Passive Properties of Canine Left Ventricle: Diastolic Stiffness and Restoring Forces


Left ventricular (LV) diastolic pressure-volume (P-V) relations arise from a complex interplay of active decay of force (i.e., relaxation), passive elastic myocardial properties, and time-varying inflow across the mitral orifice. This study was designed to quantify the passive properties of the intact ventricle and the effects of elastic recoil by separating filling from relaxation with a method of LV volume clamping with a remote-controlled mitral valve. Eleven open-chest fentanyl-anesthetized dogs were instrumented with aortic and mitral flow probes, LV and left atrium micromanometers, and a remote-controlled mitral valve. We prevented complete (end-systolic volume clamping) or partial filling at different times in diastole. The ventricle thus relaxed completely at different volumes, and we generated P-V coordinates for the passive ventricle that included negative, as well as positive, values of pressure. We then estimated ventricular volumes from ventricular weight in eight dogs, using regression equations based on data in the literature, to determine the equilibrium volume (V₀), that is, volume at zero transmural pressure, in the working ventricle. We abandoned the traditional exponential approach and characterized the P-V relation with a logarithmic approach that included maximum LV volume (Vₘ), minimum volume (V₀), and stiffness parameters (Sp and Sn) for the positive (p) and negative (n) phases: Pₚ = -Sp ln[(Vₘ - V)/(Vₚ - V₀)] and Pₙ = Sn ln[(V - V₀)/(Vₙ - V₀)]. With this formulation, the chamber compliance, dP/dV, is normalized by the LV operating volume, and Sp and Sn are size-independent chamber stiffness parameters with the units of stress. In eight ventricles with LV weight = 131 ± 20 g, Vₘ = 116 ± 18 ml, V₀ = 37 ± 6 ml, and Vₙ = 13 ± 2 ml, stiffness Sp = 14.6 mm Hg and Sn = 5.1 mm Hg were determined from the slopes of the log-linearized equations. Also, the duration of LV relaxation is increased by the process of ventricular filling (161 ± 31 msec, filling versus 108 ± 36 msec, nonfilling, measured from dP/dtᵩ₀, p<0.0001). We conclude that volume clamping is a useful method of studying restoring forces and that the logarithmic approach is conceptually and quantitatively useful in characterizing the passive properties of the intact ventricle. (Circulation Research 1988;62:1210-1222)
method of volume clamping in the intact left ventricle with a remote-controlled mitral valve (RCMV) either to prevent filling completely or to stop it at any time in diastole.\textsuperscript{10} We are thus able to separate the effects of filling from relaxation and to plot the diastolic P-V relations in both the positive and negative phases. Also, these relations were quantified with a logarithmic approach, which is in contrast to the usual exponential model.

Materials and Methods

Theory

Equilibrium volume. The concept of equilibrium volume is critically important to the approach of this paper and must be clarified here. We define the equilibrium volume as the volume of the resting ventricle at zero transmural pressure. Discussed first by Brecher\textsuperscript{7} and investigated further by Tyberg et al,\textsuperscript{9} this concept provides the mechanical model that forms the physiological basis of diastolic suction: ventricular contraction to an end-systolic volume below the equilibrium volume stores energy in the ventricular walls; this stored energy provides an internal restoring force that facilitates filling at low pressures.

This concept can be clarified by considering a chamber that has actively contracted to below its equilibrium volume and that has been clamped at that volume. During relaxation active wall stresses decrease, and when the internal elastic forces tending to restore the chamber to its initial configuration are greater than the decaying active wall forces, there must be a concurrent decrease of chamber pressure to maintain a balance of forces. Thus, the external pressure becomes greater than the internal pressure; that is, the transmural pressure becomes negative. When the external pressure is atmospheric, as in the open-chest preparation, the pressure in a chamber clamped below its equilibrium volume will be negative (Figure 1). Diastolic suction is a concept that has been supported by many experiments.\textsuperscript{3-7,9,11} We therefore conclude that a complete description of the passive diastolic properties of the left ventricle must include its behavior both above and below its equilibrium volume.

At this point, it will be useful to clarify some terminology and concepts. We define relaxation as the active decay of force due to intrinsic myocardial processes, and we distinguish it from pressure decline because the latter is determined by both active force decay and passive elastic forces. On the other hand, during isovolumic "relaxation," there is no relengthening, hence no change in elastic forces, and it is appropriate to use a time constant of relaxation (see below) determined from the decline of left ventricular pressure. Based on these concepts, we assume that the fall in pressure after volume clamping below the equilibrium volume is due to elastic recoil and relaxation, whereas a fall in pressure due to volume clamping above the equilibrium volume can only be due to relaxation.

Also, note that we have deliberately avoided use of the term "unstressed volume" for equilibrium volume because of evidence that there may be residual stresses in the relaxed myocardium at zero transmural pressure.\textsuperscript{12} In the absence of a change in material properties (e.g., due to edema or incomplete relaxation) equilibrium volume is assumed to be constant during an experiment. Note also that this concept of diastolic suction can be based on a negative transmural pressure due to sarcomere shortening as contrasted with a negative pressure due to a volume withdrawal that leads only to shape changes without sarcomere shortening.

P-V relations above the equilibrium volume. The passive diastolic P-V relation of the left ventricle has traditionally been described by an exponential of which the most general form is

\[ P = \frac{b}{a} \left[ \exp \left( \frac{a(V - V_d)}{b} \right) - 1 \right] \]  

(1)

where \( a \) and \( b \) are material properties, \( -b/a \) is the pressure asymptote, and \( V_d \) is the equilibrium volume.

