Determinants of Instantaneous Pressure in Canine Left Ventricle

Time and Volume Specification

HIROYUKI SUGA, KIICHI SAGAWA, AND LINDA DEMER

SUMMARY Instantaneous pressure (P) in the canine left ventricle is determined predominantly by the simultaneous volume (V) of the ventricular lumen; that is, the instantaneous P-V relation is reasonably well approximated by a regression line of isochronous pressures from different beats on the simultaneous volume values. Strictly speaking, however, the P-V data points from differently loaded contractions slightly scatter around the regression line, indicating that V is not the sole determinant of P. To identify the secondary determinants of P at a given V, we forced the ventricle to have a fixed V at a specified time in the cardiac cycle while changing the end-diastolic volume and the velocity of ejection over a wide range under a constant inotropic background. We found that, at any specified time and V, P decreased with increases in the simultaneous velocity of ejection (-dV/dt, ml/sec), the peak velocity of ejection (peak -dV/dt, ml/sec), and the volume ejected by the specified time (/-dV, ml). Multiple regression analysis of the data yielded a formula: \( \%P = 100 - 0.14(-dV/dt) - 0.07(\text{peak} -dV/dt) - 0.54(dV) \), in which \( \%P \) denotes P of an ejecting beat in percent of the isovolumic P at the same time and V. All those partial regression coefficients are statistically significant (\( P < 0.005 \)). The results indicate that the instantaneous ventricular pressure can be reduced from isovolumic pressure by 10-20% if the magnitude of those ejection parameters are near physiological maxima. *Circ Res* 46: 256-263, 1980

IN a naturally loaded systole, the left ventricle first develops pressure (P) and then reduces its volume (V) by ejecting blood. The instantaneous ventricular P-V data point moves counterclockwise in the P-V plane, drawing a P-V loop trajectory. The ventricle produces different P-V loops depending on the end-diastolic volume and ejection pressure even under a constant inotropic background (Fig. 1). We showed that, given an inotropic background, the P-V data points that exist on those P-V loops at a specified time in the cardiac cycle gather around a line (Suga et al., 1973; Suga and Sagawa, 1974). In Figure 1A, for example, three P-V loops are shown. The three larger points on them represent the P-V data at 100 msec from the onset of contraction in this example. Other smaller points are on other P-V loops which are not shown in the figure and also represent P-V data at the same point of time from the onset of contraction. We approximated the instantaneous P-V relationship at this specified time by drawing a linear regression line through those isochronous P-V points (Suga and Sagawa, 1974). The regression line rotates counterclockwise with time in systole until it attains a maximal slope at the end of systole. During diastole, the line rotates backward to the curve for the end-diastolic P-V relationship.

We recognized, however, that the isochronous P-V data points from different beats scattered, although within a relatively narrow zone, around the linear regression line (Suga et al., 1973; Suga and Sagawa, 1974). The scatter suggested to us that, in addition to the instantaneous volume, there are other determinants of instantaneous ventricular pressure. The purpose of the present study was to identify the secondary determinants. To this end, we developed a new experimental technique which we call "specification of time and volume." This experimental technique enabled us to make the instantaneous ventricular V at any specified time in systole to be precisely equal to a desired constant volume regardless of the preceding course of P and V within the same beat. This is illustrated schematically in Figure 1B. We correlated the variation in P at the specified time and V with the differences in ejection parameters which we suspected to be responsible for the variation of P. To confine the scope of investigation to mechanical factors within the same contraction cycle, we analyzed only the steady state variation of P in this report. We assumed that the influence of the long-term history of the preceding contractions was absent from the steady state contractions.
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FIGURE 1  A: P-V data points at a specified time in the cardiac cycle of many contractions of the left ventricle under a stable inotropic background. The larger circles belong to the three P-V loops drawn in the figure. The smaller circles belong to other loops not shown. The broken line is a linear regression line for those data points. B: P-V data points at a specified time in the cardiac cycle and also at a specified volume in the three contractions during a stable inotropic state. The dotted line was drawn to show that all the points have the same volume.

Methods

Surgical Preparation

A total of 12 isolated, cross-circulated hearts was prepared. A pair of dogs, comprising a larger dog (14 ~ 18 kg, mean = 16 kg) and a smaller dog (10 ~ 16 kg, mean = 13 kg), were anesthetized with sodium pentobarbital (30 mg/kg, iv). The hearts of the smaller dogs (left ventricular weight = 62 ~ 110 g, mean = 72 g) were isolated and supported by cross-circulation with the arterial blood from the larger dogs.

