Assessment of Cardiac Contractility

The Relation Between the Rate of Pressure Rise and Ventricular Pressure During Isovolumic Systole

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SUMMARY

It was considered that the relationship between dp/dt and simultaneously developed pressure during the course of isovolumic contraction might afford a more accurate measure of contractility than the maximum rate of intraventricular pressure rise (peak dp/dt). In six cat papillary muscles contracting isometrically from any given preload, the ratio of the rate of tension development (dT/dt) to simultaneously occurring isometric tension always varied directly with the contractile state. This ratio rose slightly as preload was increased, but it was not affected by changes in afterload. In 17 experiments in an intact canine heart preparation in which left ventricular end-diastolic pressure was constant, dp/dt at any given pressure during isovolumetric contraction again was observed to be a function of the contractile state when the latter was enhanced by norepinephrine and acetylstrophanthidin. High-fidelity left ventricular pressures and dp/dt were recorded throughout isovolumic contraction in eight patients. Isoproterenol and exercise raised the level of dp/dt at any given pressure prior to ejection. Interventions known to alter ventricular loading but not to influence the contractile state, such as elevation of ventricular end-diastolic pressure by leg raising and increases in aortic pressure induced by methoxamine, did not influence this relation significantly. In conclusion, the determination of dp/dt and intraventricular pressure throughout isovolumic contraction in the presence of variable arterial pressure and small changes of preload provides a useful, simple, and experimentally verified approach to the assessment of alterations of the contractile state of the heart in intact man.

Additional Indexing Words:
Left ventricular function  Myocardial contractility  Papillary muscle mechanics
Preload  Afterload

IT IS NOW acknowledged that the performance of the heart is governed by three principal factors: (a) the preload, which may be equated with the ventricular end-diastolic fiber length, (b) the afterload, which is closely related to the intramyocardial systolic tension, and (c) the contractile or inotropic state of the myocardium.1 In the evaluation of cardiac function, it has been possible to measure, or at least to obtain an accurate index of, the first two determinants, but it has been far more difficult to assess the contractile state.2 Hemodynamic measurements of cardiac output, stroke volume, ventricular end-diastolic volume and pressure, and systolic ejection time and the derivatives of these variables, such as the mean systolic ejection...
rate and ejection fraction, have added considerably to our ability to evaluate cardiac performance. However, the value of these measurements has been limited in the assessment of myocardial contractility, since they are not only influenced by alterations in the inotropic state but are greatly affected by alterations in the preload and the afterload as well.\(^1\)\(^3\)

One approach to the accurate assessment of contractile state is the determination of the relation between the velocity of myocardial fiber shortening and intramyocardial tension.\(^4\) However, application of this method is technically complex; it requires the performance of cineangiography, and it is relatively laborious since extensive analyses of the cineangiograms are required. The purpose of this paper is to describe another approach for the assessment of cardiac contractility, based on the relation between the rate of pressure rise and intraventricular pressure during isovolumic systole.

Observations in experimental animals and man have shown that the first derivative of systolic ventricular pressure (dp/dt) is greatly modified by cardiac contractility\(^5\) and have led to the measurement of peak dp/dt in the analysis of this fundamental property of the myocardium.\(^6\)\(^8\) However, it is now appreciated that dp/dt itself is a complex function which, in addition to the contractile state, is also influenced by ventricular preload and afterload.\(^8\)\(^,\)\(^9\) Thus, alterations in ventricular end-diastolic pressure and arterial diastolic pressure can alter dp/dt when the inotropic state is constant. Since changes in loading of the intact ventricle almost always accompany alterations in the inotropic state in the intact organism, the dp/dt per se has been found to be of limited value as an independent measure of myocardial contractility.