Chamber stiffness (dP/dV) is derived from Equation 1 by differentiation:

\[ \frac{dP}{dV} = \frac{aP + b}{V} \]  

(2)

This is a convenient approach because the chamber properties can be determined from a linear regression analysis of dP/dV versus P. Its major shortcoming is due to the fact that chamber stiffness is a function of volume and is thus not a material property that can readily be used as an index of ventricular compliance.\textsuperscript{13} In addition, Equation 1 can be criticized because it provides no limit on the maximum ventricular volume, that is, the volume at which the myocardial tissue will yield and permanently change its properties. We overcome both of these problems by following the lead of others and by characterizing the positive portion of the P-V relation with a logarithmic approach:\textsuperscript{14-16}

\[ P_p = -S_p \ln \left( \frac{V_m - V}{V_m - V_0} \right) \]  

(3)

where \( V_m \) is the maximum attainable volume of the ventricle, that is, the volume asymptote, \( S_p \), is a material property (see below), and the subscript (\( p \)) refers to

![Figure 1. Representative plot of a measured diastolic pressure-volume (P-V) loop in a normally filling ventricle, superimposed on a passive P-V relation, \( V_d \), volume at zero transmural pressure; \( V_m \), minimum volume, and \( V_m \), maximum volume. Arrow, trajectory of a completely isovolumic (i.e., nonfilling) relaxation to a negative pressure.](image-url)
the positive portion of the P-V relation. The logarithmic approach to the P-V relation is the equivalent of an exponential V-P relation and is heuristically desirable because it scales the passive ventricle to function within the natural limits of its rest and yield volumes. Differentiating:

\[ \frac{dP_n}{dV} = \frac{S_n}{(V-V_d)} \quad \text{and} \quad (4) \]
\[ S_n = \frac{(dP_r/dV)}{(V-V_d)} \quad (8) \]

Thus, \( S_n \) is seen to be a constant defined as the chamber stiffness normalized by scaling the instantaneous volume to the operating range of the ventricle. This contrasts to Mirsky's\(^{13}\) approach in which \( dP/dV \) is normalized by the instantaneous volume (i.e., \( (dP/dV)/V \)). Because \( S_n \) is measured in units of pressure, it is reasonable to conclude that it is related to the wall stress modified by a geometric factor.

**P-V relations below the equilibrium volume.** A similar approach is followed for the negative portion of the P-V relation:

\[ P_n = S_n \ln\left(\frac{(V-V_d)}{(V_0-V_d)}\right) \quad (6) \]
\[ \frac{dP_n}{dV} = S_n/(V-V_d) \quad \text{and} \quad (7) \]
\[ S_n = (dP_n/dV)/(V-V_d) \quad (8) \]

where the subscript \( n \) denotes the negative portion of the P-V relation. Here again, \( S_n \) is seen to be a constant with the units of stress and is defined by the local stiffness normalized by the operating range of the ventricle, which is between the equilibrium volume and a nonzero minimum volume \( V_d \).

**Experimental Methods**

**Volume clamping.** Ventricular diastolic volume was controlled with an RCMV shown schematically in Figure 2 and described in detail elsewhere.\(^{10}\) Briefly, a modified ball-in-cage prosthetic valve was implanted in series with an electromagnetic flow probe in the mitral anulus. A controller was triggered by a suitable physiological signal, and after a programmed delay, it rapidly closed the valve. The valve can be closed during systole (end-systolic volume clamping) or at any other time after filling has started (Figure 3).

**Animal preparation.** Eleven adult mongrel dogs (26.7 ± 1.1 kg) were premedicated with atropine (0.01 \( \mu \)g/kg i.v.). Anesthesia was induced with sodium pentothal (15 mg/kg i.v.) followed by intubation and artificial ventilation at 100% \( O_2 \) with a pressure-controlled respirator. Fentanyl (5–10 \( \mu \)g/kg) was administered every 30 minutes and supplemented with vecuronium (0.1 mg/kg). After a midline sternotomy and left thoracotomy at the fourth intercostal space, the heart was supported in a pericardial cradle. Pacing leads were sutured to the right atrium, and the sinoatrial node was crushed either to achieve sinus arrest or to lower the heart rate to approximately 100 beats/min or less. Pacing was performed when necessary.

During standard cardiopulmonary bypass, the left atrium was opened, the mitral leaflets removed, and the RCMV was implanted with the control cable exiting through the ventricular apex. Millar micromanometers (Millar Instruments, Houston, Texas) were placed in the left ventricle and left atrium through the apex and pulmonary vein. The flow probe cable was brought out of the atrial appendage; the atriotomy was repaired; and the dog was weaned from bypass. A noncannulating electromagnetic flow probe was placed around the cleaned ascending aorta.

Flows were measured with a two-channel flowmeter (Carolina Medical Electronics, King, North Carolina). Pressures were calibrated for equal gain and common zero. Pressures, flows, ECG, dP/dt, and left ventricular diastolic pressure were recorded at high gain and high speed (100 mm/sec) on a photographic recorder (DR-12, Electronics for Medicine, White Plains, New York) and at low speed on a pen recorder (Model 2600, Gould, Cleveland, Ohio). Arterial pH, \( P_{CO_2} \), and \( P_{O_2} \) were measured periodically and maintained normal by adjusting ventilatory volume or frequency and/or by administering sodium bicarbonate intravenously. If necessary, phentylephrine was infused to maintain arterial blood pressure, and lidocaine was given as either a bolus or infusion to control arrhythmias. Contractile function was controlled with infusions of dobutamine. Anesthetic level was constantly monitored by the absence of a corneal reflex and of a pain response, indicated by a sudden increase in heart rate or pressure. Data were recorded only when the dogs were in a stable steady state with the respirator turned off. All data were recorded with the chest and pericardium open so that the measured pressures were identical to the transmural pressures.

**Protocols.** A typical run was as follows: 10 control beats, a mitral valve occlusion during systole, 10 beats (to return to control conditions), a mitral valve occlusion after a small amount of filling, 10 beats, a mitral valve occlusion slightly later in time, etc. Each occlusion was held for only one beat so that with a typical seven occlusions per run at a heart rate of 100 beats/min, less than 50 seconds of apnea was required per run. To determine whether the inotropic state influenced the...
diastolic P-V relations, we increased the rate of dobutamine infusion (maximum 11 μg/kg/min), and when a new steady state was achieved, another run was recorded. At the same level of inotropic state, preload was increased by infusing volume from the oxygenator, and the above procedure was repeated.

Great care was taken to accurately measure left ventricular diastolic pressure. The side lumen of the micromanometer was connected to a Statham gauge (Los Angeles, California) positioned at the midventricular level, and the baseline was checked frequently. At the end of the experiment, the heart was arrested in diastole with potassium chloride, vented to the atmosphere, and calibrations and baselines were checked. The left ventricles, including the septum, were weighed in the last eight dogs. Because a knowledge of left ventricular weight is necessary for much of the analysis in this paper, except where otherwise noted, results will be presented for the last eight dogs only.

Data analysis. The oscillographic records were digitized with a sonic digitizer (Model GP-7, Science Accessories, Southport, Connecticut) coupled to an IBM-PC. Changes in volume were calculated from the integrals of aortic and mitral flow. In essence, we assumed that the end-systolic volume remained constant throughout each run, and subsequent volumes were determined from inflow and outflow.

