The Rate of Change of Left Ventricular Volume in Man

I. Validation and Peak Systolic Ejection Rate in Health and Disease

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SUMMARY
The rate of left ventricular volume change (dV/dt) is by definition left ventricular ejection rate during systole and filling rate during diastole, and in the absence of valvular regurgitation or intracardiac shunts, is equal to systolic aortic valve flow and diastolic mitral valve flow respectively. A computerized technique for the calculation of instantaneous left ventricular dV/dt from cineangiographically measured left ventricular volume is presented. Curve smoothing was accomplished by passing a second degree polynomial through nine consecutive volume points using the least squares technique. Validity of this technique was demonstrated by the high degree of correlation of systolic dV/dt with instantaneous ascending aortic blood velocity (flow) measured simultaneously with an electromagnetic catheter-tip velocity transducer in ten patients. Peak left ventricular systolic ejection rate ($S dV/dt$) was calculated from single plane cineangiographically measured left ventricular volumes in 113 adult patients and related to other measures of cardiovascular function. Mean $S dV/dt$ for the group of 29 normal patients was 427 ± 129 cc per second and was not significantly different in patients with coronary artery disease (21), aortic stenosis (13), mitral stenosis (11), or cardiomyopathy (9), but was increased significantly in patients with valvular regurgitation (19). $S dV/dt$ correlates poorly with the ejection fraction and with left ventricular end-diastolic pressure (LVEDP) and is not a reliable measure of left ventricular function. The primary determinant of $S dV/dt$ appears to be total left ventricular stroke volume. When $S dV/dt$ is divided by end-diastolic volume (EDV), the resultant $S dV/dt/EDV$ correlates well with peak normalized circumferential fiber shortening rate ($r = 0.89, P < 0.01$) and with ejection fraction ($r = 0.69, P < 0.01$). The correlation coefficient of $S dV/dt/EDV$ with LVEDP was $r = 0.36 (P < 0.01)$ and with arterio-venous oxygen difference, $r = 0.38 (P < 0.01)$. Thus, $S dV/dt/EDV$ appears to be a measure of ventricular function. $S dV/dt$ occurs in midsystole in normal subjects and in patients with mitral regurgitation and is not delayed in patients with aortic stenosis. The three patients with idiopathic hypertrophic subaortic stenosis appeared to have characteristic changes in the left ventricular ejection rate curve with an increase in $S dV/dt$ (and especially $S dV/dt/EDV$), with $S dV/dt$ occurring earlier in systole than normal.

Additional Indexing Words: Left ventricular ejection rate Left ventricular function Peak systolic dV/dt Aortic blood flow Velocity transducer

Very little quantitative data on the rate of left ventricular filling and ejection in man are available, although aortic root blood velocity and flow can be measured with catheter-tip velocity transducers. The development of quantitative left ventricular angiography has made possible the calculation in man of left ventricular volume and a number of derived parameters of

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cardiac function such as ejection fraction and left ventricular mass. The application of this technique to the single-plane cineangiogram allows 60 or more volume measurements per second, thus making possible quantitative analysis of a portion of the cardiac cycle such as rate of ejection and filling of the left ventricle. This study was undertaken to develop and validate a technique for the calculation of the instantaneous rate of change of left ventricular volume (dV/dt) in man, and to make a detailed analysis of systolic dV/dt in a group of 113 patients with and without various forms of heart disease.

Normal values of peak systolic left ventricular ejection rate (S dV/dt) are given together with measurements for various disease groups. The usefulness of S dV/dt as a measure of left ventricular function is compared with other measures of ventricular performance. Ejection rate curves for patients with aortic stenosis, mitral regurgitation, and idiopathic hypertrophic subaortic stenosis (IHSS) are analyzed and discussed.

Methods
Technique of Calculation of dV/dt
Left ventricular volume was calculated from each frame of the cineangiogram using the area-length method of Kasser et al. This technique results in a slight consistent overestimation of actual left ventricular volume. Therefore, in this laboratory regression equations have been computed for correction to actual volume by comparison of single-plane cineangiographic end-diastolic and end-systolic volumes with comparable volumes calculated from the biplane large film angiogram in the same patient at the same study approximately 30 min apart.

