A New Technique for the Study of Left Ventricular Pressure-Volume Relations in Man

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SUMMARY
Study of left ventricular pressure-volume relations in man has been limited by technical problems associated with left ventricular angiography. A new approach to this problem using simultaneous recording of left ventricular pressure and left ventricular volume (determined by echocardiography) was applied in 21 patients. Pressure-volume plots, constructed from pressure and volume values sampled at 20 or 40 msec intervals, had characteristic shapes for the states studied: normal, pressure overload, volume overload, and myocardial disease. These curves closely resembled pressure-volume plots previously determined by others from quantitative angiography.

The area inscribed by these plots was integrated to calculate left ventricular stroke work. Left ventricular stroke work index (gram-meters/m²) was in the range previously reported for the various states: normal—41 ± 12, pressure overload—102 ± 14, volume overload—136 ± 36, myocardial disease—65 ± 19. Inspection of the pressure-volume plots allowed assessment of valvular regurgitation by the characteristic deformation of the loop during "isovolumic" contraction and relaxation. Study of diastolic filling allowed qualitative assessment of left ventricular compliance. Patients with pressure overload had stiffer ventricles, with high diastolic pressure at lower volume, than normal or volume overload patients.

In summary, a new method is described for the beat-to-beat analysis of left ventricular pressure-volume relations in man.

Additional Indexing Words:
Echocardiography
Left ventricular stroke work
Diastolic compliance

Consideration of the relationship between left ventricular pressure and volume has long been recognized to be of importance in the evaluation of left ventricular performance. Examination of the systolic aspect of this pressure-volume relationship has allowed more precise definition of ventricular work and its various components, while analysis of the diastolic left ventricular pressure-volume relationship has permitted attempts at the measurement of ventricular compliance.

A major problem encountered in the study of left ventricular pressure-volume relations is the technical difficulty associated with the simultaneous and continuous measurement of left ventricular pressure and volume. The recent demonstration that left ventricular chamber volume can be accurately estimated by echocardiography, combined with technical advances that have allowed continuous strip chart echocardiographic recording, has opened the possibility of a new approach to the study of left ventricular pressure-volume relations.

This report presents the results of studies in 21 patients in whom simultaneous strip chart recordings of left ventricular pressure, left ventricular volume echocardiogram, and electrocardiogram were obtained at the time of diagnostic cardiac catheterization, and illustrates how this technique for simultaneous pressure-volume measurement may be applied to clinical and physiological problems.
Methods and Materials
Twenty-one patients were studied at the time of diagnostic right and left heart catheterization. The patients have been divided into four groups according to their predominant cardiac diagnosis. Group I is composed of five patients with normal left ventricular function by standard criteria. Group II contains five patients with left ventricular pressure overload lesions due to aortic stenosis (four patients) and coarctation of the aorta (one patient). Group III includes six patients with left ventricular volume overload due to significant mitral, aortic or combined mitral and aortic valvular regurgitation. The five patients in Group IV had predominant myocardial disease due to ischemia or a cardiomyopathic process. All of the patients were in normal sinus rhythm, and clinical and hemodynamic data for each patient are summarized in Table I. Studies were conducted in the fasting state following 5 to 10 mg of diazepam premedication given intramuscularly.

Brachial arteriography and retrograde left ventricular catheterization were performed with standard 8F French catheters in ten patients, and with micromanometer tipped catheters (Millar, Mikrotip) in 11 patients. The pulse transmission delay in the fluid-filled system was measured to be less than 20 msec. All pressures were recorded on an Electronics for Medicine DR-12 photographic recorder. The echocardiogram of the interventricular septum and left ventricular posterior wall was obtained by previously described techniques using a Smith-Kline Ekoline-20 ultrasonoscope with a 2.25 megaHertz transducer of 0.5 inch diameter. The Ekoline-20 machine was interfaced to the DR-12 recorder to give strip chart recordings of the simultaneous interventricular septal and left ventricular posterior wall echocardiogram, left ventricular pressure, and electrocardiogram at a paper speed of 100 mm/sec with 20 msec time lines. A typical record is seen in figure 1. Following the echocardiographic studies, left