It should be noted that we did not measure absolute ventricular volumes so that all volume measurements are referenced to an unknown end-systolic volume that is constant for each run. It was thus important that there should be no change in hemodynamic state during a run. This was tested by examining the control beats before each occlusion and accepting only those runs in which there was no change in the control pressures and flows. For the remainder of this paper, when we refer to a volume as a “relative” volume, it should be understood to be relative to the end-systolic volume for the run, and we define it with an asterisk. For example, \( V_{0*} \) is the difference between the equilibrium and the end-systolic volumes. Furthermore, since filling when the ventricle is below the equilibrium volume occurs under conditions of elastic recoil, and since \( V_{0*} = V_0 - V_s \) (where \( V_s \) is end-systolic volume), it can be characterized as a “suction volume.”

The inability to measure volume led to an inability to control it; we could only estimate volume changes from changes in end-diastolic pressure. This has, of course, increased the variance in the data. To minimize its impact, we describe an “average” dog based on pooled data regardless of which dog the data came from and without weighting any dog by number of runs. This approach implies that our samples are from the same population.

The time constant (T) of left ventricular relaxation after volume clamping at end-systole was calculated as described previously from the relation

\[
P = (P_0 - P_s) \exp(-t/T) + P_s
\]

where \( P_0 \) is the pressure at the onset of isovolumic relaxation (taken at \( dP/dt_{max} \)), and \( P_s \) is the pressure asymptote, determined experimentally (Figure 3). For comparison, T was also calculated from the isovolumic pressure points, by using zero pressure as the baseline and by assuming a zero asymptote.

Determination of equilibrium volume and P-V relations. Figure 4, Panel A shows a typical mitral flow waveform, with the numbers (1–6) indicating increasing times during diastole when the mitral valve was occluded. In particular, 1 represents a systolic occlusion, and 7 is the last point preceding the onset of ventricular contraction (i.e., the end-diastolic point), which was determined from the rapid upstroke of \( dP/dt \). Panel B shows the left ventricular volume, relative to end-systole, at each of these times. The high-gain left ventricular pressure traces for each of these occlusions is shown in Panel C. The solid trace is the control with 7 being the control left ventricular end-systolic pressure. The broken traces indicate the time variation of pressure after the mitral valve occlusion. The numbered points in Panel C indicate the minimum pressure reached during the occlusion.

Points 1–4 in Panel C are evidence of elastic recoil and diastolic suction. They occur at volumes below the equilibrium volume, hence the fall to a negative pressure (see Figure 1); and they mark the end of
relaxation because volume is constant and because pressure has stopped falling. Conversely, points 5 and 6 are greater than the equilibrium volume so that volume clamping at those times did not lead to negative pressure. Since pressure continued to fall to point 5, we conclude that relaxation had not yet ended at the time of occlusion; and by the same reasoning, point 6 occurred after the cessation of relaxation. Finally, Panel D shows the result of removing time as a parameter and plotting the complete diastolic P-V relation for this run. (Note again that all volumes are relative to the end-systolic volume.) It is clear that the equilibrium volume can be determined with relative ease from the shape of the curve.

Results

Equilibrium Volume

Table 1 summarizes the control hemodynamic conditions during a total of 51 runs for the eight dogs in which we measured left ventricular weight. Except for heart rate, which we tried to maintain at approximately 100 beats/min, but was higher during dobutamine infusions, the standard deviations are large enough to indicate that a wide range of hemodynamic conditions was covered in the course of the study. Table 1 also includes hemodynamic data for one typical run in each dog at a relatively low inotropic state, and it includes one run at a relatively high inotropic state. These conditions were determined by the infusion rates of dobutamine and verified by dP/dt and peak left ventricular pressure. It should be noted that the hemodynamic profile (mean, as well as high and low inotropic states) for the three dogs in which left ventricular weights were not measured, does not differ from the values of Table 1.

In 72 of 75 runs in the 11 dogs, the equilibrium volume was greater than the end-systolic volume, indicating that diastolic suction was the norm in this study. The remaining three runs were under conditions of low contractility and large volumes. Figure 5 shows the diastolic P-V relations for the eight dogs, determined by the method of Figure 4. Because the equilibrium volume should be invariant in the course of a study, the different runs were superimposed with a common equilibrium volume, and all volumes are relative to the end-systolic volume. The measured value of relative equilibrium volume for the subgroup of eight dogs is presented in Table 2.

To investigate the dependence of suction volume on inotropic state and heart rate, we examined 24 runs in eight dogs in which there were consecutive runs at high and low inotropic states with no change in volume. We could thus look at changes in suction volumes due to changes in heart rate and inotropic state. Relative equi-
TABLE 1. Hemodynamic Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low</th>
<th>Inotropic state</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>106 ± 17</td>
<td>99 ± 16</td>
<td>NA</td>
</tr>
<tr>
<td>PLVP (mm Hg)</td>
<td>118 ± 22</td>
<td>105 ± 12</td>
<td>127 ± 24</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>4.7 ± 2.4</td>
<td>3.7 ± 2.4</td>
<td>4.8 ± 3.1</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>24.2 ± 8.5</td>
<td>21.2 ± 3.8</td>
<td>NA</td>
</tr>
<tr>
<td>dP/dt_{max} (mm Hg/sec)</td>
<td>2,670 ± 950</td>
<td>2,080 ± 620</td>
<td>3,200 ± 940</td>
</tr>
<tr>
<td>dP/dt_{min} (mm Hg/sec)</td>
<td>1,850 ± 580</td>
<td>1,490 ± 290</td>
<td>2,040 ± 540</td>
</tr>
<tr>
<td>P_{x} (mm Hg)</td>
<td>-5.1 ± 4.1</td>
<td>-5.3 ± 4.4</td>
<td>-6.7 ± 4.6</td>
</tr>
<tr>
<td>T_{x} (msec)</td>
<td>29.6 ± 10.9</td>
<td>37.8 ± 8.4</td>
<td>26.9 ± 3.8</td>
</tr>
<tr>
<td>T_{0} (msec)</td>
<td>32.0 ± 12.0</td>
<td>34.5 ± 10.4</td>
<td>24.2 ± 4.3</td>
</tr>
<tr>
<td>n</td>
<td>(51)</td>
<td>(8)</td>
<td>(8)</td>
</tr>
</tbody>
</table>

Column 1: Mean ± SD of all 51 runs from eight dogs. Columns 2 and 3: mean of one run from each dog at relatively low and high inotropic states.

