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# Radionuclide determination of the relationship between left ventricular contractile state and ejection fraction

**To determine whether the relationship between various measures of left ventricular (LV) contractile state and ejection fraction (EF) is linear in man, we studied 30 patients during right atrial pacing over a range of loading conditions. With the use of micromanometer LV pressures and radionuclide LV volumes, pressure-volume (P-V) loops were generated for each loading condition. Then isochronal, instantaneous P-V data points were obtained by linear regression analysis to attain the maximum slope ($E_{max}$) of these time-varying isochrones. Other measures of LV end systole were also used to calculate end-systolic P-V relations in a similar fashion, and indirect P-V relations were obtained from the linear regression analysis of brachial artery peak pressure vs minimum LV volume data points. When the slopes of these LV contractile measures were compared to the radionuclide LV EFs, the linear correlation coefficients ranged from 0.53 to 0.67. After natural log transformation of the LV contractile state and EF data, the correlation coefficients for the polynomial curve fits ranged from 0.80 to 0.88. When the correlation coefficients for the polynomial curve fits of the natural log transformed data were compared to those for the linear regression analyses of the raw data, significant improvements were evident ($p < 0.05$). Thus the relationship between various measures of LV contractile state and EF obtained with radionuclide angiography is best approximated by a complex, curvilinear relationship that is due, in part, to the wide range of LV contractile states within the relatively narrow normal range of LV ejection fractions. (Am Heart J 1988;116:790.)**

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The linear relationship between left ventricular (LV) end-systolic pressure vs volume (P-V) data points obtained from multiple loading conditions has been demonstrated in excised, supported LV and conscious animal preparations to be a measure of LV contractile state.[1-6] The theoretic relationship between measures of LV contractile state and shortening characteristics, measured by stroke volume or ejection fraction (EF) has been predicted to be curvilinear.[3] Nivatpumin et al.[7] have shown in man that the maximal P-V ratio obtained from a single beat has a curvilinear relationship with LV EF. This single-beat ratio, however, may be sensitive to loading conditions in addition to LV contractile state.[8-10] In contrast, invasive and noninvasive studies in man[11,12] have reported a linear relationship between measures of LV contractile state calculated from multiple loading conditions and LV EF values. A linear relationship, however, does not incorporate low LV EF values, and therefore a curvilinear function might better represent this relationship over the full range of LV contractile states and EF values.[3,11] Whether the relationship between LV contractile state and EF is optimally predicted by a linear or curvilinear function in man has not been established. Moreover, whether various measures of LV contractile state all have a comparable relationship with shortening characteristics has also not been defined. Accordingly, the purpose of this investigation was to determine whether the relationship between various measures of LV contractile state and EF obtained with radionuclide angiography is optimally predicted by a simple linear or by a more complex, curvilinear function in man.

## METHODS

**Patients.** The patient population consisted of 30 patients, 16 normal subjects, nine patients with aortic regurgitation, one patient with mitral regurgitation, two patients with cardiomyopathy, and two patients with a prior myocardial infarction. There were 23 men and seven women, with an age range of 23 to 71 years (mean 48 ± 11 [SD] years). Each patient was referred for diagnostic right and left heart catheterization to establish the presence or absence of coronary artery disease or to establish the hemodynamic severity of his/her cardiovascular disease. Each patient gave written informed consent for this investigation on a form approved by the Human Studies Committee at the University of Michigan or Veterans Administration Medical Centers, Ann Arbor, Mich., or the University of Texas Health Science Center, San Antonio, Texas. Eight patients were taking no medication, while the remaining 22 patients were taking one or more of the following: diuretics (eight patients), beta-adrenergic blocking agents (four patients), $Ca^{++}$-entry blocking agents (five patients), vasodilators (six patients), or nitrate preparations (15 patients). All medications were discontinued 24 to 48 hours prior to cardiac catheterization. Twenty-eight of the 30 patients had normal coronary arteriograms, while the two patients with a prior myocardial infarction had single-vessel coronary artery disease with an occluded vessel to the previously infarcted myocardial region.

**Protocol.** After completion of the diagnostic catheterization, each patient entered the protocol, which consisted of the simultaneous acquisition of micromanometer measured LV and ascending aortic pressures and fluid measured brachial artery pressures with gated equilibrium radionuclide angiograms under control conditions and during methoxamine and nitroprusside infusions. The average methoxamine infusion was 761 ± 781 (SD) μg/min, and the mean nitroprusside infusion was 79 ± 93 μg/min. Right atrial pacing was used to maintain heart rate constant during all three loading conditions. Steady state was defined as a 10 mm Hg or less variation in the micromanometer and fluid pressure measurements during each radionuclide acquisition.

