Influence of Cardiac Sympathetic and Vagal Nerve Stimulation on the Relation Between Left Ventricular Diastolic Pressure and Myocardial Segment Length

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That the catechol amines or cardiac sympathetic nerve stimulation will increase the vigor of ventricular contraction has been established.1-8 Further, it is now known that the ventricle will contract more forcefully from any given filling pressure under these influences.6-8 The early studies of Anrep1 and other more recent studies5-10 indicate that a changed myocardial extensibility cannot, of itself, account for the increased ventricular contraction. However, whether or not the augmented stroke work is produced solely by a more forceful contraction from a given diastolic ventricular fiber length, or whether changes in the relation between ventricular diastolic pressure and fiber length contribute to the observed augmentation, has not been established. The development of a technic which makes it possible to examine the relation between left ventricular diastolic pressure and myocardial segment length facilitated a study of this problem.11 Also the effect of vagal efferent stimulation on the relation between left ventricular diastolic pressure and segment length was investigated. A preliminary report of this work has appeared.12

Methods

The changes in length of a segment of left ventricular myocardium were measured simultaneously with ventricular pressure during diastole.11 The measurements were made over a wide range of pressures so that curves relating left ventricular diastolic pressure and myocardial segment length could be plotted (pressure-length curves). This relation was examined before and during sympathetic or parasympathetic stimulation, both at a point after a period of slow filling (diastasis) and at the end of diastole.

Experiments were performed on mongrel dogs of both sexes weighing 11.0 to 23.0 Kg. The anesthesia, instruments used, and technics of measurement employed were the same as those described elsewhere in this issue11 with the following additions:

The rami to the left stellate ganglion were sectioned, care being taken to leave the connections to the heart undisturbed. Both vagi were sectioned in the neck. The left stellate ganglion and the peripheral end of one vagus nerve were each placed in a bipolar electrode connected to a Grass impulse generator. The parameters of the stimulus to each nerve were adjusted to yield the desired intensity of response. The heart was paced from a third Grass impulse generator by means of 2 small electrodes attached to an atrial appendage.

Data for a control pressure-length curve were first obtained and the procedure was then repeated during stimulation of either the stellate ganglion or the vagus nerve. In some instances, data for poststimulation control curves were also obtained. Data for pressure-length curves were obtained, both with a large, single, rapid infusion and with smaller, stepwise infusions.

In some experiments, in order to ensure that the relation between ventricular diastolic pressure and myocardial segment length was being examined at or near an equilibrium state (during diastasis), it was desirable to have a slow heart. Three technics were used for inducing bradycardia.11

Results

Stellate Ganglion Stimulation

Effect of Stellate Ganglion Stimulation on Ventricular Diastolic Pressure and Myocardial Segment Length

Figure 1A shows that the decrease in ventricular diastolic pressure produced by stellate ganglion stimulation is associated with decreased diastolic myocardial segment length. Left atrial pressure fell and aortic pressure rose. This concomitant change in segment length, ventricular diastolic pressure, and...
AUTONOMIC INFLUENCE ON PRESSURE-LENGTH CURVE

Figure 1A
LA = left atrial pressure; Ao = aortic pressure; LV-D = left ventricular diastolic pressure; M.S.L. = myocardial segment length; + = elongation; − = shortening. Full-scale deflection represents about 8 mm. change in length of myocardial segment. Atrium paced at 162/min. Panel at left is control tracing at 1.00 mm./sec. At middle of center panel, left stellate ganglion was stimulated; tracing at 2.5 mm./sec. Panel at right is 100 mm./sec, tracing taken during stellate stimulation.

atrial pressure, was consistent and was repeatedly observed in 28 dogs. During these experiments, a constant heart rate was maintained; it was of interest that the rate of development of ventricular pressure was increased and the duration of ventricular ejection diminished, thereby resulting in a lengthening of diastole during stellate ganglion stimulation.

Observations during Stellate Ganglion Stimulation When Ventricular Diastolic Pressure Is Restored to the Control Level by Infusion

The results of one such experiment are shown in figure 1B. Stellate stimulation, applied between the left and middle panels of figure 1B resulted, as noted above, in a parallel decrease of ventricular diastolic pressure and segment length. While the stellate stimulation was maintained, blood was then infused in such amounts as to restore the ventricular diastolic pressure to its previous level; myocardial segment length thereupon returned to its control value (fig. 1B, right panel).

Diastolic Pressure-Length Curves (Diastasis Points)

Figure 2 shows tracings from an experiment in which a rapid infusion was made while changes in ventricular diastolic pressure and segment length were recorded in a dog with heart block. The top segment of figure 2 is the control tracing; the bottom segment shows the tracing obtained during stellate stimulation.

Experiments comparing pressure-length curves before and during left stellate ganglion stimulation were done 30 times in 11 dogs. Of these experiments, 21 were done with the rapid infusion technic shown in figure 2. Of these rapid infusion experiments, 3 were done in dogs with A-V heart block, 18 were with the marked bradycardia or asystole produced by vagal stimulation. Nine pressure-length curve comparisons were made with the stepwise infusion sequence. Of these, 6 were made in dogs with intact conduction systems and 3 were made in dogs with A-V heart block. Figure 3 contains 6 curves showing the type of result obtained. In no instance did left stellate ganglion stimulation produce a change in the ventricular pressure-length relation under the experimental conditions used.

