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Left Ventricular End-Systolic Wall Stress-Velocity of Fiber Shortening Relation: A Load-Independent Index of Myocardial Contractility

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The velocity of circumferential fiber shortening (Vcf) is an index of myocardial performance which, although sensitive to contractile state, has limited usefulness because of its dependence on left ventricular loading conditions. This study investigated the degree and velocity of left ventricular fiber shortening as it relates to wall stress in an attempt to develop an index of contractility that is independent of preload and heart rate while incorporating afterload. Studies were performed in 78 normal subjects using M-mode echocardiography, phonocardiography and indirect carotid pulse tracings under baseline conditions. In addition, studies were performed on 25 subjects during afterload augmentation with methoxamine, 8 subjects before and during afterload challenge after increased preload with dextran and 7 subjects with enhanced left ventricular contractility with dobutamine. The relation of end-systolic stress to the velocity of fiber shortening and to the rate-corrected velocity of shortening (corrected by normalization to an RR interval of 1) was inversely linear with correlation coefficients of −0.72 and −0.84, respectively. Alterations in afterload, preload or a combination of the two did not significantly affect the end-systolic wall stress/rate-corrected velocity of shortening relation, whereas during inotropic stimulation, the values were higher, with 94% of the data points above the normal range. Age did not appear to affect the range of normal values for this index. In contrast, the end-systolic wall stress/fractional shortening relation was not independent of preload status, responding in a manner similar to that seen with a positive inotropic intervention.

Thus, the velocity of circumferential fiber shortening normalized for heart rate is inversely related to end-systolic wall stress in a linear fashion. Accurate quantitation can be performed by noninvasive means and a range of normal values determined. This index is a sensitive measure of contractile state that is independent of preload, normalized for heart rate and incorporates afterload. In contrast, the end-systolic wall stress/fractional shortening relation is dependent on end-diastolic fiber length in the range of physiologically relevant changes in preload.

The velocity of left ventricular fiber shortening (Vcf) is an index of myocardial performance that can be accurately measured by noninvasive means and is capable in certain situations of distinguishing patients with normal myocardial performance from those with impaired function(1–3). Although sensitive to changes in contractile state, the velocity of fiber shortening is highly dependent on cardiac loading conditions and heart rate (4–8). As with other ejection phase indexes including ejection fraction and percent fractional shortening, the clinical utility of shortening velocity is limited by its inability to distinguish between the effects of altered loading conditions and abnormalities in left ventricular contractility. Efforts to overcome these limitations have focused unsuccessfully on the relation of velocity of shortening to afterload, quantitated as either instantaneous left ventricular wall stress (9–12) or peak left ventricular wall stress (4). Recently, several investigators (13–16) observed a unique preload-independent relation between left ventricular volume and afterload at end-systole. On the basis of these observations, we previously investigated (17) the relation of fractional shortening to end-systolic wall stress, the force that limits fiber shortening at end-systole. This index is sensitive to contractile state while incorporating afterload. The use of the left ventricular wall stress/shortening relation has also been reported by other investigators (18–21). Our recent experience, however, indicated that this index may not accurately reflect contractile state in the presence of abnormal left ventricular preload conditions. We, therefore, investigated the preload dependence of the left ventricular wall stress/shortening relation in normal subjects over a wide range of arterial pressures.

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Additionally, because mean velocity of fiber shortening is known to be independent of initial fiber length, the relation of end-systolic wall stress to velocity of shortening was evaluated as a potentially preload-independent index of contractility that incorporates afterload status. Our previously reported (17,22,23) noninvasive method was used to examine the response of the end-systolic stress/velocity of shortening relation to afterload challenge (infusion of the pure alpha-adrenergic agonist methoxamine [24,25]), preload augmentation (dextran infusion) with and without afterload challenge and inotropic stimulation (dobutamine infusion) (26) with and without afterload challenge.

Methods

Study subjects. The study group consisted of 68 healthy subjects (40 male, 28 female) aged 3 to 70 years. None had known cardiovascular disease on the basis of history, physical examination, electrocardiogram and two-dimensional and M-mode echocardiogram, and none was taking cardioactive medications.

Recordings. Data acquisition was performed using previously described methods (17). An Irex or Hewlett-Packard ultrasound imaging system with a 2.25 or 3.5 MHz transducer was used for echocardiographic, external carotid pulse and phonocardiographic recordings. Phonocardiograms were recorded from the right upper sternal border. The Dinamap 845 vital signs monitor (Critikon) was used to obtain peak systolic and diastolic blood pressure measurements. We previously documented (27) the high degree of accuracy and reproducibility of measurements made with this device.

Protocol. For each study, simultaneous recordings of left ventricular echocardiogram, phonocardiogram, indirect carotid pulse tracing, electrocardiogram and systolic and diastolic blood pressures were obtained. All 78 subjects were studied under rest conditions. In 25 subjects, we also obtained data during afterload manipulation. Each of these subjects was premedicated with atropine, 0.01 mg/kg intravenously, to maintain a stable heart rate during the subsequent studies. After several baseline recordings had been made, an intravenous infusion of methoxamine (25 μg/kg per min, maximal rate 1 mg/min) was begun in all 25 subjects. Repeat recordings were made every 1 to 2 minutes during a gradual increase in peak systolic blood pressure to 30 to 60 mm Hg above baseline. The methoxamine infusion was then discontinued. In seven subjects after a 10 to 15 mm Hg decrease in blood pressure below the peak systolic level had occurred, an intravenous infusion of dobutamine, 5 μg/kg per min was begun. Recordings were obtained every 1 to 2 minutes during the gradual dissipation of the methoxamine pressor effect. In eight other subjects, a 500 ml infusion of dextran was administered over a 20 to 30 minute period after the first methoxamine study had been completed. The foot of the patient's bed was then raised to an angle of 30° and the infusion of methoxamine was repeated as just described. In summary, recordings were made under rest conditions in 68 subjects, over a wide range of afterload conditions at stable heart rates in 25 subjects, with and without inotropic augmentation (dobutamine infusion) in 7 subjects and with and without increased preload (dextran) in 8 subjects.