HR, heart rate; PLVP, LV pressure maximum; LVEDP, end-diastolic LV pressure; SV, stroke volume; dP/dt, first derivative of LV pressure; P_{x}, minimum LV pressure obtained in nonfilling beats (end-systolic clamp); T_{x}, time constant calculated from Equation 9 with experimentally determined P_{x}; T_{0}, time constant calculated from Equation 9 with P_{x} = 0; NA, not applicable; n, number of runs.

* Test between low and high inotropic states.

Equilibrium volume did not correlate with dP/dt_{max}, and it correlated only weakly with heart rate (r = 0.60, n = 12, p < 0.05).

Estimation of Absolute Volumes

The inability to measure absolute volume is a major shortcoming of this study; without such information, Equations 3–8 cannot be solved. To overcome this constraint, we used the following approaches to estimate V_{0}, V_{m}, and V_{d}. We reasoned that the functional operating volume of the ventricle should be related to its mass. This is consistent with the concept of scaling that led us to propose Equations 3 and 6. Using published data from studies that included left ventricular weight (LVW) and absolute volumes for 35 dogs (LVW = 90 ± 27 g, range 41–147 g), we performed a linear regression through the origin to determine V_{0} = 0.29 LVW (r = 0.955, n = 35) and V_{m} = 0.89 LVW (r = 0.981, n = 23). When the regression was not constrained to go through the origin, the intercepts were not significantly different from zero, and the slopes did not differ from those of the previous method; hence, we conclude that the approach is both conceptually and quantitatively correct.

To solve Equations 4 and 5, we assumed that V_{d} = 10 ml/100 g of left ventricle. This is a reasonable assumption since V_{d} is the smallest volume that can be achieved in an unloaded contraction. The measured left ventricular weights and the volumes calculated from the regressions for the eight dogs of this study are presented in Table 2. These values were used to determine the stiffness parameters. The value of equilibrium volume was also used to estimate the absolute value of the end-diastolic volumes in each run (point 7, Figure 4). Stroke volume (SV) was related to end-diastolic volume by SV = 0.47V_{m} − 1.6 (r = 0.51, p < 0.001, n = 51).

Estimation of the Stiffness Constants, S_{p} and S_{n}

All the data points above the equilibrium volume in each dog were pooled and used with the estimated absolute volumes (Table 2) in a regression analysis of
Inotropic State? Are the Stiffness Constants Influenced by
due to the influence of inotropic state on diastolic suc-
be due to the more dynamic nature of the negative
phase of the P-V relation as compared to the more
passive positive phase. The large variation may also be
from all the runs to give \( S_p = 14.6 \text{ mm Hg} \) (\( r = 0.917, n = 8 \)) is due partly to the
by pooling all the points from each dog to give \( S_n = 5.1 \text{ mm Hg} \) (\( r = 0.632, n = 8 \)).
Analysis of covariance revealed no significant difference among the values of \( S_p \). An ensemble mean \( S_p \) was also calculated from Equation 6 using the data in
we calculated \( S_p \) from Equation 6 using the data in
the log-linearized equation. With this approach, \( S_p \) is
the slope of the regression line. The results for each
dog are shown in Table 2. An analysis of covariance revealed no significant difference among the values of \( S_p \). An ensemble mean \( S_p \) was also calculated from a single regression analysis by pooling all the data points from all the runs to give \( S_p = 14.6 \text{ mm Hg} \) (\( r = 0.917, n = 318 \)). This value is identical to the mean value of
Table 2 (\( S_p = 14.5 \pm 1.5 \text{ mm Hg}, n = 8 \)) and reflects the usefulness of the volume scaling approach and reflects the low variance in the data (coefficient of variation = 10%).

Again, assuming that all the P-V coordinates below the equilibrium volume could be pooled in each dog, we calculated \( S_p \) from Equation 6 using the data in
Table 2. The results for each dog are also shown in Table 2. There were no significant differences among the values of \( S_p \). The ensemble mean \( S_p \) was calculated by pooling all the points from each dog to give \( S_p = 5.1 \text{ mm Hg} \) (\( r = 0.632, n = 175 \)). The large difference between the ensemble mean \( S_p \) and the mean from Table 2 (\( S_p = 8.7 \pm 7.9 \text{ mm Hg}, n = 8 \)) is due partly to the variance within and between dogs, which in turn may be due to the more dynamic nature of the negative phase of the P-V relation as compared to the more passive positive phase. The large variation may also be due to the influence of inotropic state on diastolic suction in contrast to the known lack of such influence on the positive portion of the P-V relation (see below).

Are the Stiffness Constants Influenced by Inotropic State?
To test the hypothesis that the negative portion of the diastolic P-V relation was influenced by inotropic state, we selected one run at high and one run at low inotropic states from each of seven dogs (Table 3). (The other dog with known left ventricular weights did not have enough data points in any one run to make a meaningful comparison.) Analysis of covariance was used to compare the slopes and intercepts of the log-linearized equations at high and low inotropic states in each dog. Six of the seven dogs showed significant differences in \( S_p \) due to inotropic state; the pooled values at each inotropic state for all seven dogs were significantly different (Table 3). A simple correlation of \( S_p \) and \( \Delta \text{dP/dt} \text{max} \) reached the 0.05 level with \( r = 0.548 \). It is clear from both Tables 2 and 3 and from the data points in the negative phase (Figure 5) that there is considerable scatter in the P-V coordinates. As was expected, \( S_p \) was not influenced by inotropic state (Table 3).

Effect of Ventricular Weight
\( S_p \) did not correlate with left ventricular weight (\( r = 0.015 \)). Figure 6 illustrates the entire diastolic P-V relation in two dogs of different left ventricular weights. In particular, note that although the left ventricular weights and functional operating ranges of these two ventricles differ widely and that the chamber compliances, \( \Delta \text{dP/dV} \), are different at either equal volumes or pressures, the stiffness parameters, \( S_p \), are equal to each other (Table 2). There was a strong negative correlation between the value of \( \Delta \text{dP/dV} \) at equilibrium volume and left ventricular weight (\( r = -0.856, p < 0.01, n = 8 \)). The widely scattered points in the negative pressure range preclude drawing similar conclusions for that sector.

