Duration of the Phases of Left Ventricular Systole

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The influence of hemodynamic variables on the duration of certain phases of ventricular systole has been studied by several investigators in intact animals and in isolated heart preparations. Even in isolated hearts, it is not possible to change one hemodynamic variable without inducing changes in one or more intrinsic determinants of the heart's performance. For example, augmenting stroke volume at constant aortic pressure increases ventricular end-diastolic pressure and fiber length. Similarly, changes of aortic pressure or heart rate are each accompanied by adjustments of myocardial contractility. We felt, however, that a systematic analysis of the effects of changing selected hemodynamic variables on the duration of each phase of left ventricular systole might help to characterize further the intrinsic mechanisms of cardiac adaptation. This report describes the effects of altering separately stroke volume, mean aortic pressure and heart rate on the duration of left ventricular isovolumic contraction, ejection and total systole. The effects of digitalization and norepinephrine infusion are also described.

Methods

Mongrel dogs weighing from 16 to 28 kg were anesthetized with a mixture of chloralose (60 mg/kg) and urethane (600 mg/kg) given intravenously. Coagulation was prevented by an initial dose of 75 mg of heparin followed by 10 mg doses hourly. Respiration was maintained by a Starling Ideal pump.

The chest was entered through a transverse incision in the fourth or fifth intercostal space. The pericardium was opened and used to support the heart. A right heart by-pass was established as shown in figure 1. All venous blood was led from the right atrium (RA) and right ventricle (RV) to a reservoir (Res) by a large multiholed cannula introduced through the right atrial appendage. Blood was pumped by a roller pump from the reservoir through a bubble trap and heat exchanger and returned to the main pulmonary artery. The return cannula was introduced through the right ventricular outflow tract and tied securely by a tape previously passed around the main trunk of the pulmonary artery. Inferior to the pulmonary artery (cardiac output) was measured by a Potter electrodinamometer (Ptd) and could be controlled by adjusting pump rate. The temperature of blood entering the pulmonary artery was maintained between 36° and 38°C.

Central aortic pressure was measured through a short metal sound introduced in the left subclavian artery. Mean aortic pressure could be controlled by adjusting a mechanical resistance (M.R.) on an aortic by-pass or by varying the resistance on a shunt (A.V.S.) between the aortic by-pass and reservoir. Left ventricular pressure was measured through a sound introduced through the apical dimple. Left atrial pressure was also measured. All sounds were connected to Statham strain gauge transducers. The dynamic response of the aortic and ventricular pressure recording systems was linear from 0 to 30 c.p.s. The heart was paced with a bipolar electrode sutured to the right atrium using a Grass (model S4) impulse generator. Records were taken on a Sanborn direct-writing oscillograph at a paper speed of 100 mm/sec. Respiration was stopped for five to ten seconds while records were taken.

Immediately prior to each study ganglionic blockade was induced with mecamylamine (10 mg/kg). Blockade was verified by observing the fall of spontaneous heart rate after the drug, and the absence of reflex tachycardia or increased blood pressure when the head was subsequently rendered ischemic by ligation of the brachial artery. Both vagi were cut. In some animals the sinoatrial node was crushed in order to obtain slower heart rates.

Definitions

Duration of total left ventricular systole is defined as the interval between the onset of left ventricular pressure rise and the incisural notch of the aortic pressure pulse. This interval includes the period of protodiastole. Ejection duration is defined by the interval between the onset of aortic pressure rise and the incisural notch. Isovolumic
systole is measured from the onset of left ventricular pressure rise to the onset of aortic pressure rise. Each interval was measured to the nearest .005 second and measurements of two to four consecutive cardiac cycles were averaged.

