Echocardiographic Determination of Left Ventricular Stress-Velocity Relations in Man

With Reference to the Effects of Loading and Contractility

By Miguel A. Quinones, M.D., William H. Gaasch, M.D., James S. Cole, M.D., and James K. Alexander, M.D.

SUMMARY

The time course of left ventricular (LV) circumferential stress and fiber shortening velocity (VcF) were determined at 20 msec intervals in 30 patients from simultaneous recordings of LV pressure (micromanometer) and LV dimensions (echography). In 12 patients with normal LV function, endocardial and midwall maximal (max) VcF, VcF at peak stress, and endocardial mean VcF were significantly greater than in eight patients with myocardial disease. Peak stress was less in the normal subjects (mean = 241 g/cm², range 180 to 310 g/cm²) than in those with myocardial diseases (mean = 371 g/cm², range 280 to 513 g/cm²). VcF was reduced in five out of seven patients with chronic LV volume overload, while peak stress ranged from normal in three to increased in four. Max VcF, mean VcF, and peak stress were normal in three patients with chronic LV pressure overload; VcF at peak stress was normal in two. Good correlation was observed between angiographic determinations of mean VcF and endocardial max VcF, VcF at peak stress and mean VcF.

Induced changes in preload in five patients (dextran infusion at constant heart rate) produced a 12.2% increase in peak stress (P < 0.05), and insignificant changes in max VcF (3.7% increase, P = NS), in VcF at peak stress (5% decrease, P < 0.05), in mean VcF (0.7% increase, P = NS). Increasing afterload with angiotensin in seven patients (peak stress increased by 45%, P < 0.01) reduced max VcF, VcF at peak stress and mean VcF by 33%, 39%, and 37% respectively. Lowering afterload in one patient (amyl nitrite) produced an increase in VcF. Improvement in VcF was observed in all instances during positive inotropic stimulation (isoproterenol and digoxin in four with myocardial disease). The response of endocardial and midwall VcF to loading and contractility were similar.

In man VcF is an index of myocardial contractility which is affected minimally by changes in preload but responds inversely to changes in afterload. Its sensitivity to acute afterload changes may, at times, limit its clinical applicability.

Additional Indexing Words:
Left ventricular contractility
Volume overload
Endocardial circumferential stress
Echocardiography

Preload
Pressure overload
Stress-strain

Afterload
Cardiomyopathy
Digitalis

CIRCUMFERENTIAL FIBER SHORTENING
velocity (VcF) has been proposed by several investigators as a reliable index of left ventricular performance which reflects the isotropic state of the left ventricular (LV) myocardium.1-2 The effects of acute changes in loading conditions on VcF, however, have not been studied in man. In recent years the echocardiogram has been shown to be a reliable method of determining the mean endocardial circumferential fiber shortening velocity.3-6 In this presentation we have used left ventricular echography in combination with simultaneous high fidelity pressure recordings to determine the time course of VcF and of left ventricular circumferential wall stress during ejection, to study the relationship between stress and VcF in various disease states of the left ventricle, and to evaluate the effects of induced changes in loading and contractility on VcF in man.

