Reduction in Baroreflex Cardiovascular Responses Due to Venous Infusion in the Rabbit

HENRY O. STINNETT, PH.D., VERNON S. BISHOP, PH.D., AND D. FRED PETERSON, PH.D.

SUMMARY We studied reflex bradycardia and depression of mean arterial blood pressure (MAP) during left aortic nerve (LAN) stimulation before and after volume infusion in the anesthetized rabbit. Step increases in mean right atrial pressure (MRAP) to 10 mm Hg did not result in a significant change in heart rate or MAP. After volume loading, responses to LAN stimulation were not as great and the degree of attenuation was proportional to the level of increased MRAP. A change in responsiveness was observed after elevation of MRAP by only 1 mm Hg, corresponding to less than a 10% increase in average calculated blood volume. After an increase in MRAP of 10 mm Hg, peak responses were attenuated by 44% (heart rate) and 52% (MAP), and the initial slopes (rate of change) were reduced by 46% (heart rate) and 66% (MAP). Comparison of the responses after infusion with blood and dextran solutions indicated that hemodilution was an unlikely explanation for the attenuation of the reflex responses. Total arterial baroreceptor denervation (ABD) abolished the volume-related attenuation of the cardiovascular responses, whereas attenuation was still present following bilateral aortic nerve section or vagotomy. It thus appears that the carotid sinus responds to changes in blood volume and influences the reflex cardiovascular responses to afferent stimulation of the LAN. On the other hand, cardiopulmonary receptors subserved by vagal afferents do not appear to be involved.

VOLUME LOADING, sufficient to raise the venous pressure and dilate the heart, has been observed to produce striking cardiovascular responses. Since Bainbridge first reported an increase in heart rate during intravenous infusion many studies have attempted to describe the efferent pathways of reflexes originating from receptors located in the cardiopulmonary region. Still, the interaction of the low pressure cardiopulmonary receptors with the arterial baroreflex system is not clear. Under conditions of arterial baroreceptor isolation or denervation, the receptors in the cardiopulmonary region that are subserved by afferent vagal fibers have been shown to exert a restraint on the sympathetic adrenergic outflow to the peripheral vasculature in the dog and rabbit. Recently, Vatner et al. found that arterial baroreflex sensitivity in dogs is reduced as atrial pressure is increased by volume loading and suggested that the set point or gain of the arterial baroreflex system is altered during infusion. These alterations might occur at either the receptor site or in the central nervous system. Although recent evidence does suggest that reflex responses from one input are modified by other afferent inputs through integration in the central nervous system, it is unlikely that specific modification of systemic arterial baroreceptors is involved. In the dog, Gupta et al. found dramatic increases in atrial type B receptor activity with volume expansion, while observing only small changes in activity of individual aortic fibers. However, later work by Edis demonstrated that the aortic baroreceptor in the dog shows little tonic activity; consequently, in the dog, one would not expect to see large changes in aortic nerve activity with modest alterations in vascular volume. On the other hand, in the rabbit, Kumada and Sagawa found the aortic baroreceptor nerve activity recorded from multiber preparations to be proportional to modest blood pressure changes during 20% volume loading and 10% blood loss.

This study was designed to investigate the influence of volume expansion on responses to aortic nerve stimulation in the intact and selectively denervated rabbit. Heart rate and blood pressure responses were measured before and after steady state alterations in mean right atrial pressure (MRAP). The relative influence of low and high pressure receptors was examined and the threshold for atrial pressure necessary to effect altered responses was determined. The rabbit was chosen as the model for study because it has an easily identified aortic nerve which subserves only baroreceptors, and the vascular responses are well defined.

