Left Ventricular Residual Volume in the Intact and Denervated Dog Heart

By Thomas A. Bruce, M.D., and Carleton B. Chapman, M.D.

The amount of blood remaining in the left ventricle at the end of systole is a factor of considerable current interest. When Harvey described the movement of the circulation in 1628 it was assumed that the heart would empty itself completely at ventricular systole. In 1856 Chauveau and Faivre, using a plethysmograph, observed that some fluid remained consistently in the heart after contraction. This was confirmed by Roy and Adami at Cambridge in 1888 by their experiments with the first cardiometer.

More recently methods have been developed for the estimation of intracardiac volume, including that of the individual chambers. These methods fall into three main groups: diameter or circumference measurements of a chamber, indicator-dilution curves, and angiocardiography. The last method has shown unusual potential in that anatomical variations in chamber size can be recorded and studied in detail at a subsequent time. Volume estimation remains less than ideal, however, so long as a single plane view is used to estimate the contents of an irregular three-dimensional chamber. A biplane cineangiofluorographic unit in this laboratory has provided the means for a more reliable determination of volume. The maximum error of the residual is ±10%, as judged by a rapidly revolving cast of the left ventricle placed before the recording cameras.

In this study the residual volume in the left ventricle has been re-evaluated, and the hemodynamic and neural mechanisms which may alter it have been explored. Studies have been made in intact, anesthetized dogs at rest and during electrically induced contractions of the thigh muscles (hereafter referred to as exercise), before and after thoracic sympathectomy and/or vagectomy.

Methods

Male mongrel dogs were isolated and observed for two weeks for signs of illness. If found healthy, they were anesthetized with chloralose-urethane 1:10 given intravenously in amounts sufficient to produce stage-3 anesthesia. A large catheter (no. 9F) was inserted from the external jugular vein into the pulmonary artery for the injection of radiocontrast material; a smaller catheter (no. 7F) was passed from the carotid artery into the left ventricle for measurement of pressure; and an endotracheal tube was placed one inch above the carina. The animal was suspended in a standing position for cineangiofluorography, breathing being controlled throughout the period of suspension by a Thompson pump respirator. Two ml/kg body weight of 90% Hypaque-M solution (Winthrop Laboratories) at 37°C were administered into the pulmonary artery by a pneumatic injector, and cineangiofluorograms were made over a six- to eight-second period at 30 frames per second. The electrocardiogram and left ventricular pressure, and in...
several instances the intraesophageal pressure, were recorded simultaneously. After the studies at rest had been completed, and with the dog still anesthetized, the thigh muscles were exercised by means of single, supramaximal stimuli, delivered at one-second intervals through needle electrodes inserted directly into the hamstring muscles. Contraction of the muscles produced vigorous kicking movements of the hind limbs, thus increasing total body oxygen consumption to between two and four times the resting value. No direct effect of electrical stimulation on the cardiac rate or force of contraction could be discerned. Cineangiofluorography was repeated 10 minutes after the beginning of the exercise, which continued during filming.

In five dogs a two-stage thoracic sympathectomy was done after base line studies had been completed. Sympathetic nerves and ganglia were removed from the sixth thoracic vertebra to the inferior cervical ganglion, including the sympathetic fibers in the vagus nerve. The animals were restudied after 10 to 14 days, when they had fully recovered from the surgical procedure. After completion of the cineangiofluorographic runs at rest and during exercise in these animals, acute bilateral vagectomy was performed, leaving the heart completely without autonomic connections, and studies were immediately repeated during resting and exercising states.

Four other dogs were studied following acute vagectomy in the presence of an intact sympathetic system, and the results were compared with their control records.

Heart rate was measured on a stroke-to-stroke basis, and converted to corresponding beats/min. Volume was calculated from the film images each 1/30 second during the passage of the radiocontrast medium through the left ventricle, using a previously described method.15

## Results

Control studies are summarized in table 1. At rest, the left ventricle retained 43% of its end diastolic volume (EDV) at the end of ejection. During exercise both the residual volume and the EDV fell (18 and 4%, respectively), and the net effect was a slight increase in stroke volume. These relationships are also shown in table 2, where the data are expressed as percentage changes from the resting EDV.

In one dog the effect of rapid intravenous infusion of isotonic saline (4 ml/kg/min for a total of 900 ml) was studied (fig. 1A). Although the EDV and the cardiac rate increased moderately, the absolute residual volume was unchanged.

In six of the unoperated dogs at rest a transient bradycardia was noted after injection of radiocontrast medium, the heart rate falling from an average of 114 beats/min before injection to 72 beats/min immediately after injection. The EDV increased significantly without change in the residual volume.

Marked atrial tachycardia caused a pronounced decrease of both residual volume and EDV, typified by dog 14 in figure 2. In one instance (dog 17, fig. 2) the reverse occurred and an essentially normal stroke volume was ejected from a greatly increased diastolic and residual volume.