Results

A. Effect of Changing Stroke Volume (see table I). In ten animals the effect was observed of augmenting stroke volume and thus left ventricular end-diastolic pressure on the duration of the phases of left ventricular systole. Heart rate and mean aortic pressure were held constant; aortic systolic pressure rose while aortic diastolic pressure fell. In six experiments no change or a decrease of the duration of left ventricular systole occurred over the range of stroke volumes studied. In four experiments the duration of systole increased 5 to 10 msec. In all studies the duration of ejection increased as stroke volume was augmented and the duration of isovolumic contraction decreased. The reduced duration of isovolumic systole occurred whether or not there was a major fall of aortic diastolic pressure.
DURATION OF THE PHASES OF LEFT VENTRICULAR SYSTOLE

TABLE 1*

<table>
<thead>
<tr>
<th>Stroke volume (10)</th>
<th>5-10 (1)</th>
<th>11-15 (1)</th>
<th>16-20 (8)</th>
<th>21-25 (10)</th>
<th>26-30 (16)</th>
<th>31-35 (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke volume (10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>155 ± 6</td>
<td>155 ± 6</td>
<td>156 ± 6</td>
<td>156 ± 6</td>
<td>156 ± 6</td>
<td>156 ± 6</td>
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<tr>
<td>W</td>
<td>124 ± 6</td>
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<td>124 ± 6</td>
<td>124 ± 6</td>
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<td>124 ± 6</td>
</tr>
<tr>
<td>I</td>
<td>31 ± 6</td>
<td>31 ± 6</td>
<td>31 ± 6</td>
<td>31 ± 6</td>
<td>31 ± 6</td>
<td>31 ± 6</td>
</tr>
</tbody>
</table>

Aortic pressure (12)

Composite data summarizing the effects of changing stroke volume (upper), mean aortic pressure (middle) and heart rate (lower) on the duration of total systole (S), ejection (E) and isovolumic systole (I). The number of animals studied is indicated in parenthesis beside each variable. Under each variable the mean ± standard error is given for each measurement in each group.

A tracing illustrating the effect of augmenting stroke volume on left ventricular diastolic and aortic pressure pulses is illustrated in figure 2 (upper) and data from a representative experiment are graphed in figure 3 (left).

B. Effect of Changing Mean Aortic Pressure (see table 1). The effect of elevating mean aortic pressure on the duration of the phases of systole was examined in sixteen experiments on eight animals. Heart rate and stroke volume were held constant. In seven experiments, elevation of aortic pressure had no measurable influence on the duration of total systole. In nine experiments systole shortened by 5 to 38 msec. The duration of ejection decreased and the duration of isovolumic contraction increased in all animals as aortic pressure was elevated. Ventricular end-diastolic pressure showed little or no change. A tracing illustrating the effect of elevating mean aortic pressure on left ventricular diastolic and aortic pressure pulses is presented in figure 2 (middle) and data from a representative experiment are graphed in figure 3 (middle).

Two experiments were performed after giving DCI* (10-20 mg/kg), an agent which blocks the positive inotropic and chronotropic effects of noradrenaline on the heart.7 8 The response to elevating aortic pressure in these two animals did not differ qualitatively or quantitatively from the other experiments.

C. Effect of Changing Heart Rate (see table 1). The effect of increasing heart rate on

*Additional tabular data summarizing results from each experiment may be obtained from the authors.

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FIGURE 2

Tracings demonstrating the influence of independently changing stroke volume, mean aortic pressure and heart rate on the durations of the phases of systole. AP = aortic pressure. LVD = left ventricular diastolic pressure. (Upper). (A) stroke volume = 10.8 ml. (B) stroke volume = 20.5 ml. (C) stroke volume = 29.0 ml. (D) stroke volume = 39.0 ml. Mean aortic pressure constant at 105 mm Hg and heart rate constant at 131.

(Middle). (A) Mean aortic pressure = 55 mm Hg. (B) Mean aortic pressure = 77 mm Hg. (C) Mean aortic pressure = 110 mm Hg. (D) Mean aortic pressure = 132 mm Hg. Heart rate constant at 118. Stroke volume constant at 16 ml. (Lower). (A) Heart rate = 100. (B) Heart rate = 158. (C) Heart rate = 187. (D) Heart rate = 222. Mean aortic pressure constant at 100 mm Hg and stroke volume constant at 15 ml.
The duration of the phases of left ventricular systole was examined in ten experiments on seven animals. Mean aortic pressure and stroke volume were maintained constant. In all animals increasing heart rate resulted in a decrease of both the duration of total systole and ejection. The period of isovolumic contraction also shortened in the majority of experiments. Left ventricular end-diastolic pressure changed only slightly as heart rate was increased. Similar findings were noted in two animals after giving DCI. The effect of increasing heart rate on aortic and left ventricular diastolic pressure pulses is illustrated in figure 2 (lower) and the graphed data from a representative experiment shown in figure 3 (right).

