Influence of Acute Myocardial Depression on Left Ventricular Stiffness and Its Elastic and Viscous Components

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ABSTRACT The influence of acute myocardial depression on ventricular stiffness and on its elastic and viscous components was studied in 19 dogs. After the animals were placed on cardiopulmonary bypass, stiffness was measured by sinusoidally injecting volume changes of 0.5 ml (ΔV) at 22 Hz into paced, isovolumically contracting left ventricles and determining the amplitude (ΔP) of the sinusoidal pressure response. Stiffness was linearly related to pressure (P) throughout the cardiac cycle, so that $\Delta P/\Delta V = \alpha P + \beta$, where α and β are constants. Myocardial depression was induced in one of three different ways: by coronary artery ligation, by administration of propranolol (Inderal), or by administration of pentobarbital. All three interventions caused significant increases in the slope, α, of the stiffness-pressure relationship, while the intercept, β, remained unchanged. Release of the coronary occlusion or administration of acetylstrophanthidin partially reversed depression and the change in α. Approximation of the mechanical nature of the left ventricle in terms of a linear second-order mechanical system permitted the division of stiffness into its elastic and viscous components. Like total stiffness, both the elastic and the viscous components were linearly related to ventricular pressure. Elastic stiffness was not changed, but the slope of the line relating viscous stiffness to pressure was significantly increased during ischemic depression, indicating that a change in viscosity was primarily responsible for the increase in total ventricular stiffness.

INTRODUCTION

Many interventions that alter left ventricular performance have been tested for their simultaneous effects on diastolic stiffness. Tests of alterations in systolic stiffness, on the other hand, have seldom been attempted, primarily because appropriate techniques have not been available. For instance, the quick-release technique, widely used to measure mechanical properties in isolated papillary muscles, has not been extended to studying ventricular mechanical properties because of the technical difficulties involved. A new method for measuring ventricular stiffness has recently been developed in our laboratory, and this technique provides a means not only for measuring total ventricular stiffness at multiple times throughout the cardiac cycle, but also for separating stiffness into its viscous and elastic components.

It is well known that large changes in tension development can alter diastolic stiffness through a mechanism involving stress relaxation (1–5). Effects of large changes in tension development on systolic stiffness, however, have not been defined. Accordingly, in the present study we have turned our attention toward determining whether and to what extent systolic stiffness is altered during severe ventricular depression and reduction in tension development.

METHODS

A detailed description of the method used for measuring ventricular stiffness has been presented previously, along

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with theoretical consideration of the analysis and an evaluation of the technique (6–11). The present study utilized sodium pentobarbital anesthesia (30 mg/kg) for 19 mongrel dogs; next, a midline thoracotomy was performed and each dog was placed on complete cardiopulmonary bypass. The extracorporeal circuit consisted of an oxygenator, a heat exchanger, and a roller pump. Heart block was produced by ligation of the bundle of His in the atrial septum, and the heart was subsequently paced at 120 beats/min by a Grass stimulator through electrodes sutured to the right ventricle (Grass Instrument Co., Quincy, Mass.). The left ventricle was made isovolumic by occlusion of the inflow and outflow tracts with Teflon buttons and insertion of a distensible balloon into the chamber through a stab incision in the apex of the heart. Thebesian blood was not allowed to accumulate between the balloon and endocardium but was drained continuously through perforations in the mitral button and around the stab incision.

The ventricular balloon was attached to a metal cannula through which the balloon was filled with 20–25 ml of saline until a diastolic pressure of between 1 and 5 mm Hg was obtained. A piston located at the external end of the cannula was driven sinusoidally at 22 Hz to produce a peak volume change in the ventricle of 0.5 ml. For this amplitude and frequency, measurable sinusoidal pressure changes produced in the ventricle during both diastole and systole were measured with a Konigsberg P21 pressure transducer inside the balloon (Konigsberg Instruments, Inc., Pasadena, Calif.). The stiffness of the balloon was negligible, and the inherent time delay at 22 Hz between the peak of a pressure cycle and a volume cycle for the system without the heart was zero for operating pressures below 90 mm Hg and 6° above 90 mm Hg. The amount of friction between the balloon and endocardium at a frequency of 22 Hz was assumed to be negligible.