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>LV end-diastolic pressure (mm Hg)</th>
<th>LV end-diastolic volume (cc/m²)</th>
<th>LV end-systolic volume (cc/m²)</th>
<th>Stroke index (mm²/m²)</th>
<th>Ejection fraction</th>
<th>Cardiac index (cc/m²)</th>
<th>LV stroke work index (gram-meter/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.P.</td>
<td>Normal</td>
<td>104</td>
<td>60</td>
<td>44</td>
<td>.42</td>
<td>2.6</td>
<td>2.8</td>
<td>57</td>
</tr>
<tr>
<td>R.Ca.</td>
<td>MS, MR</td>
<td>12</td>
<td>90</td>
<td>48</td>
<td>42</td>
<td>.54</td>
<td>2.9</td>
<td>2.6</td>
</tr>
<tr>
<td>S.P.</td>
<td>Normal</td>
<td>12</td>
<td>58</td>
<td>28</td>
<td>30</td>
<td>.52</td>
<td>2.8</td>
<td>3.9</td>
</tr>
<tr>
<td>R.C.L.</td>
<td>MS</td>
<td>5</td>
<td>71</td>
<td>31</td>
<td>40</td>
<td>.56</td>
<td>2.7</td>
<td>4.4</td>
</tr>
<tr>
<td>A.S.</td>
<td>Pulmonary HBP</td>
<td>8</td>
<td>61</td>
<td>27</td>
<td>34</td>
<td>.56</td>
<td>3.5</td>
<td>--</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td></td>
<td>10 ± 3</td>
<td>77 ± 20</td>
<td>38 ± 15</td>
<td>36 ± 6</td>
<td>.53</td>
<td>.06</td>
<td>2.9 ± .7</td>
</tr>
</tbody>
</table>

Group I (Normal Ventricle)

| J.P.    | AS               | 26                               | 84                              | 37                            | 47                    | .56               | 3.4                  | 3.5                    | 90                                   |
| A.T.    | AS               | 11                               | 95                              | 40                            | 55                    | .58               | 3.6                  | 3.4                    | 120                                  |
| W.L.    | AS               | 30                               | 62                              | 23                            | 39                    | .63               | 2.9                  | 3.4                    | 89                                   |
| S.W.    | Coartct. of aorta| 16                               | 138                             | 70                            | 68                    | .50               | 5.4                  | 4.8                    | 99                                   |
| R.B.    | AS, AR           | 25                               | 144                             | 84                            | 60                    | .30               | 3.9                  | 2.4                    | 112                                  |
| Mean ± sd |                  | 22 ± 8                           | 104 ± 35                        | 51 ± 25                       | 54 ± 11               | .53 ± .09         | 3.8 ± .9              | 3.5 ± .8                | 102 ± 14                            |

Group II (Pressure Overload)

| A.T.    | MR               | 20                               | 355                             | 156                           | 199                   | .56               | 26                   | 3.7                    | 184                                  |
| J.C.    | MR, AR, CHF      | 10                               | 399                             | 148                           | 242                   | .46               | 20                   | 2.5                    | 223                                  |
| O.W.    | AR, CHF          | 62                               | 220                             | 132                           | 88                    | .43               | 8.8                  | 3.0                    | 78                                   |
| H.H.    | MR, AI           | 19                               | 139                             | 49                            | 90                    | .65               | 8.5                  | 2.7                    | 130                                  |
| W.H.    | AR, CAD, HBP     | 24                               | 236                             | 120                           | 116                   | .42               | 8.3                  | 2.9                    | 147                                  |
| P.G.    | MS, MR, AR, CHF  | 13                               | 149                             | 92                            | 48                    | .35               | 4.5                  | 1.3                    | 56                                   |
| Mean ± sd |                  | 25 ± 19                          | 247 ± 106                       | 116 ± 40                      | 130 ± 74              | .48 ± .11         | 12.7 ± 8.4            | 2.7 ± .8                | 136 ± 36                            |