For details of the heart preparation, the reader is referred to Suga and Sagawa (1974). Briefly, the left atrium of the supported heart was opened, and all the chordae tendineae were cut. A purse-string suture was placed around the mitral annulus. A thin latex balloon with an unstressed volume of 70 ml was mounted on a metal connector (18 mm i.d., 22 mm o.d., 40 mm in length) and placed in the left ventricle. The connector was fixed at the mitral annulus, as shown in Figure 2A. A miniature pressure gauge (Konigsberg, P-21) was placed inside the apical end of the balloon. A small manifold tube was placed between the balloon and the endocardium to drain the thebesian blood by suction and thereby facilitate the fitting of the balloon on the endocardium (Suga and Sagawa, 1979).

The coronary circulation was maintained at a constant pressure between 75 ~ 150 mm Hg (mean = 105 mm Hg). The temperature of the heart was maintained at a constant level between 35 and 37°C. The heart beat with a regular sinus rhythm between 75 and 132 beats/min (mean = 112).

The balloon was connected to a recently developed volume servo pump (Suga and Sagawa, 1977) (Fig. 2A). The balloon and the pump were primed with tap water without leaving any air bubbles.

Time and Volume Specifications

We let the left ventricle take different courses of contraction from different end-diastolic volumes but contraction always went through a specific lumen volume at a specified time in the cardiac cycle. For this time and volume specification, we used a DC-restoring circuit as shown in Figure 2B. The volume command signal was generated by alternately charging and discharging a capacitor with variable time constants. This original signal then...
was floated from the ground potential by a capacitor, C. The output of this capacitor was grounded only for a short duration (10 msec) at a specified time in every cardiac cycle by a relay switch, RS. Thus, the output voltage of the circuit was forced to be zero at the specified time regardless of its preceding course and rate of change, whereas the shape of the signal remained the same as the original. This is shown on the oscilloscopic picture in Figure 2B. Stroke volume was changed by adjusting a potentiometer, R. A desired value for the specified volume was set by adding an appropriate DC voltage to the output of the DC-restoring circuit. This volume command signal was fed into the reference input of the servo pump system.

Experimental Protocol
We first selected the time in systole at which ventricular volume was to be specified at a desired value and the instantaneous P to be analyzed. The specified time covered a wide range from 48 to 200 msec from the onset of contraction, or 20 to 95% of the systolic duration. The ventricular volume at the specified time covered a normal range from 5 to 40 ml. Finally, stroke volume, onset of ejection, and velocity of ejection were changed widely in various combinations. The ranges of stroke volume and the peak velocity of ejection were 0-22 ml and 0-420 ml/sec, respectively.

Each experimental run at a given specific time and volume consisted of contractions with four to six different combinations of end-diastolic volume and ejection parameter values. In each heart, eight to 10 different experimental runs were performed.

Stability of Preparation
In any biological experiment, it is important to minimize the spontaneous (uncontrolled) fluctuation of the activity of a preparation. This was particularly so for the present study because of the relatively small magnitudes of the influence of various ejection parameters. Therefore, we frequently examined the stability of the ventricle in the same way as we did in a previous study (Suga et al., 1979). Briefly, we compared two steady state peak isovolumic pressures, one before and the other after a series of ejecting contractions involving several different combinations of end-diastolic volume and ejection parameter values. When the two steady state pressure values differed by more than 5 mm Hg, we considered the contractile state of the ventricle too unstable to accept the ejection data obtained between the two times. In a given ventricle, the stability test was performed as frequently as 10 times. Approximately 70% of the total experimental runs were stable according to this criterion and were subjected to analysis.

Data Collection
Data were collected in a steady state during which successive beats became stable, usually in about 2 minutes after each change in ejection parameters. Instantaneous P, specified V, ejection velocity (−dV/dt), ECG, and coronary perfusion pressure were recorded on a strip chart. The instantaneous P and V signals were also recorded on a storage oscilloscope to draw P-V loop trajectories. A set of superimposed P-V loops in each experimental run was photographed, as shown in Figure 3.