Effect of Filling on the Duration of Relaxation
To evaluate the effect of ventricular filling on the duration of relaxation, we reasoned as follows: if a mitral valve occlusion results in a fall in ventricular pressure at a time when ventricular volume is greater than the equilibrium volume, then relaxation is not yet completed because the fall in pressure cannot be due to elastic recoil (e.g., point 5, Figure 4). If in the same

### Table 2. Diastolic Properties of Left Ventricle

<table>
<thead>
<tr>
<th>Dog</th>
<th>BW (kg)</th>
<th>LVW (g)</th>
<th>V0* (ml)</th>
<th>Vo (ml)</th>
<th>Vm (ml)</th>
<th>Vd (ml)</th>
<th>Vm−Vo (ml)</th>
<th>Sn (mm Hg)</th>
<th>Sg (mm Hg/ml)</th>
<th>dP/dV (mm Hg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>27.2</td>
<td>157</td>
<td>13.3±7.5</td>
<td>8.5</td>
<td>139.7</td>
<td>15.7</td>
<td>95.0</td>
<td>13.3</td>
<td>4.6</td>
<td>0.140</td>
</tr>
<tr>
<td>5</td>
<td>25.6</td>
<td>124</td>
<td>12.7±1.2</td>
<td>10.2</td>
<td>35.3</td>
<td>110.4</td>
<td>12.4</td>
<td>75.1</td>
<td>22.9</td>
<td>0.169</td>
</tr>
<tr>
<td>6</td>
<td>25.0</td>
<td>93</td>
<td>3.72</td>
<td>14.2±1.8</td>
<td>15.3</td>
<td>26.5</td>
<td>82.8</td>
<td>9.3</td>
<td>56.3</td>
<td>0.250</td>
</tr>
<tr>
<td>7</td>
<td>25.3</td>
<td>126</td>
<td>4.98</td>
<td>8.9±2.1</td>
<td>7.1</td>
<td>35.9</td>
<td>112.1</td>
<td>12.6</td>
<td>76.2</td>
<td>0.190</td>
</tr>
<tr>
<td>8</td>
<td>25.8</td>
<td>145</td>
<td>5.62</td>
<td>14.0±2.8</td>
<td>9.7</td>
<td>41.3</td>
<td>129.1</td>
<td>14.5</td>
<td>87.8</td>
<td>0.186</td>
</tr>
<tr>
<td>9</td>
<td>27.3</td>
<td>133</td>
<td>4.87</td>
<td>13.9±2.8</td>
<td>10.5</td>
<td>37.8</td>
<td>118.4</td>
<td>13.3</td>
<td>80.6</td>
<td>0.245</td>
</tr>
<tr>
<td>10</td>
<td>26.7</td>
<td>120</td>
<td>4.49</td>
<td>1.4±4.8</td>
<td>1.2</td>
<td>34.1</td>
<td>108.6</td>
<td>12.0</td>
<td>72.7</td>
<td>0.221</td>
</tr>
<tr>
<td>11</td>
<td>27.8</td>
<td>146</td>
<td>5.25</td>
<td>7.4±2.9</td>
<td>5.1</td>
<td>41.6</td>
<td>129.9</td>
<td>14.6</td>
<td>88.3</td>
<td>0.231</td>
</tr>
<tr>
<td>Mean</td>
<td>26.3</td>
<td>131</td>
<td>4.94</td>
<td>9.2</td>
<td>8.5</td>
<td>37.2</td>
<td>116.2</td>
<td>13.1</td>
<td>79.0</td>
<td>0.188</td>
</tr>
</tbody>
</table>

BW, body weight; LVW, LV weight; \( V_0^* \), equilibrium volume relative to end-systolic volume (mean ± SD for all runs); \( V_o \), absolute value of equilibrium volume determined from LVW (see text); \( V_m \), maximal volume; \( V_d \), minimal volume; \( V_m−V_o \), operating range in positive phase; \( V_o−V_d \), operating range in negative phase; \( S_p \), normalized coefficient of stiffness for positive phase; \( S_g \), normalized coefficient of stiffness for negative phase (pooled value for each dog); \( dP/dV_{(0)} \), \( dP/dV \) at \( V_0 \) determined for positive pressure-volume relation; \( dP/dV_{(0)} \), \( dP/dV \) at \( V_0 \) determined from negative pressure-volume relation at low inotropic state (see text and Table 3).
TABLE 3. Effect of Inotropic State on $S_n$ and $S_p$

<table>
<thead>
<tr>
<th>Dog number</th>
<th>Inotropic state</th>
<th>$dP/dt_{max}$ (mm Hg/sec)</th>
<th>$S_n$ (mm Hg)</th>
<th>n</th>
<th>p</th>
<th>$S_p$ (mm Hg)</th>
<th>n</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>L</td>
<td>1,760</td>
<td>4.0</td>
<td>(6)</td>
<td>&lt;0.001</td>
<td>13.2</td>
<td>(7)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>2,200</td>
<td>4.9</td>
<td>(6)</td>
<td></td>
<td>14.2</td>
<td>(5)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>L</td>
<td>2,420</td>
<td>6.3</td>
<td>(7)</td>
<td>&lt;0.05</td>
<td>12.1</td>
<td>(10)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>2,860</td>
<td>9.5</td>
<td>(8)</td>
<td></td>
<td>11.0</td>
<td>(8)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>L</td>
<td>1,650</td>
<td>3.7</td>
<td>(7)</td>
<td>NS</td>
<td>13.9</td>
<td>(6)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>1,980</td>
<td>3.6</td>
<td>(6)</td>
<td></td>
<td>14.1</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>L</td>
<td>1,540</td>
<td>4.2</td>
<td>(10)</td>
<td>&lt;0.001</td>
<td>14.5</td>
<td>(11)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>3,080</td>
<td>9.6</td>
<td>(5)</td>
<td></td>
<td>14.1</td>
<td>(12)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>L</td>
<td>2,970</td>
<td>7.0</td>
<td>(4)</td>
<td>&lt;0.002</td>
<td>16.8</td>
<td>(8)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>3,740</td>
<td>14.9</td>
<td>(5)</td>
<td></td>
<td>16.4</td>
<td>(9)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>L</td>
<td>1,870</td>
<td>1.8</td>
<td>(6)</td>
<td></td>
<td>13.1</td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td></td>
<td>13.3</td>
<td>(11)</td>
<td>NS</td>
</tr>
<tr>
<td>10</td>
<td>L</td>
<td>1,760</td>
<td>7.9</td>
<td>(4)</td>
<td>&lt;0.025</td>
<td>14.0</td>
<td>(6)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>2,420</td>
<td>24.6</td>
<td>(4)</td>
<td></td>
<td>15.0</td>
<td>(8)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>L</td>
<td>1,540</td>
<td>4.6</td>
<td>(7)</td>
<td>&lt;0.001</td>
<td>15.8</td>
<td>(8)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>30</td>
<td>19.7</td>
<td>(5)</td>
<td></td>
<td>16.3</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>L</td>
<td>1,950 ± 540</td>
<td>(7)</td>
<td></td>
<td>&lt;0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>2,810 ± 650</td>
<td>(7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled</td>
<td>L</td>
<td>4.9 ± 2.0</td>
<td>(7)</td>
<td></td>
<td>&lt;0.001</td>
<td>14.1 ± 1.4</td>
<td>(8)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>12.4 ± 7.2</td>
<td>(7)</td>
<td></td>
<td></td>
<td>14.4 ± 1.6</td>
<td>(8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>4.6</td>
<td>(51)</td>
<td></td>
<td>&lt;0.05</td>
<td>14.4</td>
<td>(60)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>6.1</td>
<td>(39)</td>
<td></td>
<td></td>
<td>14.5</td>
<td>(65)</td>
<td></td>
</tr>
</tbody>
</table>