Methods

Twenty-four rabbits weighing between 1.48 and 2.23 kg were anesthetized with sodium pentobarbital (Diabutal, Diamond Laboratories), 30 mg/kg, iv, via an ear vein for...
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this study. Supplemental anesthetic was administered through a cannulated femoral vein to maintain a light level of surgical anesthesia. The descending aorta (via the femoral artery) and the right atrium (via the jugular vein) also were cannulated and connected to Statham P23Db and P23Bb strain gauges to record arterial and right atrial pressures, respectively. Heart rate was monitored through sternal needle electrodes connected to a Beckman 9847B cardiograph with parallel output signals from the arterial pressure and heart rate channels connected to a DEC PDP 8/E digital computer. A tracheostomy was performed and the rabbits were artificially ventilated by the technique published previously41 to ensure maintenance of normal blood PO2, PCO2, and pH. Through a midventral incision, the left and right aortic nerves were located in the cervical region and carefully isolated from surrounding tissue for about 1 cm.24,31 In addition, in four rabbits the vagi, and in five rabbits the carotid sinus nerves, also were carefully isolated and looped with a loose thread for identification prior to bilateral sectioning. Loss of the reflex responses due to bilateral carotid occlusion verified carotid sinus denervation.26 After carotid sinus denervation total arterial baroreceptor denervation (ABD) was considered complete when both aortic nerves also were sectioned. In all rabbits the left aortic nerve (LAN) was sectioned near the sternum and bathed in mineral oil, as previously described.34,44 The central end of the LAN was placed on a Grass SD9 stimulator. The stimulator was activated by the Schmitt trigger of the computer which was synchronized with the R wave of the electrocardiogram (ECG). Regulation of the stimulus timing and stimulus parameters, as well as continuous calculation of the length of each R-R interval and beat-to-beat mean arterial pressure (MAP), were accomplished using the computer and special computer program systems. An experimental trial consisted of: (1) 10 successive control cardiac cycles, (2) bursts of electrical stimuli coupled to each R wave of the ECG beginning with the 11th interval and continuing through 120 intervals, and (3) continuous data collection through recovery to control. Each burst of electrical stimulation was made up of 10 rectangular pulses (10 V) delivered 10 msec after the recorded R wave of the ECG. The impulse duration was 0.3 msec, the stimulus frequency was 80 Hz, and burst duration was 113 msec. For each experimental condition data from five or more trials were averaged for each rabbit. The peak change in R-R interval and blood pressure, the latencies to onset and peak responses, as well as the initial slope for each response, were calculated as previously described.48

The heart rate and blood pressure responses to LAN stimulation were studied in 14 rabbits infused with dextran in physiologic solution, 5 g/1,000 ml (dextran 40, mol wt 40,000, Pharmacia), heated at 38°C, and one rabbit was infused with whole blood from a heparinized donor. The rate of infusion through the femoral vein was adjusted to ensure a steady rise in right atrial pressure. Infusions were given over a period of 6-14 minutes. Once the MRAP had reached a predetermined level (1, 2.5, 5, or 10 mm Hg) infusion was continued at a rate necessary to maintain MRAP at that level. Trial stimulations of the LAN were initiated after heart rate and MAP reached stabilized steady state values.

Reflex responses to LAN stimulation were also studied in four rabbits which were bled after prior infusion of dextran solution. Each rabbit was bled until the volume of blood removed equaled the volume of dextran solution previously infused. In some instances, slightly more blood was withdrawn to reduce MRAP to control level (range, 0-1.5 mm Hg). In no case did the volume withdrawn plus urine volume collected during this period exceed the previously infused volume by more than 10 ml. Following each bleeding, a period of 1-2 minutes was allowed for stabilization of the rabbit's heart rate and blood pressure before further experimental trials were undertaken.

To monitor the red blood cell concentration, hematocrits were measured before and after each infusion or bleeding. In addition, urine flow and volume also were routinely monitored throughout each experiment.

Values are reported as the mean ± standard error of the mean (SEM). Statistical evaluation was made by use of the appropriate Student's t-test for paired or unpaired comparisons. P values (<0.05) were considered significant.

