Instantaneous Pressure-Volume Relationship of the Canine Right Ventricle

W. Lowell Maughan, Artin A. Shoukas, Kiichi Sagawa, and Myron L. Weisfeldt

SUMMARY The instantaneous isovolumic and ejecting pressure-volume relationship of the right ventricle was studied in 11 cross-circulated, isolated canine hearts to characterize the right ventricular contractile state. Accurate measurement of volume was achieved by the use of a water-filled, thin latex balloon in the right ventricle connected to a special volume loading and transducing chamber. Pressure was measured with a miniature pressure transducer mounted within the balloon. Wide variations in loading conditions were achieved by changing the volume of air above the volumetric chamber. The pressure and volume data were collected from multiple beats under a constant contractile state in the same mode of contraction while the left ventricle was vented to air. Linear regression analysis applied to each of the isochronal pressure-volume data sets at 20-msec intervals from the onset of contraction showed a highly linear correlation between the pressure and the volume. Both the slope and the volume intercept of the regression lines changed with time throughout the cardiac cycle. The maximal slope of the regression line (E_max) averaged 2.50 ± 0.49 mm Hg/ml (mean ± SD) for ejecting beats and 2.68 ± 0.55 mm Hg/ml for isovolumic beats. Epinephrine infusions of 12.5 μg/min and 25.0 μg/min increased E_max by 31% and 82%, respectively (P < 0.005). We conclude that: (1) The instantaneous pressure-volume relationships of the right ventricle in the isovolumic and ejecting modes can be regarded as linear, at least within the physiological range; however, these two modes of contraction did not yield an identical relationship. (2) The slope of these pressure-volume relationship curves changes with a change in the contractile state. Circ Res 44: 309-315, 1979

IT IS WELL KNOWN that there are major anatomical and physiological differences between the right and left ventricles. Compared with the left ventricle, the right ventricle has a greater regional variation in wall thickness and a more complex geometric shape. The developed pressure in systole is much smaller, and intraventricular pressure falls considerably while ejection proceeds.

Much recent research has been focussed on left ventricular function, yet there is little quantitative information concerning the right ventricle, particularly with respect to the question of how to characterize contractile state and pumping ability. Those indices of contractile state used in characterizing left ventricular function have not been quantified in and shown to be valid for the right ventricle.

Since there are major differences between left and right ventricles, we investigated whether right ventricular contractile state could be described in a similar fashion as left ventricular contractile state. In this study we determined the time-varying ratio of instantaneous pressure to volume, which has been shown to be sensitive to changes in left ventricular contractile state and nearly independent of preload, afterload, and heart rate (Suga et al., 1973; Suga and Sagawa, 1974).

Methods

Surgical Preparation

The preparation consisted of an isolated, perfused canine heart containing a water-filled balloon and a pressure transducer in the right ventricle. The preparation allowed continuous measurement of instantaneous pressure and volume under well-controlled loading conditions for several hours.

Eleven pairs of mongrel dogs weighing 20-25 kg (21.4 ± 1.6 kg) were used. Each pair was anesthetized with sodium pentobarbital (25 mg/kg, iv). The chest of one dog was opened under artificial ventilation. The subclavian artery and right atrium were cannulated and connected to the femoral arteries and veins, respectively, of the support dog. The azygos vein, superior and inferior venae cavae, brachiocephalic artery, and descending aorta were ligated. Cross-circulation was completed by ligation of the pulmonary hili. The heart was removed from the chest and suspended above a funnel (Fig. 1). Coronary flow was adjusted by means of a roller pump so that the mean perfusion pressure of the isolated heart was between 100 and 125 mm Hg. Coronary flow remained at this preset level for the duration of the experiment independent of coronary pressure. The coronary perfusion line passed through a thermostatic bath to maintain cardiac temperature at 37°C.

The pericardium was removed and the right atrium opened wide to allow coronary venous re-
turn to drain freely into the funnel and back to the femoral veins of the support dog. The chordae tendinae were cut through the tricuspid valve anulus, and a small, flat metal vent with multiple side holes was placed in the apex of the right ventricle.