The pacing stimuli, left ventricular pressure with its sinusoidal response, and the sinusoidal volume displacement, as recorded by a differential transformer connected to the shaft of the piston, were recorded on analog tape during the experiments and later were processed on PDP-12 and PDP-10 computers (Digital Equipment Corp., Cleveland, Ohio). The pacing stimulus, which was in synchronization with a preset number of volume cycles, was used to trigger the computer to begin digitizing the ventricular pressure and the volumetric displacement wave forms at a sampling rate of 1,000/s. 16 successive pressure and volume wave forms were averaged to yield single pressure and volume wave forms to remove nonperiodic noise arising from equipment vibration. Fourier series analysis was performed on the ventricular pressure wave form. This analysis assumes that the pressure wave form consists of a finite number of sine and cosine waves, whose frequencies are multiples or harmonics of the fundamental frequency or heart rate. By choosing a perturbation frequency of 22 Hz, the pressure response to the volumetric forcing function is contained in harmonics higher than those harmonics contained in an unperturbed ventricular pressure waveform. Consequently, by eliminating the lower-order harmonics (first to the eighth) that constitute the unperturbed ventricular pressure wave form for one cardiac cycle and resynthesizing the higher-order harmonics (above the eighth), a wave form that is a function of the volumetric forcing function can be constructed. The use of Fourier analysis to filter the sinusoidal pressure response from the perturbed pressure wave form gives essentially the same results as subtracting an unperturbed pressure wave form from a perturbed one (9). The pressure wave form obtained by Fourier analysis is sinusoidal, having a frequency of 22 Hz and a varying peak amplitude that increases in size during contraction and decreases during relaxation. The peak amplitude (ΔP) [1] for each perturbation divided by the change in volume that produced it (ΔV) is defined as volume stiffness ($\Delta P/\Delta V$), and analysis of the entire contraction cycle yields 22 values for volume stiffness at varying pressures. For each experimental condition, ventricular stiffness ($\Delta P/\Delta V$) was found to be linearly related to ventricular pressure (P) throughout the cardiac cycle ($r > 0.94$, Fig. 1): $\Delta P/\Delta V = \alpha P + \beta$, where α and β were the slope and intercept with the ordinate, respectively. From this expression, it is seen that the units for the slope and intercept are $(ml)^{-1}$ and (mm Hg)/ml, respectively. Previous studies conducted in our laboratory have shown that changes in ventricular volume, heart rate, norepinephrine (8), coronary blood flow (10), and serum osmolality (9) have not altered the linearity of the relationship between stiffness and pressure.

To divide stiffness into its elastic and viscous components, the response of the mechanical system, consisting of the piston, steel cannula, balloon, and left ventricle, was assumed to be that of a linear second-order system. Justification for this assumption has been discussed in detail previously (7, 11). In short, the assumption of system linearity is based on the experimental observation that the pressure response of the system to the sinusoidal volumetric forcing function is also sinusoidal. A second-order system is assumed since it was observed experimentally that the peak of each pressure cycle occurred before the peak of the nearest volume cycle. This observation implies that the system has not only a static or elastic response but a dynamic response due to both viscosity and inertia.

Accordingly, the mechanical system, consisting of the piston, connecting cannula, balloon, and left ventricle, is represented by this equation of motion:

$$\frac{1}{K}\frac{d^2P(t)}{dt^2} + \frac{1}{\eta}\frac{dP(t)}{dt} + \frac{1}{m}P(t) = \frac{1}{\alpha}\frac{d^2V(t)}{dt^2} \qquad (1)$$

where K is elastic stiffness, η is viscous damping, m is the equivalent mass, and α is a constant relating linear displacement to spherical volume changes. The sinusoidal forcing function, $V(t)$, and the system pressure response for a given ventricular pressure, $P(t)$, are sinusoids and may be expressed as follows:

$$V(t) = Vo \cos wt,$$
$$P(t) = Po \cos (wt + \Psi), \qquad (2)$$

where Vo and Po are amplitudes of volume and pressure, w is angular frequency, and Ψ is the difference in time between the occurrence of the peak of a pressure cycle and the peak of a volume cycle. By making Ψ positive, the pressure sinusoid leads the volume sinusoid in time as observed experimentally. For a linear system in which pressure and volume are the parameters, Eq. 1 demonstrates that the pressure of the elastic, viscous, and inertial elements are proportional to volume and its first and second derivatives with time, respectively. For instance, by setting the first two terms in the sum appearing in Eq. 1 at zero, Newton's second law of motion is obtained.