Results

In 14 rabbits MRAP was elevated to 5 mm Hg and in seven of these, to 10 mm Hg, using an average of 41 and 71 ml of dextran solution. This acute volume expansion did not significantly affect either heart rate or blood pressure (Table 1). Representative changes in response to LAN stimulation are shown in Figure 1 before and after step increases in right atrial pressure. The duration of stimulation used (120 cardiac cycles) previously has been shown to produce maximum heart rate and blood pressure responses.26 Note that following the increases in MRAP, the amplitude of each response was further decreased (Fig. 1). The average maximum increase in R-R interval of 45.4 ± 3.0 msec (n = 14) induced by aortic nerve stimulation was significantly reduced (P < 0.01) to 31.6 ± 4.2 (n = 14) and 25.4 ± 3.2 (n = 7) following increases in MRAP of 5 and 10 mm Hg, respectively (Fig. 2A). Similarly, for the same rabbits, the average preinfusion MAP response of -30.0 ± 2.3 mm Hg was reduced to -17.6 ± 2.4 (P < 0.005) and -14.3 ± 1.0 (P < 0.005), respectively (Fig. 2B). Neither the latency to onset (LTO) nor the latency to peak (LTP) was significantly altered for either reflex response and both were similar to those previously described.46 However, the initial slopes for both responses (Fig. 2C and D) were diminished with each increase in atrial pressure and this change, in conjunction with the lower maximum responses, would account for the essentially unchanged LTP's. The initial slope of the heart rate response decreased from 9.29 ± 0.88 msec/sec to 5.66 ± 0.84 (P < 0.01) and 5.03 ± 0.85 (P < 0.05). Similarly, the initial slope of the control MAP response, 3.68 ± 0.34 mm Hg/sec, was decreased to 2.14 ± 0.41 (P < 0.005) and 1.25 ± 0.13 (P < 0.005) by increases in MRAP of 5 and 10 mm Hg, respectively.

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TABLE 1  Responses to Volume Infusion in Rabbits with and without Vagi Intact

<table>
<thead>
<tr>
<th>Group condition</th>
<th>n</th>
<th>R-R (msec)</th>
<th>MAP (mm Hg)</th>
<th>Hct (% RBC)</th>
<th>Dextran volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vagi intact</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>14</td>
<td>233 ± 10</td>
<td>84.5 ± 6.4</td>
<td>34.9 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>ΔMRAP +5 mm Hg</td>
<td>14</td>
<td>236 ± 8</td>
<td>90.0 ± 5.7</td>
<td>22.3 ± 0.9</td>
<td>41.0 ± 2.7</td>
</tr>
<tr>
<td>Vagotomized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4</td>
<td>234 ± 10</td>
<td>83.9 ± 6.3</td>
<td>33.5 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>ΔMRAP +5 mm Hg</td>
<td>4</td>
<td>234 ± 10</td>
<td>83.9 ± 6.3</td>
<td>33.5 ± 0.4</td>
<td></td>
</tr>
</tbody>
</table>

Reflex responses also were quantitated in seven rabbits prior to and after MRAP increases of 1.0, 2.5, and 5.0 mm Hg, to estimate the threshold of the volume-loading influence. Average control heart rate and MAP, as well as LTO and LTP responses, were not found to be significantly different in these rabbits when compared to those previously studied. Progressive decreases in both average initial slope and peak change were observed for both reflex responses as MRAP was increased (Fig. 2). When MRAP was increased by 1 mm Hg there were significant changes (P < 0.05) from control averages in the maximum MAP response (-21.9 ± 2.9 mm Hg) and initial slope (2.82 ± 0.37 mm Hg/sec). The mean heart rate responses also were reduced (peak, 40.5 ± 5.0 msec; initial slope, 8.16 ± 0.94 msec/sec), but these changes were not found to be significant. However, with subsequent increases in MRAP of 2.5 and 5.0 mm Hg, the peak and initial slope for both reflex responses were significantly (P < 0.05) reduced. For an increase in MRAP of 2.5 mm Hg the maximum heart rate change was 34.0 ± 3.6 msec and the initial slope was 6.63 ± 0.99 msec/sec; comparable values for the MAP reflex change were: maximum, -18.9 ± 3.3 mm Hg, and initial slope, 2.59 ± 0.36 mm Hg/sec.

