Phasic Right Coronary Artery Blood Flow in Conscious Dogs with Normal and Elevated Right Ventricular Pressures

Howard S. Lowensohn Ph.D., Edward M. Khouri, Donald E. Gregg, Ph.D., M.D., R. Lee Pyle, V.M.D., and Randolph E. Patterson, M.D.

SUMMARY We studied phasic right coronary blood flow in well trained normal dogs and dogs with pulmonic stenosis. We installed electromagnetic flow transducers and pressure tubes under anesthesia to monitor right coronary blood flow, cardiac output, central aortic blood pressure, and right ventricular pressure. In normotensive dogs, systolic flow amplitude equaled early diastolic flow levels. The ratio of systolic to diastolic flow at rest was substantially greater in the right coronary bed than in the left circumflex bed (13 ± 3.6%). Right diastolic flow runoff, including the cove late in diastole, resembled left circumflex runoff. Blood flow to the normotensive right (37 ± 1.1 ml/min 100 g) and the left (35 ± 1.0 ml/min 100 g) ventricular myocardium indicated equal perfusion of both cardiac walls.

IN 1937, GREGG described phasic right coronary artery blood flow in the anesthetized open-chested dog. Gregg et al. constricted the pulmonary artery to elevate right ventricular pressure, and observed an increase in right coronary artery blood flow. Subsequently, other investigators confirmed augmentation of right coronary artery blood flow as a result of elevated right ventricular systolic pressure by pulmonary artery constriction or pulmonary emboli. Ross briefly characterized phasic right coronary blood flow at rest in two conscious dogs. The purpose of this study was to define phasic right coronary artery blood flow during the cardiac cycle. We studied blood flows at rest and during peak reactive hyperemia in well trained, conscious, unsedated, normotensive dogs and dogs with established congenital subpulmonic and/or pulmonic stenosis.

Methods

We studied five normal dogs (dogs 1-5) and four dogs with congenital pulmonic stenosis (dogs 6-9). The normal dogs, used as controls, appeared healthy and had normal electrocardiograms, and Knott's test for Dirofilaria immitis was negative. The diagnosis of pulmonic stenosis was based on auscultation, electrocardiogram, angiocardiogram, and right heart catheterization and subsequently was confirmed post mortem. After initial screening and diagnosis, we trained each dog to lie on its right side on a padded table for long periods of time without restraint. We administered 1 g of streptomycin sulfate and 1.5 x 10^8 U of procaine penicillin intramuscularly immediately preceding and for 3 days following surgery. We produced surgical anesthesia by intravenous injection of sodium pentobarbital (65 mg/kg). Subcutaneous injection of atropine sulfate (2.0 mg) preceded endotracheal intubation. A Harvard small animal respirator maintained ventilation with room air. We performed surgery under sterile conditions.

An incision in the 4th intercostal space exposed the base of the right heart and ascending aorta. On retraction of the right atrial appendage, we installed an electromagnetic flowmeter (2.0 mm or 2.5 mm) and a pneumatic cuff on the right coronary artery 1.0 to 2.0 cm from its origin. The cuff usually was very close to the 1st major marginal branch. Because of the acute curvature of the right coronary artery and its location deep in the friable fat of the atrioventricular sulcus, we stabilized the flowmeter with Ivalon sponge bridges and overlays. Electromagnetic flow transducer installation about the ascending aorta followed a previously described procedure. Wound closure and terminal connector placement completed the surgical procedure. A 5- to 25-day period provided sufficient recovery time prior to experimental studies. Several days after chest surgery, we implanted chronic catheters by transvascular methods under sodium thiopental (25 mg/kg) anesthesia.
A polyvinyl tube (0.038 x 0.070 in.) sheathed with Silastic tubing (0.040 x 0.085 in.) that extended approximately 1 cm beyond its tip, placed at the brachiocephalic artery origin via the left common carotid artery with fluoroscopic assistance, served as the catheter for measurement of aortic pressure and blood sampling. We installed a chronic right ventricular pressure tube (construction similar to the aortic pressure tube) in the right ventricle via the left jugular vein, using fluoroscopy, in dogs 1 and 2. In dog 3 an indwelling right ventricular catheter was implanted in the infundibular region by a modification of the Herd and Barger technique13 during a separate left thoracotomy.