Methods

Thirty patients were studied during diagnostic right and left heart catheterization in the postabsorptive state following premedication with 10 mg of intramuscular diazepam.
Informed consent was obtained from each patient. Nine patients had chest pain syndrome with normal coronary arteriograms, one patient had a functional murmur, two patients had mitral stenosis, five patients had aortic insufficiency, three patients had mitral regurgitation, two patients had aortic stenosis (one valvular, one subvalvular membranous), one patient had hypertension with secondary left ventricular hypertrophy, and seven patients had myocardial disease with varying degrees of left ventricular dysfunction (table 1). None of the patients had arteriographic evidence of significant (>50%) coronary artery disease or abnormalities of segmental wall motion. Pressure and echocardiographic data were obtained prior to angiography. Left ventricular (LV) pressure was measured with a Millar Instruments 5F (four patients) or 5F (26 patients) catheter-tip micromanometer, and recorded in an Electronics for Medicine DR-8 multichannel photographic recorder. The high fidelity pressures were calibrated either by matching the signal from the micromanometer with a simultaneous lumen pressure (Millar SF), using a Statham P-23 Db transducer with reference to a zero level 5 cm below the angle of Lewis, or by a predetermined electronic calibration constant (Millar 5F catheter). In each patient a central aortic pressure or a brachial artery pressure was recorded simultaneously with LV pressure. The ultrasound recordings were obtained with a Smith-Kline ultrasonoscope interfaced to the multichannel recorder, using a 2.25 MHz, 0.5 inch transducer focused at 5 cm, with a repetition rate of 1,000 impulses/sec. Echograms from the interventricular septum, posterior wall endocardium, and epicardium were obtained as described previously. Briefly, the transducer was placed in the third, fourth, or fifth intercostal space, to the left of the sternum and the ultrasound beam was directed posteriorly to the mitral valve and then inferolaterally in order to traverse the interventricular septum, fragments of the mitral valve apparatus and the posterior wall. The echograms, the LV pressure, and the central aortic or brachial artery pressure were recorded simultaneously on the multichannel recorder at a paper speed of 100 mm/sec.

**Measurements and Calculations**

The LV internal diameter (D) was measured in cm from the posterior wall endocardium to the interventricular septum (fig. 1). Measurements of D and of LV pressure were obtained every 20 msec from the time of the LV end-diastolic pressure recording (EDP) to end systole (time when the LV pressure descent crosses the level of the incisura in the central aortic or brachial artery pressure) utilizing an X-Y digitizer and programmed calculator. Posterolateral wall thickness (h) at end diastole and at end systole was measured as the distance from epicardial to endocardial echoes; intermediate points between end diastole and end systole were calculated every 20 msec assuming a linear change in h from end diastole to end systole. The time course of endocardial VCf was determined as:

\[
V_{Cf} \text{ (circ/sec)} = (D_1 - D_2)/t \times D_1
\]

where D1 and D2 represent sequential measurements of D, and t = the time between the two measurements (20 msec). In order to attenuate the random motion associated with the manual planimetry, the posterior wall endocardial and the interventricular septal echoes from a single beat were digitized five times: each D represented the average of 5 measurements. Mean VCf was calculated as:

\[
\text{Mean } V_{Cf} = \frac{D_d - D_s}{LVET \times D_d}
\]

where Dd and Ds represent measurements of D at end diastole and end systole respectively, and LVET = the LV ejection time measured from the time when the LV pressure trace crosses the level of the diastolic central aortic or brachial artery pressure to end systole; in patients with mitral regurgitation LVET was measured from end diastole to end systole. The velocity of circumferential fiber shortening at the midwall was derived as:

\[
\text{Midwall } V_{Cf} = \frac{D_1 + h_1 - (D_2 + h_2)}{t \times (D_1 + h_1)}
\]

The time course of LV circumferential wall stress was determined using the formula utilized by Gaul and associates with an angiographic technique. Thus:

\[
\text{LV stress (g/cm}^2\text{)} = (P \times r/h) (1 - 2r^2/L^2)
\]

where P = intracavitary pressure in g/cm²; r = intracavitary radius (D/2) in cm; and L = long axis of the LV which was assumed in this study to be twice the minor diameter (D) in all instances. The reliability of the echogram in estimating the internal LV minor axis, wall thickness, and circumferential wall stress has recently been demonstrated.

All measurements were processed by the programmed calculator, and time plots of endocardial VCf, midwall VCf, and LV hoop stress were constructed (fig. 1). A fifth order polynomial equation was fitted to the VCf curves. From these graphs the following data were derived: maximal (max) VCf, peak LV stress, and VCf at peak stress.