Data Analysis
We used multiple regression analysis to estimate the statistical relationships between the instantaneous P at the specified time and V and the three ejection parameters that we suspected to be the

Figure 3 Oscilloscopic picture of P-V trajectories (upper panel) and strip chart records of pressure, volume, and velocity of ejection (lower panel) in five steady state contractions in one experimental run. The numbers 1-5 in the two panels show corresponding contractions. The indicator points to the variation of the instantaneous ventricular pressure at the specified time and volume. The triangles in the lower panel indicate the specified time. The numerical values written in the pressure channel indicate the instantaneous pressures at the specified time; the values in the volume channel the specified volume and the volume ejected by the specified time (∫−dV); those in the velocity channel the instantaneous velocity of ejection at the specified time and the peak velocity of ejection.
secondary determinants of P. The statistical analysis is essentially the same as the standard method for multiple regression analysis described by Snedecor and Cochran (1969). To facilitate the analysis of a total of 510 sets of data from 111 experimental runs in 12 ventricles, we used a statistical program for digital computer (Nie et al., 1975). By the combinatorial solution procedure, we performed stepwise multiple regression analysis and examined a number of regression equations with all possible combinations (including the order of inclusion) of the ejection parameters. The computer program yielded statistical data including the standard error of estimation by each equation, multiple regression coefficients, their standard errors, standardized regression coefficients, the square of the multiple correlation coefficient (R²), and the incremental squared correlation coefficient (incremental R²) for each term in multiple regression.

**Results**

Figure 3 shows representative tracings from one experimental run. In this example, we specified ventricular volume to be 24 ml at a specified time (120 msec) while widely varying end-diastolic volume and ejection velocity. We found that the instantaneous P at the specified time and volume varied considerably, as shown at the tip of the indicator in the oscilloscope picture and also by the numerical values on the pressure tracings. The instantaneous P at the specified time and volume appeared to decrease with increases in (1) instantaneous -dV/dt, (2) peak -dV/dt before the specified time, and (3) volume ejected by the specified time (f -dV). Figure 4 is a plot of these individual relationships. Similar relationships were observed in other runs with various combinations of specified time and volume in this and all other ventricles studied. These relationships curves were relatively linear but slightly concave toward the abscissa. The slopes of these relationship curves were steeper when the pressure values were greater (P < 0.01) but had no significant correlations with the specified time and volume (P > 0.05). Therefore, P's at a specified time and volume were normalized with reference to the isovolumic pressure at the same specified time and volume. Percent P (%P) hereafter stands for this normalized P at a specified time and volume. The normalization enabled us to pool the data from all the different runs and hearts for the statistical analysis.

<table>
<thead>
<tr>
<th>TABLE 1 Correlation Coefficients between %P, -dV/dt, Peak -dV/dt, and ( f -dV )</th>
<th>%P</th>
<th>-dV/dt</th>
<th>Peak -dV/dt</th>
<th>( f -dV )</th>
</tr>
</thead>
<tbody>
<tr>
<td>%P</td>
<td>1</td>
<td>0.759</td>
<td>0.750</td>
<td>0.549</td>
</tr>
<tr>
<td>-dV/dt</td>
<td>1</td>
<td>0.852</td>
<td>0.515</td>
<td></td>
</tr>
<tr>
<td>Peak -dV/dt</td>
<td>1</td>
<td>0.582</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As a more direct measure of the contribution of these multiple ejection parameters to the variation of %P, we computed partial correlation coefficients \( r_{y1,23} \), \( r_{y2,13} \), and \( r_{y1,12} \), in which suffixes \( 1, 2, \) and \( 3 \) represent %P, -dV/dt, peak -dV/dt, and \( f -dV \), respectively. Coefficient \( r_{y1,23} \), for example, stands for the correlation between variables \( y \) and \( 1 \) while variables \( 2 \) and \( 3 \) are held constant. The values of the partial coefficients were \( r_{y1,23} = 0.364, r_{y2,13} = 0.186, \) and \( r_{y1,12} = 0.149, \) all being statistically significant (P < 0.01). The data indicate that -dV/dt is the most important among the secondary determinants of the instantaneous P at a given time and volume.

Table 2 lists the multiple regression equations (1-7) with all possible combinations of the three ejection parameters. Equations 1–3 include only one ejection parameter. Equations 3–6 include two ejection parameters. Equation 7 includes all the three ejection parameters. All the coefficients, except one for \( f -dV \) in Equation 6, are statistically significant (P < 0.01). The magnitude of the regression coefficients for the ejection parameters is influenced by the choice of measurement unit for each variable. To eliminate this influence, the multiple regression coefficients can be normalized by changing the values of each variable until its variance becomes unity. The regression coefficients calcu-
lated with these normalized variables are called standardized regression coefficients. The standardized multiple regression equation is:

\[
\%P = 100 - 0.46 \left( -\frac{dV}{dt} \right) - 0.28 \left( \text{peak } -\frac{dV}{dt} - 0.12 \left( \int -dV \right) \right). \tag{7}
\]

The standardized regression coefficients provide the only sensible way to compare the relative effects of those ejection parameters on \%P.