Group III (Volume Overload)

| W.C.    | CM, HBP          | 10                               | 107                             | 49                            | 58                    | .54               | 3.9                  | 3.9                    | 87                                   |
| N.E.    | CM               | 16                               | 119                             | 88                            | 31                    | .26               | 2.5                  | 2.9                    | 41                                   |
| H.J.    | CAD              | 11                               | 76                              | 37                            | 30                    | .55               | 2.6                  | 3.1                    | 48                                   |
| J.J.    | Post myocarditis | 13                               | 186                             | 123                           | 65                    | .38               | 4.5                  | 3.4                    | 72                                   |
| J.H.    | CAD, CHF         | 22                               | 116                             | 45                            | 71                    | .61               | 3.8                  | 2.4                    | 76                                   |
| Mean ± sd |                  | 14 ± 5                           | 121 ± 40                        | 68 ± 32                       | 52 ± 17               | .47 ± .14         | 3.5 ± .8              | 3.1 ± .6                | 63 ± 19                              |

Group IV (Myocardial Disease)

Abbreviations: LV = left ventricle; AR = aortic regurgitation; AS = aortic stenosis; CAD = coronary artery disease; CHF = congestive heart failure; CM = cardiomyopathy; HBP = hypertension; MR = mitral regurgitation; MS = mitral stenosis.

The P values represent the significance level for each parameter as compared with Group I.
ventricular cineangiography was performed in each case, and patients with regional abnormalities of left ventricular contraction were excluded.

The left ventricular internal diameter (D) was measured as the vertical distance between the echoes from the endocardial surfaces of the interventricular septum and left ventricular posterior wall (fig. 1) and was expressed in centimeters of tissue. Left ventricular volume was estimated from this internal diameter using a simplification of the formula for the ellipsoidal model: \( V_{LV} = \frac{\pi}{6} D_1 D_2 L \), as proposed by Pombo et al.: \( V_{LV} = D^3 \). This method assumes the minor axis in two perpendicular planes (D₁ and D₂) to be equal and assumes the long axis (L) to be twice the minor axis in length. It has been correlated with angiocardioographic volume studies, and has been found to give reasonably accurate values over a large range of ventricular volumes.⁷,⁸ In the present study left ventricular chamber volume was calculated from this formula at 20 or 40 msec intervals throughout the cardiac cycle starting from the onset of the QRS of the electrocardiogram. Three to five consecutive cardiac cycles were examined for each patient. All data reported represent the mean pressure and volume at each point in time for the total number of cycles examined. All volumes were normalized for body surface area and are expressed as cc/m². Quantitative left ventricular angiocardioigraphy was not performed in all of these patients, and the ventricular volume data reported herein were derived by the echocardiographic technique.

**Results**

Pressure-diameter and pressure-volume plots were constructed for each patient. An example of these plots is shown in figure 2, which represents data from patient H.J. who had mild coronary atherosclerosis and presumably normal left ventricular function. Initially there is a rapid rise in pressure with no change in internal diameter or calculated ventricular volume; this corresponds to the period of isovolumic contraction. As aortic diastolic pressure is exceeded, ventricular ejection commences and volume can be seen to decrease, reaching its nadir just as left ventricular pressure begins to decline. Ventricular pressure then falls rapidly with little change in volume, the period of isovolumic relaxation. As ventricular pressure falls to levels below left atrial pressure in early diastole, the rate of volume increase is maximal, defining the phase of rapid filling. During mid-systole the volume slowly continues to increase with only minimal change in left ventricular pressure. In late diastole, the rate of volume increase declines, but left ventricular diastolic pressure rises at an increasing rate. This figure illustrates the typical left

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**Figure 1**

Simultaneous left ventricular volume echocardiogram, left ventricular pressure, first derivative of left ventricular pressure, and phonocardiogram. The endocardial surface of the posterior wall is irregular because of the recording speed (100 mm/sec). The line drawing illustrates how the best smooth line representing the endocardial surface of the septum and posterior wall was drawn for the purpose of measuring the internal diameter D.
ventricular pressure-volume relationship found in all of the normal patients.