[1] *Abbreviations used in this paper:* α, slope of stiffness-pressure relationship; β, intercept of stiffness-pressure relationship; LAD, left anterior descending; $\Delta P/\Delta V$, volume stiffness.

Substituting Eq. 2 into 1 and solving for the conditions where the first and second derivatives of $V(t)$ with respect to time are zero yield expressions for elastic and viscous stiffness, respectively, at any particular ventricular pressure.

$$\text{Elastic stiffness} \triangleq K = \frac{\alpha m w^2 \, \text{Po}}{\text{Vo}\, m w^2 \cos \Psi + \text{Po}\, \alpha} \quad (3)$$

$$\text{Viscous stiffness} \triangleq \eta w = \frac{\alpha \, \text{Po}}{\text{Vo} \sin \Psi} \quad (4)$$

These expressions are functions of the ventricular stiffness (Po/Vo) and the phase angle (Ψ) both of which can be measured from the recordings of sinusoidal volume variation and the pressure response of the system obtained by Fourier analysis.

In Eq. 1, the coefficients K, η, and m are constant. However, Eq. 3 shows elastic stiffness or K to be dependent upon stiffness and the phase angle, both of which are observed to vary directly with pressure during the cardiac cycle. Consequently, Eq. 1 applies only when stiffness and the phase angle are constant, which in turn is true when pressure is constant, as during diastole. To broaden the scope of the model to include systole as well as diastole, the dynamic response of the left ventricle is modeled piecewise. That is, it is assumed that at a given developed pressure of the ventricle and a given active state of the muscle, the response to a single sinusoidal volume cycle is given by the equation of motion (Eq. 1) with constant coefficients. Moreover, it is assumed that since the developed pressure and active state are changing relatively slowly with respect to the period of each volume perturbation, each pressure cycle can be analyzed as if it were one period of a pure sinusoidal pressure response at that particular developed pressure and active state.

The chosen equation of motion (Eq. 1) contains mass. The value chosen for mass in the calculations was the sum of the fluid mass in the balloon and cannula plus the mass of the left ventricle. This is an approximation of the true effective mass of the system. This use of an approximation will not influence the report of relative changes in stiffness. However, it is assumed that mass does not significantly change during ischemia, for this would influence the results.

Computer programs were developed to calculate the viscous and elastic stiffness from the stiffness and phase angle data measured from the digitized sinusoidal volume wave form and the sinusoidal pressure response obtained by Fourier analysis. The peak values of each pressure and volume sine wave were measured and the stiffness ($\Delta P/\Delta V$) calculated. The sampling theorem (12, 13) was programmed to reconstruct both the volume and pressure wave forms to permit measurements within 1° of the times of occurrence of the peaks of the pressure and volume cycles.

In the present study, isovolumic ventricles of five dogs were ventricularly paced at 120 beats/min and perfused with an aortic pressure of 75 mm Hg. Control recordings on analog tape were made of the sinusoidal piston displacement, ventricular pressure, and the pacing stimulus. A reversible ligature was placed around the proximal left anterior descending coronary artery (LAD) immediately after the origin of the first septal branch. Placing the ligation at this position did not make the entire ventricle ischemic; instead we wanted a level of depression that gave a measurable developed pressure. This level of depression could then be described by a linear stiffness-pressure relationship, comparable with that for the control state. After ligation of the proximal LAD coronary artery, recordings of the previously mentioned parameters were made after 2, 5, 10, 15, and 20 min in four dogs and at 5-min intervals for 1 h in one dog. In two animals, removal of the LAD ligation was accomplished without producing ventricular fibrillation. In these animals, recordings were made periodically for 10 min after the release during stable ventricular pacing. In a second group of 11 dogs, a large cardiodepressant dose of propranolol (Inderal, Ayerst Laboratories, New York) (8 mg/kg) was infused intravenously and recordings made before and after the drug was given. In a subset of this group, five animals were given an initial dose of 1 mg/kg to investigate the influence of a beta-blocking dose of propranolol (14) on ventricular stiffness at a time when only minimal direct ventricular depression occurred. In three animals, severely depressed by 8 mg/kg of propranolol, acetylstrophanthidin (0.44 mg/kg) was administered at a time of maximal ventricular depression. In three additional dogs, the influence of depressant doses of sodium pentobarbital (16 mg/kg/min until developed pressure was reduced by half or more) on stiffness was investigated. These animals also received acetylstrophanthidin to test its influence on stiffness again in the setting of myocardial depression.