**Experimental Protocol**

Measurements were made at rest in all 30 patients. In 12 of the 30 patients data were collected during one or more of the following interventions: (A) Acute preload increase: In five patients with normal LV function 250 to 400 cc of dextran were infused in a 10 to 15 minute period to achieve an increase in LVEDP from normal to 16-20 mm Hg. Heart rate was kept constant by atrial pacing in all five patients. (B) Acute afterload increase: In seven patients (5 with normal LV function, 1 volume overload, 1 myocardial disease) angiotensin (2 mcg/cc) was infused at a rate sufficient to produce an increase in arterial pressure. Heart rate was held constant by atrial pacing in five of the seven patients. In one patient, afterload was subsequently reduced acutely by amyl nitrite inhalation. (C) Changes in isotropic state: Three patients with normal LV function were studied during isoproterenol infusion; four patients with LV dysfunction were studied before and one hour after acute digitalization with 1 mg of digoxin intravenously.

A left ventricular cineangiogram (right anterior oblique, 60 frames/sec) was obtained in each patient with the injection of 50 cc of contrast medium (Renografin 76) at 12 cc/sec. Measurements of mean VCf were performed as described previously. In brief, the angiographically visualized LV cavity was drawn at end diastole (first frame with the largest cavity silhouette) and at end systole (frame showing the smallest cavity). A major axis was drawn from the LV apex to the angle formed by the junction of the mitral and aortic valves, and bisected by a perpendicularly drawn minor axis (D'). Mean VCf was calculated by sub-

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*Hewlett Packard Model 9100B.
Figure 1

Example of left ventricular echogram recorded simultaneously with left ventricular and brachial artery pressure. Measurements of dimensions and pressures allow calculations of the time course of circumferential fiber shortening velocity (V<sub>CF</sub>) and of left ventricular hoop stress (see Methods). Abbreviations: LV = left ventricle, IVSE = interventricular septum, PWE = posterior wall endocardium, h = posterior wall thickness, BA = brachial artery, EKG = electrocardiogram.

Patients #14 to #19 were diagnosed as having myocardial disease (LV dysfunction without mechanical overload, normal coronary arteriograms). All of them had reduced angiographic mean V<sub>CF</sub> (<1.20 circ/sec), and all except one had ejection fractions of less than 50%. Endocardial max V<sub>CF</sub>, V<sub>CF</sub> at peak stress, and mean V<sub>CF</sub> were lower than in any of the patients with normal LV. In two additional patients (#13 and #20) the diagnosis of myocardial disease was also strongly considered. Patient #13 had reduced endocardial max V<sub>CF</sub> and V<sub>CF</sub> at peak stress with a low normal value for mean V<sub>CF</sub>; all three velocities increased to normal following digitalization (fig. 4). Likewise, angiographic mean V<sub>CF</sub> was normal after digitalis (no control angiographic data available). End-diastolic volume index was slightly greater than

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Summary of Data in 30 Patients

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*Left ventriculogram done under influence of dextraux.
**Left ventriculogram done under influence of digoxin.

Abbreviations: BSA = body surface area; F = female; M = male; LV = left ventricle; AO = arterial pressure; Ddi = echocardiographic LV internal diameter at end diastole; ΔD = percent shortening of D during systole; h = LV posterior wall thickness; dh = percent thickening of h from end diastole to end systole; Endo = endocardial; VCF = circumferential fiber shortening velocity; Max = maximal; S = stress; EDVI = end diastolic volume index; SEF = systolic ejection fraction; CA = coronary arteriograms; AI = aortic insufficiency; Myo = myocardial; MR = mitral regurgitation; SAS = subvalvular membranous aortic stenosis; AS = aortic stenosis; Hypert = hypertension; LVH = left ventricular hypertrophy.