A similarly made plot for a patient with severe mitral regurgitation is shown in figure 3. In this case the underlying pathophysiology is illustrated by the absence of an isovolumic contraction period, and by the very rapid rise in volume in early diastole. There is no discernible change in volume in the last 80 msec of diastole, an observation in keeping with the known preponderance of early rapid filling with severe volume overload lesions.

Pressure-volume figures, constructed by plotting the pressure against the corresponding echocardiographically determined ventricular volume to form loops, were made for all patients, and representa-tive plots are shown in figure 4. These plots have the typical shape for the various states studied: normal, pressure overload, and volume overload. The figures for all patients with regurgitant lesions had the characteristic deformation caused by absence of an isovolumic contraction period in mitral regurgitation and absence of an isovolumic relaxation period in aortic regurgitation.

Left ventricular stroke work was calculated by planimetrically integrating the area of the pressure-volume curves. The left ventricular stroke work index for each patient and the mean value for each group are presented in Table 1. Groups II, III, and IV had significantly greater left ventricular stroke work indexes as compared to the normal patients of Group I. The range of values in each group is

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Figure 2

Simultaneous left ventricular pressure, internal diameter (D), and estimated left ventricular chamber volume plotted against time starting with the onset of the QRS of the electrocardiogram.

Figure 3

Simultaneous left ventricular pressure, minor axis dimension, and estimated left ventricular chamber volume. Note the absence of an isovolumic contraction period and the rapid increase in volume in early diastole.
approximately the same as that obtained by others in similar patients using quantitative angiography to estimate ventricular volume.

The usefulness of this graphic analysis of stroke work is illustrated by the study of pressure-volume relationships in a patient with severe aortic stenosis and mild aortic regurgitation as shown in figure 5. Simultaneous left ventricular pressure, volume and aortic pressure have been plotted. This graph illustrates total stroke work or the sum of diastolic work (spent distending the left ventricle) and systolic work. Systolic work can be further divided into: (a) the work dissipated in overcoming the obstruction to ejection (“impedance work”), represented as the area between ventricular systolic pressure and the aortic pressure; and (b) “effective” stroke work (the pressure-volume work required if there were no outflow obstruction to be overcome), represented as the area between aortic pressure and left ventricular diastolic pressure.

The application of this technique after an intervention is illustrated in figure 6. The pressure and corresponding volume averaged for five consecutive beats at rest and during the second minute of rapid atrial pacing have been plotted against time. The mean and standard deviation for each point are illustrated. During rapid atrial pacing, end-diastolic volume and stroke volume fell significantly, the end systolic volume decreased slightly, and the cardiac index increased slightly. Although stroke work fell from 54 to 40 gram-meters per minute, minute work increased from 3400 to 4800 gram-meters per minute.

The diastolic portion of the pressure-volume plots allowed qualitative assessment of left ventricular diastolic compliance. Representative plots in figure 7 show a wide variation in left ventricular compliance ranging from J.H., a patient with severe coronary artery disease but normal left ventricular function (echocardiographic ejection fraction .61), who has a high end-diastolic pressure at a near normal end-diastolic volume (low compliance); to

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**Figure 4**

Pressure-volume plots of representative cardiac cycles from patients with no hemodynamic evidence of heart disease (normal), aortic stenosis and mild aortic regurgitation (AS, AR), severe aortic regurgitation (AR), and severe mitral regurgitation (MR). Plots 2 and 3 illustrate the absence of an isovolumic relaxation period in aortic regurgitation and plot 4 illustrates the absence of an isovolumic contraction period in mitral regurgitation.

