Postextrasystolic Compliance of the Left Ventricle

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SUMMARY The effects of a single premature contraction (PC) on left ventricular diastolic distensibility was studied in man, in the conscious chronically instrumented dog, and in the isolated (isovolumic) blood perfused dog heart. In the isolated dog heart at a constant volume, there was no difference in end-diastolic pressure when control diastolic pressure was compared to that following a PC. In man and conscious dogs, there was no difference between the overall pressure-volume or pressure-length plots when control diastolic data were compared to data from the diastole immediately following a PC (no change in the modulus of chamber stiffness). In the intact circulation of man and dog, increased filling during the post PC pause causes the ventricle to operate higher on the steeper (stiffer) portion of its pressure-volume or pressure-length curve (decrease in preload-dependent compliance). Thus, although a PC does not alter the modulus of chamber stiffness, a preload-dependent change in compliance may occur during post PC diastole.

AUGMENTED CARDIAC PERFORMANCE is observed in the contraction following a premature contraction. The mechanisms involved in the production of this phenomenon include postextrasystolic potentiation, the time-dependent fall in left ventricular outflow impedance (aortic diastolic pressure) during the postextrasystolic pause, and the Frank-Starling mechanism (increased ventricular filling during the pause). The contribution of the Frank-Starling mechanism is difficult to assess from left ventricular pressure data alone because of the curvilinear nature of the left ventricular diastolic pressure-volume relation, and especially because of the reported increase in ventricular diastolic compliance in the pause immediately following a premature contraction. Because controversy exists on this second point, the present studies were designed to define left ventricular diastolic compliance in the diastolic interval immediately following a premature contraction. Studies were carried out in the normal left ventricles of man, the conscious chronically instrumented dog, and the isolated blood perfused dog heart.

Methods

Studies in Man

Five normal left ventricular (LV) cineangiograms were examined. The ventriculograms were considered normal on the basis of normal end-diastolic volume (< 90 cc/m²), normal systolic ejection fraction (> 55%), and a normal synergetic pattern of contraction. Left ventricular volume was determined using the area-length method (single plane cineangiography at 60 frames/sec) and LV pressure was measured during ventriculography with a micromanometer (Millar Instruments Inc.). Matching of pressure and volume data throughout diastole was accomplished by using a timing reference system which marked the recording paper at the time of each cine exposure. The details of these methods are outlined elsewhere.

Plots of pressure against volume were constructed using data from the interval between the lowest early diastolic LV pressure and end diastole. The rationale and mathematical considerations pertinent to the analysis of LV diastolic distensibility have been presented in our previous publications. Briefly, diastolic pressure-volume data was fit by a simple exponential equation:

\[ P = b e^{kV} \]

where \( P \) = pressure in mm Hg, \( V \) = volume in cc/m² of body surface area, \( e \) = base of the natural log and \( b \) and \( k \) are variables to be fitted to the data. The \( k \) value characterizes the overall diastolic pressure-volume relation and may be considered a modulus of chamber (or volume) stiffness; high values for \( k \) suggest increased chamber stiffness and low values decreased stiffness. Left ventricular operating compliance is defined by the modulus of chamber stiffness (k) and by instantaneous diastolic pressure as

\[ \frac{dV}{dP} = \frac{1}{kP} \]

where \( k \) = modulus of chamber stiffness, and \( P \) = operating diastolic pressure. In each case values for the modulus of chamber stiffness and end-diastolic operating compliance were determined from control and postpremature ventricular contraction data and paired comparisons were made using the Student's t-test.

Conscious, Chronically Instrumented Dog

Mongrel dogs weighing 25-35 kg were anesthetized with sodium pentobarbitol (1 mg/kg) and respiration was controlled. A left thoracotomy was performed, the heart was exposed and a left ventricular pressure transducer (Konigsberg Inst., Co. Model P-22) was inserted into the left ventricle through an apical stab wound and secured in place by means of a purse string suture. Tygon tubing for monitoring pressure was also inserted through the apex of the ventricle and secured in place. Ultrasonic segment length crystals were implanted in the myocardial wall 7-12 mm apart; the crystals were placed in a subendocardial location along the
TABLE 1. Left Ventricular Diastolic Pressure-Volume Data from Five Patients Studied at Cardiac Catheterization

<table>
<thead>
<tr>
<th></th>
<th>LVEDP (mm Hg)</th>
<th>LVEDV (cc/m²)</th>
<th>k</th>
<th>dV/dP_{diast}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>PVC</td>
<td>C</td>
<td>PVC</td>
</tr>
<tr>
<td>Average</td>
<td>9.1</td>
<td>11.1</td>
<td>74</td>
<td>78</td>
</tr>
<tr>
<td>SEM</td>
<td>1.1</td>
<td>1.3</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.025</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>Average % change</td>
<td>+23%</td>
<td>+5.4%</td>
<td>+5.3%</td>
<td>-22%</td>
</tr>
</tbody>
</table>

Abbreviations: LVEDP = left ventricular end-diastolic pressure (mm Hg); LVEDV = left ventricular end-diastolic volume (cc/m²); k = modulus of chamber stiffness; dV/dP_{diast} = end-diastolic compliance; C = control; PVC = premature ventricular contraction.

minor axis of the left ventricular chamber. The wires and tubing were brought through the skin in the animal’s posterior cervical area; the thoracotomy was closed and the animal was allowed to heal.