normal (98 cc/m²). These findings were interpreted as consistent with a mild cardiomyopathy. Patient #20 (mitral stenosis) had rather marked reduction in endocardial VCF by echo and an elevated LVEDP to 18 mm Hg (no angiographic data available). The extent of shortening of D in these eight patients with myocardial disease was significantly lower (P < 0.01) than in the normal group (average % reduction in D = 18.9%, range from 8 to 33%). The percent increase in wall thickness during systole was not significantly different from the normal group (average % increase in h = 40.2%, range from 33 to 60%); however, in four patients the values were lower than the normal range. Although overlap was observed between the two groups, peak stress (average = 370.8 g/cm², range from 280 to 513 g/cm²) was significantly higher in the patients with myocardial disease (P < 0.01) than in the normal group. Examples of the time course of endocardial VCF and LV hoop stress in a normal compared to a myocardial disease are shown in figure 2.

Seven patients (#21 to #27) had left ventricular volume overload (mitral regurgitation in three, aortic insufficiency in four); all except one had enlarged ventricles (end-diastolic volume index > 90 cc/m²). Peak stress in these patients ranged from normal (three patients) to increased (four patients). Likewise, the extent of shortening of D, max VCF, VCF at peak stress, mean VCF, ejection fraction and angiographic mean VCF ranged from normal to markedly reduced.
Patients #28 to #30 had LV pressure overload, but in spite of elevated intracavitary pressures, peak stress fell within the normal range (200 to 277 g/cm²). Endocardial max V\(_{CF}\) and mean V\(_{CF}\) were normal in all three; V\(_{CF}\) at peak stress was normal in two and reduced in one.

The correlation of endocardial max V\(_{CF}\), V\(_{CF}\) at peak stress, and mean V\(_{CF}\) with angiographic mean V\(_{CF}\) was good (fig. 3). The correlation analysis was performed using data collected immediately prior to the LV angiogram. Separation between normal and abnormal LV function was seen with all three measurements; discrepancy between angiographic and echocardiographic data was observed with max V\(_{CF}\) and mean V\(_{CF}\) in only one patient.

Table 2 summarizes the data (excluding V\(_{CF}\)) before and during the interventions performed in 12 patients. Figure 4 summarizes the response of V\(_{CF}\) to changes in preload, afterload, and contractility. Figure 5 shows examples of stress-V\(_{CF}\) plots during acute changes in preload, afterload, and contractility.

Preload
In five patients the rapid infusion of dextran (constant heart rate) produced an increase in LVEDP from normal values to 16-20 mm Hg, and a 9.3% increase in the end-diastolic dimension from a mean of 4.3 cm to 4.7 cm. This amount of preload increase was accompanied by a 12.2% average increase in peak stress (P < 0.05) and by a 5% average decrease in V\(_{CF}\) at peak stress (P < 0.05). The 0.7% average increase in mean V\(_{CF}\) and 3.7% increase in endocardial max V\(_{CF}\) were not statistically significant. The extent of shortening of D was augmented by preloading in all five patients from a mean of 38.4% to 44.2%.

Afterload
In seven patients (five normal, one volume overload, one myocardial disease) angiotensin infusion produced a rapid increase in blood pressure which led to a 45.1% average increase in peak stress (P < 0.01). This increase in afterload was associated with a 33.4% average reduction in endocardial max
The time course of endocardial $V_{CF}$, of left ventricular hoop stress, and a plot of stress vs $V_{CF}$ from a patient with normal left ventricular (LV) function are compared to similar measurements from a patient with myocardial disease. Differences in magnitude, orientation, and configuration of the stress-$V_{CF}$ plot are apparent between the normal and the myocardial disease.