**Hemodynamics.** Twenty cardiac cycles of a simultaneous electrocardiogram (ECG), micromanometer LV (200 mm Hg and 50 mm Hg scales) and ascending aortic pressures (200 mm Hg scale), the first derivative of LV pressure (dP/dt), and fluid brachial artery pressure (200 mm Hg scale) were recorded at the beginning, middle, and end of each radionuclide acquisition at 100 mm/sec paper speed with an Electronics for Medicine VR-12 or 16 physiologic recorder (Electronics for Medicine/Honeywell Inc., Pleasantville, N.Y.). Offset measurements were made for both the micromanometer and fluid pressure signals following each hemodynamic recording to guarantee stability of the zero reference.

The micromanometer LV and ascending aortic pressures and fluid brachial artery pressures were manually averaged for each radionuclide acquisition to obtain average pressure waveforms. The average micromanometer LV pressure waveform was then hand digitized with a Calcomp 9100 inductance tablet interfaced to an IBM PC computer (IBM Corp., Purchase, N.Y.) throughout the R-R interval beginning at the peak of the R wave, with the use of a program developed in our laboratory. This program provides instantaneous LV pressure and the first derivative of LV pressure (dP/dt) at a variable sampling frequency. The LV pressures were sampled at 5 msec intervals for this investigation.[13]

**Equilibrium radionuclide angiography.** Gated equilibrium radionuclide angiograms were obtained following in vivo red blood cell labeling with 30 mCi of technetium-99m at 30 msec/frame throughout the R-R interval for 500 cardiac cycles. A 2 ml blood sample was drawn during the middle of each radionuclide acquisition and was later counted for 2 minutes. The time delay between drawing and counting the blood sample was recorded for decay correction. Measurements were made on each patient to calculate the distance from the gamma scintillation camera in the left anterior oblique (LAO) position to the LV center of mass for attenuation correction, by means of anatomic landmarks and a simple geometric technique previously validated in this laboratory.[14,15]

Radionuclide LV volumes were calculated frame-by-frame for each of the three loading conditions with a hand-drawn region-of-interest technique and attenuation correction.[14,15] Briefly, on the background subtracted and smoothed images, an LV region-of-interest was drawn by the operator to encompass the LV but to exclude the left atrium. These LV counts were then normalized for frame duration, cardiac cycles, a decay-corrected plasma blood

**Table I.** Hemodynamic data (n = 30)

| | Control | Methoxamine | Nitroprusside |
|---|---|---|---|
| *Heart rate (beats/min)* | | | |
| A* | 78 ± 12 (SD) | 76 ± 12 | 83 ± 13 |
| B† | 79 ± 13 | 78 ± 13 | 83 ± 13 |
| C‡ | 80 ± 14 | 78 ± 15 | 83 ± 14 |
| *Brachial artery peak pressure (mm Hg)* | | | |
| A | 141 ± 19 | 179 ± 21 | 113 ± 21 |
| B | 139 ± 18 | 183 ± 20 | 114 ± 23 |
| C | 140 ± 15 | 184 ± 20 | 114 ± 22 |
| *Ascending aortic peak/dicrotic notch pressures (mm Hg)* | | | |
| A | 129 ± 19/98 ± 25 | 168 ± 25/128 ± 26 | 100 ± 20/79 ± 19 |
| B | 128 ± 21/100 ± 17 | 173 ± 21/131 ± 23 | 100 ± 21/80 ± 19 |
| C | 127 ± 16/103 ± 12 | 173 ± 20/134 ± 24 | 100 ± 21/81 ± 19 |
| *Left ventricular peak/end-diastolic pressures (mm Hg)* | | | |
| A | 133 ± 18/15 ± 6 | 172 ± 29/22 ± 10 | 103 ± 20/8 ± 5 |
| B | 131 ± 20/14 ± 8 | 174 ± 22/21 ± 9 | 104 ± 20/8 ± 5 |
| C | 131 ± 17/13 ± 6 | 176 ± 20/21 ± 9 | 103 ± 20/8 ± 5 |

*A = beginning of each radionuclide acquisition.
†B = middle of each radionuclide acquisition.
‡C = end of each radionuclide acquisition.