After a three to four week recovery period, three animals with spontaneously occurring premature contractions were selected for study. In each animal, the influence of a premature contraction on ventricular distensibility was examined by comparing the pressure-length data from the diastole following a premature beat to data from a preceding control diastolic interval. Left ventricular pressure-myocardial segment length data were plotted and examined in a manner similar to that described in the human studies (see above). Since the crystals were implanted at different distances in each of the three dogs, diastolic pressure-length data (shown in figure 4) are presented as percent change from control.

Isolated Blood Perfused Dog Heart

Studies were carried out using a supported isolated heart preparation similar to that of Brown and co-workers. Briefly, arterial blood from the femoral artery of a support dog was maintained at 37°C using a heat exchanger. It was raised to a pressure of 100 mm Hg where aortic perfusion of a second (isolated) dog heart was carried out. Coronary sinus blood was drained from the right ventricle of the perfused heart and returned to the support dog. A drain in the LV prevented accumulation of blood secondary to bleeding or thebesian drainage. A condon on a silastic mount was placed into the LV through the mitral valve and intraventricular volume was varied by inflating the condom with known volumes of saline.

Left ventricular pressure was measured with a micro-manometer (Millar Instruments Inc.) and with a standard fluid-filled catheter transducer system (Statham P23dB); pressure was recorded at a high gain (micromanometer) and a low gain (fluid filled) as shown in figure 3. In the absence of spontaneous extrasystoles, premature contractions were produced by competitive pacing of the LV or right atrium. Studies were carried out over a range of volume up to that which resulted in a peak systolic pressure of 100 mm Hg. At each increment of volume, end-diastolic pressure was measured and the modulus of stiffness (k) was determined from these pressure-volume coordinates. “Operating compliance” was calculated as the inverse tangent (dV/dP) to the static pressure-volume curve at an arbitrary volume of 20 cc. Each pair of pressures recorded in table 3 represents the average of four control and four postextrasystolic measurements. In each heart, data from the diastolic interval immediately following the premature contraction were compared to the preceding control diastolic data.

Results

Studies in Man

Diastolic pressure-volume data from five patients with normal LV function were analyzed (table 1 and figure 1). Following a spontaneous premature ventricular contraction (PVC), LV end-diastolic pressure increased 23% (9.1 ± 1.1 to 11.1 ± 1.3 mm Hg, P < 0.025) and end-diastolic volume increased 5.4% (74 ± 10 to 78 ± 10 cc/m², NS). A slight increase in the modulus of chamber stiffness was nonsignificant while end-diastolic compliance fell by 22% (2.4 ± 0.4 to 1.9 ± 0.4, P < 0.025). Thus, the pause following a premature contraction resulted in increased ventricular filling along the same diastolic pressure-volume curve; the modulus of chamber stiffness (k) remained unchanged while values for end-diastolic compliance (dV/dP) fell. In one patient, the diastole following an augmented (post PVC) systole was examined (fig. 1). Inspection of the diastolic pressure-volume data in this single case suggests that there was no change in the modulus of chamber compliance in the diastole following the augmented beat.

 Conscious, Chronically Instrumented Dog

Three animals with spontaneously occurring premature contractions (PC) were studied. The effects of three premature atrial contractions and nine premature ventricular contractions on LV distensibility (pressure-length relations) are tabulated in table 2 and an example is shown in figure 2.
Following a PC, the average percent increase in LV end-diastolic pressure was 23% (10.54 ± 0.22 to 12.92 ± 0.42 mm Hg, \( P < 0.001 \)) and the average increase in myocardial segment length was 1.3% (\( P < 0.001 \)). There was no significant change in the modulus of chamber stiffness in the diastole following a PC, but compliance (dL/dP) at end diastole fell 18% (\( P < 0.001 \)).

**Isolated Blood Perfused Dog Heart**

The LV end-diastolic pressure during the pause immediately following a premature contraction was compared with the pressure during the preceding "control" diastolic interval in six isovolumically beating dog hearts. The pressure-volume data are tabulated in table 3 and a representative recording from one experiment is shown in figure 3. The change in diastolic pressure, when post PC data was compared with control ranged from +0.1 to −0.1 mm Hg and was nonsignificant (average % change = +0.06%). Likewise, an isolated PC did not alter the modulus of stiffness or "operating compliance" in this isovolumic preparation.