The square of the multiple correlation coefficient \(R^2\), listed in Table 2, indicates the fraction of variation of \%P attributable to the multiple independent variables examined. The results reveal that both \(-\frac{dV}{dt}\) and \(\text{peak } -\frac{dV}{dt}\) contributed much more to the determination of \%P than \(f -dV\) and that \(R^2\) becomes greatest with Equation 7. The \(F\)-test indicated that all those \(R^2\) values are statistically significant \((P < 0.005)\).

The standard errors of estimation of \%P from the magnitudes of the three ejection parameters. The rest of the variation, 37%, cannot be predicted by the changes in the three ejection parameters. The contributions of all three parameters to changes in \%P were found to be substantial, although the contribution of \(f -dV\) seemed relatively small. According to the value of \(R^2\) for Equation 7, we can predict 63% of the variation of \%P from the magnitudes of the three ejection parameters. The rest of the variation, 37%, cannot be predicted by the changes in the three ejection parameters and remains to be explained by other factors.

According to Equation 7, when \(-\frac{dV}{dt}\) increases, for example, by 10 ml/sec, peak \(-\frac{dV}{dt}\) increases by 10 ml/sec and \(f -dV\) increases by 1 ml, all simultaneously; we can expect a change in \%P which is the sum of the individual effects, i.e., 1.4% + 0.7% + 0.54% = 2.6%.

The mean values of the maximal limits of normal \(-\frac{dV}{dt}\), peak \(-\frac{dV}{dt}\), and \(f -dV\) in the present left ventricles were 69 (110) ml/sec, 88 (134) ml/sec, and 4.3 (7.9) ml, respectively. The values in the

<table>
<thead>
<tr>
<th>Equation no.</th>
<th>Regression equation</th>
<th>Standard error of multiple regression coefficients</th>
<th>Standard error of estimation of %P</th>
<th>Incremental (R^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(%P = 98 - 0.23 \left( -\frac{dV}{dt} \right))</td>
<td>0.0095 ( \text{dV/dt} ) 0.0067 ( \text{dV/dt} ) 0.17</td>
<td>11.09 0.584</td>
<td>0.584 0.584</td>
</tr>
<tr>
<td>2</td>
<td>(%P = 99 - 0.18 \left( \text{peak } -\frac{dV}{dt} \right))</td>
<td>0.016 0.012</td>
<td>10.53 0.626</td>
<td>0.584 0.042 0.834</td>
</tr>
<tr>
<td>3</td>
<td>(%P = 94 - 2.53 f -dV)</td>
<td>0.010 0.15</td>
<td>10.65 0.618</td>
<td>0.584 0.034</td>
</tr>
<tr>
<td>4</td>
<td>(%P = 98 - 0.15 \left( -\frac{dV}{dt} \right) - 0.09 \left( \text{peak } -\frac{dV}{dt} \right))</td>
<td>0.016 0.014 0.17</td>
<td>10.44 0.633</td>
<td>0.584 0.042 0.002</td>
</tr>
<tr>
<td>5</td>
<td>(%P = 100 - 0.19 \left( -\frac{dV}{dt} \right) - 0.98 f -dV)</td>
<td>0.010 0.009 0.18</td>
<td>11.18 0.579</td>
<td>0.577 0.002</td>
</tr>
<tr>
<td>6</td>
<td>(%P = 99 - 0.17 \left( \text{peak } -\frac{dV}{dt} \right) - 0.27 f -dV)</td>
<td>0.016 0.014 0.17</td>
<td>10.44 0.633</td>
<td>0.584 0.042 0.007</td>
</tr>
<tr>
<td>7</td>
<td>(%P = 100 - 0.14 \left( -\frac{dV}{dt} \right) - 0.54 f -dV)</td>
<td>0.016 0.014 0.17</td>
<td>10.44 0.633</td>
<td>0.584 0.042 0.007</td>
</tr>
</tbody>
</table>
limits. Our criterion of the normal ejection parameter values was that ventricular pressure during ejection was neither markedly dipping nor monotonic decreasing. Therefore, the maximal decrease in %P in normal contraction will probably be 1.4% × 6.9 + 0.7% × 8.8 + 0.54% × 4.3 = 18% on the average. In fact, the directly measured maximal decrease in %P in normal contractions in 12 hearts was 15% on the average with the 95% confidence limits of 3 and 27%.