Measurements and calculations. Left ventricular internal dimension and left ventricular posterior wall thickness were measured at end-diastole (defined as the Q wave of the electrocardiogram) and end-systole (defined as the first high frequency component of the aortic second heart sound) in five cardiac cycles, and mean values were computed. The left ventricular percent fractional shortening was calculated as end-diastolic dimension minus end-systolic dimension, divided by end-diastolic dimension. Left ventricular ejection time was measured from the simultaneous carotid pulse tracing and taken as the average of five beats. The ejection time was rate-corrected to a heart rate of 60 beats/min by dividing by the square root of the RR interval. The mean velocity of circumferential fiber shortening of the left ventricle was calculated and normalized to the end-diastolic dimension by dividing fractional shortening by the ejection time. The rate-corrected velocity of shortening was calculated by dividing the fractional shortening by the rate-corrected ejection time.

Calibration of the carotid pulse tracings was performed as described previously (28), with assignment of systolic blood pressure to the peak and diastolic pressure to the nadir of the tracing. Linear interpolation to the level of the incisura was then performed to estimate end-systolic pressure. Values obtained in this manner differ by 3 ± 4 mm Hg (mean ± SD) from simultaneous central aortic values with a correlation coefficient of 0.97 (29).

The left ventricular end-systolic meridional wall stress was calculated by the method of Grossman et al. (30)

$$\text{Stress}_{es} = \frac{(1.35)(P_{es})(D_{es})}{(4)(h_{es})[1 + (h_{es}/D_{es})]},$$

where stress_{es} is left ventricular wall stress (g/cm^2) at end-systole, P_{es} is the left ventricular pressure (mm Hg) at end-systole, D_{es} and h_{es} are the left ventricular internal dimension and posterior wall thickness (cm) at end-systole, respectively, 1.35 is a conversion factor (mm Hg to g/cm^2), and 4 is a geometric factor that results from conversion of radius to internal dimension.

Statistical analysis. Simple linear regression by the least squares method was used to calculate end-systolic wall stress extent of shortening equations and end-systolic wall stress/velocity of shortening equations for each of the experimental conditions. The *t* test for paired data was used for statistical analysis, with a probability value of less than 0.05 consid-

Table 1. Hemodynamic Response to Increased Afterload (methoxamine infusion) in Eight Subjects

	Baseline	Peak Afterload	p Value
Heart rate (beats/min)	79 ± 19	79 ± 20	NS
P_{es} (mm Hg)	99 ± 9	141 ± 13	<0.01
D_{es} (cm)	3.20 ± 0.47	3.57 ± 0.52	<0.01
h_{es} (cm)	1.46 ± 0.18	1.34 ± 0.17	<0.01
σ_{es} (g/cm^2)	51 ± 9	92 ± 18	<0.01
D_{ed} (cm)	4.75 ± 0.67	5.02 ± 0.67	<0.01
%ΔD	32.5 ± 2.1	28.6 ± 2.9	<0.01
ET (ms)	293 ± 28	312 ± 34	<0.01
ET_c (ms)	333 ± 23	352 ± 35	<0.01
V_{cf} (circ/s)	1.12 ± 0.12	0.92 ± 0.13	<0.01
V_{cf_c} (circ/s)	0.98 ± 0.07	0.82 ± 0.11	<0.01

%ΔD = percent dimension change; D_{ed} = end-diastolic dimension, D_{es} = end-systolic dimension; ET = ejection time, ET_c = rate-corrected ejection time; h_{es} = end-systolic wall thickness; σ_{es} = end-systolic wall stress; P_{es} = end-systolic pressure; V_{cf} = velocity of circumferential shortening; V_{cf_c} = rate-corrected velocity of circumferential shortening.

ered statistically significant. All subjects were studied using a protocol approved by the Committee for the Protection of Human Subjects from Research Risks of the Boston's Children's Hospital and the University of Chicago Hospitals and Clinics.

Results

Left ventricular hemodynamics. The hemodynamic data from all 25 subjects under rest and peak methoxamine pressor conditions are summarized in Table 1. The increase in end-systolic pressure seen with methoxamine resulted in an increase in end-systolic dimension and wall stress and a decrease in end-systolic wall thickness, percent dimension change, velocity of shortening and rate-corrected velocity of shortening, with no change in heart rate. In Table 2, the individual hemodynamic responses of the eight subjects who received preload augmentation with 500 ml dextran are shown with data matched for end-systolic wall stress. No significant change in end-systolic pressure, dimension or wall stress occurred, whereas significant increases in end-diastolic dimension, percent dimension change and ejection time were

Table 2. Individual Hemodynamic Response to Preload Augmentation With 500 ml Dextran (data matched for end-systolic stress)

Case	Heart Rate (beats/min)	P_{es}	D_{es}	D_{ed}	%ΔD	ET_c	V_{cf_c}	σ_{es}
1								
C	76	113	3.30	5.15	35.9	328	1.09	55
P	64	113	3.30	5.40	38.9	342	1.14	55
2								
C	49	122	4.40	6.10	27.9	312	0.89	87
P	52	117	4.55	6.45	29.5	345	0.86	90
3								
C	78	166	3.55	4.65	23.7	310	0.76	112
P	75	163	3.55	4.80	26.0	358	0.75	110
4								
C	72	136	3.60	5.00	28.0	307	0.91	89
P	74	144	3.55	5.15	31.1	337	0.91	91
5								
C	75	138	3.45	5.00	31.0	326	0.92	81
P	70	137	3.50	5.25	33.3	351	0.94	83
6								
C	88	116	3.05	4.50	32.2	337	0.95	58
P	80	113	3.05	4.70	35.1	360	0.98	57
7								
C	75	147	4.00	5.75	30.4	358	0.85	110
P	75	147	4.10	6.05	32.2	362	0.85	113
8								
C	60	119	3.40	4.90	30.6	320	0.99	63
P	54	116	3.45	5.10	32.4	323	1.00	63
C								
Mean	72	132	3.59	5.13	30.0	325	0.92	82
± SD	12	18	0.42	0.54	3.6	17	0.10	22
P								
Mean	68	131	3.63	5.36	32.3	347	0.93	83
± SD	10	19	0.47	0.60	3.8	13	0.12	23
p value (C vs. P)	NS	NS	NS	<0.01	<0.01	<0.01	NS	NS

C = control; P = preload-augmented conditions; other abbreviations as in Table 1.