**Table II.** Hemodynamic data (n = 30)

| | *HR (beats/min)* | *BaP (mm Hg)* | *Badi (mm Hg)* | *AoP (mm Hg)* | *Aodi (mm Hg)* | *LVP (mm Hg)* | *LVEDP (mm Hg)* | *(+)dP/dtmax (mm Hg/sec)* |
|---|---|---|---|---|---|---|---|---|
| Control | 79 ± 13 | 129 ± 41 | 92 ± 16 | 126 ± 16 | 101 ± 14 | 130 ± 16 | 15 ± 6 | 1123 ± 233 |
| Methoxamine | 79 ± 13 | 176 ± 42† | 118 ± 22† | 171 ± 21† | 131 ± 20† | 174 ± 22† | 23 ± 9† | 1369 ± 291* |
| Nitroprusside | 82 ± 14 | 113 ± 21† | 75 ± 21† | 100 ± 20† | 80 ± 18† | 103 ± 19† | 9 ± 5† | 1208 ± 292 |

HR = heart rate; BaP = brachial artery peak pressure; Badi = brachial artery dicrotic notch pressure; AoP = aortic peak pressure; Aodi = aortic dicrotic notch pressure; LVP = left ventricular peak pressure; LVEDP = left ventricular end-diastolic pressure.
*$p < 0.05$.
†$p < 0.001$ vs control.

sample counts. With the calculated distance from the gamma scintillation camera in the LAO projection and assuming a linear attenuation coefficient of 0.15 $cm^{-1}$ for technetium-99m in water,[14-17] the attenuation correction factor was calculated. The LV volume indices were then multiplied by this attenuation correction factor to obtain absolute LV volumes.

**Calculation of $E_{max}$ and other P-V relations.** With the use of the corresponding LV pressure measurements and radionuclide LV volumes, P-V loops for each of the three loading conditions were constructed. Then, isochronal instantaneous P-V data points from each of the three loading conditions were obtained by linear regression analysis beginning at the R wave and continuing throughout the cardiac cycle. The maximum slope of these time-varying isochrones was defined as the maximum time-varying elastance ($E_{max}$). Additional definitions of LV end systole were used to calculate end-systolic P-V relations. These additional definitions of end-systole were the time of the maximum P-V ratio (maxPV), which occurs at the left uppermost corner of each of the P-V loops; the time of minimum LV volume (minPV); the time of peak (−)dP/dt [(−)dP/dtPV]; and the time of zero systolic flow, which was approximated by the central aortic dicrotic notch (AodiPV). To calculate the end-systolic P-V relations for the first three of these definitions of end systole, the corresponding P-V data points from the hand-digitized micromanometer LV pressure waveform and radionuclide derived LV volume curve from each of the three loading conditions, which corresponded in time to the definitions of end systole, were derived by linear regression analysis to obtain a slope value. For the AodiPV slope calculations, however, the actual aortic dicrotic notch pressures were used. The indirect P-V relations were obtained from the linear regression analysis of brachial artery peak (BaP) pressure vs minimum LV volume (minV) data points from each of the three loading conditions. LV EF was calculated in the standard fashion with the use of the radionuclide absolute LV end-diastolic and end-systolic volumes.