Acute volume loading alone resulted in significant hemodilution that was estimated to average a 26% and a 43% increase in vascular fluid volume when MRAP was elevated to 5 and 10 mm Hg, respectively (Table 1). To determine whether hemodilution was responsible for the attenuated responses, bleeding was performed in four rabbits in which the MRAP had first been increased to 10 mm Hg. As shown in Table 2, although after bleeding the hematocrit still was subnormal (20%) the reflex heart rate and MAP responses returned to near control values. To eliminate the dilution factor, whole blood from a donor rabbit was infused into one rabbit. The infusion alone did not alter resting heart rate or MAP. Attenuation of the peak and initial slope of the reflex responses to LAN stimulation (Fig. 3) was similar to that observed with comparable increases in MRAP during dextran infusion (Fig. 2). The similarity in LAN-induced changes in heart rate and MAP during increased MRAP with dextran or blood infusion suggests that these responses are influenced by the degree of volume loading and not the associated hemodilution.

In the dog, acute volume loading with subsequent increases in atrial pressure stimulates receptors with after-
ents in the vagus nerves. Accordingly, the reflex changes in heart rate and MAP were examined after vagotomy in four additional rabbits before and during increases in MRAP. As shown in Table 1, vagotomy alone had little effect on resting heart rate or MAP. In corroboration of previous results, vagotomy significantly increased the LTO for the reflex bradycardia from an average of 3.3 ± 0.6 (0.75 ± 0.12 sec) beats to 6.3 ± 0.3 (1.44 ± 0.20 sec), but had little effect on the LTO or reflex changes in MAP with LAN stimulation. Vagotomy also reduced the magnitude and slope of the reflex heart rate response (Fig. 2A and C). After vagotomy, increases in MRAP of 5 and 10 mm Hg attenuated the peak reflex increase in R-R interval from 33.5 ± 4.6 msec to 20.4 ± 3.5 (P < 0.05) and 10.9 ± 2.6 (P < 0.025), respectively. The reflex fall in MAP also was attenuated in the vagotomized rabbits at each level of increased MRAP (Fig. 2B) from a preinfusion average of −32.6 ± 0.9 mm Hg to −21.2 ± 1.7 (P < 0.025) and −12.9 ± 1.5 (P < 0.005), respectively. The LTO, LTP, and initial slope of the reflex changes in MAP were not significantly different when compared to the respective values from trials with the vagi intact. Thus, while the vagal efferent component of the reflex bradycardia was abolished by vagotomy, the sympathetic component remained intact. After vagotomy the reflex bradycardia mediated by the intact sympathetics, as well as the reflex fall in MAP, were attenuated in a

**Table 2** Assessment of Hemodilution on the Cardiovascular Reflex Responses to Aortic Nerve Stimulation: Volume Infusion followed by Bleeding in Four Rabbits

<table>
<thead>
<tr>
<th>Property</th>
<th>Control (MRAP ≤ 0-1 mm Hg)</th>
<th>Infusion (MRAP ≥ 10 mm Hg)</th>
<th>Bleeding (MRAP ≥ 0.0 mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct (%)</td>
<td>34.8 ± 1.0</td>
<td>13.9 ± 1.1*</td>
<td>20.0 ± 1.3*</td>
</tr>
<tr>
<td>Initial R-R (msec)</td>
<td>239 ± 18</td>
<td>234 ± 14</td>
<td>226 ± 10</td>
</tr>
<tr>
<td>Initial MAP (mm Hg)</td>
<td>84.1 ± 5.4</td>
<td>86.8 ± 3.3</td>
<td>78.8 ± 3.2*</td>
</tr>
<tr>
<td>LAN stimulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak ΔR-R (msec)</td>
<td>40 ± 7</td>
<td>33 ± 5*</td>
<td>39 ± 5</td>
</tr>
<tr>
<td>Peak ΔMAP (mm Hg)</td>
<td>28 ± 4</td>
<td>13 ± 2*</td>
<td>28 ± 5</td>
</tr>
</tbody>
</table>

MRAP = mean right atrial pressure; LAN = left aortic nerve; MAP = mean arterial pressure; values are mean ± 1 SEM.