Table 3. Individual Hemodynamic Response to Inotropic Stimulation (dobutamine)

Case	Heart Rate (beats/min)	P_{es}	D_{es}	%ΔD	ET_c	V_{cf_c}	σ_{es}
1							
C	83	103	3.00	32.6	368	0.89	59
D	100	127	2.85	38 7	341	1 13	59
2							
C	46	105	3.45	33.0	293	1.12	50
D	59	127	3.20	42.3	312	1.36	49
3							
C	100	102	3 15	30.0	349	0.86	56
D	101	120	2.80	38.5	325	1.18	51
4							
C	79	98	3.30	30.5	321	0.95	57
D	108	138	3.10	39 2	320	1.21	57
5							
C	69	110	3.30	31.3	311	1.01	50
D	61	134	3.15	37.6	308	1.22	50
6							
C	105	102	3 10	32.6	373	0.87	55
D	120	129	2.95	39.2	357	1.10	54
7							
C	108	100	2.70	32.5	362	0.90	50
D	115	119	2.20	45.0	332	1.36	32
C							
Mean	84	103	3.14	31.8	340	0.94	54
± SD	22	4	0.25	1.2	31	0.09	4
D							
Mean	95	128	2.89	40.1	328	1.22	50
± SD	25	7	0.34	2.6	17	0.10	9
p Value (C vs. D)	NS	<0.001	<0.001	<0.01	NS	<0.001	NS

Data are matched for end-systolic wall stress. Abbreviations as in Tables 1 and 2.

found. There was no change in the velocity of shortening or rate-corrected velocity of shortening with preload augmentation.

The hemodynamic response elicited in each of the seven subjects who received dobutamine (matched for end-systolic wall stress) are presented in Table 3. Heart rate increased by 13% (from 84 ± 22 to 95 ± 25 beats/min) during dobutamine administration. Increased contractile state re-

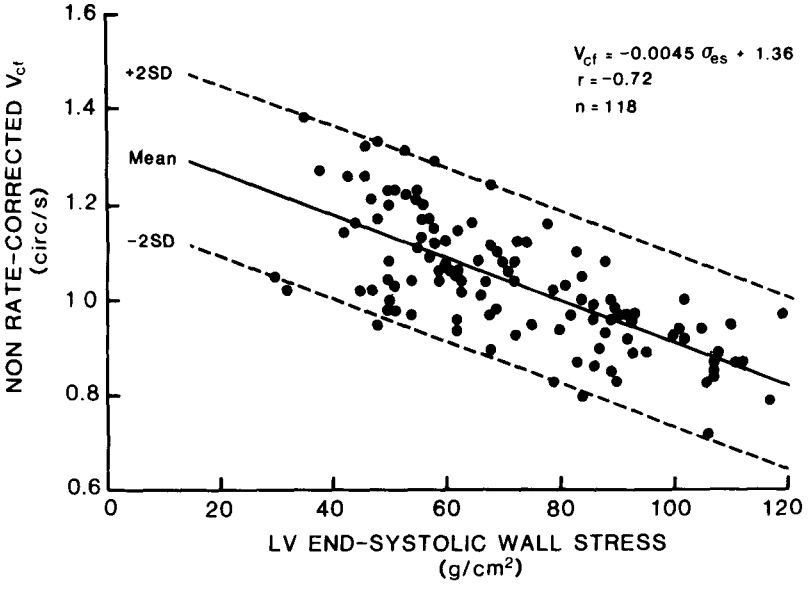


Figure 1. Relation between left ventricular (LV) end-systolic wall stress and the mean velocity of circumferential fiber shortening (V_{cf}) for 118 data points obtained in 25 subjects under rest and increased afterload conditions. The relation is inversely linear over a wide range of wall stress values (σ). The linear regression equation is given and illustrated along with 95% confidence intervals, correlation coefficient (r) and the number of data points (n).

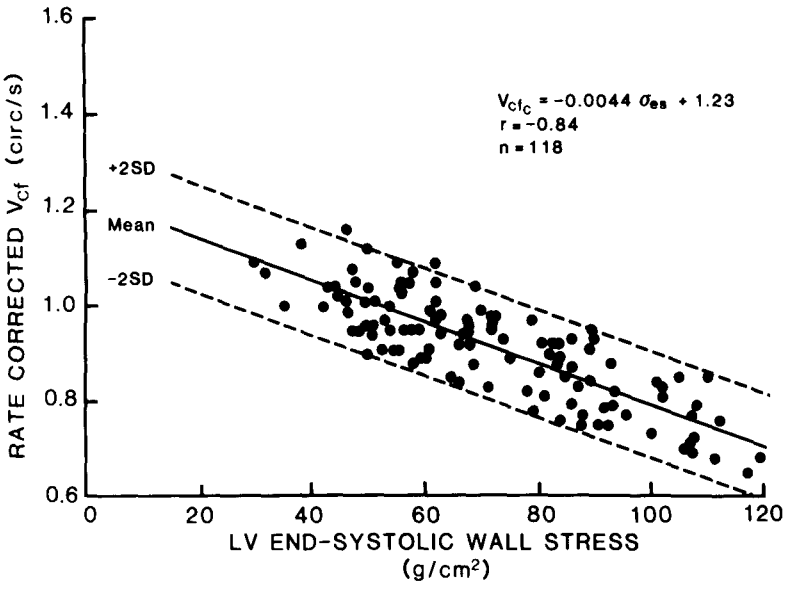


Figure 2. Relation between end-systolic wall stress (σ) and the rate-corrected mean velocity of fiber shortening (V_{cf_c}) for the same conditions as in Figure 1. A similar inverse linear relation is seen, but closer correlation and narrower confidence intervals result when the mean velocity of fiber shortening is corrected for heart rate. Linear regression equation, 95% confidence intervals, correlation coefficient (r) and the number of data points (n) are given as in Figure 1.

sulted in higher end-systolic pressures associated with lower end systolic dimensions. Percent dimension change, velocity of shortening and rate-corrected velocity of shortening were higher with shorter ejection times at equivalent end-systolic stress.

Left ventricular end-systolic stress/velocity of shortening relation. When the 118 data points from the 25 subjects studied under baseline and afterload-augmented conditions (without increased preload or contractility) were combined, the relation between left ventricular end-systolic wall stress and the velocity of circumferential fiber shortening was inversely linear with a correlation coefficient of −(72 (Fig. 1). By rate-correcting the velocity of shortening, a better correlation (−0.84) with narrower confidence intervals was found (Fig. 2). Previous studies (5,31) documented that velocity of shortening is rate-dependent and that the use of rate-corrected velocity of shortening thus increases the validity of comparisons made between subjects with disparate heart rates. We have, therefore, used rate-corrected velocity of shortening for the remainder of the data analysis.