**Table 2**

**Summary of Data During Acute Changes in Preload, Afterload, and Contractility**

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<td>100 100 165/3 120/16 165/71 120/73 3.75 4.00 37.3 43.8 185 202</td>
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|              | C AL C AL C AL C AL C AL C AL C AL |               |
| 1            | 75 75 102/10 124/17 102/64 124/100 4.20 4.30 47.6 30.2 180 310 |
| 2            | 94 94 140/9 200/12 200/97 200/120 4.80 4.90 37.5 26.5 245 430 |
| 4            | 100 100 165/3 156/10 165/70 156/90 3.70 3.80 37.8 26.3 185 222 |
| 6            | 100 88 123/4 178/10 123/85 178/118 4.35 4.66 34.0 24.9 280 383 |
| 7            | 75 75 120/8 143/20 120/71 143/95 4.40 4.50 38.6 28.7 223 300 |
| 16           | 140 140 85/25 98/30 85/70 98/80 6.30 6.44 11.7 8.6 426 524 |
| 24           | 100 100 111/3 159/8 111/60 159/68 7.00 7.25 31.4 22.8 285 415 |

|              | C ISO C ISO C ISO C ISO C ISO C ISO |               |
| 1            | 75 125 101/12 110/11 101/65 110/60 4.20 4.15 45.2 56.6 215 245 |
| 2            | 94 125 153/12 102/6 153/98 102/62 3.46 5.15 40.5 54.4 350 290 |
| 7            | 75 120 120/8 120/7 120/70 120/57 4.40 3.75 38.6 40.8 220 180 |

|              | C DIG C DIG C DIG C DIG C DIG C DIG |               |
| 13           | 58 59 150/10 160/9 150/90 160/92 5.00 4.90 32.0 38.8 300 285 |
| 14           | 107 86 130/33 140/25 130/100 140/94 6.85 6.80 18.2 22.1 513 486 |
| 15           | 107 86 120/8 130/6 120/100 130/86 4.30 4.00 7.5 15.0 340 325 |
| 16           | 140 115 85/25 92/19 85/70 92/75 6.30 6.56 11.7 15.2 426 489 |

*Patient number as in table 1.

Abbreviations: C = control; PL = preload (dextran); AL = afterload (angiotensin); ISO = isoproterenol; DIG = digoxin. The others as in table 1.
to 2.4 circ/sec), and in mean $V_{CF}$ (1.48 to 1.79 circ/sec). Thus, the data indicate an inverse relation between changes in afterload and $V_{CF}$.

**Contractility**

Isoproterenol infusion in three patients with normal LV function produced a significant increase in the extent of shortening of D as well as in endocardial max $V_{CF}$, $V_{CF}$ at peak stress, and mean $V_{CF}$ (table 2, figures 4 and 5). Peak stress increased by 14% in one patient, and decreased by 43% and 18% in the other two. Intravenous digoxin administration, likewise, produced significant increases in mean and instantaneous $V_{CF}$, as well as in the extent of shortening of D in four patients with reduced LV function secondary to myocardial disease (table 2 and fig. 4). Peak stress in-

**Figure 3**

Comparison of angiographic mean $V_{CF}$ with echocardiographic endocardial maximal $(max)$ $V_{CF}$, mean $V_{CF}$, and $V_{CF}$ at peak stress. All three velocities by echography correlated well with angiographic mean $V_{CF}$.

**Figure 4**

Summary of the response of endocardial $V_{CF}$ (maximal, at peak stress, and mean) to acute increase in preload ($PL$), afterload ($AL$), and contractility. $V_{CF}$ changed minimally with preload, was reduced by increasing afterload, and responded directly to positive inotropic stimulation. Abbreviations: Max = maximal, C = control, ISO = isoproterenol, DIG = digoxin.
increased by 15% in one patient, and fell by 5% in the other three.