These results are summarized in figure 4. In man and unanesthetized dog, and in the isovolumic canine LV, a single premature contraction does not alter the modulus of stiffness of the diastolic LV. In the intact circulation a post PC pause generally causes increased LV filling, and post PC compliance calculated at end-diastole falls.

**Discussion**

Since the diastolic pressure-volume curve of the left ventricle is nearly exponential, the slope of a tangent to this

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**Table 3. Left Ventricular Diastolic Pressure-Volume Data from Six Isolated Blood Perfused Dog Hearts**

<table>
<thead>
<tr>
<th>Left ventricular (balloon) volume</th>
<th>5 cc</th>
<th>10 cc</th>
<th>15 cc</th>
<th>20 cc</th>
<th>25 cc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>PC</td>
<td>C</td>
<td>PC</td>
<td>C</td>
</tr>
<tr>
<td>Average pressure (mm Hg)</td>
<td>1.37</td>
<td>1.37</td>
<td>2.15</td>
<td>2.16</td>
<td>3.82</td>
</tr>
<tr>
<td>SEM</td>
<td>0.22</td>
<td>0.22</td>
<td>0.50</td>
<td>0.52</td>
<td>0.55</td>
</tr>
<tr>
<td>( P )</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Average % change</td>
<td>0</td>
<td>−0.1%</td>
<td>+1.8%</td>
<td>−1.0%</td>
<td>−0.8%</td>
</tr>
</tbody>
</table>

Abbreviations: C = control diastolic pressure; PC = diastolic pressure in the pause immediately following the premature contraction.
The normal diastolic pressure-volume curve, which in turn results in a reduction in the calculated value for end-diastolic compliance.

Our conclusions, based on observations made in the normal left ventricle, may require qualification under different circumstances. In a situation in which ventricular filling is markedly time dependent (i.e., mitral stenosis), the post PVC reduction in end-diastolic compliance may be prominent. Under conditions in which filling time is not an important determinant of ventricular volume (i.e., chronic constrictive pericarditis), there may be no change in the end-diastolic compliance in the diastole following a premature beat.

In addition, the diastolic properties of a failing ventricle may differ from the normal ventricles reported herein. Using severely decompenated hearts with elevated end-diastolic pressures, Bartlestone et al. found a “variable diastolic compliance” induced by extrasystole.3 In these failing ventricles, increased compliance following the extrasystole (before the potentiated contraction) was manifest as increased volume at constant pressure as well as by reduced pressure at constant volume. Sonnenblick et al. also studied this problem in isolated cat papillary muscle and in the isovolumic dog ventricle.4 With sustained postextrasystolic potentiation, they found that resting length at a given tension may increase if systolic force is augmented, but no such change occurred in isotonic contractions. It was concluded that postextrasystolic potentiation “does not induce changes in the resting length-tension relations of heart muscle per se.” However, these investigators did not examine the diastole before the potentiated contraction, which was the prime objective in the present study.

As is shown in figure 1, there was no change in the modulus of stiffness either before or after the potentiated systole; similar observations were made in the instrumented dogs. However, in the isolated (isovolumic) dog heart studies, a slight reduction in diastolic pressure was frequently seen following the augmented beat. These observations are in agreement with the conclusions of Sonnenblick et al., who pointed out that those who have observed an increase in compliance with inotropic interventions generally have worked with isometric or isovolumic preparations.4

In these studies, we made no attempt to control heart rate, coupling interval of the premature beat, or left ventricular peak systolic pressure. Since the time course of myocardial
relaxation depends in part on these and other factors, 10 we do not know the extent to which variations in relaxation influenced our results. Another potential limitation of these studies involves the reproducibility of the angiographic measurements; in our laboratory the standard deviation for ten determinations of volume from the same (single) cine frame is 2–3 cc in ventricles ranging from 300 to 400 cc. 11 However, in any such study the limitations of single plane angiography are well known. Diastolic pressure-volume or pressure-length data may be fit by a broad variety of mathematical functions, but it is generally agreed that an exponential function is most appropriate. The addition of a third variable (P = a + b(e^k)) to the monoexponential function used in this study alters the pressure intercept (b) but does not significantly alter conclusions based on k (the modulus of chamber stiffness). While myocardial stress-strain data is required to characterize myocardial stiffness, especially when one heart is compared to another, 12 the conclusions of the present studies are not altered by such an analysis.

We have used a broad spectrum of methods in animals and in man to study the effects of a premature contraction on the diastolic properties of the left ventricle. Our data demonstrate that a premature contraction does not alter the modulus of volume stiffness in a normal ventricle. Postextrasystolic reduction in operating compliance occurs as a consequence of increased ventricular filling during the compensatory pause.

Figure 4. Summary of the change in diastolic pressure, volume (or length), the stiffness modulus, and end-diastolic compliance following an extrasystole. An extrasystole does not alter the modulus of stiffness; however, in the intact circulation of man and dog, increased filling along the same diastolic pressure-volume (or pressure-length) curve results in a reduction in end-diastolic compliance.

References

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