For the posterior-anterior (PA) cineangiogram the regression equation based on study of 25 patients in this laboratory was

\[ V_b = 0.855 V_c + 5.8 \text{ cc}, \ r = 0.97, \ \text{SEE} = 19 \text{ cc} \]

where \( V_b \) is the actual left ventricular volume calculated from the biplane large film angiogram and \( V_c \) is the PA single-plane cineangiographic volume. For the right anterior oblique (RAO) cineangiogram, the regression equation based on a second study of 25 patients is

\[ V_b = 0.792 V_c - 0.07 \text{ cc}, \ r = 0.96, \ \text{SEE} = 31 \text{ cc} \]

A typical left ventricular volume curve obtained with this technique from a patient with coronary disease and normal ejection fraction and left ventricular end-diastolic pressure is shown in the upper portion of figure 1.

Because of scatter in the primary volume data, some type of curve smoothing of the volume-time curve is necessary before differentiation is possible. Of three curve-smoothing techniques investigated in our laboratory (polynomial approximation, frequency-domain design, and time-domain design), the first was selected because the others resulted in phase shift. Instantaneous left ventricular dV/dt determined for each point of the volume curve is plotted against time in the lower half of figure 1.

Studies for Validation of Method
In ten adult patients undergoing cardiac catheterization after having given informed written consent, ascending aortic root blood velocity was measured simultaneously with angiography using a catheter-tip electromagnetic velocity (flow) transducer (Carolina Medical Electronics) introduced percutaneously into the femoral artery and positioned in the ascending aorta about 4 cm above the aortic valve. Of these ten, five, who were clinically and hemodynamically normal, had volunteered for a study evaluating the catheter-tip electromagnetic velocity (flow) transducer. In these five patients angiography was performed by injection of 1 cc/kg 75% sodium-meglumine diatrizoate (Hypaque-M) over 2–3 sec through an 8F NIH catheter into the pulmonary artery. In the remaining five patients, diagnostic left heart catheterization was performed by the transseptal route with injection into the left atrium (two patients) or left ventricle (three patients). The final cardiac diagnoses were normal in two and one each nonobstructive cardiomyopathy, mitral stenosis, and pulmonic stenosis.

Calculation of Aortic Root Blood Velocity (Flow)
The ECG, velocity signal, and a marker indicating time of exposure of each frame of cine film were recorded on paper at 100 mm/sec (Electronics for Medicine, DR-8). The cross-sectional area of the ascending aorta at the level of the catheter velocity transducer was measured throughout one systole from each frame of the cineangiogram with correction for X-
ray distortion by use of a 1 cm grid filmed at the level of the ascending aorta. The instantaneous blood velocity through one systole (simultaneous with the left ventricular cineangiogram) was measured at 16.7 msec intervals corresponding in time to the exposure of each frame of the cineangiogram and multiplied by the cross-sectional area of the aorta to calculate instantaneous aortic blood flow. The characteristics of the instrument, techniques of calibration, and calculation of velocity and flow have been previously described.\(^\text{11,12}\) The instantaneous ascending aortic blood flow measurements were then compared with the simultaneously measured dV/dt.

**Validation of Method**

If the internal cross-sectional area of the vessel is known, and assuming that the velocity profile throughout the cross-sectional area is flat as indicated by Ling et al.,\(^\text{13}\) then flow through the vessel can be calculated from the velocity signal. Systolic dV/dt in the absence of mitral regurgitation or a shunt at the ventricular level should be equal to ascending aortic root blood flow, assuming that coronary flow during systole is negligible. Figure 2 shows an example of instantaneous ascending aortic root blood flow calculated from the velocity transducer and instantaneous dV/dt for the same systole in that patient plotted on the same scale. The similarity of the two curves is apparent. Table 1 shows the statistical analysis of the relationship of left ventricular dV/dt to simultaneously measured aortic root blood flow for each of ten patients. The correlation coefficient of dV/dt vs aortic root blood flow is high for every individual patient (\(r = 0.86-0.96\)). However, in some cases, and for the entire group, the slope of the regression equation is less than unity, indicating that at high instantaneous flows dV/dt slightly exceeds aortic root blood flow. This discrepancy may be explained in part by coronary blood flow not being sampled by the velocity transducer positioned in the midascending aorta. Nevertheless, these two markedly different techniques provide remarkably similar results, both for each individual patient and for the group as a whole. Figure 3 graphically illustrates these data for 160 pairs in the ten patients. The mean value of the angiographic dV/dt (267 cc/sec) is identical to the mean value of the aortic flow (267 cc/sec) Thus, by comparison with the independent aortic flow method, the computed left ventricular dV/dt during systole appears to be valid. There is no comparable independent method of measuring instantaneous mitral diastolic flow in man. However, since the technique of calculating left ventricular dV/dt is the same during diastole as during systole, the measurement of diastolic dV/dt should be equally valid.