Consequently, we conclude that the instantaneous ventricular pressure, which is predominantly determined by the simultaneous volume in the ventricle, will be decreased by 10–20% at maximum from the isovolumic pressure at the corresponding time and at the corresponding volume if the velocity of ejection and/or volume ejected by this time is near the physiological maximum.

Discussion

Our results have indicated that the instantaneous velocity of ejection (−dV/dt) and the history of ejection within the same beat (peak −dV/dt and ∫−dV) affect the instantaneous ventricular pressure, although it is determined predominantly by the ventricular lumen volume at that instant.

In some of the ejecting contractions studied, −dV/dt was made abnormally large to reveal clearly the effect of this factor on the pressure deficit. Consequently, the ventricular pressure declined monotonically throughout the ejection period. Such contractions are certainly unphysiological but should not be considered artifactual. Rather, they are highly informative, just as were the results of the quickly unloaded (to zero force!) shortening experiment by Brutsaert et al. (1971). That ventricular ejection rather than ventricular pressure was controlled by our pump does not make the result less acceptable than the experimental results of Brutsaert et al. (1972) and Meiss and Sonnenblick (1972), in which shortening velocity of muscle was controlled instead of its force. Our volume pump helped the ventricle eject blood to variable degrees, but this does not hamper us in learning the active property of myocardium, because the ventricle does not recognize whether it is the passive impedance of the aorta or the speed of our active pump displacement which is determining its lumen pressure.

Being an active system, the pump sometimes evacuated the ventricle faster than the ventricle could do under a constant pressure. The consequence was a declining ejection pressure. We emphasize that such a contraction should be as informative as the so-called physiological contractions with relatively flat pressure during ejection, just as shortening contractions with decreasing, constant, or increasing load all are equally informative for the study of muscular contractile machine.

In our previous studies (Suga et al., 1973; Suga and Sagawa, 1974), we observed that, under a stable inotropic background, instantaneous ventricular pressure P(t) was strongly correlated to the simultaneous volume V(t) almost independently of end-diastolic volume and afterload condition. Therefore, we proposed that the instantaneous P-V relationship could be approximated with reasonable accuracy by the following equation:

\[ P(t) = E(t) [V(t) - V_d] \]  

in which \( E(t) \) is the time-varying slope coefficient of the regression line of instantaneous pressure on instantaneous volume, and \( V_d \) is the volume axis intercept of the end-systolic P-V regression line. Examples of the instantaneous regression line at times \( t_1, t_2, \) and \( t_3 \) are drawn in panel A of Figure 5. By contrast, the present results indicate that some deficit of instantaneous ventricular pressure occurs in ejecting contractions when the instantaneous ejection velocity or extent of ejection by that instant of time is large. The pressure deficit is shown schematically in panel B of Figure 5. Again, the solid
slanted lines, transcribed from panel A, represent the instantaneous P-V relationship in isovolumic contractions. The shaded zone underneath each isovolumic P-V line indicates the zone in which the instantaneous P-V data point at the corresponding time can be found in ejecting contractions. The ejection phase of the P-V loop (heavy line) deviates from the hypothetical loop (broken line) inferred from the isovolumic P-V relationship lines according to our previous contention.

Equation 8 should now be revised by incorporating the multiple regression Equation 7 in Table 2. Namely,

\[
P(t) = E^*(t)[V(t) - V_d] \left[ 1 - 0.0014(-\frac{dV}{dt}) - 0.0054 \left( \int -\frac{dV}{dt} \right) \right]
\]

in which \(E^*(t)\) represents the specific \(E(t)\) for isovolumic contractions. The terms within the second brackets on the right side of the equation are those in Equation 7 divided by 100.