End-Diastolic Pressure-Length Curves

Eight experiments were done in which the sino-atrial node was crushed but neither heart block nor vagal stimulation was used to slow the heart. Left ventricular end-diastolic pressures were plotted against end-diastolic segment lengths before and during stellate ganglion stimulation. The results from 4 such experiments are shown in figure 4. In 7 of the 8 experiments, no change was observed in the curve as a result of stellate stimulation; in the eighth experiment the changes were equivocal.
Figure 2
Bradycardia and 2:1 heart block induced by distal vagal stimulation and kept constant throughout entire experiment. Upper panel is record taken during rapid infusion before stellate stimulation. Lower panel is record taken during rapid infusion while stellate stimulation is applied.

Effect of Stellate Ganglion Stimulation on the Relation between Ventricular Pressure and Myocardial Segment Length at Various Times during Diastole

It was consistently observed that, at any given heart rate, stellate stimulation provided for the earlier onset of ventricular relaxation as the result of a shortened systole, as seen in figures 1 and 6. Such sympathetic activity thus allowed a longer interval for ventricular relaxation to become complete before the onset of the ensuing systole. Figure 5 shows data from an experiment which emphasizes the importance of this phenomenon. Figure 5A shows that the end-diastolic pressure-length curve was not altered by stellate stimulation as described above. Closer inspection, however, revealed certain interesting phenomena. In the absence of stellate stimulation (fig. 5B), 50 ms. prior to systole the myocardial segment was substantially shorter at any given pressure and this effect was even more marked at 70 ms. prior to the onset of systole. During stellate stimulation (fig. 5C), 50 ms. prior to the onset of systole, there was no change in the pressure-length relation and at 70 ms. prior to systole the myocardial segment was only slightly diminished in length at any given pressure. It is likely that, in this experiment, had the heart rate or stroke volume been increased or the heart further depressed to a point at which diastole was shortened by as little as 50 ms., the relation between pressure and segment length at the end of diastole would have shifted to the left (as shown in figure 5B). Subsequent stellate stimulation would have appeared to produce an increased ventricular diastolic extensibility (see Discussion), whereas in fact, by shortening systole, it simply permitted time for inertial and viscous factors to be dissipated and for relaxation to become more complete. That this is an important operative consideration is indicated by the tracings in figure 6. In this experiment, with the heart deprived of sympathetic efferents from both stellate ganglia and paced at a rate of 201/min., diastole was limited to 69 ms. out of a total cycle time of 296 ms. (fig. 6, left). Left stellate ganglion stimulation not only increased the force of contraction from a lower end-diastolic pres-
sure but doubled diastolic time, thus increasing the time available for a more complete ventricular relaxation (fig. 6, right).

Certain reservations must be attached to the data shown in figure 5. No instrumental means with which to examine the frequency response characteristics of the fully assembled lever-ventricle system is immediately available. Further, the rotational motion of the heart during ventricular systole and early diastole imposes the danger of artefact. For these reasons, the data shown in the middle panel of figure 5 must be regarded as suggestive but not conclusive.

Vagal Stimulation

Studies similar to those performed with stellate ganglion stimulation were also performed with vagal nerve stimulation. The relation between left ventricular diastolic pressure and myocardial segment length during conditions approximating an equilibrium state was studied in 16 experiments on 9 dogs. Figure 7 contains 4 curves showing the type of result obtained. In no experiment was vagal nerve stimulation observed to alter the relation between left ventricular diastolic pressure and myocardial segment length during conditions approaching an equilibrium state. In addition to the lack of vagal stimulation on ventricular myocardial extensibility, it was observed that the end-diastolic pressure-length curve was also unmodified by vagal stimulation at the heart rates studied.

Discussion

The term "extensibility," as used in this study, refers to the change in length of a segment of myocardium when subjected to stress (uniform distending pressure). It is concerned with a static property of the tissue under examination and does not vary with the rate of application of stress. We assume that an increase in the length of a segment of myocardium between the lever arms, brought about either by an increase in pressure or a change in extensibility of the tissue, would reflect directionally similar changes occurring elsewhere in the ventricular myocardium. In order to investigate effects on ventricular myocardial extensibility, left ventricular pressure was related to myocardial segment length during diastole only in states at or approaching equilibrium. Presumably, at such times, effects secondary to viscosity and inertia would not be present. The plot of left ventricular diastolic pressure against changes in myocardial segment length was used to express ventricular myocardial extensibility. Neither stellate ganglion nor vagal efferent nerve stimulation was observed to alter ventricular myocardial extensibility.