It has been observed in isovolumetrically contracting heart muscle that changes in contractility are reflected in the ratio of the peak rate of tension development to peak systolic tension despite changes in preload.\(^10\)\(^–\)\(^18\) However, since in the ejecting ventricle isovolumic dp/dt usually reaches a peak at the opening of the semilunar valves,\(^19\) this ratio, as well as peak dp/dt itself, are influenced profoundly by the level of arterial diastolic pressure, and, therefore, the value of these measurements as indices of myocardial contractility are seriously limited.\(^8\) In the present investigation, the possibility was considered that the relation between dp/dt and the simultaneously developed pressure throughout the course of isovolumic contraction, or the dp/dt at a given level of intraventricular pressure during isovolumic systole, might provide an accurate and practical measure of ventricular contractility independent of changes in preload and afterload. In order to examine the validity of this concept, we tested it initially in the isolated cat papillary muscle, then in dogs with controlled circulations, and then extended it to intact man. A preliminary report has been presented previously.\(^20\)

**Methods**

**Isolated Cardiac Muscle**

The relation of developed tension (T) and rate of tension development (dT/dt) was examined in six isolated right ventricular cat papillary muscles. Cats were anesthetized with intraperitoneal sodium pentobarbital (25 mg/kg) and the papillary muscles were rapidly removed and suspended in a myograph, as previously described.\(^21\) One end of the muscle was fixed by a spring-loaded clip, while the other end was rigidly attached to a force transducer (Statham 64-1000) for the measurement of tension. The muscle was bathed in buffered Krebs’ solution, aerated with 95% O\(_2\) and 5% CO\(_2\) and maintained at 30°C. Muscles were stimulated at a frequency of 12 per min with a pulse of 6-msec duration and a voltage which was 10% above threshold by mass electrodes placed parallel to the muscle. Only muscles with cross-sectional areas of 1.0 mm\(^2\) or less were utilized. Studies were carried out with the muscles contracting isometrically as well as in a variably afterloaded manner, i.e., in which isotonic shortening follows isometric contraction. The rate of force or tension development (dT/dt) was determined by electrical differentiation, and this measurement, along with the tension developed and the stimulus signal, was recorded on an Electronics for Medicine photographic recorder. The addition of norepinephrine and of paired electrical stimulation was employed to alter the muscles' contractile state.

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**Canine Heart**

Seventeen mongrel dogs weighing an average of 20.3 kg (14.1–32.2 kg) and anesthetized either with sodium pentobarbital (35 mg/kg) or with a combination of morphine sulfate (2.8 mg/kg), chloralose (96/mg/kg), and urethane (620 mg/kg) were studied. The experimental preparation utilized has been described in detail previously. Briefly, it consisted of a right heart bypass preparation in which stroke volume, heart rate, and mean aortic pressure were controlled. Left ventricular pressure, aortic pressure, aortic flow rates, and the rate of change of left ventricular pressure (dp/dt) were recorded on a multichannel oscillograph † at paper speeds of 100 mm/sec. The dynamic characteristics of the differentiating circuit and the flowmeter have been previously described. The relation between developed pressure (instantaneous left ventricular pressure minus left ventricular end-diastolic pressure) and dp/dt were obtained at 10-msec intervals during the isovolumic phase of left ventricular contraction. The onset of ejection was determined from the flowmeter tracing corrected for the time lag of the instrument.

Following control measurements, the effects of norepinephrine infusion (0.1–0.3 μg/kg/min) were studied in six experiments in five animals, and the effects of the administration of acetyl-strophantidin (0.19–0.40 cat units/kg) were studied in six additional dogs. All determinations were made at a constant heart rate, mean aortic pressure, and stroke volume. In three of the six experiments with norepinephrine, the output of the pump was increased to maintain left ventricular end-diastolic pressure constant.

In six other experiments the effects of increasing left ventricular end-diastolic pressure on the relation between developed left ventricular pressure and the corresponding dp/dt were examined; stepwise increases in cardiac output were produced at a constant mean aortic pressure and heart rate. In four of these dogs the effects of changes in afterload on the relation between dp/dt and developed pressure at a constant left ventricular end-diastolic pressure were examined. In order to control intraventricular pressure, we inserted a solenoid-triggered valve into the descending aorta so that aortic flow could be diverted to a separate reservoir bottle, as has been described previously. By regulating the pressure within this reservoir and triggering the valve during diastole, we could produce stepwise single beat changes in aortic pressure while maintaining left ventricular end-diastolic pressure constant. In these experiments, aortic diastolic pressure was increased from 45 to 150 mm Hg.