**Table 1**  

<table>
<thead>
<tr>
<th>Patient</th>
<th>(n)</th>
<th>(r)</th>
<th>(\bar{x})</th>
<th>(\bar{y})</th>
<th>Range of (x)</th>
<th>Range of (y)</th>
<th>Regression equation</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS</td>
<td>17</td>
<td>0.93</td>
<td>284</td>
<td>381</td>
<td>66-418</td>
<td>79-631</td>
<td>(y = 1.51x - 48.2)</td>
<td>70.3</td>
</tr>
<tr>
<td>CJ</td>
<td>18</td>
<td>0.86</td>
<td>224</td>
<td>264</td>
<td>73-336</td>
<td>95-410</td>
<td>(y = 1.10x + 18.3)</td>
<td>46.6</td>
</tr>
<tr>
<td>OM</td>
<td>22</td>
<td>0.96</td>
<td>239</td>
<td>236</td>
<td>34-470</td>
<td>10-458</td>
<td>(y = 1.01x - 4.9)</td>
<td>41.9</td>
</tr>
<tr>
<td>DR</td>
<td>17</td>
<td>0.87</td>
<td>159</td>
<td>140</td>
<td>41-269</td>
<td>22-243</td>
<td>(y = 0.66x + 35.0)</td>
<td>30.6</td>
</tr>
<tr>
<td>EW</td>
<td>19</td>
<td>0.93</td>
<td>236</td>
<td>262</td>
<td>56-408</td>
<td>42-421</td>
<td>(y = 0.84x + 64.9)</td>
<td>40.2</td>
</tr>
<tr>
<td>CR</td>
<td>7</td>
<td>0.90</td>
<td>581</td>
<td>418</td>
<td>397-577</td>
<td>259-486</td>
<td>(y = 0.82x - 57.9)</td>
<td>33.0</td>
</tr>
<tr>
<td>MS</td>
<td>15</td>
<td>0.91</td>
<td>291</td>
<td>322</td>
<td>24-537</td>
<td>48-567</td>
<td>(y = 0.95x + 42.2)</td>
<td>51.2</td>
</tr>
<tr>
<td>BH</td>
<td>12</td>
<td>0.89</td>
<td>435</td>
<td>302</td>
<td>182-702</td>
<td>46-543</td>
<td>(y = 0.98x - 125)</td>
<td>71.6</td>
</tr>
<tr>
<td>OM</td>
<td>18</td>
<td>0.96</td>
<td>266</td>
<td>261</td>
<td>65-476</td>
<td>73-402</td>
<td>(y = 0.67x + 81.8)</td>
<td>31.0</td>
</tr>
<tr>
<td>CT</td>
<td>15</td>
<td>0.92</td>
<td>223</td>
<td>180</td>
<td>58-329</td>
<td>18-258</td>
<td>(y = 0.93x - 28.2)</td>
<td>27.5</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>160</strong></td>
<td><strong>0.86</strong></td>
<td><strong>267</strong></td>
<td><strong>267</strong></td>
<td><strong>24-702</strong></td>
<td><strong>10-631</strong></td>
<td>(y = 0.86x + 36.7)</td>
<td><strong>76.2</strong></td>
</tr>
</tbody>
</table>

Abbreviations: \(n\) = number of pairs of data points compared; \(r\) = simple linear correlation coefficient; \(\bar{x}\) = mean of angiographic dV/dt (cc/sec); \(\bar{y}\) = mean of aortic root blood flow (cc/sec); \(\text{SEE}\) = standard error of estimate (cc/sec).

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Figure 3

Instantaneous aortic root blood flow determined from blood velocity measured with an electromagnetic catheter-tip velocity transducer is plotted (Y-axis) versus the corresponding simultaneously measured left ventricular dV/dt (X-axis). The data include 160 pairs from one systole in each of ten patients.