**Figure 5**

Pressure-volume plot from a patient with aortic stenosis and aortic regurgitation. Ventricular work has been divided into its various components. The extra load imposed by the obstruction to left ventricular ejection is represented as "impedance work."
ECHO AND PRESSURE-VOLUME RELATIONS

NORMAL SINUS RHYTHM

EDV = 80 cc/M²
ESV = 40 cc/M²
SV = 40 cc/M²
EF = .50
CI = 2.64 L/min/M²

ATRIAL PACING 120/MIN

EDV = 60 cc/M²
ESV = 32 cc/M²
SV = 28 cc/M²
EF = .47
CI = 3.36 L/min/M²

Figure 6

Simultaneous pressure and volume plotted against time throughout the cardiac cycle at rest and after two minutes of atrial pacing. The values represent the mean for five consecutive beats. The standard deviation for each point is shown. EDV = end diastolic volume, ESV = end systolic volume, SV = stroke volume, EF = ejection fraction, CI = cardiac index.

Discussion

The value of pressure-volume plots as illustrated above in the analysis of left ventricular pressure-volume relations throughout the cardiac cycle has been emphasized by others. Ventricular work as calculated from these plots involves fewer assumptions than work calculated from the average forward stroke volume and aortic pressure. This is

patient J.C. with severe volume overload secondary to mitral and aortic regurgitation who has a normal end-diastolic pressure at an inordinately high left ventricular volume (high compliance). In addition to such a single point comparison of diastolic compliance, the time course of "observed" compliance (the ratio of changing volume to changing pressure) throughout diastole can be assessed by inspection of the entire diastolic pressure-volume plot. It is apparent from the changing slope of each curve that "observed" compliance not only varies widely between the patients, but changes throughout diastole in each patient. Of particular interest is patient O.W. who had severe aortic regurgitation and in whom end-diastolic pressure equalled the aortic diastolic pressure. It can be seen from figure 7 that compliance in this patient was markedly reduced in late diastole as pressure increased tremendously with only a slight increase in ventricular volume.

Figure 7

Representative diastolic pressure-volume plots illustrating the marked variation in diastolic pressure-volume relations among the patients. Differences in "observed" compliance can be qualitatively assessed by comparing the slope of each curve. The dot at the lower right termination of each curve represents end-diastolic pressure and volume.
particularly obvious in those patients with regurgitant lesions or shunts. The components of total work can be separated, and the extra work imposed on the left ventricle by both obstructive and regurgitant lesions can be readily appreciated by comparing the results for left ventricular stroke work in Groups II and III with Group I (table 1). The determinants of total ventricular work—pressure, volume, or both—can be independently evaluated in each individual patient, and the type of hemodynamic derangement can be easily assessed. The importance of knowing both left ventricular pressure and volume in evaluating the response to an abnormal hemodynamic burden is apparent from a comparison of the pressure overload with the volume overload patients. All but one of the pressure overload patients (Group II) had significantly increased left ventricular end-diastolic pressures together with increased left ventricular mean systolic pressures, increased stroke work indexes, and normal or slightly increased left ventricular end-diastolic volumes. The increase in stroke work in these patients thus resulted chiefly from the increased afterload. The patients with predominant volume overload lesions (Group III) also had significantly greater stroke work indexes than the normal patients. The major differences between this group and the remainder of the patients were significantly larger end diastolic volumes and stroke indexes. The increased ventricular work in these patients is therefore related to increased left ventricular preload. The importance of differentiating predominant pressure work from predominant volume work and the effect of each on left ventricular performance has been previously stressed by others.\textsuperscript{14-17}