**Clinical Studies**

Twenty-three studies were carried out in eight patients, aged 28 to 63 years, with normal sinus rhythm in the course of postoperative left heart catheterization. These patients are described in detail in the complementary approach to quantification of contractility of determining maximal velocity of contractile element shortening. All patients had undergone successful replacement of the mitral and/or aortic valves with Starr-Edwards prostheses (five aortic, two mitral, and one combined aortic mitral) an average of 7 months prior to study. Each patient was markedly improved clinically and hemodynamically following operation, and none had regurgitation around his prosthesis.

Catheterization of the left ventricle was performed by the percutaneous apical insertion of a 6-inch Teflon catheter ‡ having an internal diameter of 0.053 inches and was attached directly to a Statham P23DB pressure transducer. The frequency response of this system is even greater than the standard left ventricular puncture needle (above 30 cycles/sec), and the phase lag is linear with frequency in this range. The left ventricular dp/dt was continuously calculated with an R-C differentiating circuit having a time constant of 9.4 × 10⁻⁵ sec, which provided differentiation of linear amplitude without phase distortion to 50 cycles/sec.

All patients were studied in the postabsorptive state following premedication with 100 mg pentobarbital. After placement of a Cournand needle in the brachial artery and the catheter in the left ventricle, 15 min were permitted to elapse for the patient to reach a stable state. Control measurements of intraventricular and brachial arterial pressures and of the left ventricular dp/dt were then recorded at a paper speed of 200 mm/sec intermittently during a 5-min period and were continued during each of the following interventions. In six patients, left ventricular end-diastolic pressure was elevated by increasing systemic venous return by rapidly raising the legs while the trunk remained in the horizontal position. In five patients, the aortic pressure was increased with the stimulating agent of the alpha-adrenergic receptor, methoxamine (1–2 mg), infused intravenously over a 1-min period. Isoproterenol (1 or 2 μg/min) was administered

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*Biotronex (Model BL 410 electromagnetic flowmeter), Biotronex Laboratories, Silver Springs, Maryland.
†Hewlett Packard Model 770, Waltham, Massachusetts.

‡Becton, Dickinson and Co., Rutherford, New Jersey, No. 01-0050.

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The relationship between the rate of change of force (dF/dt in g/sec) and active force (g) in isometric contractions from an isolated cat papillary muscle, plotted at 25-msec intervals up to the point of maximum dF/dt. (A) The relationship between dF/dt and active force at Lmax (squares, maximum tension = 6.48 g) and at a muscle length equaling 96% of Lmax (open circles, maximum tension = 5.52 g). This 14.8% decrease in active force is equivalent to an alteration in active force produced by a change in left ventricular end-diastolic pressure exceeding 6 mm Hg. (B) The effects of a concentration of 10^{-6}M norepinephrine (NE) on the relationship between dF/dt and active force. (C) The effects of paired electrical stimulation (PES) at a basic frequency of 12 per min and an interstimulus interval of 510 msec.

In six right ventricular papillary muscles, initial muscle length was varied between the midportion and the apex of the length-active tension curve. While developed tension increased with increasing muscle length, the time intervals from stimulation to peak tension and to the peak rate of tension development (dT/dt) were not altered. In contrast, with the addition of norepinephrine (10^{-6}M) to the bath, developed tension rose, while the time to peak tension and to peak dT/dt fell.

The rate of tension development was also plotted as a function of developed tension during isometric contractions, as seen in figure 1, which is representative of the results in all muscles. As initial muscle length was reduced from maximum active tension (Lmax) to a length at which isometric tension was reduced by 15% of peak levels, i.e., to 0.96 Lmax (fig. 1A), the maximum dT/dt declined, as did the peak developed tension. However dT/dt at any given level of tension showed little change. Similarly, during the isometric phase of afterloaded isotonic contractions, the relation of dT/dt to the corresponding level of developed tension was not altered by an increase in the afterload.

