
<td>42.2 ± 22.7</td>
</tr>
<tr>
<td>Dobutamine, 5 μg/kg/min vs Dobutamine, 5 μg/kg/min</td>
<td>1.87 ± 0.44</td>
<td>57.4 ± 27.4</td>
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<td>1.55 ± 0.34</td>
<td>42.2 ± 22.7</td>
</tr>
</tbody>
</table>

The level of significance for t tests between values in adjacent inotropic states are given in parentheses. Measurements obtained with and without infusion of nitroglycerin are pooled for each inotropic state.

the determination of TTP, where the difference between observers averaged 14.8%. Since mean acceleration is calculated as PV/TTP, it reflects the interobserver variability for the determination of TTP, with a mean difference between observers of 16.8%. The mean interobserver difference for SVI was 10.7%.

Discussion

The results of the current study demonstrate that Doppler echocardiographic measurements of ascending aortic blood velocity are very sensitive to changes in left ventricular systolic performance. That PV and mean acceleration are more sensitive than the TTP or the SVI is demonstrated by their superior ability to detect differences in inotropic states and by their better correlations with conventional invasive indexes. The finding that these correlations were not appreciably affected by adjustment for heart rate or preload suggests that the Doppler indexes are no more influenced by these variables than are the conventional invasive indexes studied.

Some overlap of index measurement in different states was noted for each Doppler and conventional index studied, and may be partially attributed to variation between animals with respect to responses to the agents used to alter contractility and to the fact that the range of variation in preload differed between animals. Doppler indexes share the basic limitation of all indexes of ventricular function, namely that they do not measure contractility directly. Thus, while we have found Doppler measurements of aortic PV and mean acceleration to be as sensitive as conventional indexes to changes in contractility, they are no better than conventional indexes in defining inotropic state in an absolute way and are not practical for comparison of contractile states between individuals. This limitation of Doppler indexes of function has been described by others, and suggests that the value of this technique lies in its ability to detect changes in ventricular function in a given individual.

TABLE 2
Correlations between Doppler (horizontal rows) and invasively derived (vertical columns) indexes of left ventricular function for all six animals studied

<table>
<thead>
<tr>
<th></th>
<th>Q max</th>
<th>Max dQ/dt</th>
<th>Max dp/dt</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>.96</td>
<td>.95</td>
<td>.92</td>
</tr>
<tr>
<td>r(HR)</td>
<td>.95</td>
<td>.94</td>
<td>.91</td>
</tr>
<tr>
<td>r(SL)</td>
<td>.94</td>
<td>.93</td>
<td>.89</td>
</tr>
<tr>
<td>Acceleration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>.90</td>
<td>.92</td>
<td>.91</td>
</tr>
<tr>
<td>r(HR)</td>
<td>.88</td>
<td>.91</td>
<td>.88</td>
</tr>
<tr>
<td>r(SL)</td>
<td>.87</td>
<td>.91</td>
<td>.88</td>
</tr>
<tr>
<td>TTP</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>r</td>
<td>-.67</td>
<td>-.70</td>
<td>-.70</td>
</tr>
<tr>
<td>r(HR)</td>
<td>-.60</td>
<td>-.63</td>
<td>-.61</td>
</tr>
<tr>
<td>r(SL)</td>
<td>-.56</td>
<td>-.61</td>
<td>-.63</td>
</tr>
<tr>
<td>SVI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>.79</td>
<td>.75</td>
<td>.69</td>
</tr>
<tr>
<td>r(HR)</td>
<td>.83</td>
<td>.80</td>
<td>.76</td>
</tr>
<tr>
<td>r(SL)</td>
<td>.78</td>
<td>.72</td>
<td>.64</td>
</tr>
</tbody>
</table>

r = correlation coefficient for variables indicated by row and column heading; r(HR) = partial correlation coefficient adjusted for heart rate; r(SL) = partial correlation coefficient adjusted for segment length.
FIGURE 3. Relationship between Doppler-determined aortic PV and \( Q_{\text{max}} \) (electromagnetic flowmeter) is shown for each of six animals. The pooled correlation coefficient without adjustment for heart rate or changes in preload was .96.

FIGURE 4. Histogram illustrating percent difference between two observers for individual measurements of each Doppler index.
catheter-tipped velocity probes found maximum acceleration to be the most sensitive index of function.\textsuperscript{2-4} The Doppler technique that we used differs in that it measures mean rather than maximum acceleration. This difference may account for the fact that we found acceleration to be somewhat less sensitive than PV in detecting changes in inotropic state. Prior work evaluating Doppler echocardiographic assessment of left ventricular function has focused on the agreement of Doppler measurements with ejection fraction values\textsuperscript{11, 15} and, when combined with determination of aortic cross-sectional area, with results of traditional methods of measuring cardiac output. Ejection fraction and cardiac output are strongly influenced by loading conditions, however. It is encouraging that Doppler measurements of PV and mean acceleration are highly sensitive to changes in contractile state over the range of preload likely to be encountered clinically.

The need to make our measurements under stable hemodynamic conditions in different inotropic states precluded variation of both preload and afterload in a single study. Further studies are therefore required to evaluate the effect of afterload on Doppler indexes of left ventricular performance, and to help identify the Doppler index that best reflects changes in contractility in settings in which afterload is not constant. Further studies are also needed to confirm work with catheter-tipped velocity probes demonstrating the sensitivity of aortic blood flow velocity and acceleration to changes in regional as well as global ventricular function.\textsuperscript{2-3}

The most important technical problem encountered in making Doppler measurements was the occasional difficulty in correctly identifying the onset and termination of ventricular ejection, events that are sometimes obscured by baseline artifacts. As the histogram demonstrated (figure 4), the relatively higher mean differences between observers for time-dependent Doppler indexes (acceleration, TTP, and SVI) resulted from proportionately large differences on only a few occasions. Predictably, these instances occurred when the heart rate was very high and TTP and ejection time were short. Further developments in instrumentation may result in more reproducible recordings of acceleration or permit accurate measurement of maximum acceleration, making this measurement more useful.

The finding here that Doppler indexes of left ventricular function are comparable to conventional indexes in their sensitivity to changes in contractility at varying levels of preload and heart rate lends impetus to the study of potential clinical uses of this technique. Productive areas for investigation may include application of Doppler echocardiography to exercise stress testing and to serial evaluation of left ventricular function after therapeutic interventions.

In conclusion, while each of the Doppler indexes studied showed significant correlation with conventional invasive indexes, peak velocity appears to be the best of the Doppler indexes, showing the closest correlation with the least interobserver variation. Although the effect of changes in afterload remains to be defined, the Doppler indexes studied appear no more dependent on preload or heart rate than are the conventional invasive indexes. Thus, the Doppler echocardiographic determination of ascending aortic blood velocity offers a promising noninvasive method for the assessment of changes in left ventricular performance in individuals in a wide variety of clinical situations.

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