Patient Population

One hundred thirteen consecutive patients undergoing cardiac catheterization at two laboratories (USPHS Hospital, Baltimore, and VA Hospital, Denver) and who had technically adequate cardiac cineangiography for left ventricular volume measurement formed the basis for this report. The ages ranged from 18-69 years with a mean of 46. There were 103 males and ten females.

The patients were divided into six major diagnostic categories depending on the predominant cardiovascular lesion identified at cardiac catheterization. There were 29 patients (mean age 35) who had normal left ventricular function based on clinical and catheterization findings. Sixteen of these were normal cardiovascular subjects who had volunteered for right heart and aortic catheterization as part of a study evaluating an electromagnetic catheter-tip velocity probe. In these patients cardiac angiography was performed by injection into the pulmonary artery. The remaining 13 had left and right heart catheterizations because of a systolic murmur (7), atypical chest pain (2), mild pulmonic stenosis (2), unexplained cardiomegaly (1), and a questionable diastolic murmur of mitral stenosis (1). In all of these latter patients, left ventricular hemodynamics were judged to be normal by the criteria of left ventricular end-diastolic pressure (LVEDP) less than 13 mm Hg, cardiac index greater than 2.2 L/min/m², ejection fraction greater than 0.50, and no evidence of valvular or coronary disease (normal selective coronary angiography in four patients).

There were 21 patients (mean age 50) with symptomatic coronary disease, all documented with selective coronary angiography. All had at least a 50% stenosis of one major coronary vessel, and most had severe diffuse disease. Fifteen were functional class III, four, class IV, and two, class II.

Nineteen patients (mean age 51) had left ventricular volume overload due to either aortic or mitral regurgitation or both, ten having primarily aortic regurgitation, seven predominantly mitral regurgitation, and two both. Nine were functional class III; eight, class II; and one each, classes I and IV. The amount of valvular regurgitation estimated by the quantitative angiographic technique of Sandler et al.¹⁴ varied from 0.5 L/min to 14.1 L/min (7-84% of left ventricular output) with a mean of 6.1 ± 3.7 L/min (55 ± 21% of left ventricular output).

Of the thirteen patients (mean age 55) with predominantly aortic stenosis, all save one (who also had mild mitral stenosis) had isolated, calcific aortic stenosis. Eight were functional class III, and five class II. The generally severe nature of the valvular obstruction is indicated by an average peak-to-peak gradient of 80 ± 26 mm Hg (range 42-123 mm Hg), average mean systolic gradient of 65 ± 19 mm Hg (range 31-88 mm Hg), and a calculated valve orifice area¹⁵ of 0.8 ± 0.3 cm² (range 0.5-1.4 cm²). Four of these patients had evidence of LV failure on clinical grounds, marked elevation of LVEDP, and/or reduced ejection fraction. More than trivial aortic regurgitation was present in only one patient.

Ten patients (mean age 48) had mitral stenosis as the predominant lesion ascertained at cardiac catheterization. Two in this group had mild mitral regurgitation, and one had mild mitral and aortic regurgitation. Seven were functional class III and three class II. The average mean mitral diastolic gradient was 11.2 ± 7.2 mm Hg (range 5-27 mm Hg), and the average calculated orifice area¹⁵ was 1.3 ± 0.5 cm² (range 0.5-1.9 cm²).

Nine patients (mean age 46) were found to have primary myocardial disease as the predominant lesion. The criteria used were a history of congestive failure with no clinical or catheterization evidence of valvular dysfunction or coronary disease sufficient to account for the symptoms. Six were functional class III; two, class II; and one, class IV.

The last group of 12 patients (mean age 46) is a heterogeneous group and is included where the data for all 113 patients are evaluated. Three had idiopathic hypertrophic subaortic stenosis (IHSS) and will be discussed separately. Four patients were studied postoperatively: one with mitral valve replacement, one with aortic and mitral valve replacements, one who had a mitral commissurotomy and residual severe tricuspid regurgitation, and one following saphenous vein bypass graft for angina pectoris (free of angina at the time of study). One each had mixed mitral and aortic valve disease, constrictive pericarditis, patent ductus arteriosus, primary pulmonary hypertension, and systemic hypertension. Five were functional class III; three each, classes I and II; and one, class IV.