A thin balloon, with an unstressed volume of 55 ml and mounted through its side on a metal adapter, was placed in the right ventricle. The neck of the balloon was pulled out through a small opening in the pulmonary artery, and the metal adapter was secured with a purse-string suture in the tricuspid annulus (Fig. 1). The space between the balloon and ventricular wall was minimized by applying continuous suction through the vent which previously had been implanted. The adapter then was connected to the volumetric chamber through a short section of tubing. Changes in volume in the chamber were measured as a change in conductance across two stainless steel electrodes.

All data were recorded simultaneously on a pen recorder (Brush model 480) and also digitized on line by a computer (Nova 1220) and stored on magnetic tape. Only selected portions of the digitized data were permanently recorded on magnetic tape for future data analysis. The pressure-volume loops also were monitored on line by the use of an x-y storage oscilloscope (Tektronix model 1564).

To determine the absolute right ventricular lumen volume it was necessary to add a correction to the balloon water volume, since the ventricle contained not only the water in the balloon but also the balloon wall, the pressure transducer and wire, a ventricular vent, and the adapter for mounting and securing the balloon. These volumes were determined by water displacement and were found to total 6.0 ml. Isovolumic contractions were achieved by clamping the short outflow tube from the balloon. Clamping the tube displaced 0.3 ml of water into the volume chamber, causing an underestimation of the volume by that amount. The absolute isovolumic volume was therefore equal to the volume chamber measurement plus an additional 6.3 ml. All data are presented as means and standard deviation of the means unless otherwise stated.

**Experimental Conditions and Protocols**

Initially, it was not clear what output impedance would be required to yield physiological pressure and volume cycles in the isolated ejecting right ventricle. We attempted to match the arterial resistance and compliance parameters of the pulmonary circulation of the dog (Shoukas, 1975). Resistance was altered by changing the diameter of the outflow tube, and compliance was altered by changing the volume of the air-filled space above the water in the volumetric chamber. The pressure-volume loops under these conditions were triangular in shape, in contrast to the more rectangular left ventricular pressure-volume loops. We were concerned that this shape might be a consequence of inappropriate impedance. However, the same impedance system loaded on the left ventricle produced the characteristic square left ventricular pressure-volume loops. Previously published data on pulmonary artery flow and right ventricular pressure (Elzinga, 1972; Elzinga et al., 1974) suggested that the ventricle would produce a more triangular pressure-volume loop rather than a square loop. We confirmed this by simultaneously measuring pulmonary artery flow and right ventricular pressure during systole in an in vivo heart preparation. By constructing a pressure-volume loop from the integrated flow signal, we found a triangular-shaped pressure-volume loop very similar to that observed in the right ventricle of excised hearts (Fig. 2).

An experimental run consisted of the following procedure. Under an initial loading condition, an ejecting pressure-volume loop was recorded. This initial loading condition was chosen so that the peak systolic pressure of the ejecting beat was between 50 and 60 mm Hg. The peak systolic ventricular pressure then was lowered by sequentially decreasing the volume of air in the loading system. At each volume, both ejecting and isovolumic curves were obtained after steady state had been achieved in 0.5–2 minutes. From four to six ejecting and from four to six isovolumic curves (Fig. 3) were obtained, and at the end of each run the pressure-volume loop...
40-30 u 20-15 20 25 VOLUME (ml)

FIGURE 2 A right ventricular systolic pressure-volume plot of data obtained from an open-chested dog in which right ventricular pressure measurements were made in vivo with an electromagnetic pulmonary artery flow probe and miniature transducer. The right ventricular volume was determined by arbitrary selection of an end-diastolic volume of 30 ml and subtraction of the integrated flow.

Result

Baseline Conditions

A family of pressure-volume diagrams obtained in a single dog heart and representing a single experimental run is shown in Figure 3. The six vertical lines represent isovolumic contractions at six different volumes, and the five open loops are the pressure-volume trajectories of ejecting beats under five different loading conditions. As the broken line (drawn in) suggests, the end systolic (peak) isovolumic pressures appear to be linearly related to the volumes.

To examine whether a linear relationship existed between isochronal pressure and volume throughout the cardiac cycle (that is, pressure-volume points at the same interval of time from the onset of the cardiac cycle), a linear regression of pressure on volume was applied and the correlation coefficients were examined. Based on the method of least squares fitting, linear regression lines of pressure on volume, determined from the isochronal instantaneous pressure-volume points from the differently loaded beats of a given experimental run, were calculated at 20-msec intervals from the time of the stimulus throughout the cardiac cycle. This procedure is illustrated in Figure 4 with data from one experimental run. In this example, isochronal points were taken from isovolumic beats at six different volumes as shown in the upper panel, and from ejecting beats under four different loading conditions as shown in the lower panel. A more complete set of these regression lines for isovolumic beats of a ventricle in the baseline contractile state is illustrated in the lower left panel of Figure 5, and for ejecting beats in the lower right panel.