Experimental studies spanned a 2-week period. Studies consisted of measurement of phasic and mean right coronary blood flows at rest and the resultant peak values during the reactive hyperemia that followed release of 10-second occlusions. Recording of central aortic blood pressures, cardiac outputs, electrocardiograms, right ventricular pressures, and right coronary artery blood flows were made simultaneously in dogs 1-3. In all other dogs we recorded right ventricular pressures once via a Brockenbrough catheter (dog 8) or a no. 5 Fr. Swan-Ganz catheter17 on the day of, or up to 4 days after, completion of coronary hemodynamic studies. To obtain right ventricular pressures we used intravenous sodium pentobarbital anesthesia (25 mg/kg) in dogs 6, 8, and 9. In dogs 4, 5, and 7 we recorded right ventricular pressures under light sedation with sodium pentobarbital (120 mg) and [10-\beta-(dimethylamino)propyl]phenothiazin-2-yl-methyl ketone [acepromazine, Ayerst] (20 mg), with procaine HCl infused into the skin over the left jugular vein at the site of catheter entry. Hematocrits for all dogs ranged about 0.1 second after the associated P wave.

We used Biotronix model 310 gated sine wave electromagnetic flowmeters to measure right coronary artery blood flow (1,000 Hz carrier frequency) and cardiac output (400 Hz carrier frequency). Statham model P23Db electromanometers monitored aortic and right ventricular pressures. Standard and augmented leads provided information on the electrical correlates of the hearts studied. We used an Electronics for Medicine recorder, model DR8, for these studies.

Postmortem evaluation included gross thoracic examination, cardiac histopathological studies, and heart weight determinations. Control heart weights were from dogs 1, 4, and 5, and from 15 other normal experimental dogs representing body sizes used in this study. We sectioned and weighed the free right myocardial wall by the method of Latimer14 and used this to estimate right coronary artery blood flow per 100 g of myocardium.

Results

RIGHT CORONARY ARTERY BLOOD FLOW IN DOGS WITH NORMAL RIGHT VENTRICULAR PRESSURE

Figure 1 illustrates the pattern of right coronary artery blood flow obtained from all normal dogs at rest. The systolic flow (black area) commenced with a rapid increase in flow after the opening of the aortic valves. This increase in flow reached a peak rapidly, then declined immediately to a substantially high plateau that remained through pro-

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TABLE 1

<table>
<thead>
<tr>
<th>Dog</th>
<th>Wt (kg)</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
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<td>1</td>
<td>26</td>
<td>61 ± 4</td>
<td>119 ± 4</td>
<td>66 ± 4</td>
<td>91 ± 5</td>
<td>21 ± 2</td>
<td>43 ± 4</td>
<td>0.09 ± 0.01</td>
<td>0.24 ± 0.03</td>
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</tr>
<tr>
<td>2</td>
<td>26</td>
<td>77 ± 9</td>
<td>129 ± 8</td>
<td>85 ± 7</td>
<td>106 ± 9</td>
<td>4.4 ± 0.3</td>
<td>16 ± 1</td>
<td>0.06 ± 0.01</td>
<td>0.14 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>71 ± 9</td>
<td>119 ± 7</td>
<td>71 ± 7</td>
<td>93 ± 7</td>
<td>3.8 ± 0.1</td>
<td>15 ± 2</td>
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<tr>
<td>4</td>
<td>28</td>
<td>53 ± 6</td>
<td>105 ± 4</td>
<td>69 ± 5</td>
<td>88 ± 4</td>
<td>2.0 ± 0.1</td>
<td>14 ± 0.5</td>
<td>36 ± 1</td>
<td>0.06 ± 0.00</td>
<td>0.17 ± 0.01</td>
</tr>
<tr>
<td>5</td>
<td>22</td>
<td>62 ± 5</td>
<td>114 ± 4</td>
<td>74 ± 5</td>
<td>92 ± 5</td>
<td>14 ± 0.5</td>
<td>36 ± 1</td>
<td>0.06 ± 0.00</td>
<td>0.17 ± 0.01</td>
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Normal dogs