RESULTS

The distribution of Pearson's r values for the linear stiffness-pressure relationships, determined both before and after LAD coronary artery ligation and before and during administration of propranolol, is shown in Fig. 1. 80 stiffness-pressure relationships were analyzed, and none had a Pearson's r value of less than 0.94. Consequently, the stiffness-pressure relationships for the cardiac cycle both during the control state and during myocardial depression can be approximated with the linear equation $\Delta P/\Delta V = \alpha P + \beta$, where $\Delta P/\Delta V$ is stiffness, P is ventricular pressure at which the stiffness was determined, and α and β are constants. Thus, analysis of changes in the constants α and β provides a convenient means for documenting the influence of myocardial depression on ventricular stiffness.

The influence of coronary artery ligation on the linear stiffness-pressure relationship in a single representative

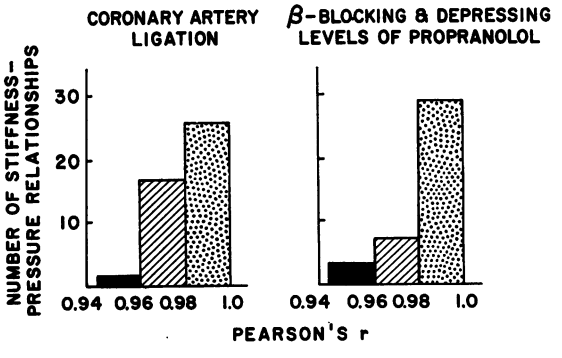

FIGURE 1 The distribution of Pearson's r values for the linear regression equations determined for the ventricular stiffness-pressure relationships before and after either coronary artery ligation or propranolol administration.

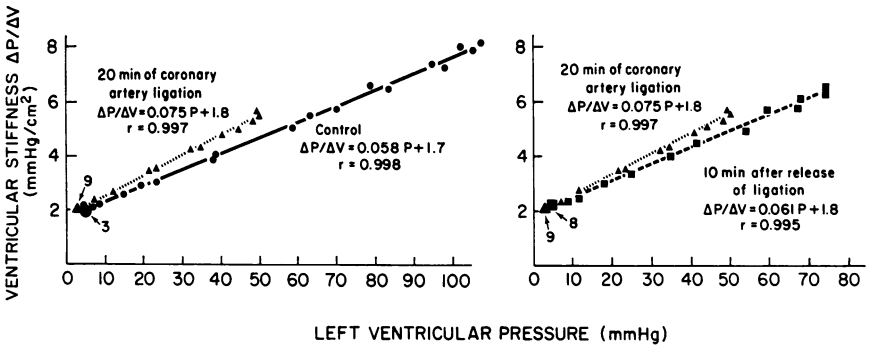

FIGURE 2 Ventricular stiffness-pressure relationships before, during, and after the release of a ligation midway down the left anterior coronary artery. The data points were obtained in an isovolumically contracting left ventricle and from an average of 16 ventricular pressure wave forms. Stiffness ($\Delta P/\Delta V$) was determined with a forcing function, which induced a sinusoidal volume change with a peak amplitude (ΔV) into the ventricular cavity, and measuring the peak of each pressure cycle (ΔP) from the resulting sinusoidal pressure response. As shown on the left, the stiffness after coronary artery ligation (▲) is higher than the stiffness during control (●). Comparison of the relationships on the right shows that stiffness after release of the ligation (■) is lower than during the ligation (▲).

dog is shown in Fig. 2. 20 min after coronary artery ligation, stiffness at any given systolic pressure was increased, whereas release of the temporary occlusion reversed this change. Changes in diastolic stiffness, if present, were too small to be detected within the resolution power of the system.