With the addition of norepinephrine (fig. 1B) or the institution of paired electrical stimulation (fig. 1C) to muscles contracting isometrically at a constant length, the dT/dt at any given level of tension rose. These changes were considerably greater than those that occurred when preload alone was altered (fig. 1A). The results of a group of muscles are compared in figure 2. The relation of dT/dt to isometric tension in five isometrically contracting muscles is shown in the control state and after either the addition of norepinephrine or the institution of paired electrical stimulation. With both interventions, the ratio of dT/dt to isometric tension was augmented significantly (P < 0.01). Similar results on the effects of inotropic interventions on the ratio
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of left ventricular ejection (fig. 4A, arrows) was not significantly changed during either norepinephrine or acetylstrophanthidin infusion. However, the ratio of dp/dt to the highest common level of left ventricular isovolumic pressure occurring during both the control contractions and after the administration of either drug, (dp/dt)/CPIP, rose significantly (fig. 5).

The effects of acute changes in afterload produced by alterations of aortic diastolic pressure on the relation between developed pressure (P) and left ventricular dp/dt for a representative experiment are depicted in figure 6. In this experiment, aortic diastolic pressure was increased progressively from 25 to 127 mm Hg, while left ventricular end-diastolic pressure was held essentially constant. The relation between left ventricular dp/dt and P, prior to the opening of the aortic valve, was not affected by alterations in afterload. However, when the aortic valve was opened before left ventricular dp/dt had reached its peak, i.e., when the left ventricle was ejecting while dp/dt was rising (fig. 6, closed circles) left ventricular dp/dt at any given level of P was lower than during isovolumic systole, emphasizing the importance of making this determination prior to the onset of ejection.

The effects of stepwise increases in left ventricular end-diastolic pressure on the relation between developed pressure and dp/dt in a representative experiment are shown in figure 7. It is evident that there was a progressive upward shift of the curves as left ventricular end-diastolic pressure was increased, while heart rate and mean aortic pressure were held constant. Figure 8 combines the results in all six animals in which the effects of alterations in left ventricular end-diastolic pressure were studied. The dp/dt at a pressure of 40 mm Hg, which was always reached during isovolumetric contraction, is plotted for contractions with progressively higher left ventricular end-diastolic pressure. A significant correlation (P < 0.01) between end-diastolic pressure and the dp/dt at a

![Graph](http://circ.ahajournals.org/)

**Figure 2**

Relation between dT/dt and developed tension (T) as determined in five muscles. (Cross-hatched bars) Before the addition of norepinephrine or paired electrical stimulation. (Open bars) After the addition of norepinephrine or during paired electrical stimulation.

The vertical lines represent ±SEM.

of dT/dt to tension were also observed in the isometric portions of afterloaded isotonic contractions.

Canine Heart

The effects of norepinephrine infusion on the relationship between left ventricular dp/dt and developed pressure are shown in figure 3. At pressures exceeding 20 mm Hg there was a significant (P < 0.05) elevation of left ventricular dp/dt. Figure 4 illustrates the effects of acetylstrophanthidin administration in the intact canine heart. There was a significant elevation of left ventricular dp/dt at all levels of developed pressures during isovolumic contraction. The left ventricular pressure at the end of isovolumic systole, i.e., at the onset

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pressure of 40 mm Hg is evident. For comparison of the effect of increasing preload with that of altering contractility on the relation between dp/dt and pressure, the averages of the norepinephrine and acetylsystrophanthidin studies depicted in figures 3B and 4B are also shown in figure 8. These two interventions increased dp/dt at a pressure of 40 mm Hg by 750 mm Hg/sec, an extent equal to that produced by an elevation of left ventricular end-diastolic pressure of approximately 10 mm Hg.

Clinical Studies

In any given patient, measurements of the relation between dp/dt and developed pressure throughout isovolumic systole were highly reproducible during the control periods. The deviation of the four separate measurements of dp/dt at peak isovolumic pressure averaged 0.9% of the mean value in the eight patients studied.