Figures 3 and 4 present individual plots of the end-systolic stress/shortening and stress/rate-corrected velocity of shortening relations over a range of afterload conditions, both with and without preload augmentation in the eight subjects who received intravenous dextran. Both relations varied inversely with afterload in all subjects, with slope values that closely paralleled the mean regression line of the pooled data (Fig. 2). In each subject, augmentation of left ventricular preload resulted in an upward shift of the end-systolic wall stress/fractional shortening relation in a manner similar to that seen during a positive inotropic intervention (17). In contrast, the end-systolic wall stress/rate-corrected velocity of shortening relation was not altered. Thus, preload variation has no effect on the end-systolic wall stress/rate-corrected velocity of shortening relation, but does influence the end-systolic wall stress/fractional shortening relation.

Inclusion of the end-systolic wall stress/rate-corrected velocity of shortening data points collected under preload augmented conditions permitted calculation of the regression line and confidence intervals for the end-systolic wall stress/rate-corrected velocity of shortening relation with normal contractile state over a broad range of afterload and preload conditions. The results were not different from those obtained without increased preload. The end-systolic wall stress/rate-corrected velocity of shortening relation thus appears to be independent of preload and to incorporate afterload.

The position of the 34 end-systolic wall stress/rate-corrected velocity of shortening data points obtained during dobutamine infusion are illustrated in Figure 5. The enhanced contractile state resulted in increased rate-corrected velocity of shortening values at all levels of end-systolic stress, with 94% of the dobutamine data points above the 95% confidence interval for the normal end-systolic wall stress/rate-corrected velocity of shortening relation. When the subjects were considered individually, there was an upward shift of the linear end-systolic wall stress/rate-corrected velocity of shortening relation in each case (Fig. 6).

The effect of age on the end-systolic wall stress/rate-corrected velocity of shortening relation is displayed in Figure 7. The data of all 78 rest studies are pooled in panel A. The individual groups of patients aged 3 to 18, 18 to 40 and 40 to 75 years are then shown in panels B, C and D, respectively. For all panels, the confidence intervals from Figure 2 are shown for comparison purposes. No differences in these groups could be found. Thus, age does not appear to influence the end-systolic wall stress/velocity of short-

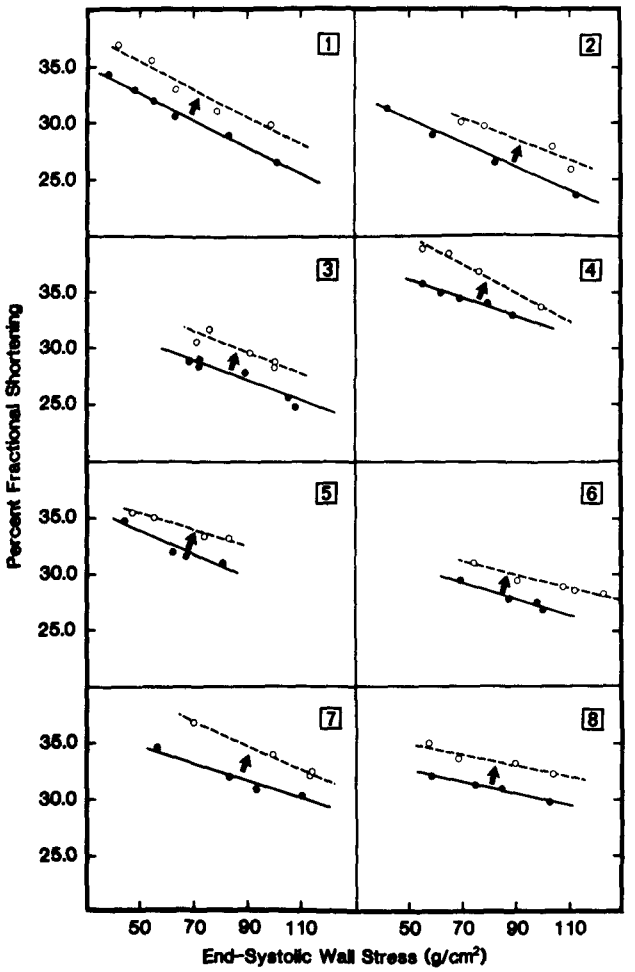


Figure 3. Relation of end-systolic wall stress to left ventricular percent fractional shortening in eight subjects before (**closed circles**) and after (**open circles**) dextran infusion over a wide range of afterload conditions. In each case, preload augmentation resulted in a significant upward shift (**arrows**) of the stress/shortening relation in a manner similar to that seen with positive inotropic intervention. Linear regression lines before (**solid**) and after (**dashed**) dextran infusion are shown.

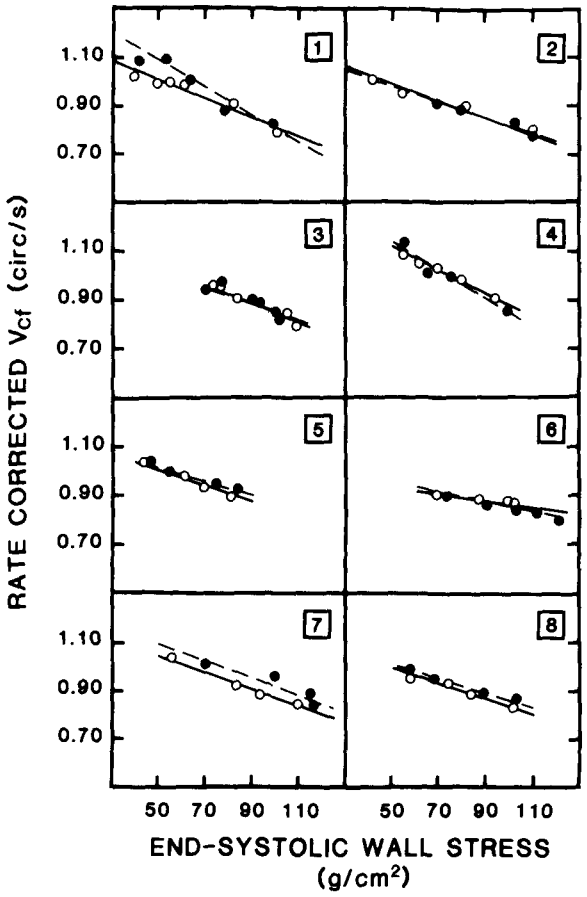


Figure 4. Relation of end-systolic wall stress to rate-corrected velocity of fiber shortening (V_{cf}) in eight subjects before (**closed circles**) and after (**open circles**) preload augmentation over a wide range of afterload conditions. There was no significant change. Linear regression lines before (**solid**) and after (**dashed**) dextran infusion are illustrated.

ening relation over the broad range of 3 to 75 years. A similar analysis according to gender did not reveal a difference in end-systolic wall stress/velocity of shortening values between male and female subjects.