Regurgitant lesions are apparent from the characteristic deformation of the pressure-volume plot caused by the absence of an isovolumic contraction or relaxation period. Since the data are recorded in continuous analog form both instantaneous pressure and volume can be sampled during these brief periods of the cardiac cycle. By comparing the total stroke volume determined by ultrasound to the forward stroke volume determined by the Fick or indicator-dilution method, the severity of regurgitant or shunt lesions can be assessed. Previous reports of the echocardiographic method have shown a strong correlation between the left ventricular stroke volume estimated from the echocardiogram and by the Fick method.\textsuperscript{9} Popp and Harrison using a slightly different echo technique estimated the change in ventricular size along both the transverse and apex to base axes and found excellent correlation between regurgitant volume estimated angiographically and echocardiographically.\textsuperscript{18} More recently, left ventricular volume has been estimated from the single transverse internal diameter measured echocardiographically.\textsuperscript{7-12} This dimension is either cubed\textsuperscript{7} or used in a regression equation\textsuperscript{8, 9} to estimate ventricular volume. It should be pointed out that both approaches will lead to overestimation of ventricular volume in enlarged ventricles which tend to be more spherical than ellipsoidal.\textsuperscript{8, 19} This source of error may magnify the regurgitant volume or cause a greater discrepancy between the echo and Fick cardiac outputs in patients with significantly dilated left ventricles. Although this source of error may magnify the difference, it is clear from table 1 that those patients in Group III had considerably larger cardiac indexes as estimated by the echocardiographic technique when compared to the forward cardiac index measured by the Fick method. In two patients (S.W. and J.J.) without regurgitant lesions who had larger echocardiographic cardiac indexes than Fick cardiac indexes the left ventricular volume tended to be abnormally large. Complete volume curves derived from quantitative biplane left ventricular angiography by using the area-length method,\textsuperscript{20} in two of our patients showed acceptable correlation with the echocardiographic volume curves, as illustrated in figure 8. This is reassuring but it must be emphasized that a constant geometric reference figure is assumed for the left ventricle in the echocardiographic volume calculation, and this formulation may not fit all hearts. As noted before this is especially true in enlarged dilated left ventricles. Proper identification of the echocardiographic representation of the interventricular septum and posterior left ventricular wall is obviously critical and requires practice and experience with the technique. One potential source of error that must be excluded is the result of regional abnormalities of ventricular contraction. This circumstance invalidates the assumptions necessary for echocardiographic volume determinations, and patients with dyskinesis must be excluded. It is important that the transducer be placed in a consistent location, the third or fourth left intercostal space near the sternal edge, in each patient. The anterior leaflet of the mitral valve serves as a landmark from which the transducer is directed just inferiorly and laterally to obtain representative and reproducible echo signals from

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the interventricular septum and posterior left ventricular wall. It proved expeditious in the current study to practice obtaining adequate echocardiograms the day prior to cardiac catheterization. Although echocardiograms of adequate resolution cannot be obtained in all patients, particularly those with large, thick wall chests, emphysema, or unusual intrathoracic anatomy, approximately 70% of the studies attempted thus far in our laboratory have been successful.

The major difficulties with angiographic ventricular volume studies are the inability to repeat them frequently, the significant incidence of arrhythmias or more serious complications, the time consuming analysis required, the radiation received by the patient, and the limitation of the number of cardiac cycles that may be studied. The use of the echocardiographic volume method obviates some of these difficulties and, with certain limitations, it provides a method that may be easily repeated and that allows frequent measurement of instantaneous volume throughout multiple cardiac cycles. High resolution strip chart echocardiograms are necessary; but once the technique is learned, the data can be gathered in a minimal period of time.

In summary, a new approach to left ventricular pressure-volume measurements has been described. The method, utilizing simultaneous strip chart recordings of the left ventricular volume echocardiogram and left ventricular pressure, has made possible measurement of pressure and volume at frequent intervals throughout multiple cardiac cycles. Studies in 21 patients have permitted the quantitation of total stroke work and its various components, the qualitative evaluation of diastolic compliance, and assessment of the severity of regurgitant valvular lesions. Results obtained using this technique are similar to results previously reported by others using angiographic volume determinations. This new approach, with certain assumptions, is a useful alternative to angiographic volume measurements and should have wider application than previous techniques.

References
Correction

Klein HO: Circulation 47: 758, 1973. On page 759, in the legend to figure 1, line 9, sentence should read: "Extrasystoles induced thereafter lead to lengthened post extrasystolic cycles." On page 763, the second line of column two should read, "conduction delay. The second mechanism may be..."
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