The methodology and experimental conditions used in the above studies vary substantially from those used by other workers. It may be pertinent, however, to indicate that the above findings are consonant with the studies of Lundin on isolated mammalian papillary muscle, with those of Ulrich on the isometrically contracting canine left ventricle, and with the more recent work of Rosenbluth et al. on the canine right ventricle. They are also in agreement with the
observations of Blinks, who found no change in the pressure-volume relation of isolated mammalian atria when exposed to concentrations of epinephrine which produced a marked positive inotropic effect. The results shown above appear to be at variance with the experiments of Rushmer et al., who found an increased "distensibility" during epinephrine infusion and with those of Katz et al., who suggested that norepinephrine produced an "increase in ventricular diastolic tone."

The relation between end-diastolic left ventricular pressure and segment length was also unmodified by either stellate or vagal stimulation at the heart rates studied. It must, however, be emphasized that the relation between ventricular pressure and myocardial segment length during diastole may involve other factors in addition to extensibility. If diastole is abbreviated, the relation between pressure and segment length will involve the extent to which relaxation has taken place and to which inertial and viscous factors have been dissipated. During states in which diastole is curtailed, the myocardial segment length for any given ventricular pressure may be decreased. This problem has been well formulated by Buckley et al., who described the observed phenomena in terms of mechanical impedance (ratio of ventricular pressure to ventricular inflow). In the isolated mammalian ventricle, norepinephrine was found to decrease mid-filling impedance and provide a lengthened time available for filling when impedance was at its lowest. The data shown in figures 5 and 6, wherein the observed changes were induced by stellate stimulation, are compatible with the findings of Buckley and indicate that sympathetic pathways are capable of producing the same type of change in the heart in situ.

The shortening of systole and the consequent lengthening of diastole resulting from sympathetic stimulation would appear to be of great importance at high rates and/or large stroke volumes which tend to shorten the ratio of diastole to total time. The positive inotropic effect of sympathetic efferent impulses and the consequent shortening of systole is, therefore, a most appropriate concomitant of the tachycardia induced by sympathetic chronotropic influences. This effect of sympathetic impulses provides means whereby the "normal" ventricular pressure-length relation is more likely to be retained at high heart rates. Such a view is reminiscent
of the 1920 studies of Wiggers and Katz, who found that the length of systole during accelerator stimulation and during the action of epinephrine was markedly less than that indicated by the theoretical curve for what these values should have been at the increased rates. They concluded "that the accelerator nerves have a specific effect on the ventricular musculature which operates to reduce the contraction period."

Finally, the above data indicate that, unless diastole is unduly limited, the myocardial fiber may be expected to have the same length at any given ventricular end-diastolic pressure, whether or not the positive inotropic effect of stellate ganglion stimulation is present. Under such circumstances, when the ventricle contracts more forcefully from a given pressure, it is doing so without a change in the fiber length from which the contraction begins.

**Summary**

During the continuous and simultaneous recording of left ventricular diastolic pressure and changes in the length of a segment of left ventricular myocardium it was demonstrated that neither cardiac sympathetic nor vagal efferent nerve stimulation produces a change in ventricular myocardial extensibility. It was further shown that, at the heart rates studied, autonomic nerve stimulation does not modify the end-diastolic pressure-length curve. These data indicate that, during cardiac sympathetic stimulation, the augmented ventricular stroke work from any given end-diastolic pressure is accomplished without a change in end-diastolic fiber length.

Evidence was obtained, however, which suggests that the abbreviation of diastole at high imposed heart rates or large stroke volumes may leave an inadequate time for ventricular relaxation to take place and for inertial and viscous factors to be dissipated. Under these circumstances, sympathetic stimulation, by shortening systole and thereby lengthening diastole, permits the ventricle to remain on its "normal" pressure-length curve.
curve. This component of cardiac sympathetic efferent activity is peculiarly appropriate to the tachycardia that occurs with increased sympathetic outflow to the heart.

**Summario in Interlingua**

Durante la continuo e simultanea registrazion del pression diastolico sinistro-ventriculare e del cambiamento in le longor de segmentos de myocardio sinistro-ventriculare il essesva demonstrato que ni la stimulazio del nervos cardiac sympathetic ni la stimulazio del nervos efferent vagal produce un cambiamento in le extensibilidade del myocardio ventriculare. Essess essesva demonstrato que, con le frequencia cardiac stantiale, la stimulazio del nervos autonomo non modifico le curvas termino-diastolico de pression e longor. Istes datos indican que durante un stimulatio cardiac sympathetic, le augmentato trabecto ventriculare per pulso a omne pression termino-diastolico particular es completo sin un cambiamento in le longor del fibras al termino del diastole.

Nonobstante, datos essesva obtenito que permitte la conclusion que le abbreviation del diastole a alte induente frequencias cardiac o a grande volumine per pulso potto resultar in un periodo inadequate de temporo pro le relaxation ventricular e pro le dissipatio de factoris de inertia e viscositate. Sub iste circumstantias le stimulatio sympathetic, per accurar le systole e assi allongar le diastole, permette al ventriculo remanere in su "normal" curva de pression e longor. Istes componento de l'offerente activitate sympathetic cardiac es distinctemente associate con le tachycardia que occorre con augmentate effuxo sympathetic al cordo.

**References**


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