Effects of decreased aortic compliance on performance of the left ventricle

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URSCHEL, CHARLES W., JAMES W. COVELL, EDMUND H. SONNENBLICK, JOHN ROSS, JR., AND EUGENE BRAUNWALD. Effects of decreased aortic compliance on performance of the left ventricle. Am. J. Physiol. 214(2): 298-304. 1968.—The effects of decreased aortic compliance on the performance of the left ventricle were studied in eight dogs by diverting their aortic blood flow through a rigid bypass. Despite unchanged myocardial contractility, judged by the force-velocity relation during isovolumic systole, direction of blood into the rigid bypass caused increases in peak systolic pressure, duration of ejection, and left ventricular end-diastolic pressure. Stroke volume was unchanged and the ejection fraction therefore declined. Peak and integrated myocardial fiber tension rose as a result of the increases in left ventricular pressure and size and because of the increase in tension, circumferential fiber and contractile element velocities decreased. Further, it was shown that at any instant during ejection, the performance of the ventricle was dependent on the interrelations between myocardial fiber length, tension, velocity, and the impedance to ejection. In other experiments, aortic blood flow was diverted through the rigid bypass while preload was held constant. Under these circumstances, stroke volume fell and left ventricular tension rose to a smaller extent than when preload was allowed to rise. These experiments illustrate that the mechanical performance of the left ventricle is altered by the physical characteristics of the arterial tree. Decreased aortic compliance, as occurs during aging in man, therefore increases the impedance to ejection and the tension load on the myocardium.

force-velocity relation; rigid aorta; myocardial fiber length; ventricular tension; impedance to ejection

There is general agreement that the contractile behavior of isolated cardiac muscle is controlled primarily by mechanical factors such as preload and afterload and by the contractile state of the myocardium. During the past few years considerable effort has been directed toward extending these concepts to the intact heart (2, 3, 5-8, 11, 14, 15) and it has become apparent that the mechanical performance of the intact heart resembles that of the isolated papillary muscle in its responses to changes in preload and to alteration in the force-velocity relation induced by inotropic influences (7, 12). In the studies on isolated heart muscle, the effects of changes in afterload are easily determined since the load is constant throughout contraction. In the intact circulation, however, the ventricle contracts auxotonically, the afterload changing constantly during the course of ejection. Instantaneous afterload, i.e., wall tension, is determined by a variety of closely interrelated factors. These include: 1) ventricular volume (myocardial fiber length) and wall thickness, which, acting through the La Place relation, control myocardial wall tension at any level of pressure; 2) the impedance to ejection, which is an important determinant of intraventricular pressure (impedance itself is a function of the resistance of the systemic vascular bed as well as the compliance of the central arterial tree); and 3) the shortening characteristics of the myocardial fibers, which affect the stroke volume and the velocity of ejection; the latter two variables interact with the impedance to ventricular outflow and determine myocardial wall tension.

In recent studies on simulated aortic and mitral regurgitation in the intact canine heart (13) it was found that the afterload at any instant during contraction plays a dominant role in determining the dynamic characteristics of contraction. Since, as indicated above, the compliance of the aorta is one of the important determinants of instantaneous afterload, it was considered of interest to determine the manner in which alterations in the elasticity of the aortic wall affect the ejection characteristics of the left ventricle.

METHODS

A bilateral thoracotomy was performed in eight dogs, weighing 14.5-23.5 kg (avg = 20.9 kg) anesthetized with sodium pentobarbital (30-40 mg/kg) and ventilated with positive pressure. By placing a rigid stainless steel bypass line (i.d. = 1.2 cm) between the aortic arch and
Aortic pressure was measured above and below the bypass by short polyethylene catheters attached to Statham P23Db gauges. Ascending aortic blood flow was measured with a Statham type QH flow probe placed around the ascending aorta, and a gated sine-wave flowmeter (model M 4000, Statham Instruments, Inc., Los Angeles, Calif.). All flow measurements were corrected for a constant time delay of 10 msec in the instrument. Left ventricular pressure was measured with a Statham P23Db gauge attached to a 4 mm i.d., 2.0 cm rigid cannula. The first derivative of left ventricular pressure, dp/dt, was determined with an R-C differentiating circuit, exhibiting a constant phase shift of 90° ± 1° from 0 to 160 cycles/sec (Electronic Gear, Inc., Valley Stream, N. Y.). Left ventricular end-diastolic pressure was controlled by phlebotomy or transfusion of previously exchanged donor blood through a femoral vein. Heart rate was maintained constant at 115–140/min by electrically stimulating the right atrium after crushing the sinoatrial node.