Endocardial vs Midwall $V_{CF}$

The time course of midwall $V_{CF}$ was determined in all 30 patients at rest, and in several patients during the various interventions. Although the absolute values for midwall $V_{CF}$ were lower than endocardial $V_{CF}$, the morphology of the two curves was identical and the correlations between endocardial max $V_{CF}$ and midwall max $V_{CF}$, and between endocardial $V_{CF}$ at peak stress and midwall $V_{CF}$ at peak stress were excellent ($r = 0.97$ and 0.95 respectively). As shown in figure 7, good correlation between endocardial and midwall $V_{CF}$ was seen not only during single control measurements but also during the various interventions, thus indicating that the responses of midwall $V_{CF}$ to acute changes in preload, afterload, and contractility were similar to those of endocardial $V_{CF}$.

Discussion

The time course of circumferential fiber shortening velocity at the midwall and of left ventricular hoop stress was first described in man by Gault and associates using simultaneous left ventricular pressure and angiographic LV dimensions. Since velocity of fiber shortening is equal to the algebraic sum of the contractile element velocity ($V_{CE}$) and the series elastic lengthening (or shortening) velocity ($V_{SE}$), and since at peak stress $V_{SE}$ equals zero, velocity of fiber shortening at peak stress is equivalent to $V_{CE}$. Gault et al. found that the magnitude of values for max $V_{CF}$ and for $V_{CE}$ at peak stress was significantly higher in patients with normal LV function when compared to patients with myocardial disease. Qualitative differences in the stress-$V_{CF}$ plots between the two groups of patients were also observed. The same group of investigators subsequently presented data suggesting that measurements of the mean endocardial circumferential fiber shortening velocity by angiography could be used as a simplified index of LV performance which separated normal from abnormal LV function. Peterson and associates measured the time course of LV wall tension and endocardial $V_{CF}$ in patients with normal and abnormal LV function by using simultaneous LV pressure and central aortic blood flow (electromagnetic velocity probe) assuming a thin-walled spherical model for the left ventricle. Results similar to those of Gault et al. with the angiographic technique were observed. Mean endocardial $V_{CF}$ has also been measured using echocardiography by different investigators; correlation with the angiographic technique has been excellent, particularly in the absence of LV asynergy.

In this study, echocardiography, in combination with simultaneous high fidelity LV pressure record-
ing, was used to plot the time course of LV hoop stress, endocardial V_{CF} and midwall V_{CF} in man. An important assumption in measuring endocardial V_{CF} by echocardiography is that the size and motion of the echocardiographic left ventricular internal diameter reflects the size and motion of the minor axis of the LV. Previous studies have validated this assumption.\(^9\),\(^10\) Left ventricular circumferential wall stress was measured using a prolate ellipsoid as a reference figure assuming a fixed ratio of long axis to minor axis of 2:1. Even though this assumption failed to hold when comparisons were made, Ratshin and associates found an excellent correlation between measurements of stress at end diastole and at the time of aortic valve opening by angiography versus echocardiography (using the 2:1 assumption) in 48 subjects with a variety of heart diseases.\(^10\) In addition, due to the nature of the formula for wall stress used in this study, if the true ratio of L to D is other than 2:1 the error in over or underestimation of wall stress will be small. For example, if at the time of peak stress the ratio of L to D is 1.5:1 (as may occur in a large dilated LV), peak stress will be overestimated by 11%; if the L to D ratio is 3:1 (as may occur in a small elongated LV), peak stress will be underestimated by 8%. Accepting this potential error in the absolute value of LV hoop stress, the time to peak stress should be affected minimally and therefore measurements of V_{CF} at peak stress (or V_{CE}) should be valid. When spherical models are used and tension (force per unit length) rather than stress (force per unit cross-sectional area) is calculated, the time to peak tension and stress are nearly identical.\(^15\)

An accurate measurement of LV wall thickness (h) is essential in calculating LV hoop stress. The reliability of the echocardiogram in measuring h at end diastole has been well established.\(^10\),\(^16\) In this study h was measured at end diastole and at end systole, intermediate points were calculated assuming a linear change throughout ejection.\(^1\),\(^7\),\(^8\) The percent wall thickening during ejection found in our patients with normal LV function (average = 49.6%) is in general agreement with that obtained by Eber and associates using a constant LV mass and an angiographically measured end diastolic h,\(^7\) but is slightly greater than the values observed by Mitchell et al. in dogs using endocardial and epicardial markers (25–45%).\(^8\) Even though some patients with myocardial disease had an increase in h of less than the normal range, the mean for the group was not significantly different from normal. Midwall V_{CF} was measured assuming a uniform wall thickness throughout the left ventricular circumference; none of the patients studied had asymmetric septal hypertrophy.