Following vagectomy the cardiac rate rose immediately to an average of 169 beats/min

### TABLE 1

End Systolic or Residual Volumes (ESV) and End Diastolic Volumes (EDV) at Rest and During Electrically Stimulated Muscular Exercise in 28 Intact, Anesthetized Dogs*

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
<th>Change</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESV, ml</td>
<td>22 ± 15</td>
<td>18 ± 9</td>
<td>-18%</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>EDV, ml</td>
<td>49 ± 27</td>
<td>47 ± 23</td>
<td>-4%</td>
<td>ns‡</td>
</tr>
<tr>
<td>ESV/EDV, %</td>
<td>43 ± 11</td>
<td>38 ± 10</td>
<td>-12%</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Cardiac rate, beats/min</td>
<td>94 ± 28</td>
<td>109 ± 36</td>
<td>+16%</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>15.1 ± 2.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

‡ns: not significant.
**TABLE 2**

**Effect of Electrically Stimulated Muscular Exercises on Left Ventricular Volumes and Cardiac Rate Before and After Cardiac Denervation**

<table>
<thead>
<tr>
<th></th>
<th>Cardiac rate</th>
<th>EDV*</th>
<th>ESV*</th>
<th>Total strokes studied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>beats/min</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td><strong>1. Intact control (28 dogs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>94</td>
<td>100</td>
<td>42.5</td>
<td>171</td>
</tr>
<tr>
<td>Exercising</td>
<td>109</td>
<td>96.5</td>
<td>36.4</td>
<td>143</td>
</tr>
<tr>
<td>P-values</td>
<td>&lt;.005</td>
<td>ns†</td>
<td>&lt;.005</td>
<td></td>
</tr>
<tr>
<td><strong>2. Vagectomy (4 dogs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>169</td>
<td>59.7</td>
<td>14.5</td>
<td>41</td>
</tr>
<tr>
<td>Exercising</td>
<td>166</td>
<td>69.4</td>
<td>17.4</td>
<td>43</td>
</tr>
<tr>
<td>P-values</td>
<td>ns</td>
<td>&lt;.005</td>
<td>&lt;.025</td>
<td></td>
</tr>
<tr>
<td><strong>3. Sympathectomy (5 dogs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>119</td>
<td>91.7</td>
<td>35.0</td>
<td>28</td>
</tr>
<tr>
<td>Exercising</td>
<td>124</td>
<td>102.8</td>
<td>41.2</td>
<td>32</td>
</tr>
<tr>
<td>P-values</td>
<td>ns</td>
<td>&lt;.005</td>
<td>&lt;.005</td>
<td></td>
</tr>
<tr>
<td><strong>4. Total denervation (5 dogs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>131</td>
<td>72.2</td>
<td>29.2</td>
<td>39</td>
</tr>
<tr>
<td>Exercising</td>
<td>131</td>
<td>80.6</td>
<td>28.0</td>
<td>33</td>
</tr>
<tr>
<td>P-values</td>
<td>ns</td>
<td>&lt;.005</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>

*Calculated as per cent of each dog's own resting control EDV.
†ns: not significant.

**B. BRADYCARDIA**

**FIGURE 1**

A. Left ventricular residual volume (lined area) before and after infusion of 900 ml isotonic saline during a 17-minute period to a healthy 15-kg dog. EDV: end diastolic volume; ESV: end systolic (residual) volume. B. Average residual volume in six dogs during bradycardia produced by radiocontrast medium injection, and in the remaining control dogs that showed no bradycardia after injection.
and did not increase further during exercise. Left ventricular volumes at rest (fig. 3) became much smaller: EDV decreased to 59.7% of the control value, and residual volume decreased to the lowest levels recorded in the course of the entire study, 14.5% of the control.

**FIGURE 2**

Left ventricular residual volume before and after the onset of tachycardia, measured in two different dogs.

**FIGURE 3**

Left ventricular volume during the resting state in groups of intact control, vagectomized, sympathectomized, and totally denervated dog hearts. EDV: end diastolic volume; ESV: end systolic (residual) volume.
control EDV. During subsequent exercise, both systolic and diastolic volumes increased, especially the latter (table 2).

After sympathectomy, there was little change in the resting ventricular volumes from the control state, considering the slightly faster mean cardiac rate (fig. 3). The response to exercise was different, however, in that ventricular filling increased, and a greater amount of residual blood remained after ejection (table 2).

Total denervation was characterized by an EDV between the two extremes of sympathectomy and vagectomy (fig. 3). As in the sympathectomized animals, exercise increased the EDV, significantly but in this instance no change in residual volume was seen.

Discussion

A considerable volume of residual blood has been found in the left ventricle at all times. Under control resting conditions it remained at 30 to 55% of the EDV. During exercise, tachycardia, and unopposed sympathetic control (produced by vagectomy) the residual volume diminished. Even under severe stress, however, it remained above 10% of the diastolic volume.