Throughout the cardiac cycle, the linear regression appeared to be an excellent approximation of the pressure-volume relation. The mean values of coefficients of correlation averaged from nine dogs are shown in Table 1 for each 40-msec interval through the cardiac cycle for beats in the baseline contractile state. Even the minimal value of the coefficients of correlation that occurred at the time of the stimulus averaged 0.977, indicating a highly linear correlation between isochronal pressure and volume.

The relation between \( P(t) \), the instantaneous pressure, and \( V(t) \), the instantaneous volume, can therefore be written as:

\[
E(t) = \frac{P(t)}{V(t)} - V_d(t),
\]

where \( E(t) \) is the slope and \( V_d(t) \) the volume intercept of the regression line at time \( t \). In the left

FIGURE 3 Right ventricular pressure-volume relationships for isovolumic (vertical lines) and ejecting (loops) beats. See text for details.
ventricle, the maximal slope of the line has been termed $E_{\text{max}}$ (Suga and Sagawa, 1974). The $E_{\text{max}}$ value for eight of the hearts under the baseline contractile condition is shown in Table 2 and aver-
aged $2.26 \pm 0.59$ mm Hg/ml for isovolumic beats and $2.60 \pm 0.60$ mm Hg/ml for ejecting beats.

Unlike in the left ventricle, $V_d$ (the volume intercept) varied continuously throughout the cardiac cycle, as seen in Figure 5. We plotted $V_d$ as an explicit function of time for eight dogs. As shown in Figure 6, $V_d$ reached a minimal value shortly before the time of $E_{\text{max}} (T_{\text{max}})$. The values of $V_d$ at $T_{\text{max}}$ for the baseline isovolumic determinations in eight hearts are listed in Table 2. The variation of $V_d$ at $T_{\text{max}}$ was grossly correlated with heart size ($r = 0.85$).

**Change in the Pressure-Volume Relationships with Inotropic State**

With epinephrine infusion, there was a large increase in the slope of $E_{\text{max}}$ whether the ventricle was contracting isovolumically or ejecting. An example is shown in Figure 7, in which ejecting beats under the baseline contractile state are shown in solid lines and those during infusion of 25 µg/min epinephrine in broken lines. The top panels of Figure 5 illustrate the change in the isochronal regression lines with epinephrine. Notice that at any given time during systole, epinephrine caused the slope of the regression line to increase for both the isovolumic and ejecting beats.

**TABLE 1 Coefficient of Correlation between Right Ventricular Pressure and Volume at Various Times within One Cardiac Cycle**

<table>
<thead>
<tr>
<th>Time (msec)</th>
<th>Ejecting beats ($n = 9$)</th>
<th>Isovolumic beats ($n = 9$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$SD$</td>
</tr>
<tr>
<td>0</td>
<td>0.996</td>
<td>0.032</td>
</tr>
<tr>
<td>40</td>
<td>0.977</td>
<td>0.018</td>
</tr>
<tr>
<td>80</td>
<td>0.980</td>
<td>0.014</td>
</tr>
<tr>
<td>120</td>
<td>0.979</td>
<td>0.019</td>
</tr>
<tr>
<td>160</td>
<td>0.988</td>
<td>0.009</td>
</tr>
<tr>
<td>200</td>
<td>0.995</td>
<td>0.003</td>
</tr>
<tr>
<td>240</td>
<td>0.997</td>
<td>0.002</td>
</tr>
<tr>
<td>280</td>
<td>0.995</td>
<td>0.007</td>
</tr>
<tr>
<td>320</td>
<td>0.991</td>
<td>0.017</td>
</tr>
<tr>
<td>360</td>
<td>0.987</td>
<td>0.018</td>
</tr>
</tbody>
</table>

All values significant to 1% level.