D. Effect of Sympathomimetic Amines. In six animals the effect of a continuous infusion of norepinephrine (3 to 10 μg/min) was observed while mean aortic pressure, stroke volume and heart rate were maintained constant. In each animal norepinephrine reduced left ventricular end-diastolic pressure and shortened all phases of ventricular systole. A representative experiment is shown in figure 4 (upper).

The duration of the isovolumic period is the difference between total systole and ejection.

E. Effect of Cardiac Glycosides. Five animals were digitalized with acetyl strophanthidin (332 to 500 μg) injected into the pulmonary artery cannula. Ventricular end-diastolic pressure fell consequent to the glycoside action while stroke volume, heart rate and mean aortic pressure were held constant. In all animals the durations of total systole and ejection were reduced. Isovolumic contraction shortened in three of five experiments. See figure 4 (lower).

Discussion

The results of this investigation emphasize three aspects of left ventricular contraction. First, changes of considerable magnitude can occur in the duration of the isovolumic period. Second, it is evident that changes of the duration of ejection are not always paralleled by quantitatively, or at times even qualitatively, similar changes of total systole. Finally, as a result of elevating aortic pressure, and as a result of increasing heart rate the ventricle alters its performance characteristics to eject the same stroke volume from the same end-diastolic pressure in a substantially shorter period of time.

The major effects of augmenting stroke vol-
FIGURE 4
(Upper). Influence of norepinephrine (10 gamma/min infusion) on the duration of each phase of systole. AP = aortic pressure. LVD = left ventricular diastolic pressure. Mean aortic pressure constant at 100 mm Hg, heart rate constant at 162, stroke volume constant at 15 ml. Panel (A) Control. Duration of ejection = 150 msec. Duration of systole = 220 msec. Isovolumic systole = 70 msec. Panel (B) Norepinephrine. Duration of ejection = 130 msec. Duration of systole = 370 msec. Isovolumic systole = 60 msec. (Lower). Influence of acetyl strophanthidin (500 gamma) on the duration of each phase of systole at constant mean aortic pressure of 100 mm Hg, constant heart rate of 162, constant stroke volume of 15 ml. Panel (A) Control. Duration of ejection 138 msec. Duration of systole 208 msec. Isovolumic systole 70 msec. Panel (B) acetyl strophanthidin. Duration of ejection 115 msec. Duration of systole 275 msec. Isovolumic systole 60 msec.

The duration of total systole did not change in the majority of studies. Frank first suggested a relation between stroke volume and...
the duration of the phases of systole. He demonstrated in the frog heart that augmentation of filling prolonged ejection, shortened the strain (isovolumic) phase, and delayed aortic valve closure. These results were later confirmed by Peserico in the turtle heart, by Katz in the isolated dog heart, and by Wiggers in the intact dog. The observations reported in this paper support the view that augmenting stroke volume prolongs ventricular ejection. In contrast to previous reports, we have found that alterations of stroke volume had no consistent effect on the duration of total systole; the prolongation of ejection was accompanied by an equal, but opposite change of the isovolumic phase. The data of Wiggers, indicating that total systole lengthened when stroke volume was augmented may have resulted from reflex withdrawal of cardiac sympathetic tone, since arterial pressure was allowed to increase in the presence of intact baroreceptors. In the isolated heart, Katz also concluded that augmented filling prolonged total systole. He noted, however, that prolongation of total systole was always small compared to the simultaneous lengthening of the ejection phase and commented that in several animals practically no change of the duration of total systole occurred.

The effects of elevating aortic pressure at constant heart rate and stroke volume were to decrease left ventricular ejection time and to prolong isovolumic contraction. Total systole either did not change or decreased. Frank found similar effects in the frog. He noted that raising aortic resistance prolonged the strain phase, shortened ejection and had little effect on the time of aortic valve closure. Peserico noted that when aortic pressure was increased the duration of systole was reduced. Wiggers reported variable results depending on the method employed to increase aortic resistance. His experiments are difficult to compare to those reported in this paper, since heart rate and stroke volume were not controlled and since reflex alterations of sympathetic tone to the heart were not excluded. In a separate publication, however, Wiggers and Katz were obviously impressed with the finding that when aortic resistance was increased by clamping the aorta above the diaphragm, the duration of ejection decreased despite the same or even a greater stroke volume.