Discussion

The mean velocity of fiber shortening has been calculated by several different techniques, depending on the method used for determining end-diastole and end-systole as well as measurement of ejection time (2–4,32,33). The approach used in this study results in highly reproducible determinations of end-systolic and end-diastolic dimension, with insignificant inter- or intraobserver variation in measurement (34). Ejection time calculated from externally recorded carotid pulse tracings is not significantly different from an intraarterial standard (35). When determined by a similar approach with a combined echocardiogram and carotid pulse tracing, velocity of shortening correlates well (r = 0.94) with angiographically determined values (33).

Rate-corrected velocity of shortening. Because velocity of shortening is calculated as a rate of change in length per unit length (dl/dt per unit length), it represents a strain rate (strain is defined as "change in length per unit length or dl/L). Conceptually, velocity of shortening represents a "normalized velocity" and allows one to compare hearts of different sizes (36,37). Although normalized for end-diastolic diameter, mean velocity of shortening values are directly related to heart rate (5,31). This was demonstrated in the study of Hirshleifer et al. (5), in which a 13% increase in mean velocity of shortening was induced by a 55% increase in heart rate. However, when velocity of shortening from the Hirshleifer data is rate-corrected, velocity of shortening actually decreases 9%. This decrease in rate-corrected

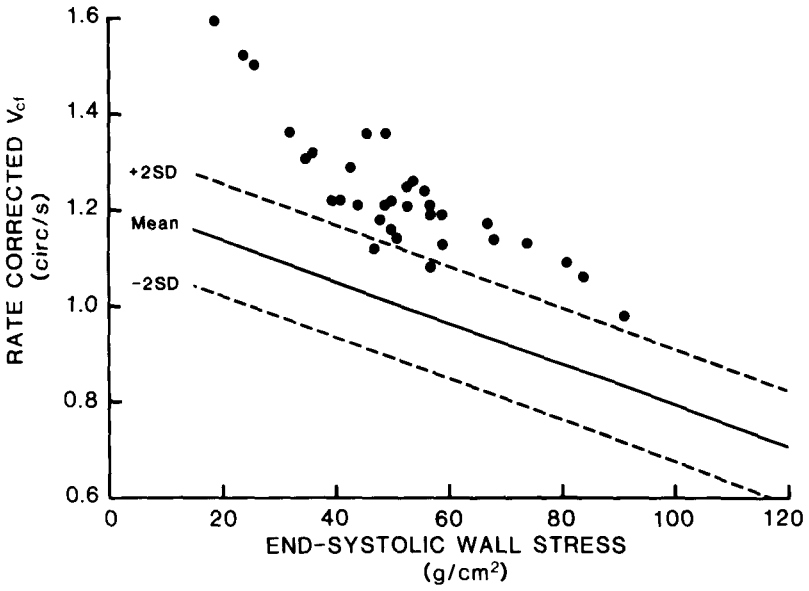
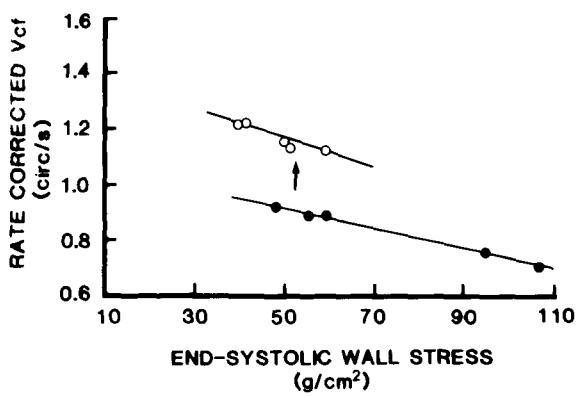


Figure 5. Relation of end-systolic stress to rate-corrected velocity of fiber shortening (V_{cf}) during dobutamine infusion in eight subjects, showing the sensitivity of this relation to inotropic state. Ninety-four percent of these data points were more than 2 standard deviations above the mean value for control data (Fig. 2).

velocity of shortening corresponds to the 7% increase in blood pressure observed during the higher heart rates and is the expected response of velocity variables to increased afterload (4,5). In our study, the use of rate-corrected velocity of shortening resulted in decreased scatter of normal data and narrowed confidence intervals for the end-systolic wall stress/velocity relation, thus permitting more meaningful comparison of subjects with different heart rates. Additionally, this method allows the inotropic and chronotropic effects of dobutamine to be distinguished from changes due to heart rate alone.

Velocity of shortening/force relations. Exploration of the relation between the velocity of shortening of the contractile element of muscle and developed force can be categorized as follows:

Figure 6. Comparison of baseline (**closed circles**) and increased contractile state (**open circles**) values of the end-systolic wall stress/rate-corrected velocity of fiber shortening (V_{cf}) relation in a representative subject. During the dobutamine infusion, velocity of fiber shortening was higher for any equivalent end-systolic wall stress.



1) Analysis of the instantaneous force/velocity/length relation throughout systole (12,38–40). It is clear that for any given contractile state, the instantaneous shortening velocity is determined by the instantaneous force and length (40). Therefore, simultaneous quantitation of these three variables permits a comprehensive description of left ventricular systolic function including contractile state. Difficulties with this method include the need for the use of a velocity-sensing catheter (40) and the complex three-dimensional constructs involved in data analysis. Finally, adequate delineation of the individual force/velocity/length profile necessitates afterload manipulation, usually by pharmacologic means.

2) Calculation of V_{max}. By extrapolation from measured values, one can theoretically determine the velocity of contractile element shortening for no load on the ventricle (V_{max}) (41). The theoretical basis and methodologic problems of this index have been discussed in detail by Mirsky et al. (37). In addition to uncertainty concerning the correct method for extrapolating to V_{max}, it is inherent within the process of extrapolation that the error of the calculation increases as the distance between the point of extrapolation and the measured data grows larger. It has also been reported that this index is not independent of preload status (42,43).

3) Relation of mean velocity of fiber shortening to peak left ventricular wall stress. In some cases, this relation is able to distinguish normal from abnormal myocardial function (4,6); afterload manipulation improves this ability (9–11). Because of the preload dependence of early systolic wall stress (12), this relation is influenced by end-diastolic fiber length (6), limiting its value as an index of contractility.