Catheterization Techniques and Calculations

Right and left heart catheterizations were performed (after each patient gave his informed verbal and written consent) with the patient fasting, lightly sedated, supine, and at rest. Pressures were measured through 7 or 8F fluid-filled catheters, 100 to 125 cm in length with a Statham P23Db strain gauge. LVEDP was measured at the beginning of the rapid rise in left.
ventricular pressure. Physiologic data were recorded optically (Electronics for Medicine, DR-8). Cardiac output was measured by the indicator dilution technique (PHS Hospital) or the Fick principle (VA Hospital). Following measurement of pressures and cardiac output, cineangiography was performed by power injection of 45–60 cc 75% sodium-meglumine diatrizoate (Hyopaque-M) over two to three seconds into the pulmonary artery, left atrium, or left ventricle. Left ventricular volume was calculated from each frame of the cineangiogram exposed at 60 frames per second using the area-length method.4,8 Previous studies in these laboratories have demonstrated that rapid intracardiac injection of radiographic contrast material has minimal effect on cardiac function until the contrast material reaches the peripheral circulation 10 to 15 seconds after injection.12 The effect of contrast material on cardiac function for the first 10 to 15 seconds following injection does not vary greatly with the site of injection.12 The first 36 consecutive patients were studied in the posterior-anterior (PA) projection: the last 77 were studied in the 45° right anterior oblique (RAO) projection because of better visualization of the mitral valve and the elimination of the spine from the cardiac silhouette. Overestimation of true volume by the single-plane technique in both the PA and RAO projections was corrected by application of the appropriate regression equations, as previously described. Angiographic volume measurements were made on one or more complete cardiac cycles omitting premature beats and the sinus beat immediately following a premature beat. In the case of atrial fibrillation, supraventricular beats with a representative preceding R–R interval were selected.

The instantaneous dV/dt was calculated from the left ventricular volume data as described above. S dV/dt together with end-diastolic volume (EDV), end-systolic volume (ESV), total left ventricular stroke volume (SV = EDV – ESV), and ejection fraction (SV/EDV) were calculated from the same beat(s) of the cardiac cineangiogram. When volumes were calculated on more than one cycle, the data were averaged. The equatorial circumference (C) of the left ventricle midway between endocardium and epicardium was calculated from the projected area (A), length (L), and wall thickness (h) for each frame of the cineangiogram according to the formula: C = 4A/L + πh. The instantaneous first derivative (dC/dt) was calculated for each cine frame after curve smoothing as previously described. Maximum circumferential fiber shortening rate (VCF) expressed in muscle lengths/sec was taken as maximum absolute value of dC/dt during systole and normalized by dividing by end-diastolic circumference.

Statistical analyses were performed using standard techniques, including the Student t-test for difference between means, and a simple linear regression for correlation coefficients.

**Results**

Table 2 lists the left ventricular volume data and ejection characteristics for each group. The volume data for the normal group are very similar to that reported by Kennedy et al.,16 obtained by biplane angiocardiography. In the present report, the group with volume overload (regurgitant lesions) showed the largest SV and a comparably large EDV, both of which were significantly increased above normal (P < 0.01, table 2). The ejection fraction was significantly depressed in all disease groups (P < 0.05 or < 0.01), except those with aortic stenosis, and was lowest in patients with cardiomyopathy and mitral stenosis. S dV/dt for 29 normal adults was 427 ± 129 cc/sec and was not statistically different in any of the disease groups except the group with valvular regurgitation where S dV/dt was increased to 653 ± 290 cc/sec (P < 0.01). S dV/dt corrected for end-diastolic volume (S dV/dt/EDV) was 2.84 ± 0.50 sec⁻¹ for the normal group and was significantly decreased only in the cardiomyopathy