**Statistical analysis.** The raw and natural log-transformed LV contractile slope values for $E_{max}$, the end-

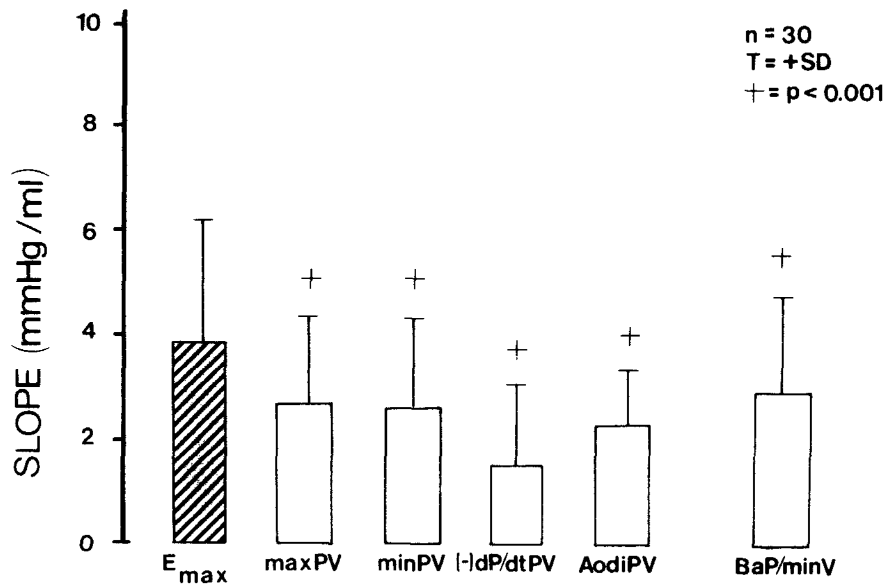


**Fig. 1.** The isochronal $E_{max}$ slope value *(cross-hatched bar)* is compared to the other end-systolic P-V and indirect P-V relations *(open bars)*. The bars represent the mean ± 1 SD. Significant differences are shown.

systolic P-V relations, the indirect P-V relations, and LV EF data were compared by linear regression analysis and polynomial curve fitting. Correlation coefficients for each of these LV contractile state and EF comparisons were compared by Fisher's $Z$ transformation. The mean values for $E_{max}$, the end-systolic P-V relations, and the indirect P-V relations are presented as the mean ± 1 standard deviation and were compared by an analysis of variance. When a significant $F$ statistic was obtained, $t$ tests with a Bonferroni correction were performed to identify where these differences occurred. Similar comparisons were performed for LV, ascending aortic, and brachial artery pressures obtained during the beginning, middle, and end of each radionuclide acquisition to establish whether hemodynamic stability existed during each radionuclide acquisition, and for these pressures under the control condition and during the methoxamine and nitroprusside infusions to establish whether differences in these hemodynamic variables occurred between conditions. A probability value of 0.05 or less was considered significant.

## RESULTS

**Hemodynamic data (Tables I and II).** During each radionuclide acquisition, a hemodynamic steady state was maintained, as shown in Table I. Notably, heart rate, brachial artery pressure, ascending aortic pressure, and LV pressure did not differ significantly between the beginning, middle, and end of each radionuclide acquisition.

In contrast, as shown in Table II a significant hemodynamic effect was produced by the methoxamine and nitroprusside infusions in comparison to control. Because of right atrial pacing, heart rate did not differ significantly between the three loading conditions. However, brachial artery, ascending aortic, and LV pressures increased during the methoxamine infusion ($p < 0.001$ for each) and decreased during the nitroprusside infusion ($p < 0.001$ for each) compared to control. There was an increase in (+)dP/dtmax during the methoxamine infusion ($p < 0.05$), but there was no significant effect of nitroprusside on the rate of LV pressure development compared to control.

**Comparison of various measures of LV contractile state to $E_{max}$.** The average isochronal $E_{max}$ slope value for the 30 patients was 3.94 ± 2.24 mm Hg/ml, and it was underestimated by the other end-systolic and indirect P-V relations ($p < 0.001$ for all, Fig. 1). The maxPV relations averaged 2.61 ± 1.73 mm Hg/ml, the minPV relations averaged 2.50 ± 1.73 mm Hg/ml, the (−)dP/dtPV relations averaged 1.56 ± 1.71 mm Hg/ml, and the AodiPV relations averaged 2.16 ± 1.38 mm Hg/ml. The average BaP/minV relation was 2.69 ± 1.90 mm Hg/ml.

The average isochronal $E_{max}$ extrapolated volume-axis intercept was 47 ± 93 ml. Although the mean unstressed volume ($V_0$) values for the other end-systolic and indirect P-V relations were less than that for $E_{max}$, they did not underestimate it significantly, due to the wide variance in these values (17 ± 94, 27 ± 149, −2 ± 148, −1 ± 57, and −2 ± 49 ml, respectively).