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<th>Dog</th>
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<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
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<td>6</td>
<td>18</td>
<td>80 ± 11</td>
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<td>82 ± 11</td>
<td>110 ± 8</td>
<td>1.5 ± 0.02</td>
<td>20 ± 3</td>
<td>33 ± 5</td>
<td>0.06 ± 0.01</td>
<td>0.18 ± 0.02</td>
</tr>
</tbody>
</table>

Moderate hypertension

<table>
<thead>
<tr>
<th>Dog</th>
<th>Wt (kg)</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
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<tbody>
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<td>7</td>
<td>9</td>
<td>57 ± 6</td>
<td>106 ± 6</td>
<td>60 ± 8</td>
<td>76 ± 7</td>
<td>0.94 ± 0.17</td>
<td>14 ± 2</td>
<td>35 ± 6</td>
<td>0.03 ± 0.01</td>
<td>0.22 ± 0.03</td>
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</table>

Severe hypertension

<table>
<thead>
<tr>
<th>Dog</th>
<th>Wt (kg)</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
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<tbody>
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<td>8</td>
<td>26</td>
<td>60 ± 6</td>
<td>105 ± 4</td>
<td>49 ± 6</td>
<td>68 ± 6</td>
<td>2.6 ± 0.4</td>
<td>37 ± 2</td>
<td>33 ± 2</td>
<td>0.05 ± 0.03</td>
<td>0.57 ± 0.04</td>
</tr>
<tr>
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<td>31</td>
<td>59 ± 9</td>
<td>122 ± 6</td>
<td>54 ± 5</td>
<td>75 ± 4</td>
<td>4.1 ± 0.5</td>
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<td>30 ± 1</td>
<td>0.13 ± 0.03</td>
<td>0.88 ± 0.09</td>
</tr>
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</table>

5. We found a high systolic-diastolic blood flow ratio of 36 ± 7.6% (sd) (n = 36 observations, five dogs).

After release of a 10-second occlusion of the right coronary artery, mean blood flows ranged from 30 to 52 ml/min at the time of maximal hyperemic response (Table 2). Peak flow response was 300 ± 20% (sd) (n = 22 observations, four dogs; range = 130-430%) of preocclusion values at rest. A typical peak phasic pattern for normal right coronary flow showed an initial rapid increase in systolic flow (Fig. 1, black area) to a nearly level summit of approximately the same amplitude as maximum diastolic flow. Systolic flow terminated at a notch as described above for the resting flow. Early diastolic flow remained level or ascended slightly for a period nearly equivalent to systole, then gradually fell to a coved depression similar to that recorded at rest, but remained at a much greater amplitude. A stroke systolic to diastolic flow ratio of 30 ± 2.0% (se) (n = 22 observations, four dogs) represented the average pulsatile flow distribution during peak reactive hyperemia. Peak hyperemia accounted for 1.1% and 1.2% of cardiac output in dogs 2 and 3, respectively.

RIGHT CORONARY ARTERY BLOOD FLOW IN DOGS WITH ELEVATED RIGHT VENTRICULAR PRESSURE.

Dogs with right ventricular hypertension represented different hemodynamic categories in this study, as determined by the relationship of systolic arterial pressure to systolic right ventricular pressure (Fig. 3 and Table 2). In the presence of moderate hypertension (dog 6), the markedly elevated right ventricular systolic pressure was considerably less than arterial systolic pressure. With high hypertension (dog 7) systolic arterial and right ventricular pressures were nearly equal. Severe hypertension (dogs 8 and 9) described the condition in which right ventricular systolic pressure was markedly higher than arterial systolic pressure. Attenuation of the latter two-thirds of control systolic flow primarily characterized right coronary artery blood flow in right ventricular hypertension. The severity