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**Table 2**

Angiographic Left Ventricular Volume Data and Ejection Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>EDV (cc/M² ± sd)</th>
<th>SV (cc/M² ± sd)</th>
<th>Ejection fraction (± sd)</th>
<th>S dV/dt (cc/sec ± sd)</th>
<th>S dV/dt/EDV (sec⁻¹ ± sd)</th>
<th>VCF (muscle lengths/sec ± sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>29</td>
<td>78 ± 15</td>
<td>50 ± 13</td>
<td>0.64 ± 0.07</td>
<td>427 ± 129</td>
<td>2.84 ± 0.50</td>
<td>1.28 ± 0.33†</td>
</tr>
<tr>
<td>CAD</td>
<td>21</td>
<td>97 ± 47</td>
<td>46 ± 15</td>
<td>0.53 ± 0.20*</td>
<td>448 ± 151</td>
<td>2.80 ± 1.29</td>
<td>1.06 ± 0.61</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>19</td>
<td>140 ± 63†</td>
<td>78 ± 28†</td>
<td>0.58 ± 0.11*</td>
<td>653 ± 290†</td>
<td>2.66 ± 0.63</td>
<td>1.18 ± 0.38**</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>13</td>
<td>100 ± 38*</td>
<td>54 ± 15</td>
<td>0.50 ± 0.20</td>
<td>455 ± 123</td>
<td>2.50 ± 0.92</td>
<td>1.05 ± 0.53</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>11</td>
<td>90 ± 24</td>
<td>44 ± 15</td>
<td>0.40 ± 0.09†</td>
<td>408 ± 107</td>
<td>2.43 ± 0.68</td>
<td>0.96 ± 0.44*</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>9</td>
<td>143 ± 74*</td>
<td>48 ± 17</td>
<td>0.40 ± 0.18§</td>
<td>495 ± 186</td>
<td>2.04 ± 0.98†</td>
<td>0.77 ± 0.45†</td>
</tr>
</tbody>
</table>

*Statistically different from normal (P < 0.05).
†Statistically different from normal (P < 0.01).

Abbreviations: EDV = end-diastolic volume; SV = total left ventricular stroke volume; sd = one standard deviation; S dV/dt = peak systolic ejection rate; S dV/dt/EDV = peak systolic ejection rate divided by end-diastolic volume; VCF = peak circumferential fiber shortening rate; CAD = coronary artery disease.

†27 patients.
§18 patients.

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group. Similarly, VCF in the normal group was 1.28 ± 0.33 muscle lengths/sec and was significantly decreased only in the groups with cardiomyopathy and mitral stenosis.

Figure 4 shows characteristic curves of instantaneous LV dV/dt versus time for patients with no heart disease, with mitral regurgitation, with aortic stenosis, and with IHSS. The resemblance of these systolic dV/dt curves to previously published aortic root blood velocity tracings1–3 is apparent and was confirmed previously in the methods section of this report. Regurgitant lesions resulted in increased peak dV/dt with no qualitative difference between mitral or aortic regurgitation. Note that the curves for the normal patient and the patient with aortic stenosis are similar. In only one of the 13 patients with aortic stenosis was the rate of rise of left ventricular ejection rate markedly delayed on visual inspection. The time from onset of ejection to S dV/dt was not significantly different for aortic stenosis patients (177 ± 57 msec) compared to the normal group (167 ± 45 msec). In the seven patients with mitral regurgitation S dV/dt occurred at an average of 201 ± 32 msec after the onset of ejection.

The patients with IHSS demonstrate an interesting and probably characteristic abnormality in the systolic ejection rate curve, i.e., rapid ejection early in systole (fig. 4). The individual data for each of the three patients with this diagnosis are given in table 3. In two of the three, S dV/dt was greater than one standard deviation above the normal mean, and in all three S dV/dt/EDV was two standard deviations or more above the normal mean. S dV/dt was achieved significantly earlier than the normal mean of 167 ± 45 msec in the two IHSS patients with the most significant outflow tract obstruction.

For the entire population S dV/dt has no relationship to LVEDP (r = 0.09), cardiac index

\[ r = 0.06 \]

or arteriovenous oxygen difference \((\Delta A - VO_2)\) (r = 0.14). The correlation coefficient for ejection fraction is \( r = 0.21 \) (P < 0.05 where P is the probability of \( r = 0 \)). The relationship between S dV/dt and ejection fraction for each of the patient groups is illustrated in figure 5. The normal, mitral stenosis, and coronary artery disease groups show statistically significant correlations between S dV/dt and ejection fraction (r = 0.54, 0.61, and 0.51, respectively). In those patients with valvular regurgitation and the small group with cardiomyopathy, there was no significant relationship between S dV/dt and ejection fraction.