We can only speculate on the mechanisms underlying the observed pressure deficit in ejecting contractions. The \(-\frac{dV}{dt}\) term, which represents a viscous effect of the ventricular volume change, is most likely the manifestation of the inverse force-velocity relation of cardiac muscle (Sonnenblick, 1965; Braunwald et al., 1976). In this respect, we have already shown (Suga and Sagawa, 1972) that Equation 8 includes the force-velocity relation as it is obtained by the afterloaded isotonic contraction method (Abbott and Mommaerts, 1959; Covell et al., 1969). This force-velocity relation relates the graded afterloaded forces and the velocities of shortening against them at a constant muscle length. However, the time within the contraction cycle, at which the force-velocity relation is studied, is gradually delayed with the increases in the afterloaded isotonic force. Therefore, this force-velocity relation is different from the force-velocity relation obtained by the quick-release isotonic method in which the relation is studied at a constant time in cardiac contraction (Brady, 1965; Sonnenblick, 1967). Since the \(-\frac{dV}{dt}\) term was added to Equation 8 to recast Equation 9, the latter implies the force-velocity relation at a fixed time in systole as obtained by the quick-release method. In addition, the \((-\frac{dV}{dt})\)-dependent pressure deficit might be caused partly by mechanical viscosity against shear between ventricular muscle layers and deformation of ventricular shape.

The peak \(-\frac{dV}{dt}\) and \(\int -\frac{dV}{dt}\) terms are probably the manifestations of deactivation, or uncoupling, of the contractile machinery by shortening of cardiac muscle (Bodem and Sonnenblick, 1974; Brutsaert et al., 1972; Suga and Yamakoshi, 1977). The deactivation effect seems to disappear exponentially within a relatively short time (50–100 msec) in cardiac muscle (Bodem and Sonnenblick, 1974). In the present study, the specified time at which ventricular pressure was studied was relatively close to the peak velocity of ejection. This is probably the reason that we observed the deactivation effect in proportion to peak \(-\frac{dV}{dt}\) in the present study. An integral of instantaneous \(-\frac{dV}{dt}\) from the onset of contraction to the specified time is \(\int -\frac{dV}{dt}\). The higher the peak and other instantaneous velocities before the specified time, the greater \(\int -\frac{dV}{dt}\). This seems to explain the apparently high correlation between the pressure deficit and \(\int -\frac{dV}{dt}\) listed in Table 1.

An implication of Equation 9 in relation to \(E(t)\), i.e., instantaneous pressure-volume ratio, would be that \(E(t)\) for ejecting contractions is smaller than \(E^*(t)\) for isovolumic contractions by the amount within the second brackets on the right side of Equation 9. This dependence of \(E(t)\) on ejection conditions seems to explain the slight difference between \(E(t)\)'s of naturally loaded contractions and artificially loaded contractions (Suga and Sagawa, 1974). Ejection velocities in the latter were lower than the former in general. This probably explains why those \(E(t)\) curves obtained from the artificially loaded contractions were closer in shape to the isovolumic \(E^*(t)\) curve, and why \(E(t)\) curves from naturally loaded contractions had somewhat smaller values during ejection than \(E(t)\) from artificially loaded ejecting contractions.

Several studies (Kaufmann et al., 1971; Jewell and Rovell, 1973; Parmley and Chuck, 1973; Donald et al., 1976; Lakatta and Jewell, 1977; Brutsaert and Paulus, 1977; Suga and Sagawa, 1978) indicated complex effects of previous contractile events on the contractile state of myocardium. Thus, Jewell (1977), among others, proposed that loading conditions, particularly muscle length, alter the internal state of the contractile machine. If we accept this thesis, we would have to conclude that the internal state of myocardium in our experiment changed every time we altered end-diastolic volume and the ejection parameters. Hence, we can only state that we attempted to maintain the inotropic state of the preparation by holding extracardiac factors (such as coronary perfusion pressure, temperature, blood gas, and the general state of the support dogs) as constant as possible, and we used only those data which satisfied our stability criteria described in Methods. During the experimental runs with altered ejection parameters, we could not prevent possible changes in the contractile state due to the internal effect of loading conditions, nor can we estimate the magnitude of the contribution of this mechanism to the observed pressure deficit.

The P-V relationship of the left ventricle has been simulated by a time-varying elastance or capacitance model as shown in the bottom of panel A of Figure 5. The behavior of either model is described by Equation 8 (with the addition of \(V_d\)). However, the present study indicated that the single-element model is not adequate to describe the details of the instantaneous P-V relationship in
contracts with large velocity and extent of ejection. A new model should at least look like either the mechanical or electrical analog shown at the bottom of panel B of Figure 5. With the addition of a resistance (R) and a second elastance (E₂) or capacitance (1/E₂), the model incorporates those terms in the second brackets of Equation 9. From the coefficients in Equation 9, the tentative values of the model elements can be estimated as follows: R = 0.14 mm Hg/(ml/sec), E₂ = 1.4 mm Hg/ml, and E*(t) changes with time from an end-diastolic value of nearly 0 to an end-systolic value of 5–10 mm Hg/ml.

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