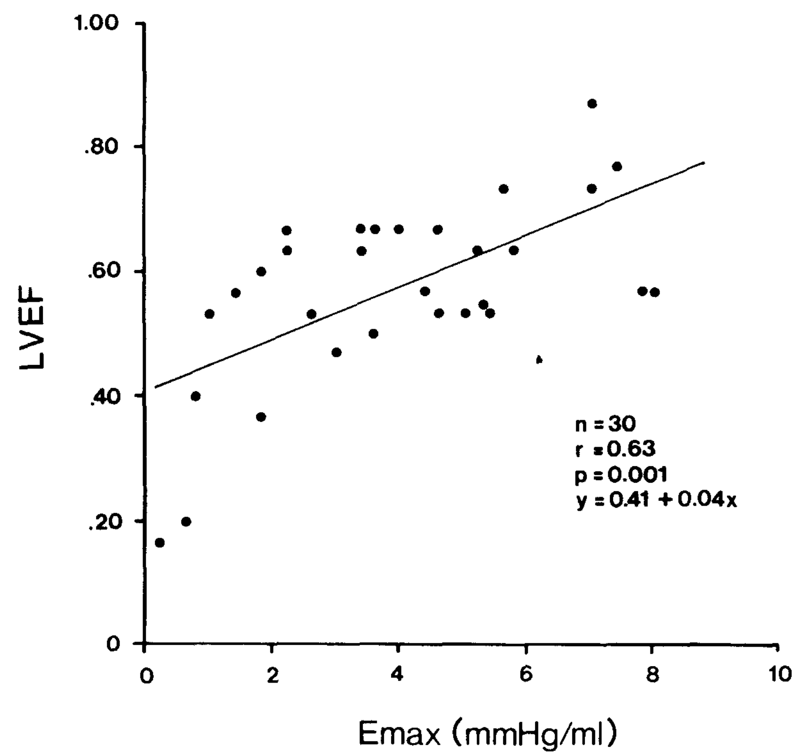


**Fig. 2.** The individual left ventricular ejection fraction *(LVEF)* values *(on the ordinate)* and their corresponding isochronal $E_{max}$ slope values *(on the abscissa)* are compared by linear regression analysis. The line of best fit, correlation coefficient *(r)*, and regression equation are shown.

**Table III.** Correlation between measures of LV contractile function and ejection fraction (n = 30)

| | $E_{max}$ | *maxPV* | *minPV* | *(−)dP/dtPV* | *AodiPV* | *BaP/minV* |
|---|---|---|---|---|---|---|
| Raw data | | | | | | |
| Linear regression | 0.63 | 0.64 | 0.67 | 0.20 | 0.53 | 0.65 |
| Polynomial curve fit | 0.71 | 0.70 | 0.71 | 0.20 | 0.66 | 0.70 |
| Natural log transformed data | | | | | | |
| Linear regression | 0.80 | 0.79 | 0.78 | 0.23 | 0.77 | 0.79 |
| Polynomial curve fit | 0.84† | 0.88* | 0.83† | 0.24 | 0.80* | 0.86* |

$E_{max}$ - maximum time-varying elastance; maxPV = time of maximum P-V ratio; minPV = time of minimum LV volume; AodiPV = time of zero systolic flow approximated by the central aortic dicrotic notch; BaP = brachial artery peak pressure; minV = minimum LV volume.
*$p \le 0.05$.
†$p < 0.10$ vs linear regression of raw data.

**Comparison of LV contractile state and EF (Table III).** The correlation coefficients between measures of LV contractile state and EF are shown in Table III, and they are displayed for isochronal $E_{max}$ in Figs. 2 to 4. As demonstrated in Fig. 2, the correlation coefficient for the linear regression of isochronal $E_{max}$ and EF was $r = 0.63$ ($p = 0.001$). When a polynomial curve fit was applied to these data, the correlation coefficient improved to $r = 0.71$ ($p < 0.001$, Fig. 3). When the isochronal $E_{max}$ slope values and LV EF data were natural log transformed, the correlation coefficient for the linear regression of these data improved to $r = 0.80$ ($p < 0.001$, Fig. 4). A further improvement in the correlation coefficient to $r = 0.84$ ($p < 0.001$, Fig. 4) was observed when a polynomial curve fit was applied to the natural log transformed data. When the correlation coefficients for the linear regression of the raw data and the polynomial curve fit of the natural log transformed data were compared, there was a marginal improvement in correlation between these data ($0.10 > p > 0.05$).

Similar comparisons between the end-systolic P-V slope value relations and LV EF data demonstrated a progressive improvement in the correlation