The correlation between stroke volume and S dV/dt is high (r = 0.88; P < 0.01) (fig. 6) and

Table 3

<table>
<thead>
<tr>
<th>Patient</th>
<th>Resting gradient (mm Hg)</th>
<th>Stimulated gradient (mm Hg)</th>
<th>Ejection fraction</th>
<th>S dV/dt (cc/sec)</th>
<th>S dV/dt/EDV (sec^-1)</th>
<th>Time to S dV/dt (msec)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP</td>
<td>0</td>
<td>93</td>
<td>0.91</td>
<td>405</td>
<td>3.82</td>
<td>117</td>
<td>68</td>
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<tr>
<td>HS</td>
<td>0</td>
<td>69</td>
<td>0.82</td>
<td>676</td>
<td>4.48</td>
<td>117</td>
<td>75</td>
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<tr>
<td>KM</td>
<td>4–8</td>
<td>16</td>
<td>0.73</td>
<td>666</td>
<td>3.88</td>
<td>150</td>
<td>80</td>
</tr>
</tbody>
</table>

*Isoproterenol.

Abbreviations: S dV/dt = peak left ventricular systolic ejection rate; S dV/dt/EDV = peak left ventricular systolic ejection rate divided by end-diastolic volume.
The ejection fraction is plotted against S dV/dt for each of the 113 patients with each disease group identified. Correlation coefficients (r) and significance levels (P) are given for the total population and each of the disease groups.

Figure 5

The relationship between EDV and S dV/dt (fig. 7) is somewhat less for the entire patient population, (r = 0.60) but still highly significant (P < 0.01). For the diagnostic groups, the correlation with EDV is statistically significant only for the normal and valvar regurgitation groups (fig. 7). S dV/dt has a low correlation with VCF (r = 0.26, P < 0.01), and no significant correlation with heart rate (r = 0.17).

While S dV/dt appears to correlate poorly with generally used measures of cardiac function and does not differ from normal in disease states (except regurgitant lesions where S dV/dt is increased), S dV/dt/EDV correlates well with ejection fraction (r = 0.69, P < 0.01) and VCF (r = 0.99, P < 0.01), and to a lesser degree with LVEDP (r = 0.38, P < 0.01) and ΔA-VO₂ (r = 0.38, P < 0.01) for the entire patient population. The correlation of S dV/dt/EDV with cardiac index (r = 0.20) is not significant. The relationship between S dV/dt/EDV and ejection fraction for each of the patient groups is shown in figure 8; a significant degree of correlation exists in all disease groups.

Discussion

Peak left ventricular systolic ejection rates (S dV/dt) in man have not been previously reported.

Figure 8

The ejection fraction is plotted against left ventricular systolic ejection rate corrected for end-diastolic volume (S dV/dt/EDV) with each of the disease groups identified. Correlation coefficients (r) and significance levels (P) are given.
in detail. The data reported here can be compared with peak aortic flow rates obtained with various types of catheter-tip velocity transducers. In the absence of mitral regurgitation and a ventricular shunt, S dV/dt differs from peak aortic flow rate only by the very small amount of blood entering the coronary arteries during systole. There was a high degree of correlation between left ventricular dV/dt and aortic flow rates measured by an electromagnetic velocity (flow) probe (table 1). The value of S dV/dt of 427 ± 129 cc/sec for 29 normal patients is somewhat greater than the peak aortic flow rate of 347 ± 51 cc/sec for seven patients without cardiovascular disease obtained by the pressure gradient technique reported by Snell et al. However, these authors used an average value for the aortic flow radius in converting blood velocity to flow; this will tend to underestimate peak flow by 5–10%, as the cross-section of the aorta expands with systole by 5–10%. In a group of seven patients with nonvalvular heart disease (one atherosclerotic and six primary myocardial disease) Snell et al. report no deviation in peak aortic flow rate (340 ± 76 cc/sec) from their normal value. This corresponds well with our findings that in patients with heart disease without valvular regurgitation, S dV/dt was in the normal range. Harley et al. have reported peak aortic flow, measured with the pressure-gradient technique in five patients with complete heart block, varying from about 200–450 cc/sec, correlating well with the stroke volume, which in turn varied with the timing of atrial contraction.