Current study. The force/velocity analysis undertaken in this study has shown that an inverse linear relation exists between the mean velocity of fiber shortening and left ventricular end-systolic wall stress. This relation is sensitive to

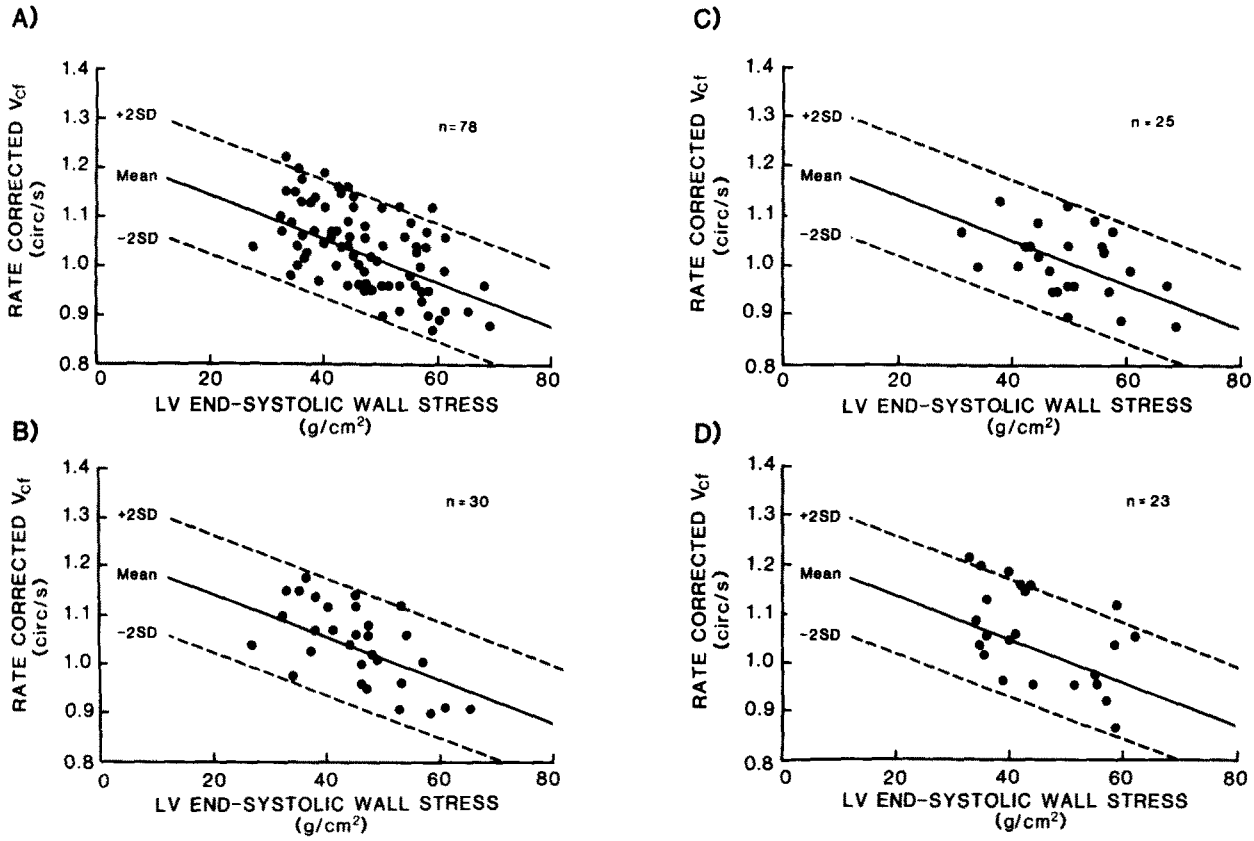


Figure 7. Relation of end-systolic wall stress/rate-corrected velocity of shortening (V_{cf}) to age. Rest data points for all 78 subjects are illustrated in **panel A**. Data are then divided into groups aged 3 to 18 years (30 subjects, **panel B**), 19 to 40 years (25 subjects, **panel C**) and 41 to 75 years (23 subjects, **panel D**). In all cases, the normal confidence limits from Figure 2 are shown for comparison. No influence of age on the end-systolic stress/rate-corrected velocity of shortening relation was discernible.

altered contractile state, is independent of preload, incorporates both afterload and heart rate and can be accurately determined by noninvasive means without manipulation of loading conditions.

The lack of influence of end-diastolic fiber length on the relation of end-systolic wall stress to rate-corrected velocity of shortening derives from the fact that neither of these variables is preload-dependent. Although instantaneous ve-

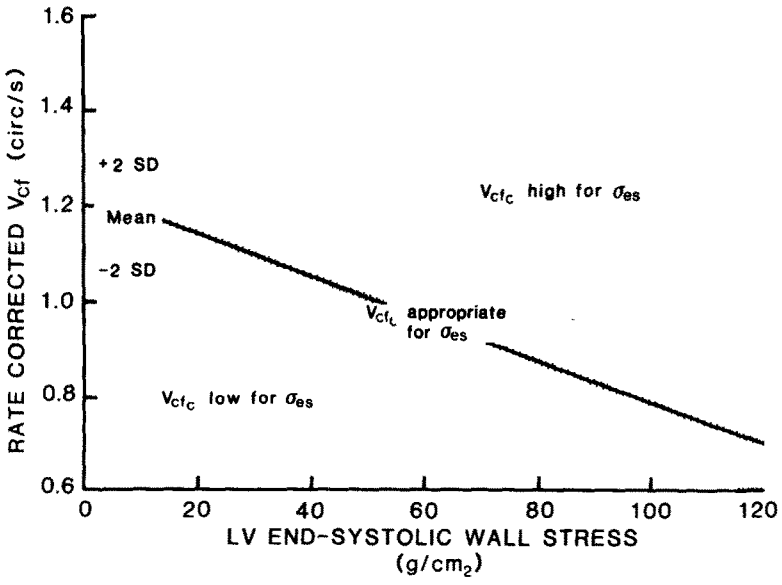


Figure 8. Diagram of the end-systolic wall stress (σ_{es})/rate-corrected velocity of fiber shortening (V_{cf}) relation. Depressed contractile state (V_{cf_c} low for the level of σ_{es}) may be distinguished from situations in which contractility is normal but afterload is increased (V_{cf_c} appropriate for the level of σ_{es}). Velocity of fiber shortening, which is high for the level of end-systolic wall stress, is characteristic of increased inotropic state.

locity is higher during preload augmentation in papillary muscle preparations (44) and isolated canine hearts (12), concomitant prolongation of ejection time and elevation of early systolic wall stress results in mean velocity of shortening values that are independent of preload over the physiologic range (4,7,45). Additionally, end-systolic wall stress, in contrast to peak stress, is not related to preload status. When isolated, ejecting canine hearts are subjected to increased filling volumes while the absolute level of ejection pressure is held constant, higher early systolic wall stress (including peak stress) is attained, while end-systolic wall stress is unchanged (40). Thus, if afterload is defined in terms of wall stress, then only at end-systole is afterload independent of preload. This influence of end-diastolic fiber length on early systolic wall stress results in the preload dependence of the mean velocity of shortening/peak wall stress relation. Only by relating mean velocity of shortening to afterload at end-systole is it possible to define a preload-independent index of contractility.