The effects of bypassing the normal aorta and directing blood through the rigid prosthesis were studied in two separate types of experiments. The first, designated "preload allowed to vary" consisted of a comparison of myocardial function following a simple change from the normal aorta to the rigid bypass without control of any hemodynamic variable other than heart rate. Eighteen such experiments were performed in eight dogs. This

### Table 1. Effects of directing blood from the normal aorta through the rigid bypass

<table>
<thead>
<tr>
<th></th>
<th>A. Preload Allowed to Vary</th>
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<th>B. Preload Constant</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Rigid bypass</td>
<td>Control</td>
<td>Rigid bypass</td>
</tr>
<tr>
<td><strong>AA systolic press., mm Hg</strong></td>
<td>122 ± 6</td>
<td>133 ± 8†</td>
<td>113 ± 11</td>
<td>125 ± 11†</td>
</tr>
<tr>
<td><strong>AA diastolic press., mm Hg</strong></td>
<td>87 ± 4</td>
<td>93 ± 4</td>
<td>77 ± 10</td>
<td>80 ± 7</td>
</tr>
<tr>
<td><strong>AA mean press., mm Hg</strong></td>
<td>100 ± 5</td>
<td>90 ± 5</td>
<td>92 ± 11</td>
<td>90 ± 10</td>
</tr>
<tr>
<td><strong>AB mean press., mm Hg</strong></td>
<td>94 ± 5</td>
<td>91 ± 5†</td>
<td>86 ± 11</td>
<td>83 ± 9</td>
</tr>
<tr>
<td><strong>LVEDP, mm Hg</strong></td>
<td>5.1 ± .5</td>
<td>6.0 ± .6†</td>
<td>7.9 ± 1.5</td>
<td>8.0 ± 1.5</td>
</tr>
<tr>
<td><strong>LVEDV, ml</strong></td>
<td>28.3 ± 1.8</td>
<td>31.4 ± 1.9†</td>
<td>33.6 ± 4.3</td>
<td>33.8 ± 4.4</td>
</tr>
<tr>
<td><strong>Cardiac index, liter/min per m²</strong></td>
<td>1.71 ± 0.16</td>
<td>1.36 ± 0.17†</td>
<td>1.91 ± 0.40</td>
<td>1.69 ± .35†</td>
</tr>
<tr>
<td><strong>SV, ml</strong></td>
<td>11.3 ± 1.0</td>
<td>10.5 ± 1.1</td>
<td>12.2 ± 1.5</td>
<td>10.9 ± 1.3†</td>
</tr>
<tr>
<td><strong>SV/EDV</strong></td>
<td>0.42 ± 0.04</td>
<td>0.35 ± 0.04†</td>
<td>.38 ± .05</td>
<td>.34 ± .05†</td>
</tr>
<tr>
<td><strong>Peak flow, ml/sec</strong></td>
<td>95 ± 12</td>
<td>87 ± 13†</td>
<td>90 ± 19</td>
<td>87 ± 23</td>
</tr>
<tr>
<td><strong>Stroke work, g-m</strong></td>
<td>18.1 ± 2.6</td>
<td>18.1 ± 3.1</td>
<td>17.4 ± 4.2</td>
<td>16.0 ± 3.8</td>
</tr>
<tr>
<td><strong>Peak tension, g/cm²</strong></td>
<td>121 ± 7</td>
<td>143 ± 8†</td>
<td>130 ± 15</td>
<td>136 ± 14†</td>
</tr>
<tr>
<td><strong>Integrated tension, g-sec/cm²</strong></td>
<td>25.0 ± 1.8</td>
<td>29.7 ± 1.8†</td>
<td>29.2 ± 4.0</td>
<td>31.1 ± 3.9†</td>
</tr>
<tr>
<td><strong>CE work g-m</strong></td>
<td>165 ± 17</td>
<td>175 ± 20</td>
<td>182 ± 37</td>
<td>169 ± 34</td>
</tr>
<tr>
<td><strong>CF work</strong></td>
<td>126 ± 16</td>
<td>131 ± 19</td>
<td>136 ± 32</td>
<td>124 ± 29†</td>
</tr>
<tr>
<td><strong>Vmax , cm/sec</strong></td>
<td>35 ± 4</td>
<td>35 ± 5</td>
<td>35 ± 4</td>
<td>35 ± 5</td>
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</tbody>
</table>