L, low inotropic state; H, high inotropic state. $S_n$, normalized coefficient of stiffness for negative phase; $S_p$, normalized coefficient of stiffness for positive phase. n, number of runs. NS, not significant.

run, pressure starts to fall from the same level and reaches its asymptote in a total occlusion before this time (e.g., point 1, Figure 4), then we may conclude that filling slows left ventricular relaxation and prolongs the time to end relaxation.

We then selected the 32 runs in which there was a total occlusion and one or more occlusions that occurred after equilibrium volume with a consequent pressure fall. Because in any one run all the control beats had the same hemodynamic conditions, the isovolumic relaxation time and the atrioventricular pressure crossover at the onset of filling were the same, and $dP/dt_{min}$ was chosen as the reference time.

The time to end relaxation in the partially filling beats was greater than the time to reach the equilibrium volume (161 ± 31 versus 143 ± 39 msec, p<0.05) and was very much greater than the time to end relaxation in the completely isovolumic beats (108 ± 36 msec, p<0.0001). Note that the actual value of the time to end relaxation is greater than 161 msec; for example, it is somewhere between points 5 and 6 in Figure 4. Filling thus appears to have a profound effect on the duration of relaxation.

Discussion

Clinical and laboratory investigations of diastolic properties and function are growing rapidly. The adverse effects of late diastolic dysfunction, that is, of decreased compliance, have long been known; the current emphasis is on early diastole, that is, on the rate and duration of left ventricular relaxation. There is a solid body of clinical evidence indicating that diastolic function may become impaired before systolic function and that the dysfunction is often related to the operating volume range, $V_{\text{max}} - V_{\text{f}}$, increases with LVW, the chamber stiffness, $dP/dV$, at any given pressure is inversely proportional to LVW. Similarly, at any given volume, $dP/dV$ is smaller in large ventricles. Dots are the raw data points; solid curves are extrapolations from the logarithmic fit. See Table 2 for individual data.
to the passive and active left ventricular properties early in diastole. The rate of left ventricular pressure decay is now routinely used as an index of early diastolic function with some investigators demonstrating the significance of the extent of relaxation as well as of its rate.

**Concept of Diastolic Suction and Equilibrium Volume**

We have demonstrated here and elsewhere that the left ventricle can relax to a negative pressure in the absence of filling. We have also shown that end-systolic volume clamping need not necessarily lead to negative pressures, but it does lead to a pressure that is lower than the pressure that would have existed with filling. Brecher has defined suction as filling due to a pressure difference created by the ventricle lowering its pressure below that of the atrium. This definition avoids the issue of negative pressure, but it raises a conceptual problem: mitral flow is always associated with an atrioventricular pressure gradient, and left atrial pressure must fall as the atrium empties; therefore, filling must occur while left ventricular pressure is falling. Since ventricular filling is due to both relaxation and restoring forces, we think it is incorrect to conclude that relengthening while LV pressure is falling indicates active filling due only to restoring forces. The absence of a gradient is incompatible with life; hence, if we accept Brecher’s definition, the ventricle always fills itself by suction, even when the end-systolic volume is greater than the equilibrium volume.

An attempt to avoid this dilemma can be extracted from the teleological argument that once the ventricle starts to fill it relaxes more rapidly under the load and thus expedites its own filling. This approach negates the need to postulate restoring forces as the mechanism of suction; indeed, Brutsaert and coworkers (Goethals et al) have maintained that the ventricle does not contract to below its equilibrium volume. Noble et al have also concluded that diastolic suction is unlikely because the end-systolic volume is usually greater than the equilibrium volume, but their own data do not support that conclusion. Using their exponential approach (Table 1 of Noble et al) and their measured end-systolic volume, we calculate that V0 - Vss is 14.5 ml, or 46% of their stroke volume. This is almost identical to the 45% obtained in this study (Tables 1 and 2). Our data do not support the arguments that diastolic suction occurs infrequently.

Contraction below the equilibrium volume is analogous to contraction below slack length in an isolated muscle. It is well known that an unloaded papillary muscle or myocyte will contract and relengthen in the absence of any external forces. There must, then, be internal restoring forces in the ventricular chamber when it contracts to below the slack length of the sarcomeres within its wall. There may also be restoring forces due to a ventricular shape change that occurs after sarcomere shortening has ended. This is most evident in the right ventricular outflow tract, which is frequently seen to invaginate late in systole. The P-V relations across the aortic valve have long been known to reflect an inertial system. It is not unreasonable to conclude that, because of momentum in aortic outflow, blood may continue to leave the ventricle after the sarcomeres have ceased shortening, thereby leading to a deformation that can store elastic energy even in the absence of contraction below equilibrium volume. The more vigorous the outflow, the greater is the likelihood of a shape change. Perhaps this is why the negative portion of the P-V curve was influenced by the inotropic state (increased S, see Table 3) and showed so much variability.

We propose to define diastolic suction as that property of the left ventricle that relies upon internal restoring forces to establish the pressure gradient for filling. Since storage of energy requires an expenditure of at least an equal amount of energy, it appears that the functional role of diastolic suction is to maintain the integrity of the lungs by keeping the filling pressure low. Although it is not the scope of this study to determine the source of restoring forces, it is worth noting a recent study that relates the extracellular matrix of the myocardium to its mechanical parameters.