Mean data for all five dogs in which coronary occlusion was induced are shown in Table I. Diastolic pressure was not significantly altered in these isovolumic ventricles, but developed pressure fell significantly by 2 min, reaching a plateau by 10 min after ligation. The slope of the stiffness-pressure relationship rose throughout the 20-min period, the most marked increase occurring between 2 and 5 min or immediately after the most severe decrease in developed pressure. The intercept of the stiffness-pressure relationship, β, was unaffected.

The time course of changes in the linear stiffness-pressure relationships for an hour after coronary ligation is shown by data from a single dog in Fig. 3. 10 min after ligation the slope reached its maximal value and remained at that level for the rest of the period of occlusion. The intercept varied minimally, tending to rise slightly toward the end of the hour.

A level of propranolol (1 mg/kg) known to produce beta-receptor blockade in dogs caused a moderate re-

TABLE I

Influence of Coronary Artery Ligation on Left Ventricular Mechanics and Stiffness

	Control	Change from control to 2-min ligation	Change from 2-min to 5-min ligation	Change from 5-min to 10-min ligation	Change from 10-min to 15-min ligation	Change from 15-min to 20-min ligation
Diastolic pressure, *mm Hg*	3.8±0.68	−0.7±0.50 NS	−0.1±0.07 NS	+0.2±0.25 NS	−0.3±0.33 NS	+0.1±0.09 NS
Developed ventricular pressure, *mm Hg*	94.6±5.76	−31.0±6.60 $P < 0.005$	−5.0±2.24 NS	−1.4±1.86 NS	−0.3±0.63 NS	±0.8±0.25 NS
Slope (α) of stiffness-pressure relationship, ml^{-1}	0.068±0.0095	+0.005±0.0039 NS	+0.013±0.0027 $P < 0.005$	+0.003±0.0019 NS	+0.001±0.0010 NS	+0.002±0.0005 NS
Intercept (β) of stiffness-pressure relationship, *mm Hg/ml*	1.0±0.33	−0.1±0.08 NS	−0.1±0.03 NS	+0.1±0.03 NS	+0.1±0.02 NS	−0.1±0.06 NS

Mean control values ±SEM are shown for diastolic pressure, left ventricular pressure, the slope (α) and intercept (β) of the linear stiffness-pressure relationship for five dogs. During coronary ligation these parameters were again measured and are reported as the mean differences from the immediately preceding condition.

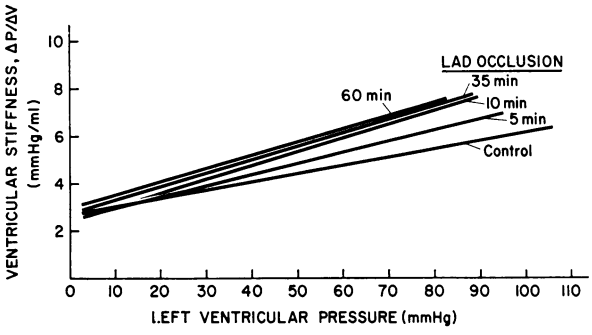

FIGURE 3 Ventricular stiffness-pressure relationships from a single animal showing the influence of coronary artery ligation for up to 1 h.

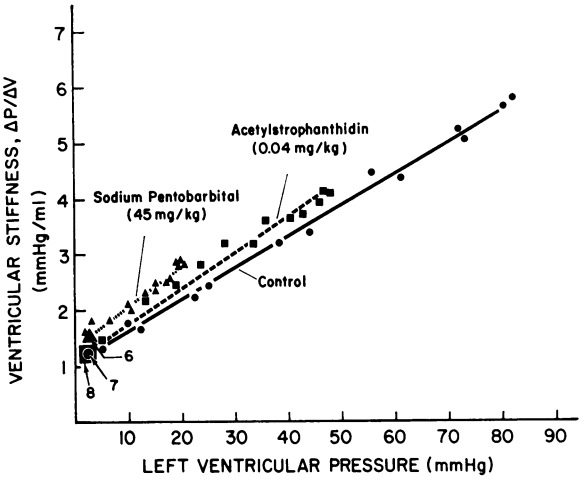

FIGURE 4 The influence of sodium pentobarbital and acetylstrophanthidin on the stiffness-pressure relationship. Comparison of control data (●) with data after sequential administration of sodium pentobarbital (▲), and acetylstrophanthidin (■) shows that depression evoked by sodium pentobarbital is characterized by greater stiffness, which is lessened by a subsequent dose of acetylstrophanthidin.