**AA** = ascending aorta; **AB** = aortic bifurcation; **LVEDP** = left ventricular end-diastolic pressure; **LVEDV** = left ventricular end-diastolic volume; **SV** = stroke volume; **SV/EDV** = ejection fraction; **CE** = contractile element; **CF** = circumferential fibers.

*P < 0.05. †P < 0.01 compared to control computed using a t test (9).
intervention elevated left ventricular end-diastolic pressure (LVEDP), i.e., preload. Accordingly in six experiments, in order to determine the effects of changing aortic compliance at a constant preload, after a steady hemodynamic state had been achieved while blood flowed through the rigid bypass, flow was returned to the normal aorta and the LVEDP then elevated to the same level which had existed when blood flowed through the rigid bypass. These experiments were designated "preload constant." Five of the eight dogs were studied after the administration of dl-propranolol, 5 mg iv, in order to obviate reflex changes in contractility.

Following completion of the experiment the heart was arrested with KCl, and passive pressure-volume curves were determined by a method previously described (7). The left ventricle, including the interventricular septum, was then dissected free from the right ventricle and atria, and weighed.

CALCULATIONS

Left ventricular pressure (LVP) and its derivative (dp/dt) and aortic flow, were determined at 10-msec intervals during representative ejecting beats. Left ventricular end-diastolic volume (LVEDV) was determined from the pressure-volume curve of the KCl arrested heart and instantaneous ventricular volume at a given point in ejection was calculated as the difference between LVEDV and the integrated flow to that moment.

The left ventricle was considered to be a thick-walled sphere, and its external volume was taken as the sum of LVEDV and muscle volume. An even distribution of left ventricular muscle was assumed and the radii of the external and internal volumes were computed, ventricular wall thickness comprising their difference. Assuming force to be evenly distributed across the ventricular wall, i.e., identical at all radii, it can be shown mathematically that this average stress or tension (T in gm/cm²) is equal to Pr/2h where r₁ = internal radius, and h = ventricular wall thickness (8). In brief, this derivation assumes that the total force to be supported by the ventricular wall is equal to the product of the LVP and the internal surface area of the ventricle. It is appreciated that this equation, derived for a thin-walled sphere, will provide a small overestimation of true wall tension because of the thickness of the left ventricular wall (12). The relationship of Pr/2h to true wall tension is also affected by the mode

![Graph](http://aiplib.org/Download/9.jpg)

**FIG. 2.** Tracings from a typical experiment: Recordings of aortic pressure (Ao. P) left ventricular pressure (LVP) at low and high sensitivities, first derivative of LVP (dp/dt), and aortic flow (Ao. Flow) are shown during periods of flow through the dog's normal aorta (A) and through the rigid bypass (B).
of coupling of force to the wall and the actual stress distribution, neither of which can be defined at present.