Leg Raising

In the six patients in whom leg raising was carried out, the left ventricular end-diastolic
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Effects of norepinephrine and acetylstrophanthidin (ACS) on the ratio of LV dp/dt to the highest common developed isovolumic pressure (CPIP) in the open-chest anesthetized dogs. (Cross-hatched bars) Average control values. (Open bars) Average increments produced by the two inotropic agents.

pressure was augmented by between 4 and 17 mm Hg (average, 8 mm Hg). The relationship between dp/dt and the simultaneously developed pressure throughout isovolumic systole was not affected significantly by leg raising. Similarly, there was no significant elevation of the ratio (dp/dt)/CPIP, which averaged 29.8 ± 3.2 sec⁻¹ prior to and 30.8 ± 3.0 sec⁻¹ following leg raising (figs. 9 and 10).

Methoxamine

In the five patients who received methoxamine, the systolic brachial arterial pressure was elevated by an average of 23 mm Hg (range, 16–34 mm Hg), while the diastolic brachial arterial pressure rose by an average of 13 mm Hg (range, 5–20 mm Hg). These increments of arterial pressure were accompanied by elevations of left ventricular end-diastolic pressure, which averaged 4 mm Hg and ranged from 3 to 6 mm Hg (fig. 9). This intervention did not alter the relation between dp/dt and the simultaneously developed pressure throughout isovolumic systole (figs. 9 and 11), or the ratio (dp/dt)/CPIP, which averaged 31.1 ± 3.8 sec⁻¹ prior to and 31.6 ± 4.0 sec⁻¹ after methoxamine was administered (P > 0.1).

Isoproterenol

In contrast to leg raising or methoxamine infusion, interventions that elevated preload and afterload, the administration of isoproterenol to five patients elevated dp/dt at any given pressure throughout isovolumic systole (fig. 12). Also (dp/dt)/CPIP rose significantly (P < 0.01), from 31.2 ± 3.2 sec⁻¹ to 44.0 ± 4.5 sec⁻¹ (figs. 9 and 12). These changes were associated with small declines of left ventricular end-diastolic pressure, which averaged 3 mm Hg and ranged between 2 and

Figure 5

Effects of increasing aortic diastolic pressure on the relation between developed pressure and left ventricular dp/dt during five individual contractions in an open-chest dog. Left ventricular end-diastolic pressure (LVED) was maintained relatively constant, and aortic diastolic pressure varied between 25 and 127 mm Hg. The vertical arrows on each curve represent the end of isovolumic contraction, i.e., the onset of ejection.

Ao dist. press. = aortic diastolic pressure in mm Hg; Peak LV Pr = peak left ventricular pressure in mm Hg; SV = stroke volume in ml.
Effects of varying left ventricular end-diastolic pressure on the relation between developed pressure and LV dp/dt while heart rate, aortic pressure, and stroke volume were maintained constant. The arrows indicate the termination of isovolumic contraction.

6 mm Hg (fig. 9), and with slight decreases in arterial diastolic pressure, which averaged 8 mm Hg and ranged from 2 to 16 mm Hg.

Exercise
In the seven patients in whom the effects of supine leg exercise were studied, dp/dt at any pressure throughout the period of isovolumic contraction rose significantly (P < 0.01), while (dp/dt)/CPIP increased strikingly, from 29.6 ± 2.1 sec⁻¹ to 41.8 ± 5.0 sec⁻¹ (fig. 9). These changes occurred while left ventricular end-diastolic pressure rose by an average of 3 mm Hg.

Discussion
Although in the past considerable attention has been focused on the influence of variations in preload on indices of cardiac contractility,⁸,¹⁰,¹⁸ the effects of alterations of arterial pressure have not been clearly defined. It is clear from this study, as well as from previous studies,⁸,⁹ that although peak ventricular dp/dt is exquisitely sensitive to changes in the inotropic state, it also can be affected to some degree by alterations of arterial diastolic pressure, which is a function of ventricular afterload and, therefore, of the peripheral vascular bed. Unless diastolic pressure is markedly elevated, peak dp/dt usually occurs at the instant of opening of the semilunar valves in ejecting beats.¹⁰ Under these circumstances, simple elevation of arterial diastolic pressure, unassociated with a change of contractility, raises peak dp/dt, while a decrease in arterial diastolic pressure lowers it (fig. 6). Therefore, only when peak dp/dt occurs before the onset of ejection is it independent of afterload.