Our results indicate that both endocardial max V_{CF}, V_{CF} at peak stress, and mean V_{CF} were reliable in identifying normal versus abnormal LV function. As anticipated, the correlation between echocardiographic V_{CF} and angiographic mean V_{CF} was good (fig. 3). Even though echocardiographic mean V_{CF} correlated well with max V_{CF} (r = 0.93), a few instances were observed in which mean V_{CF} was either normal (\(\geq 1.10\) circ/sec) or nearly normal (table 1, #13 and

\[\text{Figure 7}\]

Comparison of endocardial and midwall V_{CF} in the patients at rest and during some of the interventions. As shown by the strong correlation coefficient, midwall V_{CF} does not offer any advantage over endocardial V_{CF} in patient separation or in degree of responsiveness to loading and contractility.
patient #14 postdigoxin, mean \( V_{CF} = 1.07 \) (circ/sec) while max \( V_{CF} \) was clearly depressed. This finding suggests that at times measurements of the time course of \( V_{CF} \) may be more meaningful than mean \( V_{CF} \) in assessing LV performance. Measurements of \( V_{CF} \) at 20 msec intervals is a time consuming procedure requiring the use of an X-Y digitizer and programmed calculator for accuracy. An estimate of the time course of \( V_{CF} \) may be simply obtained by measuring the internal LV diameter \( D \) manually from end diastole to end systole at further spaced intervals (such as 60 msec) so that dimensional changes may be easily visualized. Since the calculated velocity is normalized (equation #1), measurements of \( D \) may be performed with a standard metric scale. This type of analysis can be done with the aid of a desk calculator in less than 10 minutes. An example of an endocardial \( V_{CF} \) curve derived from sampling at 60 msec intervals is shown in figure 8 and compared to a 20 msec interval curve obtained with the digitizer from the same beat. Data from the 30 patients in this study are also shown. Due to the excellent correlation observed between the two measurements \( (r = 0.99) \), the simplified method seems to be a practical alternative for clinical use.

In this study, the values obtained for peak stress in the normal group were within the range observed by other investigators. The largest values were seen in patients with myocardial disease and in some patients with LV volume overload. Of interest are three patients with pressure overload who in spite of very high intracavitary pressures had normal values for peak stress (afterload) due to small intracavitary radii and to LV hypertrophy. Differences in magnitude, orientation, and configuration were observed in the stress-\( V_{CF} \) plots between patients with normal LV function and those with myocardial disease (fig. 2).

The response of \( V_{CF} \) to acute changes in loading and contractility has not been previously evaluated in man. In this study, an acute increase in preload was accompanied by small increases in peak stress and by minor changes in \( V_{CF} \); the extent of shortening of the internal diameter \( D \), however, was significantly augmented. An example of the change in the stress-\( V_{CF} \) plot during preloading is seen in figure 5. Of interest is that even though the changes in velocity were small, the total area under the curve (an index of muscle fiber power) was significantly greater during the increased preload. An acute increase in afterload (45.1% average increase in peak stress) was accompanied by significant reduction in \( V_{CF} \) and in the extent of fiber shortening. In one patient in whom afterload was acutely reduced, \( V_{CF} \) was significantly augmented. In this patient \( V_{CF} \) at peak stress in the three afterload curves are theoretically falling on the same force-velocity curve (fig. 6).