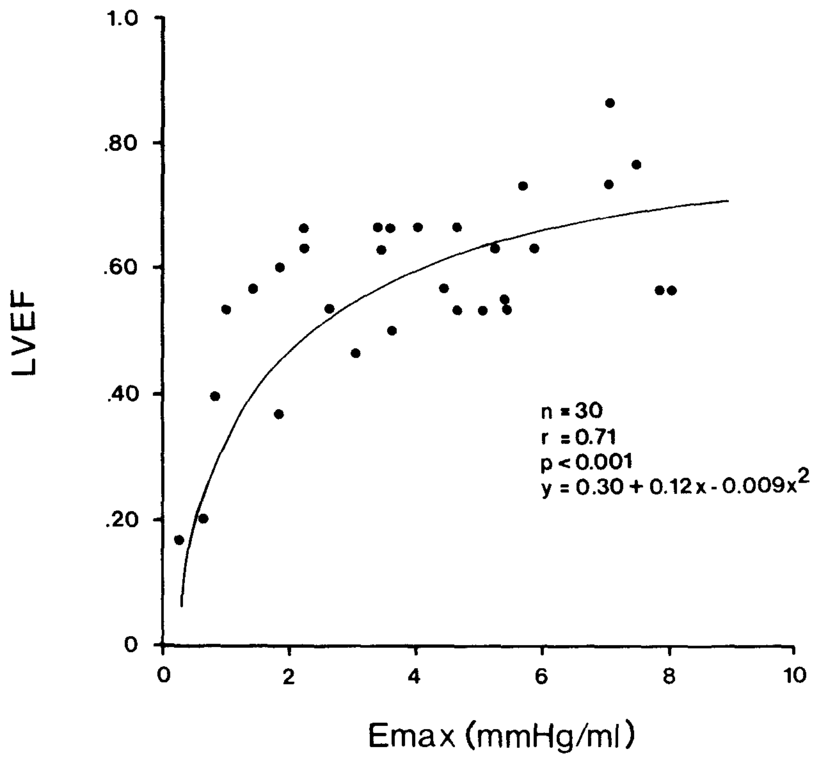


**Fig. 3.** In a format similar to that of Fig. 2, the LVEF and isochronal $E_{max}$ slope values are compared by means of a polynomial curve fit.

coefficients from the linear regression of the raw data to the polynomial curve fit of the natural log transformed data (Table III). A significant improvement in the correlation coefficients was noted for the maxPV and the AodiPV relations ($p < 0.05$ for both), while a marginal improvement was noted for the minPV relations ($0.10 > p > 0.05$). The correlation coefficients between the (−)dP/dtPV relations and LV EF data remained consistently poor.

The indirect P-V relations (BaP/minV) also demonstrated a progressive improvement in correlation coefficients between the BaP/minV slope values and the LV EF data. Compared to the linear regression analysis of the raw data, the polynomial curve fit of the natural log transformed data significantly improved the correlation coefficient between these data ($p < 0.05$).

## DISCUSSION

The data in the present investigation indicate that the LV maximum time-varying elastance ($E_{max}$) slope values have only a weak linear relationship with their corresponding LV EFs. The relationship between isochronal $E_{max}$ slope values and LV EF is more closely approximated by a complex, curvilinear function. When other end-systolic P-V slope value relations were compared to the LV EF data, weak correlation coefficients were obtained with linear regression analysis of the raw data, while better correlation coefficients were observed when polynomial curve fitting was applied to the natural log transformed data. Moreover, the indirect P-V (BaP/minV) slope value relations also demonstrated an improvement in correlation with the LV EF data with polynomial curve fitting of the natural log transformed data in comparison to linear regression analysis of the raw data. Thus despite differences in the mean isochronal $E_{max}$, end-systolic P-V relations, and indirect P-V relations, they all, except for the (−)dP/dtPV relations, have a comparable relationship with LV shortening characteristics as measured by LV EF.

Sagawa et al.[3] suggested that knowing the end-systolic P-V ratio from a single beat, one can theoretically predict LV stroke volume or EF if LV end-diastolic volume and end-systolic pressure are known. The LV EF is then equivalent to: $EF = 1 - [ESP/EDV(E_{max})] - V_O/EDV$; where ESP = end-systolic pressure, EDV = end-diastolic volume, $V_O$ = the unstressed volume, and $E_{max}$ in this construct is the end-systolic P-V ratio obtained from a single beat. The value $V_O/EDV$ is presumed to be