duction in developed pressure and, simultaneously, stiffness increased slightly (Table II). The decrease in developed pressure and the increase in the slope of the stiffness-pressure relationship were more severe after a larger depressant dose of propranolol (8 mg/kg), as is also shown in Table II.

Similarly, severe depression elicited by sodium pentobarbital caused a decline in developed pressure and an increase in stiffness. Fig. 4 depicts data from one dog. There was a shift upwards in the stiffness-pressure relationship due to an increase in both slope and intercept, reflecting an increase in stiffness at any given pressure. When depression was partially reversed by acetylstrophanthidin, the changes in stiffness and pressure were also reversed.

These results demonstrate that depression of left ventricular tension development, evoked by coronary artery ligation or by administration of either propranolol or sodium pentobarbital, is characterized by a rise in the dynamic stiffness of the left ventricle for any given pressure. To determine whether the change in stiffness with depression is attributable to elastic stiffness or viscous stiffness, the response of the left ventricle to a sinusoidal forcing function was approximated by an equation of motion (Eq. 1), which is a linear second-order differential equation. As explained in the Methods, elastic and viscous stiffness were derived from K and η, coefficients of the equation of motion, in terms of the total stiffness ($\Delta P/\Delta V$) and the phase angle (Ψ).

The relationships between elastic and viscous stiffness and ventricular pressure before and 20 min after ligation of the proximal LAD coronary artery are shown for one representative dog in Fig. 5. The apparent linearity of both the elastic and viscous stiffness-pressure relationships indicated by Fig. 5 was true for all five dogs, since the r values for all the relationships

TABLE II

Influence of Blocking Dose (1 mg/kg) and Depressing Dose (8 mg/kg) of Propranolol on Left Ventricular Mechanics and Stiffness

	$n = 5$		$n = 11$	
	Control	Propranolol 1 mg/kg	Control	Propranolol 8 mg/kg
Diastolic pressure, *mm Hg*	5.1±1.20	−0.7±1.02 NS	3.9±0.89 (SEM)	−0.2±1.02 NS
Developed ventricular pressure, *mm Hg*	93.8±5.79	−21.8±4.43 ($P < 0.005$)	98.6±3.55	−49.4±4.58 ($P < 0.001$)
Slope (α) of stiffness-pressure relationship, ml^{-1}	0.052±0.0031	+0.004±0.0008 ($P < 0.005$)	0.054±0.0038	+0.011±0.0017 ($P < 0.001$)
Intercept (β) of stiffness-pressure relationship, *mm Hg/ml*	0.8±0.11	+0.1±0.11 NS	0.6±0.18	0.0±0.13 NS

The data are presented as in Table I. The results after propranolol are expressed as a change from control.