This principle is also illustrated by the preload dependence of the end-systolic stress/fractional shortening relation documented in this study. Fractional shortening is known to be preload-dependent, whereas end-systolic stress is not influenced by end-diastolic fiber length. Comparison of pre- and post-dextran infusion data points at similar levels of end-systolic stress (Table 2) shows that fractional shortening increased 7.6 ± 1.9%. Thus, their ratio is responsive to alterations in loading under conditions that are clearly physiologically relevant. This load dependence limits the usefulness of the stress/shortening relation as an index of contractile state. As also shown in Table 2, the concomitant 7.1 ± 4.9% increase in ejection time during preload infusion resulted in the velocity of shortening being unchanged. Figure 8 illustrates the use of the end-systolic stress/velocity of fractional shortening relation for the interpretation of clinical data. For any given end-systolic stress, a normal range of rate-corrected velocity of shortening values can be defined. It is thereby possible to distinguish reduced velocity of shortening due to excessive afterload from the effects of depressed contractility. Both rate-corrected mean velocity of shortening and wall stress are normalized for heart size, permitting comparison of patients with different heart sizes and ages. Normalization of mean velocity of shortening for heart rate enables inter- and intrapatient comparison under changing physiologic conditions.

Limitations. The potential limitations of this method of left ventricular wall stress quantitation have been previously discussed in detail (17,22,23). It should be noted that measurements from multiple cardiac cycles were averaged for each wall stress and rate-corrected velocity of shortening computation. Additionally, conclusions are based on the analysis of individual responses over a wide range of afterload conditions. By these means, the influence of random measurement error is minimized. This method of quantification of meridional wall stress as a measure of left ventricular afterload yields accurate results by noninvasive methods (46). Although quantitatively different from circumferential wall stress, these two measures of afterload correlate well (47) and relate similarly to left ventricular performance (48). Even in conditions with altered left ventricular geometry, such as aortic regurgitation and congestive cardiomyopathy, a correlation of 0.94 has been found between the two orthogonal stress determinations (20). We chose to use meridional wall stress as a measure of afterload in this analysis because of the ease and reproducibility of the measurements involved. Clinical conditions in which the usual relation of meridional and circumferential wall stress is significantly disturbed may require an alternative approach.

Clinical implications. The end-systolic stress/rate-corrected velocity of fiber shortening relation is obtainable in the rest state by noninvasive means without need for alteration of loading conditions, rendering it ideal for longitudinal studies assessing the effects of therapeutic interventions, disease progression and so forth. In particular, this index may be especially advantageous in situations in which preload status is either unpredictable or known to be abnormal, such as hereditary anemias, vasodilator therapy or the postoperative state. Further investigations of the clinical utility of this method are needed.

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References

1. Karliner JS, Gault JH, Eckberg D, Mullins CB, Ross J Jr. Mean velocity of fiber shortening. A simplified measure of left ventricular myocardial contractility. Circulation 1971;44:323–33.
2. Fortuin NJ, Hood WP, Craige E. Evaluation of left ventricular function by echocardiography. Circulation 1972;46:26–35.
3. Paraskos JA, Grossman W, Saltz S, Dalen JE, Dexter L. A noninvasive technique for the determination of velocity of circumferential fiber shortening in man. Circ Res 1971;29:610–5
4. Quinones MA, Gaasch WH, Cole JS, Alexander JK. Echocardiographic determination of left ventricular stress-velocity relations in man. With reference to the effects of loading and contractility. Circulation 1975;51:689–700.
5. Hirshleifer J, Crawford M, O'Rourke RA, Karliner JS. Influence of acute alterations in heart rate and systemic arterial pressure on echocardiographic measures of left ventricular performance in normal human subjects. Circulation 1975;52:835–41.
6. Sasayama S, Kotoura H. Echocardiographic approach for the clinical assessment of left ventricular function. the analysis of end-systolic pressure (wall-stress)-diameter relation and force-velocity relation of ejecting ventricle. Jpn Circ J 1979,43:357–66.
7. Mahler F, Ross J JR, O'Rourke RA, Covell JW. Effects of changes in preload, afterload and inotropic state on ejection and isovolumic phase measures of contractility in the conscious dog. Am J Cardiol 1975;35:626–34.
8. Rosenblatt A, Clark R, Burgess J, Cohn K. Echocardiographic as-

sessment of the level of cardiac compensation in valvular heart disease. Circulation 1976;54:509–18.