The slow upstroke of the central aortic pressure tracing is characteristic of valvular aortic stenosis, yet there is no delay (within the limits of accuracy of this technique) in the rise of the dV/dt curve in aortic stenosis (fig. 4) or prolongation of time from onset of ejection to S dV/dt. It should be noted that these time intervals cannot be measured with a precision greater than 17–33 msec (1–2 cine frames). However, errors of this nature should be random and cancelled by averaging a number of patients. The explanation for the normal dV/dt curve in aortic stenosis is illustrated in figure 9. In the top portion of the figure left ventricular (LV) and central aortic (Ao) pressure tracings from a case of severe aortic stenosis are reproduced. The instantaneous LV-aortic gradient and the square root of the gradient calculated for each hundredth of a second are plotted on the same time scale below. Flow across a stenotic orifice should be proportional to the square root of the gradient. Note that the configuration of the square root of gradient curve is virtually identical to the dV/dt curves of normal subjects and patients with aortic stenosis in figure 4. The peak of the square root of gradient curve (fig. 9) occurs 150 msec after the onset of systole.

Measurement of instantaneous aortic blood flow at thoracotomy in patients with severe mitral regurgitation shows rapid early ejection into the aorta. The dV/dt curve in mitral regurgitation does not peak early (fig. 4), but represents the summation of ejection into the aorta and left atrium. This is compatible with the conclusion of Elkins et al. that regurgitant flow across the mitral valve is greatest in late systole.

The pathophysiologic characteristics of IHSS are an early rapid ejection with obstruction to left ventricular outflow developing in mid and late systole. Our data are compatible with this concept in that there is an increase in S dV/dt (particularly when corrected for EDV) which peaks in early systole in two patients with the most significant obstruction (fig. 4, table 3). Hernandez et al. measured aortic flow in five patients with IHSS using the pressure gradient technique and demonstrated no increase in peak flow as compared to five control subjects, but did note a marked increase in the percent of flow in the first half of systole.

Figure 9

Shown above are left ventricular (LV) and aortic (Ao) pressure curves and electrocardiogram (ECG) from a patient with severe valvular aortic stenosis. Shown below are the instantaneous LV gradient and square root of the gradient measured at each hundredth of a second and plotted on the same time scale.
ventricular volume calculations in patients with IHSS may be inaccurate, especially near end-systole because of the irregular outline of the chamber due to marked trabeculation and hypertrophied papillary muscles. However, the abnormalities described here are in early systole, when volume measurements are most likely to be accurate.

The data presented indicate that S dV/dt was not closely related to ventricular function, particularly in patients with valvular regurgitation. The ejection fraction was significantly depressed in all disease groups except patients with aortic stenosis; however, S dV/dt was normal or increased in each of the disease groups (table 2). The correlation between S dV/dt and ejection fraction for the entire patient population was low (r = 0.21) (fig. 5). However, in some of the groups without valvular regurgitation (normals, mitral stenosis, aortic stenosis and coronary disease) higher levels of correlation exist (r = 0.54, 0.61, 0.54, 0.51, respectively) suggesting that in the absence of valvular regurgitation, S dV/dt may be, in part, a function of left ventricular performance (fig. 5).

Total stroke volume appears to be the primary determinant of S dV/dt (r = 0.88; P > 0.01). This is not unexpected since the duration of ejection varied over only a narrow range (usually not more than ± 30%), while total stroke volume varied sevenfold. (The normal mean stroke volume was 95 cc; the range in all disease categories was 41–283 cc). Since the configuration of the systolic dV/dt curve is relatively unchanged (except in IHSS), an increase in total stroke volume must result in an increase in S dV/dt if duration of ejection remains relatively constant. A high correlation between total stroke volume and peak aortic flow, both measured with the pressure gradient technique, has been previously described.19

Because S dV/dt in this group of 113 patients was primarily related to the volume characteristics of the left ventricle (SV and EDV), the poor correlation of S dV/dt with measures of ventricular function such as ejection fraction or LVEDP could be anticipated. Measures of ventricular performance and degree of volume overload of the left ventricle frequently vary independently. For example, ventricular or myocardial function as measured by the ejection fraction14 or contractile element velocity at maximum wall tension22 may be normal even in the face of severe regurgitant lesions. S dV/dt/EDV is a better measure of ventricular function than S dV/dt, but probably not as reliable as the ejection fraction.

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The Rate of Change of Left Ventricular Volume in Man: I. Validation and Peak Systolic Ejection Rate in Health and Disease

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