The equation used for calculating the velocity of circumferential fiber shortening was modified from that presented by Fry et al. (3). For this derivation the ventricular wall is assumed to be a series of concentric thin walled spheres. The instantaneous circumferential shortening velocity ($V_{CF}$) in centimeters per second at the midwall can be calculated as:

$$V_{CF} = \frac{Q}{2r_0 r_1}$$

where $Q =$ instantaneous flow rate out of the ventricle in cubic centimeters per second, $r_0 =$ external radius in centimeters, and $r_1 =$ internal radius in centimeters.

$V_{CF}$ and $T$ represent the velocity of shortening and the force necessary to approximate the ends of a hypothetical 1.0 cm$^2$ cross-sectional area band of muscle encircling the ventricle at the midwall radius. All subsequent calculations describe the behavior of this hypothetical band. Contractile element velocity ($V_{CE}$) equals $V_{CF}$ plus the velocity of elongation of the series elastic ($V_{SE}$).

$$V_{SE} = \frac{dT}{dt}/kT$$

where $kT =$ the modulus of elasticity of the series elastic component of the muscle (10). The normalized value for $k$ used in this study, 28, is based upon observations on isolated heart muscle (10) which have recently been shown to pertain to the intact heart (1). Contractile element and circumferential fiber shortening power were calculated as the products of $V_{CE}$ and $T$ and $V_{CF}$ and $T$, respectively, and contractile

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**Fig. 3.** Myocardial mechanics comparing beats with the blood flowing through the aorta (control) and through the rigid bypass (rigid) in one of the experiments in which preload was allowed to vary. **CF** = circumferential fiber, **CE** = contractile element.
element and circumferential fiber work were calculated by integrating the appropriate power-time relationship for the duration of the contraction. Instantaneous impedance to ejection was calculated as the ratio of pressure (g/cm²) to flow (cm³/sec) throughout ejection.

RESULTS

1) Preload allowed to vary. The effects of diverting aortic flow from the normal aorta through the rigid bypass were studied on 18 occasions in eight dogs; 11 of these experiments were performed after propranolol. Since beta adrenergic blockade did not affect the response in any detectable manner, the results of all 18 experiments are considered together and presented in Table I.A.

Tracings from a typical experiment are shown in Fig. 2, and the data calculated from this experiment are shown in Fig. 3. When blood was diverted from its normal pathway through the rigid bypass, aortic systolic pressure rose, while diastolic and mean aortic pressures were not altered significantly; pulse pressure increased from an average of 35–48 mm Hg. The mean pressure gradient between the aortic arch and the aortic bifurcation was not significantly altered. The ascending aortic flow tracing changed in one of two characteristic ways. The first (Figs. 2B and 3B), consisted of an abnormally rapid rise in flow to a peak level approximately equal to the control, followed by a rapid deceleration, followed in turn by a secondary slower rise. This pattern was observed in those experiments in which aortic diastolic pressure fell slightly when blood was directed through the rigid bypass. Instantaneous impedance, i.e., the instantaneous pressure-to-flow ratio, was lower than control during the beginning of ejection (Fig. 3C) but rose to levels exceeding control during the course of ejection. The second pattern of ascending aortic flow which was observed when blood was directed through the rigid bypass is illustrated in Fig. 4B and was characterized by an interruption of the normal acceleration of flow, with a delayed peak. In these experiments calculated instantaneous impedance was higher throughout all except the last portion of systole, as compared to control (Fig. 4D).

LVEDP and LVEDV rose slightly but significantly, while the ejection fraction (SV/EDV) fell from 0.42 to 0.35 (P < 0.01). With the elevation in LVP and increase in ventricular size, peak and LV wall tension rose from 121 to 143 g/cm² (P < 0.01) and integrated tension...
from 25.0 to 29.7 g·sec/cm² (P < 0.01) (Fig. 3D). Concomitant with this rise in tension the velocities of shortening of the circumferential fibers (Fig. 3E) and of the contractile elements (Fig. 3P) fell throughout most of ejection in a manner which, in general, paralleled the changes in aortic flow. The peak velocity of aortic blood flow usually fell, from an average of 95 to 87 ml/sec (P < 0.01).