9. Ross J Jr. The concept of afterload mismatch and its implications in the clinical assessment of cardiac contractility. Jpn Circ J 1976; 40:865–75.
10. Ross J Jr, Franklin D, Sasayama S. Preload, afterload and the role of afterload mismatch in the descending limb of cardiac function. Eur J Cardiol 1976;4:77–86.
11. Ross J Jr. Afterload mismatch and preload reserve: a conceptual framework for the analysis of ventricular function. Prog Cardiovasc Dis 1976;18:255–64.
12. Weber KT, Janicki JS. Instantaneous force-velocity-length relations in isolated dog heart. Am J Physiol 1977;232:H241–9.
13. Suga H, Sagawa K. Instantaneous pressure-volume relationships and their ratio in the excised, supported canine left ventricle. Circ Res 1974;35:117–26.
14. Weber KT, Janicki JS, Hefner LL. Left ventricular force-length relations of isovolumic and ejecting contractions. Am J Physiol 1976;231:337–43.
15. Grossman W, Braunwald E, Mann T, McLaurin LP, Green LH. Contractile state of the left ventricle in man as evaluated from the end-systolic pressure-volume relation. Circulation 1977;56:845–52.
16. Suga H, Kitabatake A, Sagawa K. End-systolic pressure determines stroke volume from fixed end-diastolic volume in the isolated left ventricle under a constant contractile state. Circ Res 1979;44:238–49.
17. Borow KM, Green LH, Grossman W, Braunwald E. Left ventricular end-systolic stress-shortening and stress-length relations in humans. Normal values and sensitivity to inotropic state. Am J Cardiol 1982;50:1301–8.
18. Wisenbaugh T, Spann J, Carabello B. Chronic volume overload of similar severity produces different ventricular mechanics in mitral versus aortic regurgitation (abstr). Circulation 1983;68(suppl III):III-238.
19. Hirota Y, Shimizu G, Kaka K, Takaharu S, Kawamura K. Two dimensional analysis of left ventricular function by afterload-ejection fraction, and end-systolic stress-volume relationships (abstr). Circulation 1983;68(suppl III):III-238.
20. Douglas P, Reichek N, Plappert T, Muhammad A, St John Sutton M. Multiplanar analysis of left ventricular stress-shortening relationships (abstr). Circulation 1983;68(suppl III):III-239.
21. Pfeffer MA, Pfeffer JM, Iwai J. Effects of graded dietary NaCl on left ventricular hypertrophy and performance in Dahl hypertensive rats (abstr). Circulation 1983;68(suppl III):III-224.
22. Borow KM, Neumann A, Wynne J. Sensitivity of end-systolic pressure-dimension and pressure-volume relations to inotropic state in humans. Circulation 1982;65:988–97.
23. Borow KM, Propper R, Bierman FZ, Grady S, Inati A. Left ventricular end-systolic pressure-dimension relation in patients with thalassemia major: a new noninvasive method of assessing contractile state. Circulation 1982;66:980–5.
24. Duke M, Ames RP, Ablemann WH. Hemodynamic effect of methoxamine in normal human subjects. Am J Med Sci 1963;246:301–7.
25. Goldberg LI, Bloodwell RD, Braunwald E, Morrow AG. The direct effect of norepinephrine, epinephrine, and methoxamine on myocardial contractile force in man. Circulation 1960;22:1125–32.
26. Tuttle RR, Mills J. Dobutamine. Development of a new catecholamine to selectively increase cardiac contractility. Circ Res 1975;36:185–96.
27. Borow KM, Newberger JW. Noninvasive estimation of central aortic pressure using the oscillometric method for analyzing systemic artery pulsatile blood flow: comparative study of indirect systolic, diastolic, and mean brachial artery pressure with simultaneous direct ascending aortic pressure measurements. Am Heart J 1982;103:879–86.
28. Stefadouros MA, Dougherty MS, Grossman W, Craige E Determination of systemic vascular resistance by a noninvasive technique. Circulation 1973;47:101–7.
29. Marsh JD, Green LH, Wynne J, Cohn PF, Grossman W. Left ventricular end-systolic pressure-dimension and stress-length relations in normal human subjects. Am J Cardiol 1979;44:1311–7.
30. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975,56:56–64.
31. Mahler F, Yoran C, Ross J Jr. Inotropic effect of tachycardia and poststimulation potentiation in the conscious dog. Am J Physiol 1974;227:569–75.
32. Cooper RH, O'Rourke RA, Karliner JS, Peterson KL, Leopold GR. Comparison of ultrasound and cinangiographic measurements of the mean rate of circumferential fiber shortening in man. Circulation 1972;46:914–23.
33. Quinones MA, Gaasch WH, Alexander JK. Echocardiographic assessment of left ventricular function. With special reference to normalized velocities. Circulation 1974;50:42–51.
34. Lapido GOA, Dunn FG, Pringle TH, Bastian B, Lawrie TDV. Serial measurements of left ventricular dimensions by echocardiography: assessment of week-to-week, inter- and intra-observer variability in normal subjects and patients with valvular heart disease. Br Heart J 1980;44:284–9.
35. Van de Werf F, Piesseus J, Kesteloot H, DeGeest H. A comparison of systolic time intervals derived from the central aortic pressure and from the external carotid pulse tracings. Circulation 1975;51:310–6.
36. Mirsky I, Pasternac A, Ellison RC. A general index for the assessment of cardiovascular function. Am J Cardiol 1970;26:649–50.
37 Mirsky I, Pasternac A, Ellison RC, Hugenholtz PG. Clinical application of force-velocity parameters and the concept of a "normalized velocity." In: Mirsky I, Ghista DN, Sandler H, eds. Cardiac Mechanics New York: John Wiley & Sons, 1974:293–329.
38. Fry DL, Griggs DM, Greenfield JC Jr. Myocardial mechanics: tension-velocity-length relationships of heart muscle. Circ Res 1964;14:73–85.
39. Peterson KL, Uther JB, Shabetai R, Braunwald E. Assessment of left ventricular performance in man. Instantaneous tension-velocity-length relations obtained with the aid of an electromagnetic velocity catheter in the ascending aorta. Circulation 1973;47:924–35.
40. Weber KT, Janicki JS. Instantaneous force-velocity-length relations: experimental findings and clinical correlates. Am J Cardiol 1977;40:740–7.
41. Sonnenblick EH. Force-velocity relations in mammalian heart muscle. Am J Physiol 202:1962;931–9.
42. Nejad NS, Klein MD, Mirsky I, Lown B. Assessment of myocardial contractility from ventricular pressure recordings. Cardiovasc Res 1971;5:15–23.
43. Grossman W, Haynes F, Paraskos JA, Saltz S, Dalen JE, Dexter L. Alterations in preload and myocardial mechanics in the dog and in man. Circ Res 1972,31:83–94.
44. Sonnenblick EH, Parmley WW, Urschel CW. The contractile state of the heart as expressed by force-velocity relations. Am J Cardiol 1969;23:488–503
45. Nixon JV, Murray RG, Leonard PD, Mitchell JH, Blomqvist CG. Effect of large variations in preload on left ventricular performance characteristics in normal subjects. Circulation 1982;65:698–703.
46 Brodie BR, McLaurin LP, Grossman W. Combined hemodynamic-ultrasonic method for studying left ventricular wall stress: comparison with angiography. Am J Cardiol 1976;37:864–70.
47 DePace NL, Reu JF, Iskandrian AS, Kotter MN, Hakki AH, Segal BL. Correlation of echocardiographic wall stress and left ventricular pressure and function in aortic stenosis Circulation 1983;67:854–9.
48. Sandler H, Dodge HT. Left ventricular tension and stress in man. Circ Res 1963;13:91–104.