**TABLE 2 $E_{\text{max}}$ and $V_d (T_{\text{max}})$ of Baseline Contractile Beats**

<table>
<thead>
<tr>
<th>Heart</th>
<th>Heart wt (g)</th>
<th>$E_{\text{max}}$ (mm Hg/ml)</th>
<th>$V_d, T_{\text{max}}$ (ml)</th>
<th>$E_{\text{max}}$ (mm Hg/ml)</th>
<th>$V_d, T_{\text{max}}$ (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>330</td>
<td>1.73</td>
<td>16.0</td>
<td>1.81</td>
<td>14.6</td>
</tr>
<tr>
<td>2</td>
<td>181</td>
<td>3.29</td>
<td>8.8</td>
<td>3.50</td>
<td>8.2</td>
</tr>
<tr>
<td>3</td>
<td>342</td>
<td>3.25</td>
<td>16.9</td>
<td>3.37</td>
<td>15.3</td>
</tr>
<tr>
<td>4</td>
<td>270</td>
<td>2.56</td>
<td>12.1</td>
<td>2.81</td>
<td>11.2</td>
</tr>
<tr>
<td>5</td>
<td>246</td>
<td>2.55</td>
<td>10.3</td>
<td>2.58</td>
<td>9.2</td>
</tr>
<tr>
<td>6</td>
<td>324</td>
<td>2.37</td>
<td>19.1</td>
<td>2.52</td>
<td>19.6</td>
</tr>
<tr>
<td>7</td>
<td>306</td>
<td>1.83</td>
<td>24.9</td>
<td>2.01</td>
<td>24.9</td>
</tr>
<tr>
<td>8</td>
<td>247</td>
<td>3.08</td>
<td>6.9</td>
<td>2.89</td>
<td>4.8</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>287</td>
<td>2.60</td>
<td>14.4</td>
<td>2.26</td>
<td>13.5</td>
</tr>
</tbody>
</table>

$\pm 0.60 \pm 6.0 \pm 0.69 \pm 6.5$
Figure 5  Linear regression lines based on isochronal data sets under various loading conditions under the baseline contractile state (lower panels) and with epinephrine infusion of 25 μg/min (upper panels).

Figure 8 shows the magnitude of the changes in $E_{\text{max}}$ caused by the two rates of epinephrine infusion. For isovolumic beats in the baseline contractile state, $E_{\text{max}}$ was $2.68 \pm 0.55$ mm Hg/ml. This increased to $3.30 \pm 0.49$ mm Hg/ml with an infusion of epinephrine of $12.5 \mu g/min$, and to $4.19 \pm 1.09$ mm Hg/ml with an infusion of $25.0 \mu g/min$ (into the support dog). For ejecting beats, the corresponding $E_{\text{max}}$ values were $2.50 \pm 0.49$, $3.47 \pm 0.56$, and $4.14 \pm 1.07$ mm Hg/ml, respectively. An anal-

Figure 6  The variation of the volume intercept ($V_o$) with time.

Figure 7  Ejecting pressure-volume loops in a single dog heart under baseline contractile state (solid lines) and $25 \mu g/min$ epinephrine infusion (broken lines).
Figure 8  Average $E_{\text{max}}$ values for isovolumic and ejecting beats under three levels of inotropic state.

Analysis of variance showed these increases in $E_{\text{max}}$ for both isovolumic and ejecting beats to be highly significant ($P < 0.005$).

Epinephrine infusion also was associated with a change in the volume intercept at $T_{\text{max}}$, $V_d$ ($T_{\text{max}}$). As shown in Table 3, it decreased from the baseline value under both ejecting and isovolumic conditions at both epinephrine infusion rates to a statistically significant degree ($P < 0.05$). There was no significant difference in $V_d$ ($T_{\text{max}}$) between the two enhanced contractile states.

Relationship between Isovolumic and Ejecting Conditions

As seen in Figure 3, the isovolumic end-systolic pressure-volume line appears to be shifted to the left of the end-systolic pressure-volume line for ejecting beats. To see whether this difference in isovolumic and ejecting beats was caused by a change in the slope of the line ($E_{\text{max}}$), a parallel shift of the line (a change in $V_d$), or both, we compared these two parameters for three levels of inotropic state. Table 3 shows the $E_{\text{max}}$ and $V_d$ values in the same runs and their corresponding $P$ values. As shown, the $E_{\text{max}}$ values in the two enhanced contractile states are not significantly different; however, in the baseline state, $E_{\text{max}}$ for the isovolumic mode was significantly greater ($P < 0.01$). $V_d$, on the other hand, showed a consistent decrease under the isovolumic condition for all three inotropic states.