**Effect of Filling on Duration of Relaxation**

Isolated muscle experiments, in which relaxation is defined by relengthening rate, and conceptual arguments have been presented to hypothesize that the process of filling increases ventricular relaxation rate. In addition, Weisfeldt et al demonstrated that the normal filling ventricle reaches the passive P-V curve at approximately 3.5 time constants after the onset of isovolumic relaxation. The results of this study and of our previous studies do not support either conclusion.

Ventricular pressure always falls more rapidly when there is no filling (Figure 4). Thus, there is no evidence from intact heart experiments that filling increases relaxation rate. Physiologically sequenced isolated muscle studies that demonstrate a load dependency of relaxation may not be an adequate analog of the intact heart for several reasons. 1) Relengthening occurs during an isotonic load clamp that is imposed on the muscle, whereas in the intact heart, relengthening occurs while pressure is still falling, and the pressure is due to both activation decay and passive elastic recoil or stretch. 2) Relaxation in the isolated muscle is described by the rate of relengthening in contrast to the rate of pressure fall in the intact heart. Relengthening rate cannot be used as an index of relaxation in the intact heart because it is determined by all the components of the atrioventricular gradient. 3) Under normal loading conditions, the isolated muscle rarely contracts to below slack length, whereas in this study, contraction to below the equilibrium volume is normal. We therefore think that caution should be used in extending the results of isolated muscle studies to the intact heart.

We have shown previously that the decay of left ventricular pressure is not truly exponential but that the approach is reasonable. That same study also showed
that as a consequence of non-exponentiality, the calculated time constant based on a zero asymptote is approximately the same as the time constant based on the true asymptote \( P_a \). The data of Table 1 support these previous findings \( T_s = T_0 \). Furthermore, relaxation in the ventricle clamped at end-systole (i.e., completely isovolumic relaxation) is complete at 3.7T, while in the filling beats it is not completed until 5.4T. Because volume clamping is a reliable method, perhaps the only method, capable of separating the effects of filling from relaxation, we may conclude that filling slows the rate of relaxation and increases its duration. The mechanisms leading to these unexpected conclusions remain to be determined.

**Estimation of Diastolic Ventricular Properties**

A major limitation of this study is our lack of a direct measurement of absolute ventricular volume. Volume clamping, along with the measurement of ventricular inflow and outflow, only allowed us to determine the equilibrium volume relative to an unknown end-systolic volume. (Note again that we assumed that the end-systolic and equilibrium volumes remained constant throughout each run.) However, because we were able to measure the negative as well as the positive P-V coordinates, relative equilibrium volume could be accurately determined visually from the scatter plots. The accuracy of our estimates of absolute equilibrium and maximum volumes based on a regression against left ventricular weight of the calculated values of these parameters from the work of others can only be determined by future work and by comparison of our results with the results of others. To perform these comparisons, we used the data from Table 2 along with the ensemble mean values for \( S_p \) and \( S_o \) to create the “average” dog in this study.

\[
P_p = -14.6 \ln[(116 - V)/79] \quad \text{and} \quad P_p = 5.1 \ln[(V - 13)/24]
\]

Table 4 presents the results from other studies in which equilibrium and maximum volumes and \( S_p \) were calculated. (Unfortunately, many investigators only gave ranges and not means or actual data for body weight; some of the normalized data are thus estimates.) The first four rows of Table 4 contain the references from which we derived our estimates of maximum and equilibrium volumes based on left ventricular weight; hence, we cannot compare results in columns 7–10.

Our stiffness constant \( S_o \) is higher than the first two values and close to the third. Our chamber compliance at the equilibrium volume, \( dP/dV_{oe} \), is somewhat less than the three based on diastolic arrest and reasonably close to the one derived from angiograms in the conscious dog. This reflects the smaller operating volumes \( V_o - V_d \) in the former hearts, which are perhaps due to contracture in the nonperfused preparation.

The equilibrium volume of this study, normalized by body weight, is very close to that determined by diastolic arrest and is higher than that determined by vena caval occlusion. We think that vena caval occlusion underestimates equilibrium volume by tending to maintain a positive left ventricular pressure because even the small amount of filling during vena caval occlusion increases left ventricular pressure; relaxation may not be complete at the measured minimum left ventricular pressure; and filling slows relaxation. Thus, the point at which the minimum left ventricular pressure is equal to zero, which was used in those studies to determine equilibrium volume, may not be on the passive P-V curve.

It is interesting to note that when normalized by left ventricular weight, our pooled suction volume \( V_o^* \) obtained under normal afterload conditions (Table 1) is only slightly lower than that obtained by Suga et al under unloaded conditions \( 6.9 \pm 4.4 \) versus \( 7.8 \pm 3.0 \) ml/100 g). There are no independent data or studies with which to verify the calculation of maximum volume, but we will discuss an approach below.

A rough approach toward looking at the usefulness of the results is to examine the relation between sarcomere length and ventricular properties. A reasonable value for the ratio of maximum sarcomere length to slack length is 1.33 \( (2.4/1.8) \); this compares favorably with the cube root of the ratio of maximum volume to equilibrium volume \( (V_m/V_o) \), 1.46.

Given these estimates of absolute volumes and properties, we calculate that our “average” dog functioned with an end-diastolic volume of 52.3 ml, an end-systolic volume of 28.1 ml, and an ejection fraction of 46%. This is consistent with the linear regression presented above \( (stroke\; volume = 0.47V_{oe} - 1.6) \). We can further define an end-systolic volume reserve as \( (V_e - V_o)/(V_e - V_d) \) and determine that our dogs used 38% of that reserve. Similarly, the end-diastolic volume reserve is \( (V_{oe} - V_o)/(V_m - V_o) \), and our dogs used only 19% of the reserve. Thus, the Frank-Starling mechanism is readily available. Finally, at 0.95\( V_m \) the ventricular pressure is 40 mm Hg; this is consistent with the maximum end-diastolic pressures found by others. It is also consistent with the known tendency for the cardiovascular system to regulate pressure as volume varies. These approaches appear to lend credibility to the qualitative as well as quantitative results of this study.

There are no data available with which to compare our value of stiffness in the negative phase \( S_o \). To our knowledge, this is the first study that has sought to quantify the properties of the left ventricle when the volume is below the equilibrium volume and has reached that volume by active contraction rather than by passive volume withdrawal. In a previous study, we reported the interesting observation that ventricular pressure fell to a greater negative value at higher levels of contractility and similar end-systolic volumes. The tendency for \( S_o \) to be greater at higher inotropic states (Table 3) supports this result and suggests that diastolic suction may be due to a combination of elastic recoil and one or more mechanisms related to the ventricular systole.