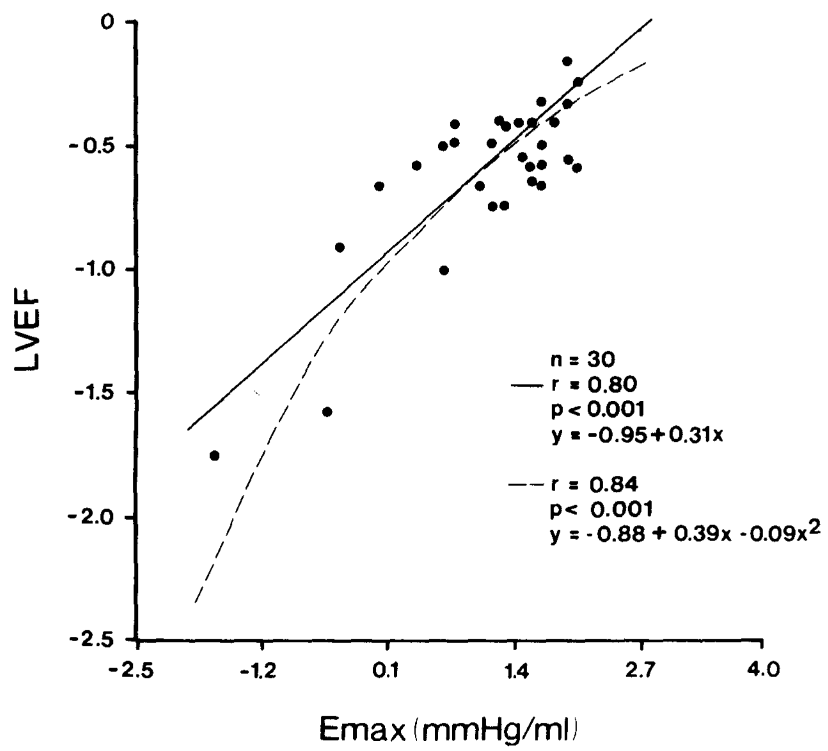


**Fig. 4.** The natural log transformed left ventricular ejection fraction *(LVEF)* values *(on the ordinate)* and the natural log transformed isochronal $E_{max}$ slope values *(on the abscissa)* are compared by both a linear regression analysis and a polynomial curve fit. The lines of best fit for the linear regression analysis *(solid line)* and for the polynomial curve fit *(dashed line)* are shown with their correlation coefficients *(r)* and regression equations.

negligible. When this relationship was plotted, a nonlinear relationship was constructed that was relatively insensitive to changes in the end-systolic P-V ratio at high values of LV EF. Thus the theoretic relationship between the single beat end-systolic P-V ratio and LV EF would appear (based on this mathematical analysis) to be a complex, curvilinear function.

The data regarding the relationship between LV contractile state and EF in man are conflicting.[7,11,12] Nivatpumin et al.[7] have shown in man that the maximal P-V ratio obtained from a single beat (as predicted by Sagawa et al.[3]) has a curvilinear relationship with LV EF. This measure, however, may be sensitive to changes in loading conditions in addition to contractile state.[8-10] Kono et al.,[8] in an excised, supported LV preparation, and Wiesenbaugh et al.,[9] in an acute canine preparation, both demonstrated that the single-beat maximal P-V ratio and stress-volume ratio, since they presume a zero volume-axis intercept, increase when arterial load is increased. This has also been suggested in man.[10] These single-beat ratios may also be dependent upon end-systolic volume.[18,19] Thus since the maximal P-V ratio calculated from a single beat and LV EF are sensitive to alterations in loading conditions,[20,21] end-systolic P-V relations, which are characterized by both a slope and $V_0$ calculated from multiple data points and are independent of loading conditions, should be used to assess LV contractile state in man.

Other studies in man[11,12] have compared end-systolic P-V slope value relations to LV EF. Mehmel et al.[11] reported correlation coefficients between the slope of the maximum end-systolic P-V relations and LV EF when a linear ($r = 0.89$) and exponential analysis was employed ($r = 0.94$). Although no difference between these correlation coefficients was evident, they noted that the linear regression analysis did not incorporate lower LV EF values, which were incorporated by the monoexponential function. The equally high correlation coefficients for both mathematical data transformations reported by these authors may be due to the relatively few data points in the low LV contractile state and EF ranges.

More recently, McKay et al.[12] calculated the LV maximum time-varying elastance with radionuclide angiography and demonstrated a correlation of $r = 0.67$ between isochronal $E_{max}$ slope values and

LV EF. Our data confirm this relatively weak linear correlation between the isochronal $E_{max}$ slope values and LV shortening characteristics. Other end-systolic P-V relations and indirect pressure-volume relations also demonstrated weak linear correlations with LV EF. Interestingly, the (−)dP/dtPV relations showed no significant correlation with LV EF, which is similar to the finding reported by McKay et al.[12] This linear relationship, however, does not incorporate the lower LV EF values, as evidenced in our data by a y-axis intercept of 41%. When we used a more sophisticated mathematical data transformation, the correlation coefficients between the isochronal $E_{max}$, other end-systolic P-V and indirect P-V slope value relations and LV EFs improved significantly. Thus these data demonstrate in man that the slope values of various measures of LV contractile state and EF are not optimally described by a linear function, but rather are more closely approximated by a complex, curvilinear function.