The decreased duration of ejection when aortic pressure was elevated occurred without a necessary increase of ventricular end-diastolic pressure (fig. 3, middle). Further, the decreased duration of ejection was seen after dichloroisoproterenol, and has been noted in other experiments when left coronary flow was maintained constant. These findings demonstrate that the shortening of the ejection period when aortic pressure is elevated does not result from a longer ventricular end-diastolic fiber length nor from an increased delivery of catecholamines to myocardial receptor sites. Also it is not dependent on an increase of coronary flow. The fact that the duration of ejection is reduced is consistent with the finding that myocardial contractility is augmented by elevating aortic pressure and supports the concept of homeometric autoregulation. According to that concept when the amount of tension the ventricle is required to develop per unit of time is increased, an increased contractility ensues.

Increasing heart rate at constant mean aortic pressure and stroke volume shortened the duration of total systole as well as the duration of ejection. The period of isovolumic contraction was also reduced. These observations confirm the findings of Braunwald et al., concerning the effect of heart rate on the duration of ejection. The increased contractility of the ventricle which results from a more rapid heart rate is another aspect of homeometric autoregulation and is an expression of the classical "trappe" seen in isolated cardiac muscle. This mechanism enables the heart to accomplish more work from a given end-diastolic pressure than if this type of autoregulation had not occurred. It has been shown that the mean rate of pressure rise during isovolumic systole, mean rate of ejection and stroke power are all increased at...
rapid heart rates. The maximal rate of rise of ventricular pressure is also increased by increasing heart rate. Thus, homeometric autorregulation not only enables the heart to eject the same stroke volume and to accomplish the same stroke work, but also confers upon it the capability of doing this work in a shorter period of time. These data are consonant with those concerning the influence of rate on isolated cardiac muscle.

The demonstration that stroke volume and heart rate are separate determinants of the duration of ejection in isolated preparations has been extended to intact man. Weissler et al. have shown in resting subjects that the duration of ejection decreased linearly as heart rate was increased, and increased linearly as stroke volume was augmented. By means of multiple regression analysis it was concluded that the heart rate and stroke volume were separate factors which influenced the duration of ejection in normal individuals.

Previous studies have indicated that catecholamine administration, direct stimulation of cardiac sympathetic nerves, and administration of digitalis, each shortens certain of the phases of systole. These findings have been confirmed in this study under more controlled conditions. Acetyl strophanthidin and norepinephrine are known to increase myocardial contractility. Each of these agents shortens the durations of isovolumic systole, ejection and total systole. The shortening of all phases of systole by both agents suggests that a feature common to their inotropic action is an increased velocity and a decreased duration of contraction. This suggestion is consonant with the findings that norepinephrine and other positive inotropic agents increase the maximal velocity of shortening and decrease the time to peak tension in the papillary muscle.

Wiggers' observations support the suggestion that the duration of isovolumic contraction is primarily dependent on the end-diastolic ventricular pressure and aortic diastolic pressure. Our data concerning the effect of augmenting stroke volume at constant mean aortic pressure as well as the effect of elevating aortic pressure at constant stroke volume are consistent with that hypothesis. Nevertheless, when stroke volume and aortic pressure were held constant, positive inotropic influences such as increasing heart rate, acetyl strophanthidin and norepinephrine each substantially shortened the isovolumic period.

**Summary**

The effects of altering stroke volume, aortic pressure and heart rate on the duration of each phase of left ventricular systole were investigated in a denervated dog heart.

Augmenting stroke volume was found to prolong ejection, shorten the isovolumic period and had little or no effect on the duration of total systole. Elevating mean aortic blood pressure shortened ejection time, prolonged the isovolumic phase and either had no effect or decreased slightly the duration of total systole. Increasing heart rate at constant aortic pressure and stroke volume reduced the duration of all phases of systole. Digitalis and norepinephrine shortened all phases of systole.

These findings demonstrate that the duration of each phase of left ventricular systole is dependent upon existing hemodynamic conditions as well as on the contractile state of the myocardium. By means of intrinsic mechanisms the ventricle exhibits the remarkable capability of being able to adjust the duration of each phase of systole in a manner appropriate to changing hemodynamic conditions.

**Acknowledgment**

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**References**

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