Ideally, if Equations 3 and 6 are to accurately characterize the entire P-V relation, they should have the
same slope at their common point, the equilibrium volume. In the “average” dog, dP/dV at V₀ is 0.185 and 0.213 mm Hg/ml for the positive and negative phases of the P-V relation, respectively. Alternatively, a paired t test between the values of dP/dV in Table 2 showed no significant difference. To assess a possible influence of inotropic state, we compared dP/dV at V₀ determined from positive pressure-volume relation.

Results: mean ± SD.

n, number of runs; BW, body weight; LVW, LV weight; V₀, absolute value of equilibrium volume determined from LVW (see text); V₀m, maximal volume; V₀ — V₀, operating range in positive phase; S₀, normalized coefficient of stiffness for positive phase; and dP/dV₀, dP/dV at V₀ determined from positive pressure-volume relation.

*One dog (number 11) is eliminated because of unrealistic value of LVW; †determined from Table 1 from Nobel et al; ‡our estimate; §determined from data in (14, 17–19); ||for 5 dogs (2, 4, 5, 6, and 7).

Functional Differences Between Exponential and Logarithmic Approaches

The classic assumption of an exponential P-V relation has led to two methods of determining the material properties of the ventricular chamber: the solution of Equation 1, typically by a nonlinear regression analysis,29 or the solution of equation 2, which is linear.18 The use of Equation 2 is always fraught with difficulty since it leads to a negative chamber stiffness at the equilibrium volume. This is physiologically impossible because the derivative tends to be noisy. A more important problem arises when the derivative is negative for positive values of transmural pressure. Diamond et al18 found this contradictory result in all of their studies and attempted to explain the data by postulating a deviation from exponentiality at pressures below 2.5 mm Hg. These data arise because of an incorrect assumption of an exponential P-V relation and its linear dP/dV versus P relation.

It can be shown that a plot of the P-V relation obtained in this study (P = −14.6 ln[(116-V)/(116–37)]) is almost identical, within the operating range of the ventricle, with the curve obtained by a least-squares exponential regression of coordinates obtained from the plot P = 6.2 (exp[0.025(V–37)]−1).

Figure 7, curve A, is the plot of dP/dV versus P derived from the logarithmic approach. Curves B, C, and D are the relations derived from a linear regression of the coordinates from curve A with points from 40–110 ml, 40–100 ml, and 40–90 ml, respectively. Curve B is impossible because the chamber compliance is negative at positive values of pressure and is analogous to the results of Diamond et al.18 The slope and intercept of curve D are very close to that obtained from the exponential shown in the upper panel. The slope of curve C is 30% greater than that of curve D, revealing the sensitivity of the material constant de-
TABLE 4. (Continued)

<table>
<thead>
<tr>
<th>$S_p$ (mm Hg)</th>
<th>$dP/dV_{0}$ (mm Hg/ml)</th>
<th>$V_0$ determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>$8.1 \pm 0.9$</td>
<td>$0.224 \pm 0.121$</td>
<td>Diastolic arrest</td>
</tr>
<tr>
<td>$9.8 \pm 1.4$</td>
<td>$0.245 \pm 0.089$</td>
<td>Diastolic arrest</td>
</tr>
<tr>
<td>$13.2 \pm 6$</td>
<td>$0.345 \pm 0.242$</td>
<td>Diastolic arrest</td>
</tr>
<tr>
<td></td>
<td>$0.166 \pm 0.139$</td>
<td>Equations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vena cava occlusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vena cava occlusion</td>
</tr>
<tr>
<td>$14.5 \pm 1.5$</td>
<td>$0.188 \pm 0.036$</td>
<td>Diastolic volume clamp</td>
</tr>
</tbody>
</table>

rived from an exponential to the range of volumes (or pressures) chosen for the acquisition of data. It is reasonable to conclude from this analysis that the logarithmic approach is functionally more acceptable than the exponential and that the data of Diamond et al.18 are consistent with a logarithmic P-V relation, which supports our data.

**Conceptual Validity of the Logarithmic Versus the Exponential Approach**

The logarithmic approach, Equations 3–8, sets upper and lower limits on the operating volumes of the ventricle that are consistent with the operating pressure range, and it yields relations for the chamber compliance that are scaled to these volumes. We are thus led to conclude that the logarithmic approach is heuristically more acceptable than the exponential. We also think that this approach will prove to be more meaningful in the analysis of ventricular properties in disease states. For example, we would predict that in hypertrophy, the maximum and equilibrium volumes would both decrease and that $dP/dV$ at the equilibrium volume would increase. A rough numerical analysis suggests that $S_r$ and $S_p$ would increase or remain unchanged as the volume parameters changed. This approach is consistent with the results of others.14,16

**Conclusion**

The technique of ventricular volume clamping has allowed us to determine that filling slows left ventricular relaxation, to quantify the diastolic properties of the left ventricle, and to characterize the diastolic P-V relations with a logarithmic model that appears to be superior to the popular exponential model. The results obtained by volume clamping the ventricle have clearly demonstrated the existence of diastolic suction. The importance of diastolic suction and of the characterization of the negative portion of the P-V relation have to be demonstrated by further work. In particular, we look forward to the application of these results to a reevaluation of the concept of P-V area based on the time varying elastance theory and to the diastolic stress-strain relations. Finally, we are concerned with our separation of the P-V relation into positive and negative phases, and we encourage an approach that unites both phases. Such an approach would be mathematically more elegant and, if physically possible, more desirable than the present separation.

**Acknowledgments**

This work could not have been done without the skilled technical help of Messrs. P. Bon, A. Leon, F. Rivera, and F. Wasserman. We thank Ms. M. Olivera for typing the manuscript, and Dr. K. Nelson for building the remote-controlled mitral valve controller.

**References**

20. Sagawa K: The end systolic pressure volume relation of the...

KEY WORDS • diastolic stiffness • diastolic suction • P-V relations restoring forces • equilibrium volume • scaling
Passive properties of canine left ventricle: diastolic stiffness and restoring forces.
S Nikolic, E L Yellin, K Tamura, H Vetter, T Tamura, J S Meisner and R W Frater

Circ Res. 1988;62:1210-1222
doi: 10.1161/01.RES.62.6.1210

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/62/6/1210

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/