2. Preload constant. In six experiments the effects of diverting blood flow through the rigid bypass were determined at a constant LVEDV. Typical data from one of these experiments are shown in Fig. 4, and the average results of all experiments are presented in Table 1B.

The changes in arterial pressure which occurred were similar to those which were observed when preload was allowed to vary. However, stroke volume declined significantly when blood was diverted through the rigid aorta at a constant preload (Fig. 4B). At a constant preload, the increases in peak tension and integrated tension which occurred were significantly smaller (P < 0.01 and P < 0.05, respectively) than when preload was allowed to vary (Fig. 4A). Thus, when diversion of blood through the rigid bypass was not permitted to elevate preload, the increase in left ventricular wall tension was reduced and stroke volume diminished significantly. The isovolumic portions of the relationship between force and instantaneous velocity curves were not altered (Fig. 5) and extrapolated velocity at zero tension (Vmax) averaged 35 cm/sec when blood was directed through either pathway, indicating that the intrinsic myocardial contractile state was unchanged (7). However, contractile element velocity during ejection was lower than during the control period.

Discussion

It was shown in an earlier investigation (13) that when ventricular afterload is reduced by allowing the left ventricle either to eject into the left atrium, a low pressure chamber, (simulated mitral regurgitation), or to commence ejection at a lower aortic diastolic pressure than normal (simulated aortic regurgitation), both the velocity and extent of shortening of the myocardial fibers and contractile elements increase, due to the lowered impedance to ejection, as well as the more rapid decrease in ventricular radius. In the present study the effects of increasing impedance to left ventricular outflow were examined and the opposite effects were observed; aortic flow rate, circumferential fiber shortening velocity and contractile element velocity were reduced during ejection (Figs. 3B, E, F; 4B; and 5).

It should be emphasized that these changes occurred despite the fact that the contractile state of the myocardium, as reflected in the extrapolated Vmax of the contractile elements (Fig. 5), remained unchanged. Furthermore, diverting the blood flow through the rigid bypass did not alter mean aortic pressure and the changes in myocardial fiber and contractile element shortening may be attributed to the elevation of systolic arterial pressure, which resulted from the reduction in the compliance of the arterial tree. In the experiments in which preload was allowed to vary, increasing the impedance to ejection resulted in small, but significant elevations of LVEDP and LVEDV (Table 1A). These tended further to increase left ventricular wall tension. However, when preload was held constant, the increases in left ventricular myocardial tension which occurred when blood was diverted through the rigid bypass, though of lesser magnitude, could be attributed entirely to alterations in aortic compliance.

The present investigation illustrates that the behavior of the myocardium is conditioned by the physical characteristics of the arterial tree. These findings are consistent with and extend earlier studies which related ventricular performance to mean impedance (2, 3, 14, 15). The normal aortic Windkessel limits the elevation of left ventricular systolic pressure and tension and allows the myocardial fibers to shorten further and more rapidly. When this expansion of the aorta is prevented by stiffening of the aortic wall, left ventricular systolic pressure and tension rise to a higher level and therefore myocardial shortening is reduced. Although the magnitude of the effects on left ventricular function demonstrated in the present investigation was modest, it is possible that when aortic compliance remains reduced over a period.

![Figure 5](http://example.com/figure5.png)

**Figure 5.** Force (tension)-velocity relations from ejecting beats with blood flowing through the aorta and the rigid bypass. The isovolumic portions of the beats extrapolate to similar intercepts on the ordinate (Vmax). The vertical arrows indicate the onset of ejection. The encircled points in the lower right-hand portion of the figure indicate contractile element (CE) force-velocity relations during ejection, at identical times, 220 msec, after the onset of systole. With blood flowing through the rigid aorta, force is higher and CE velocity is reduced.
of years this additional afterload may cause clinically significant alterations in cardiac activity. Indeed it is of interest that systolic hypertension is associated with an increased mortality rate (4).

REFERENCES