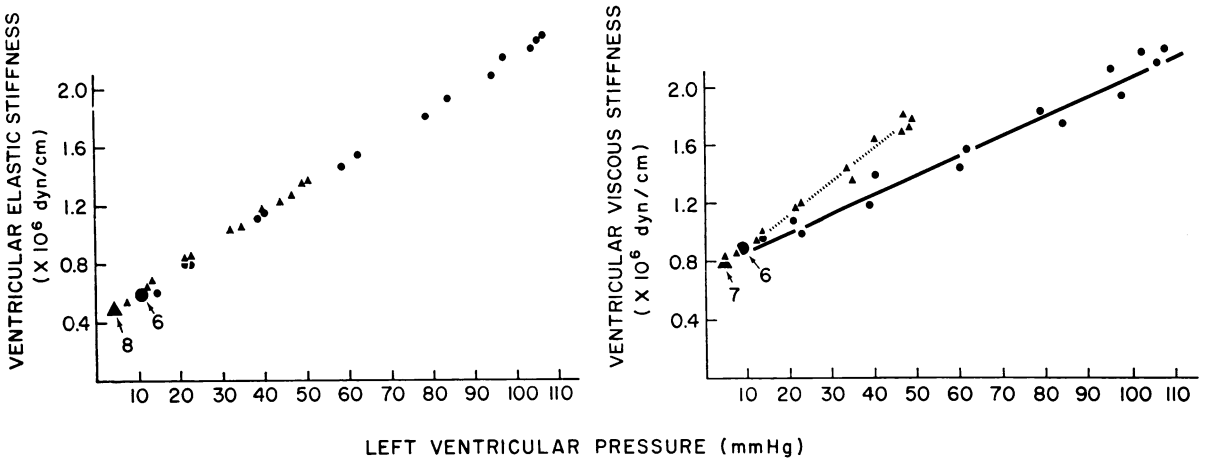

FIGURE 5 The influence of coronary artery ligation on elastic stiffness-pressure and viscous stiffness-pressure relationships (left and right, respectively). Viscous stiffness during coronary ligation (▲) is greater than that before the ligation (●), but elastic stiffness is unchanged.

were always greater than 0.95. The slopes and intercepts of these relationships were determined and are shown in Table III. As suggested by the data from the single dog in Fig. 5, the data in Table III confirm that a marked increase in viscous stiffness is responsible for the net change in stiffness. In contrast, elastic stiffness was not significantly altered after coronary ligation.

DISCUSSION

The influence of a reduction in left ventricular developed pressure on myocardial stiffness in the present study was the same whether propranolol, pentobarbital, or acute occlusion of the LAD coronary artery was used to elicit contractile depression. After each of these interventions, depression was accompanied by increased stiffness, as indicated by an increase in slope of the linear stiffness-pressure relationship. The increase in ventricular stiffness resulted from an increase in viscous stiffness, rather than elastic stiffness. Thus, our results indicate that large changes in tension development are accompanied by reciprocal alterations in systolic viscoelastic properties analogous to those previously described for diastolic properties (1–5).

TABLE III

The Influence of Coronary Ligation on the Linear Elastic and Viscous Stiffness-Pressure Relationships of the Left Ventricle

	Elastic stiffness				Viscous stiffness			
	Control		20 min after coronary artery ligation		Control		20 min after coronary artery ligation	
Dog	α	β	α	β	α	β	α	β
	ml^{-1}	*mm Hg/ml*	ml^{-1}	*mm Hg/ml*	mm^{-1}	*mm Hg/ml*	mm^{-1}	*mm Hg/ml*
1	0.0320	0.18	0.0298	0.26	0.0157	0.46	0.0250	0.37
2	0.0229	0.22	0.0227	0.18	0.0130	0.56	0.0161	0.60
3	0.0194	0.11	0.0203	0.10	0.0141	0.33	0.0191	0.37
4	0.0219	0.26	0.0223	0.29	0.0194	0.90	0.0231	0.93
5	0.0184	0.40	0.0191	0.40	0.0193	0.74	0.0220	0.68
Mean	0.0229	0.23	0.0228	0.25	0.0163	0.60	0.0211	0.59
SEM	0.00241	0.048	0.00185	0.051	0.00131	0.101	0.00156	0.105
Difference of means			−0.0001	0.02			0.0048	−0.01
SE			0.00055	0.020			0.00105	0.028
Significance			NS	NS			$P < 0.005$	NS

Both elastic and viscous stiffness were found to be linearly related to ventricular pressure. To determine the influence of a coronary artery ligation on these linear relationships, the slope (α) and intercept (β) were compared before and during coronary artery occlusion.

In interpreting these changes in myocardial stiffness, one must distinguish between the mechanical changes that might accompany cardiac depression in a normally ejecting left ventricle with a sustained aortic pressure from an isovolumically contracting ventricle such as was used in our study. In the latter, contractile depression will result in a reduction of developed tension, whereas in the former it will lead to cardiac dilatation and, by the Laplace principle, an increase in tension. Because of this consideration it is important to emphasize that the present results concern the response to ventricular depression with reduced tension; different results might be expected in hearts in which depression is accompanied by cardiac dilatation with a net increase in tension.