There may be several possible explanations for these observations. First, there is a relatively wide range of LV contractile states within the normal LV EF range (50% to 75%). These data suggest that LV EF is a poor index of contractile state. Only when LV contractile state is severely depressed will a reduced EF be manifest. Conversely, when LV EF is within the normal range, LV contractile state may be depressed. This is not surprising, considering the load dependence of LV EF.[20,21] Moreover, these data suggest that isochronal $E_{max}$ and the other P-V relations may be more sensitive to alterations in LV contractile state than shortening characteristics. This has indeed been demonstrated in an intact animal preparation[6] and in a preliminary fashion in man.[22] Second, these observations may also be due in part to the variability of the radionuclide LV EF determinations within the normal range.[23,24] Third, this range of isochronal $E_{max}$ slope values in normal subjects and in patients with cardiovascular disease processes may be due in part to the independent influence of heart size on these LV contractile measures.[5,13,25] It therefore reinforces the suggestion by Sagawa[5] that for valid comparisons of LV contractile state to be made between patient groups methods must be identified to standardize these slope values, thereby minimizing their range and thus enabling depressed LV contractile states to be detected in individual patients. Methods of performing this standardization have been demonstrated in animals[25] and in man by means of invasive techniques.[9] Thus measures of LV contractile state may be most useful in assessing patients with disease processes such as mitral regurgitation,[18,19] in whom shortening characteristics may remain normal despite depressed LV contractile state because of favorable alterations in loading conditions. Finally, once slope values of the various measures of LV contractile state become severely depressed, the LV ejection fractions demonstrate a wide range of values. This suggests that the reflex neurohumoral adjustments to LV contractile depression and their resultant effects on loading conditions may become increasingly important for establishing the absolute value of LV EF.

Potential limitations of the present investigation should be considered. First, we assumed that a constant inotropic background existed during the three loading conditions. We observed no significant change in heart rate during the three loading conditions due to right atrial pacing. In contrast, we did observe an increase in (+)dP/dtmax during the methoxamine infusion compared to control. This may be due to the preload dependence of (+)dP/dtmax.[20,21] Nevertheless, since we did not automatically block our patients in this investigation, we cannot totally exclude minor alterations in autonomic tone, which may have affected the calculation of LV contractile state. Second, we assumed that the various measures of LV contractile state were linear over the range of loading conditions employed in this investigation. Although other investigators[26,27] have also assumed linearity, recent data[28-31] have suggested that these relations may not be linear in the high LV pressure range and that they may become curvilinear in the subphysiologic LV pressure range. At least within the LV pressure range we employed in this investigation, the three P-V data points for each of the definitions of end systole demonstrated linearity. Third, although we demonstrated differences in the mean slope values for other more commonly defined measures of end systole and isochronal $E_{max}$, the relationship between the slope of these end-systolic P-V relations and LV EF was comparable to that for isochronal $E_{max}$. The one exception was the (−)dP/dtPV relations, which may be due in part to the difficulty in defining the exact timing of peak (−)dP/dt over the full range of loading conditions when the methods employed in this investigation are used. The definition of end systole may differ in patients with valvular heart disease compared to patients with other pathologic processes or normal subjects. It is important to note therefore that a number of our patients did have mitral and aortic regurgitation, and they were included in our patient population to establish this relationship. Finally, differences in the end-systolic and indirect P-V relation and $E_{max}$ slope values are probably multifactorial. Reasons for this may include the methods of altering load, the presence of intact autonomic reflexes, or the effects of increased load on the slope of the P-V relationship.[13] Nevertheless, irrespective of the underlying pathologic process or the measure of LV contractile state, it appears that a characteristic, complex, curvilinear relationship exists between LV contractile state and shortening characteristics.

In conclusion, the relationship between LV contractile state and EF is probably not linear. Rather, measures of LV contractile state have a characteristic, complex, curvilinear relationship with EF. The end-systolic P-V relationship may therefore be most useful for detecting alterations in LV contractile state in patients who have otherwise preserved shortening characteristics such as mitral regurgitation.[19, 20]

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