* P < 0.05 (paired analysis) for values significantly different from control.
manner similar to that seen prior to vagotomy. Therefore, since the magnitudes and initial slopes of the reflex responses were affected similarly by volume loading in both the intact and vagotomized rabbits, cardiopulmonary receptors subserved by vagal afferents do not seem to be involved in the observed alterations of LAN-invoked reflex changes during intravenous infusion.

To determine the possible contribution of intact arterial baroreceptors to the volume-induced attenuation of the reflex responses, bilateral aortic arch and carotid sinus denervations were performed in rabbits with intact vagi. Prior to total denervation, both aortic nerves were sectioned in two rabbits. Reflex responses to LAN stimulation were found not to be altered either before or after volume loading (MRAP = 5.0 mm Hg) when compared to control responses. In five rabbits, responses to LAN stimulation were quantitated prior to and after total arterial baroreceptor denervation (ABD) and subsequently after volume loading (MRAP = 5.0 mm Hg) of the denervated rabbits. Average control heart rate was not significantly altered by ABD, even though average resting MAP values were increased by 30 mm Hg following ABD (Table 3). The LTO’s and initial slopes were not significantly changed following ABD, but the magnitude of the peak and the LTP for the MAP response were both increased significantly (Table 3). After ABD, attenuation of the reflex responses to LAN stimulation by volume loading was not observed. Three rabbits were bled after ABD and volume loading in order to return MRAP and MAP to preinfusion levels. Subsequently, the vagi were sectioned in these rabbits. Although MAP increased on the average by 14 mm Hg following vagotomy and by an additional 19 mm Hg following infusion (MRAP = 5.0 mm Hg), no significant change in heart rate or MAP responses to LAN stimulation were observed when these responses were compared to those obtained prior to vagotomy.

**Discussion**

This study has demonstrated that acute volume loading depresses the reflex cardiovascular responses to electrical activation of the rabbit aortic nerve. The mechanism responsible for this attenuation was highly sensitive, since identifiable influences occurred after an elevation in MRAP of only 1.0 mm Hg, or a vascular volume expansion of less than 10%. Although there was significant hemodilution when MRAP was elevated by acute volume loading (Table 1), hemodilution could not explain the attenuated cardiovascular responses to LAN stimulation. Hemorrhage after volume loading caused total fluid volume, as well as the responses to nerve stimulation, to equal preinfusion values even though significant hemodilution remained (Table 2). Furthermore, an attenuation of the reflex changes during LAN stimulation was observed during infusion of blood which did not change the hematocrit (Fig. 3).

Infusion alone did not elicit any significant change in heart rate or MAP even when MRAP was increased by 10 mm Hg. This finding is contrary to results obtained for the conscious dog which indicated that volume loading, sufficient to raise mean atrial pressure to 10 mm Hg or more, produced an increase in both heart rate and MAP. Horwitz and Bishop concluded that in the conscious dog

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**Table 3 Heart Rate and Mean Arterial Blood Pressure (MAP) Changes Due to Left Aortic Nerve (LAN) Stimulation before and after Arterial Baroreceptor Denervation and following Venous Infusion in Five Rabbits**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Control (MRAP 0.5 mm Hg)</th>
<th>Penetration 0.5 mm Hg</th>
<th>Penetration 5.0 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRAP</td>
<td>221 ± 11</td>
<td>221 ± 6</td>
<td>218 ± 3</td>
</tr>
<tr>
<td>MAP</td>
<td>94 ± 3</td>
<td>124 ± 10*</td>
<td>123 ± 7*</td>
</tr>
</tbody>
</table>

**Stimulation-reflex changes**

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>µ (mm Hg)</th>
<th>37 ± 4</th>
<th>57 ± 6*</th>
<th>59 ± 6*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>5.4 ± 0.5</td>
<td>6.7 ± 0.8</td>
<td>7.1 ± 0.6</td>
<td></td>
</tr>
<tr>
<td>Hg/sec</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LTP (interval no.)</td>
<td>45 ± 4</td>
<td>73 ± 13*</td>
<td>71 ± 5*</td>
<td></td>
</tr>
</tbody>
</table>

MRAP = mean right atrial pressure; LTP = latency to peak; values are mean ± standard error.