The response of \( V_{CF} \) to acute changes in loading found in this study in man is in agreement with the findings of Covell et al. in the conscious dog. The inverse relation between \( V_{CF} \) and afterload is similar to the changes in \( V_{CF} \) observed in isolated muscle preparations during acute changes in afterload. However, in contrast to our findings in the intact human heart, increasing preload in the isolated mus-

\[ \begin{align*}
\text{Figure 8} \\
\text{Examples of the time course of endocardial } V_{CF} \text{ measured at 20 msec intervals (using a digitizer and programmed calculator) and measured directly at 60 msec intervals in the same beat. An excellent correlation between the two methods for calculating maximal (max) } V_{CF} \text{ is apparent.}
\end{align*} \]
cle preparation produces a definite increase in \( V_{CF} \) at comparable levels of afterload. One possible reason why this response was not observed in this study may be that in the intact heart it is impossible to completely separate preload from afterload, so that increasing preload leads to some increase in afterload (peak stress) which in turn attenuates the \( V_{CF} \) response.

Benning and associates measured \( V_{CF} \) during acute changes in preload, afterload, and contractility in a group of opened chest anesthetized dogs. They found a consistent inverse relation between mean \( V_{CF} \) and afterload in all of their experiments. Mean \( V_{CF} \) during volume loading was not statistically different from control; however, marked variation in the individual responses were observed. In evaluating the response of \( V_{CF} \) to changes in the inotropic state these investigators found \( V_{CF} \) (max \( V_{CF} \) and \( V_{CF} \) at peak stress) to be less sensitive to the negative inotropic effect of ischemia than mean LV hydraulic output power, another parameter of LV function. However, we have found \( V_{CF} \) to be responsive to the positive inotropic effect of isoproterenol and digoxin in man; Covell and associates found \( V_{CF} \) responsive also to the negative inotropic effect of propranolol as well as to the positive effect of isoproterenol in the conscious dog.

Since \( V_{CF} \) varies inversely with afterload, whenever a low value for \( V_{CF} \) is observed in a patient with increased LV hoop stress, the question may arise whether this value reflects a reduced inotropic state of the myocardium or a point on a normal (but afterload increased) force-velocity curve. Figure 9 shows the relation between LV peak stress and \( V_{CF} \) at peak stress \( \bar{V}_{CF} \) before and during an increase in afterload for five patients with normal LV function (average and standard error), for one patient with LV volume overload (aortic insufficiency, patient #24), and for one patient with myocardial disease (#16). The control values for both patients, if seen in relation to the curve from the normals, could be interpreted as falling on the same force-velocity curve; however, when a second afterload point is plotted it can be seen that the slope from the curves in both the volume overload and the myocardial disease are less steep, and the \( V_{CF} \) intercept at zero load are lower than in the normal group. These findings suggest that in these two patients myocardial contractility was indeed depressed.

The orientation of myocardial fibers in a cross-section of the left ventricular wall at the minor equator varies from epicardium to endocardium, so that the greatest concentration of fibers aligned along the circumference of the ventricle occurs at the midwall. Accordingly, one might expect midwall \( V_{CF} \) to be more representative of fiber shortening velocity than endocardial \( V_{CF} \). In this study, however, midwall \( V_{CF} \) did not offer any advantage over endocardial \( V_{CF} \) in patient separation or in degree of responsiveness to loading and contractility (fig. 7).

In conclusion, the time course of \( V_{CF} \) and LV hoop stress throughout ejection may be determined in man with the combined use of echocardiography and intracardiac pressure recordings. In man \( V_{CF} \) is relatively unaffected by acute changes in preload but varies inversely with afterload changes; its sensitivity to inotropic stimulation seems to be good. \( V_{CF} \) appears to adequately separate normal from reduced LV function, but its sensitivity to afterload may at times limit its clinical utility. Construction of a stress-\( V_{CF} \) curve during two afterload states may provide an improved insight into the inotropic state of a given ventricle.

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