Discussion

Quantitative information on right ventricular pumping ability and contractile state in the literature has been relatively scanty as compared to that available on the left ventricle. The reasons for this are multiple and include the concept that the right ventricle is unnecessary in resting hemodynamics (Starr et al., 1943; Kagan, 1952; Bakos, 1950), as well as the concept that the left ventricle does most of the work of generating blood flow through the circulation. Recently there has been an increased interest in the importance of the right ventricle (Brooks et al., 1971; Fixler et al., 1977; Guyton et al., 1973). A major impediment is that in vivo and in vitro studies with the right ventricle has been its complex geometric shape, which has made accurate volume measurements extremely difficult.

The purpose of this study was to examine whether the pressure-volume relationships of the right ventricle contained a significant amount of information about right ventricular pumping ability and contractile state. In this regard, the present studies are similar to the studies of Suga and his colleagues (Suga et al., 1973; Suga and Sagawa, 1974) on end-systolic pressure-volume relationships of the left ventricle. In these studies, they determined that the slope of the end-systolic pressure-volume relationship was insensitive to changes in preload and afterload but sensitive to changes in contractile state of the left ventricle. In the present studies we demonstrated similar findings, in that there was a linear relationship between pressure and volume at any specified time within the cardiac cycle for differently preloaded and afterloaded beats. Also, the maximal slope of these isochronal lines ($E_{\text{max}}$) was sensitive to changes in inotropic state. However, there are interesting qualitative as well as quantitative differences between the right and left ventricular pressure-volume relationships.

For the left ventricle, it was shown that, although $V_d$ changed with time in early systole, it was nearly constant from 100 msec to the end of systole, whereas our data on the right ventricle showed that $V_d$ continues to change until 200 msec from the onset of systole. Moreover, the $V_d$ obtained for either isovolumic or ejecting beats changed significantly with inotropic state. This is a major deviation from the findings previously reported (Suga et al., 1973; Suga and Sagawa, 1974) for the left ventricle, in which $V_d$ did not change to a statistically significant degree with inotropic state.

When we compared the pressure-volume relationships for isovolumic and ejecting beats, the two

<table>
<thead>
<tr>
<th>Table 3  Comparison of $E_{\text{max}}$ and $V_d$ ($T_{\text{max}}$) of Isovolumic and Ejecting Beats at Three Levels of Inotropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline contractile state</td>
</tr>
<tr>
<td>$E_{\text{max}}$</td>
</tr>
<tr>
<td>Isovolumic</td>
</tr>
<tr>
<td>Ejecting</td>
</tr>
<tr>
<td>$P$ &lt; 0.01</td>
</tr>
</tbody>
</table>

NS = not significant.
regression lines with the maximal slopes did not superimpose. Statistical analysis showed no consistent difference in the two slopes, but revealed a consistent difference in V_d values, suggesting a parallel shift in the pressure-volume curves with the change in contraction mode. Such a shift has not been demonstrated in the left ventricle.

Of note also is the quantitative difference in E_max and V_d values between the right and left ventricles. We found a lower E_max value (2.68 mm Hg/ml vs. 3.86 ± 0.55 mm Hg/ml) and a larger V_d (13.8 ± 5.5 ml vs. 8.2 ± 3.3 ml) for the right than for the left ventricle for isovolumic beats under the baseline contractile state (Suga and Sagawa, 1974).

Another striking difference is in the shape of the pressure-volume loops for ejecting beats. The left ventricular pressure-volume loops are nearly rectangular in shape, with a clear shoulder near end systole. The right ventricular loops are more triangular in shape, with ejection continuing well past peak pressure. This feature of right ventricular contraction makes it difficult to define the end of its systole. We can define end systole as occurring at the time of E_max, which is clearly different from the end of ejection (Fig. 7). In the left ventricle the two instants of time are very close to each other.

Of greatest importance among the present findings, however, is the observation that in the right ventricle, despite its complex geometric shape, variable wall thickness, and different pressure-ejection relationship, the instantaneous relationship of pressure to volume is as linear as that found in the left ventricle over a wide physiological range. Although the physiological basis of this linear relation is not clear at present, it does provide a convenient phenomenological method of indexing contractile state.

Acknowledgments

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