* Significant (P < 0.05) change from control (paired analysis).
tachycardia during volume loading was due primarily to reflex inhibition of vagal efferent activity. The control heart rates for rabbits in our present study ranged from 223 to 300 beats/min; these values are similar to those found for the conscious rabbit but considerably higher than the resting heart rate of the conscious dog. Since vagotomy did not (Table 1) result in a sustained change in heart rate above control levels it is likely that the tonic cardiac vagal restraint is slight in the rabbit. Consequently, changes in heart rate during volume loading would be minimal.

There is good evidence for receptors subserved by vagal afferents that are responsive to volume or tension changes in the cardiopulmonary region and that reflexly alter cardiac sympathetic activity.15-13 Additionally, in the dog49 and in the rabbit50 after sinoaortic denervation, vagal block or section results in a rise in arterial pressure. Clement et al.48 found in the anesthetized denervated rabbit a 41% decrease in renal sympathetic activity associated with a 10% increase in blood volume. In the dog, vagally mediated cardiopulmonary receptors have been shown to oppose the vasoconstriction due to carotid sinus hypotension more effectively in the kidney than in the hindlimb.29 Some interaction apparently occurs in the central nervous system between the arterial baroreceptors and the cardiopulmonary receptors, since the magnitude of the canine pressor response to vagal cold block is altered by input from the carotid sinus.48 A recent study5 using conscious dogs has suggested that the normal arterial baroreceptor restraint on heart rate is diminished during volume loading, since in spite of a substantial increase in arterial pressure a significant tachycardia occurred and the heart rate responses to LAN stimulation were unaltered by vagotomy (Fig. 2). Thus, during volume loading, cardiopulmonary receptors subserved by vagal afferents did not play a role in modifying the reflex responses to LAN stimulation. In addition, although volume loading reduced the efferent sympathetic inhibition due to LAN stimulation, the parasympathetic component of the reflex heart rate response was apparently unaltered. This last conclusion is based on the observation that the peak change in the initial slope of the heart rate responses were uniformly reduced after vagotomy when comparisons were made at each level of MRAP tested (Fig. 2A and C).

Following total ABD or ABD plus vagotomy, the reflex cardiovascular responses to LAN stimulation were no longer attenuated by volume expansion (Table 3). Earlier, Kumada and Sagawa22 suggested that variations in blood volume in the rabbit can be detected by aortic baroreceptors via the small associated changes in arterial pressure. Since the vagally mediated cardiopulmonary receptors were not found to play an important role in the attenuation of the reflex responses caused by infusion, two possible mechanisms were considered. The first involved activation of sympathetic afferents subserving cardiopulmonary receptors4-10 and the second activation of arterial baroreceptor afferents from carotid sinus and aortic arch regions responsive to volume loading. By progressive bilateral denervation it was considered that the relative contributions of each mechanism could be distinguished. When both aortic nerves were sectioned prior to carotid sinus baroreceptor denervation, no significant change in the attenuation of the reflex responses was detected. Subsequent to total ABD or ABD plus vagotomy the attenuation observed after infusion was eliminated. Were sympathetic afferents from cardiopulmonary receptors involved, some measurable attenuation would have been observed following ABD. A rise in arterial blood pressure was seen following vagotomy and volume loading in the rabbits after ABD; this indicates that vagally mediated receptors can modify blood pressure in the denervated animal, as reported by others.10-17, 28, 29

These results suggest that the carotid sinus baroreceptors detect subtle changes in arterial pressure or volume during infusion and this results in a diminished sympathetic efferent activity to the effector organ. Thus, as previously demonstrated,29 use of the absence of a change in heart rate or arterial blood pressure as a criterion for the absence of a change in carotid baroreceptor activity during an experimental intervention may lead to inaccurate conclusions.