The major finding of this investigation was that the relation between the instantaneous dp/dt and the simultaneously developed ventricular pressure during isovolumic systole...
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Average results (±SEM) in patients of the relation between left ventricular end-diastolic pressure and the ratio of dp/dt and the highest common developed isovolumic pressure (CPIP) during a control period and during each of the four interventions indicated. n = number of patients studied.

reflects the contractile state of the myocardium and is independent of the arterial pressure. In the isolated cat papillary muscle preparation, which contracted in an afterloaded, isotonic manner, the relation of dT/dt to the simultaneously developed tension was not influenced by alterations of the afterload during isometric contractions or of the isometric portion of afterloaded isotonic contractions. However, with an increase of preload, i.e., resting initial muscle length, dT/dt at any given level of tension did rise very slightly (fig. 1A). In contrast, dT/dt at any given level of tension was markedly elevated by the positive inotropic actions of norepinephrine and paired electrical stimulation (figs. 1B and 1C). Thus, in the isolated papillary muscle, the rate of isometric force development at any given level of tension was particularly sensitive to the inotropic state, not a function of afterload, and affected only slightly by changes in preload.

These observations were then extended to the left ventricle of the dog with a controlled circulation. In the right heart bypass preparation with left ventricular end-diastolic pressure (preload) held constant, large variations of aortic diastolic pressure (afterload) had little influence on the relation between dp/dt and the simultaneously recorded pressure throughout isovolumic contraction (fig. 6). When end-diastolic pressure was changed, the relation between dp/dt and developed pressure during isovolumetric contraction rose moderately (fig. 7), as did the dp/dt at a common peak isovolumetric pressure, (dp/dt)/CPIP. In contrast, the positive inotropic agents, norepinephrine and acetylcholine, produced marked elevations of dp/dt at any given pressure throughout isovolumic contraction and raised the ratio (dp/dt)/CPIP (figs. 3-5). On occasion, these differences in dp/dt were not evident at very low isovolumic pressures (fig. 3B). Since increases in preload and administration of the inotropic agents had similar qualitative effects on this ratio, a quantitative comparison of these interventions was carried out; it was observed

Figure 9

(Top) Simultaneous recording of the left ventricular (LV) pressure pulse, its first derivative (dp/dt), the brachial arterial pressure (BA), and electrocardiogram during the control period (A) and during leg raising (B). The measurements of dp/dt indicated are at the highest common developed isovolumic pressure (CPIP). EDP = LV end-diastolic pressure; D = peak isovolumic LV pressure. (Bottom) Relation between LV dp/dt and developed isovolumic pressure at 5-msec intervals throughout isovolumic systole of the contractions shown in the top panel in the control period (cont.) and during leg raising (L.R.). The arrows indicating CPIP of both curves are the points at which the ratio (dp/dt)/CPIP was calculated.
that the changes produced by norepinephrine and acetylstrophanthidin were far greater than those produced by moderate elevations of ventricular end-diastolic pressure (fig. 8). Moreover, the alterations in end-diastolic pressure usually produced by the changes in contractile state in the intact organism tend to exert an opposing effect on the (dp/dt)/CPIP ratio. Thus, an increase in the ratio in the presence of a decrease in left ventricular end-diastolic pressure clearly reflects an increase in contractile state. These observations in the open-chest anesthetized dog were consistent with those made on isolated myocardium, and these studies were then extended to the assessment of myocardial contractility in patients.

Methoxamine, an alpha-adrenergic stimulant which has no direct effect on myocardial contractility, elevated arterial pressure and tended to raise ventricular end-diastolic pressure. However, it did not alter the relation between dp/dt and the simultaneously developed ventricular pressure throughout isovolumic contraction, nor did it alter the ratio (dp/dt)/CPIP (figs. 9 and 11). Similarly, significant elevations of left ventricular end-diastolic pressure produced by leg raising had little effect on those indices (figs. 9 and 10). Indeed, in these clinical studies, alterations of preload appeared to exert substantially less influence on the relation of dp/dt to the simultaneously occurring pressure during isovolumic contraction than it did in the canine heart. The explanation for this difference is not clear. Perhaps some of these patients had residual ventricular hypertrophy and reduced ventricular compliance, leading to disproportionately marked elevations of ventricular end-diastolic pressure accompanying only small increases of end-diastolic volume; i.e., perhaps the changes in preload induced were smaller than suggested by the elevations of left ventricular end-diastolic pressure. Alternatively, reflex withdrawal of sympathetic stimulation of the heart may have occurred as an indirect consequence of increased preload and the resultant elevation of arterial blood pressure, while these reflex mechanisms might have been attenuated in the open-chest anesthetized dog.