Several previous reports have tended to place the normal resting residual volume as high as 65 to 80 of the EDV.9-11 Holt found that residual volume in dogs, swine, cattle, and horses averaged 57% of the EDV of the ventricle, regardless of species studied and of the range of their heart sizes. He also reported a group of dogs in which the residual volume was 75% of the EDV when the heart rate was rapid (mean, 163 per minute), and 54% when the rate was slower (mean, 79 per minute).7 All these studies, in which the residual volume accounted for more than 50% of the total ventricular volume, were done by the indicator-dilution method. Swan and Beck,22 and more recently Hallemann et al.,23 have warned about the special difficulties in this method of nonmixing of indicator, which can produce excessively large figures for residual volume.

The anesthetic agent may also be a cause of excessively large volume figures. Rapaport et al.11 noticed that during pentobarbital anes-

thesia the residual volume was 79.1% of the EDV, but that when a chloralose-urethane mixture was substituted, the residual volume fell to 66% of the EDV. Our own results would confirm this: the first 5 dogs studied were anesthetized with pentobarbital and residual volume was 60%, whereas the mean for the group given chloralose-urethane was 43%.

Alterations in some of the circulating hormones, particularly epinephrine, might have resulted in some of the changes we have ascribed to exercise. There was no evidence of pain during electrical stimulation of the hamstrings, however, because of the plane of anesthesia. The absence of changes in heart rate during exercise in the denervated animals suggest also that changes in the concentrations of circulating catecholamines had little or no effect on the final result. The role of autonomic factors in cardiac control has been discussed in a previous report from this laboratory.26

Cineangiographic volume studies from other laboratories, using methods different from our own, have given data similar to those published in this report. Gribbe et al.16 reported that the residual volume in 22 anesthetized dogs was 39.3% of the EDV. In three unanesthetized dogs the residual volume was 42.5%, and after repeated studies, 40.7%. Dodge et al.4 reported left ventricular volumes in a series of patients with heart disease studied by angiography. In the two patients considered to have normal left ventricles, the residual volumes (calculated from their data) were 30 and 45% of the EDV.

The effect of the radiocontrast material itself may account for some of the differences found in the results obtained from the angiographic and indicator-dilution methods. Hemodynamic changes were seen following the injection of radiocontrast material in about half of the dogs reported. Peak ventricular pressure immediately after contrast injection was reduced by an average of 12% of the preinjection pressure. Friesinger et al.29 have reported also that, for a short period, the
force of myocardial contraction is diminished following the injection of radiocontrast materials. In our study, when the group of dogs that did develop bradycardia from contrast material is compared with the group that did not (fig. 1B), it can be seen that no change of residual volume occurred in spite of an increase of EDV.

Cournand and co-workers\textsuperscript{20} have reported a study in which separate right and left ventricular volumes were determined at rest and during treadmill exercise in two groups of patients: one trained in muscular exertion and the other sedentary. Volumes were determined from precordial scintillation curves after injection of \textsuperscript{131}I-albumin into the right atrium. Right ventricular residual volume at rest (calculated from the figures reported) averaged 49.8\% of the EDV in the six trained subjects and 43.4\% in the four untrained subjects. Left ventricular residual volumes were 54.8 and 46.3\%, trained and untrained, respectively. Ten seconds after exercise was begun, left ventricular residual volume fell to 40.1\% of the EDV in the trained subjects but rose to 64.9\% in the untrained group.

In our own study, the largest ventricular residual volumes encountered were in the resting control state. The close resemblance of ventricular volumes in the sympathectomized and in the intact animals emphasizes the predominating vagal influence on the normal resting heart. An increase of residual volume was observed in only two situations: during the mechanical inefficiency produced in one dog by arrhythmia, and during exercise with unsupported vagal control because of sympathectomy.

Previous reports, that the residual volume bears a linear relationship to the EDV,\textsuperscript{27, 28} seem to hold true only in the resting state, since either the EDV or the residual volume at times vary independently of the other. For instance, the ventricle responded to a slower heart rate and to an increased venous inflow by a progressive diastolic engorgement, resulting in a larger stroke volume. Cardiac output was thus maintained without diminution of residual ventricular blood. This lack of linearity was seen also in the cineangiographic study of dogs by Rushmer and Thal\textsuperscript{14} who concluded that the diastolic ventricular area varied with the ventricular filling pressure, whereas the end systolic (residual) area remained constant.

**Summary**

Left ventricular volumes were measured at rest and during electrically stimulated muscular exercise in 28 anesthetized dogs. Volumes were calculated from images obtained during biplane cineangiofluorography. Under control resting conditions from 30 to 55\% of the diastolic volume of the left ventricle remained after ejection. This residual volume of blood became an immediate source of the increased ventricular output during the beginning of exercise. Following vagectomy, sympathectomy, and total cardiac denervation, the ability to increase cardiac output during exercise persisted, but was accomplished by increased ventricular filling rather than by diminution of the residual volume.

**Acknowledgment**

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**References**

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