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Ventricular Pressure-Volume Curve Indices Change with End-Diastolic Pressure

STANTON A. GLANTZ, PH.D.

SUMMARY Many indices have been proposed to describe the diastolic pressure-volume curve mathematically and permit quantification of the elastic properties of the myocardium itself in hopes that changes in the muscle caused by disease would be reflected in the diastolic pressure-volume curve. To date, none of the proposed indices has been shown convincingly to discriminate one group of patients from another. While this situation in part reflects the high variability of the diastolic pressure-volume curve from a segment like that which capillaries of the left ventricle's geometry and the myocardium's elasticity. The accepted view of the diastolic pressure-volume curve reflects this change. For example, if muscle stiffens with ischemia, a partially ischemic ventricle should exhibit a higher or steeper pressure-volume curve than normal. Since the extent and severity of ischemia play an important role in deciding whether to attempt to revascularize ischemic myocardium through coronary artery bypass graft surgery, considerable attention has been devoted to studying pressure-volume curves of patients with coronary artery disease. By computing various parameters from the pressure-volume curve, the investigators hoped to quantify the extent of ischemia. Similar studies have been directed at explaining the relationship of the aortic and carotid sinuses to nonhypotensive hemorrhage and to transfusion. Am J Physiol 211: 1429-1437, 1966


SUMMARY Many indices have been proposed to describe the diastolic pressure-volume curve mathematically and permit quantification of the elastic properties of the myocardium itself in hopes that changes in the muscle caused by disease would be reflected in the diastolic pressure-volume curve. To date, none of the proposed indices has been shown convincingly to discriminate one group of patients from another. While this situation in part reflects the high variability of the diastolic pressure-volume curve, and the values of all diastolic pressure-volume curve parameters investigated change significantly when one uses different segments of the same pressure-volume curve to compute them. These results were derived from relatively noise-free pressure-volume curves obtained by filling nine excised dog left ventricles at a known rate and monitoring pressure. Furthermore, the change in the value of the parameters is different for different dogs (i.e., there is a significant interaction effect in the analysis of variance), and this interaction precludes a simple correction factor to account for the segment of the pressure-volume curve used to compute the parameter. Merely increasing measurement fidelity will not resolve this problem, because none of these parameters accurately characterizes the entire diastolic pressure-volume curve from a segment like that which one can reasonably expect to obtain from humans.

BECAUSE the diastolic pressure-volume relationship plays an important role in determining the left ventricle's systolic performance through the Frank-Starling mechanism, there has been considerable effort, recently reviewed by Mirsky, directed toward describing the diastolic pressure-volume relationship with a single parameter and interpreting its value in terms of the myocardium's elasticity. The accepted view of the diastolic pressure-volume curve considers the ventricle an unconstrained elastic shell that is subject to uniform internal and external pressures and that expands as it fills, with the curve reflecting the ventricle's geometry and the myocardium's nonlinear elasticity. Presumably, with different diseases the mechanical properties of the muscle change and the pressure-volume curve reflects this change. For example, if muscle stiffens with ischemia, a partially ischemic ventricle should exhibit a higher or steeper pressure-volume curve than normal. Since the extent and severity of ischemia play an important role in deciding whether to attempt to revascularize ischemic myocardium through coronary artery bypass graft surgery, considerable attention has been devoted to studying pressure-volume curves of patients with coronary artery disease. By computing various parameters from the pressure-volume curve, the investigators hoped to quantify the extent of ischemia. Similar studies have been directed at explaining how hypotension, congestive cardiomyopathy, and infarction affect the pressure-volume curve. Unfortunately, the values of the proposed parameters exhibit considerable scatter within and overlap between patient groups. In fact, an analysis of variance often fails to detect differences between the values of the parameters in different patient...
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