Relation between left ventricular dp/dt and developed isovolumic ventricular pressure before and after methoxamine (Meth.) administration. For explanation, see figure 10.

Relation between left ventricular dp/dt and developed isovolumic ventricular pressure before and after isoproterenol (Iso.) administration. For explanation, see figure 10.
In contrast to the minor influence of alterations of arterial diastolic pressure and of ventricular end-diastolic pressure on the relation between dp/dt and the simultaneously occurring pressure during isovolumic contraction, was the striking alteration of this relation in response to the beta-adrenergic stimulant, isoproterenol. Thus, there was considerable elevation of this relation (fig. 12) as well as the ratio (dp/dt)/CPIP (fig. 9). Consistent with the observation that these indices are highly sensitive to changes in contractility is the finding that they were also increased during exercise (fig. 9), in which adrenergic stimulation of the myocardium occurs.\(^{30}\)

In this study, developed pressure was used in the relation of dp/dt to isovolumic ventricular pressure (figs. 3, 4, 6, 7, and 10–12) and in the ratio (dp/dt)/CPIP (figs. 5 and 9–12). When total isovolumic pressure was employed, dp/dt and, thereby, (dp/dt)/CPIP were altered to a slightly lesser extent with changes in preload, and they were also less sensitive in absolute terms to inotropic interventions. Since total isovolumic pressure is the sum of developed pressure and end-diastolic pressure, a progressive elevation of preload with inotropic state constant results in a larger rise of dp/dt when developed pressure, rather than total pressure, is employed for the dp/dt–isovolumic pressure relationship (figs. 7 and 8). Concerning changes in contractility at any level of developed pressure compared to the corresponding higher total pressure occurring at the same initial dp/dt, a given enhancement of contractility (equal rise in dp/dt) at constant preload, produces the same relative increase of (dp/dt)/CPIP but greater absolute elevation of this ratio with CPIP as developed pressure instead of total pressure.

In the application of this method to the assessment of cardiac contractility, it is essential that the intraventricular pressure be recorded by high-fidelity recording techniques—either a catheter tip manometer or a short catheter or needle attached directly to a manometer. Standard cardiac catheter-manometer systems are not believed to be suitable for this type of analysis.\(^{6–8}\)

In calculating (dp/dt)/CPIP, it is important to point out that the dp/dt used in this ratio is that which occurs simultaneously with CPIP and is not necessarily the peak dp/dt. For example, in figure 12, the relation between dp/dt and developed ventricular pressure in a single patient is shown during isovolumic contraction in a representative systole in both the control period and following isoproterenol administration. Since the CPIP was 70 mm Hg, the dp/dt employed in the calculation (dp/dt)/CPIP in the control state was 1760 mm Hg/sec, a value which was substantially less than the peak dp/dt in this beat.

In conclusion, these investigations on isolated mammalian myocardium, on the open-chest canine heart, and on conscious patients demonstrate that the relation between the rate of pressure rise and the simultaneously occurring pressure during isovolumic contraction is not altered by acute changes in afterload. In contrast, dp/dt at any given level of pressure during isovolumetric contraction and the ratio (dp/dt)/CPIP are markedly sensitive to changes in the level of inotropic state. Although these indices are influenced to some extent by large changes in preload, when the latter are minimized they do provide an accurate method for the assessment of myocardial contractility. Finally, it is important to emphasize that this study demonstrates the validity and usefulness of the ratio (dp/dt)/CPIP in the quantification of changes in contractile state in which each heart serves as its own control. This method in its present framework is of limited value in comparisons of basal levels of contractility of different ventricles.

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