It should also be noted that the stiffness changes we observed were in response to very large alterations in tension. We have previously shown that modest inotropic interventions, in which the velocity of shortening increased significantly but in which total tension development rose only slightly, were not accompanied by measurable alterations in net stiffness (8, 10). The apparent discrepancy between that study and the present seems to us most likely to be due simply to major differences in the degree of alteration of tension. It also remains possible that depression of tension below normal control levels in some way exerts a fundamentally different effect on stiffness than does enhancement of tension development above normal, and that possibility is currently being investigated.

The concept and importance of viscous stiffness in influencing traditional determinations of left ventricular diastolic compliance or of systolic "series elasticity" as measured by quick-release experiments have been mentioned in some previous reports (9, 11, 15–17), but remain insufficiently defined. Viscous stiffness for cardiac muscle had not been quantified before the present technique was developed, and its relationship to other parameters relating velocity and force remains unclear. However, a comparison between systolic viscous stiffness and the traditional force-velocity curve has been made in skeletal muscle studies. Using a sinusoidal forcing function, Buchthal and Rosenfalck (18, 19) obtained measurements of viscous stiffness in skeletal muscle similar to those recorded in the present experiments for cardiac muscle. To compare systolic viscous stiffness to the force-velocity relationship, Buchthal derived an expression for viscous stiffness from Hill's mathematical expression of the force-velocity relationship. With typically observed values for the constants of Hill's equation, a value of the derived viscous stiffness parameter was much less than the value of viscous stiffness measured by Buchthal's sinusoidal forcing technique. Buchthal deduced from this comparison that the contractile element in Hill's model contributed to the viscous stiffness measured by the sinusoidal forcing technique but was not entirely responsible for the measured viscous stiffness.

A similar comparison between viscous stiffness and the force-velocity curve can be drawn for cardiac muscle for a better understanding of this new parameter in terms of the more widely used one. Such a comparison can be made by realizing that viscous stiffness is, by definition, the ratio of change in force (ΔF) to change in velocity (ΔV). Then, this ratio ($\Delta F/\Delta V$) is the same as the negative reciprocal of the slope of the force-velocity curve. However, it should be emphasized that the techniques used in obtaining these two expressions of muscle viscosity are quite different, and consequently the data measured by them are not strictly comparable. Since techniques are now available for measuring viscous stiffness directly and since experiments such as those described in this report have established that myocardial viscous changes exert a major influence during some interventions, it is to be hoped that greater attention will be paid in the future to defining the nature and importance of the viscous stiffness of the heart.

The increase in ventricular viscous stiffness by myocardial ischemia indicates that either the ability of the myocardium to generate a velocity at a given force has been impaired or its ability to generate tension at a given velocity has been improved. Whether this change in viscous stiffness indicates an impairment or an improvement depends on whether the contractile apparatus is more dependent upon velocity or force; e.g., whether the contractile apparatus is a velocity generator or a force generator. This distinction cannot be made at the present time. All that is known from the representation of Hill's contractile element with the force-velocity curve is that force and velocity are interrelated; we do not know which parameter is dependent on the other.

Due to technical difficulties, studies measuring the force-velocity relationship have rarely been done in the left ventricle. Some investigations have made simplifying assumptions to obtain in vivo force-velocity relationship, and a few of these have investigated the influence of ischemia on in vivo force-velocity relationships. Mason, Spann, Zelis, and Amsterdam (20) obtained relationships comparable to force-velocity curves for patients by plotting dp/dt/p versus isovolumic pressure. The slope of their relationship was greater during control than failure. The reciprocal of the slope of their relationship thus increased with failure, indicating an increase in viscous stiffness and agreeing with the change in the direct measurements of viscous stiffness during ischemia seen in our results.

Finally, it would be interesting to be able to relate studies such as ours to experiments using quick-re-

lease techniques. However, at the present, any comparison between stiffness parameters measured by quick-release and sinusoidal techniques must be guarded. As pointed out previously (9, 11, 15–17), the quick-release does not measure a pure elastic response, even though the property it reflects has been termed the "series elastic element." Strict comparison between the two techniques can be assessed only after further experimentation to see how both behave under different experimental interventions and to measure the viscous component in the response to a quick release.

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