Table 2 - Peak Reactive Hyperemia and Ventricular Pressure Data

<table>
<thead>
<tr>
<th>Dog</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
<th>RVP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68 ± 8</td>
<td>119 ± 6</td>
<td>71 ± 9</td>
<td>93 ± 9</td>
<td>30 ± 5</td>
<td>57 ± 5</td>
<td>0.12 ± 0.02</td>
<td>0.33 ± 0.07</td>
<td>22 ± 2</td>
<td>2.5 ± 1</td>
</tr>
<tr>
<td>2</td>
<td>88 ± 16</td>
<td>127 ± 9</td>
<td>87 ± 11</td>
<td>107 ± 11</td>
<td>52 ± 4</td>
<td>46 ± 7</td>
<td>0.16 ± 0.01</td>
<td>0.45 ± 0.02</td>
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<td>5.1 ± 1</td>
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<td>3</td>
<td>72 ± 9</td>
<td>115 ± 8</td>
<td>68 ± 9</td>
<td>90 ± 9</td>
<td>4.7 ± 0.6</td>
<td>118 ± 9</td>
<td>0.13 ± 0.01</td>
<td>0.61 ± 0.11</td>
<td>18*</td>
<td>3*</td>
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<tr>
<td>4</td>
<td>59 ± 11</td>
<td>105 ± 5</td>
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<td>89 ± 5</td>
<td>42 ± 3</td>
<td>14*</td>
<td>0*</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>76*</td>
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Moderate hypertension

<table>
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<tr>
<th>Dog</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
<th>RVP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>85 ± 12</td>
<td>138 ± 12</td>
<td>81 ± 10</td>
<td>110 ± 12</td>
<td>1.4 ± 0.2</td>
<td>87 ± 8</td>
<td>145 ± 13</td>
<td>0.21 ± 0.02</td>
<td>0.80 ± 0.10</td>
<td>105*</td>
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<tr>
<td>7</td>
<td>59 ± 8</td>
<td>105 ± 7</td>
<td>58 ± 4</td>
<td>77 ± 6</td>
<td>0.96 ± 0.3</td>
<td>55 ± 12</td>
<td>134 ± 30</td>
<td>0.12 ± 0.02</td>
<td>0.82 ± 0.21</td>
<td>142*</td>
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Severe hypertension

<table>
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<tr>
<th>Dog</th>
<th>HR</th>
<th>Systole</th>
<th>Diastole</th>
<th>Mean</th>
<th>CO (liters/min)</th>
<th>RCF (ml/min)</th>
<th>RCF (ml/min/100 g)</th>
<th>SSF (ml)</th>
<th>SDF (ml)</th>
<th>RVP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>67 ± 10</td>
<td>108 ± 6</td>
<td>53 ± 5</td>
<td>71 ± 5</td>
<td>2.9 ± 0.4</td>
<td>113 ± 12</td>
<td>101 ± 11</td>
<td>0.18 ± 0.05</td>
<td>1.6 ± 0.34</td>
<td>154*</td>
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<tr>
<td>9</td>
<td>65 ± 12</td>
<td>123 ± 2</td>
<td>57 ± 6</td>
<td>77 ± 10</td>
<td>4.4 ± 0.05</td>
<td>241 ± 48</td>
<td>121 ± 24</td>
<td>0.48 ± 0.15</td>
<td>3.3 ± 0.7</td>
<td>154*</td>
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All values are entered as the mean ± sd, except for the asterisked right ventricular pressures (RVP) taken under anesthesia. Abbreviations are defined in Table 1.
of this restriction increased in relation to the degree of hypertension, taking into account the magnitude of the differential between right ventricular and coronary perfusion pressures (Fig. 3 and Table 1). The example of greatest flow restriction occurred in severe hypertension. In this state, the presence of retrograde systolic flow indicated that the forces that acted on the peripheral right coronary arterial bed during this period exceeded coronary artery perfusion pressure. Early in diastole a brief, peaked segment of augmented flow occurred. This appeared in all control hypertensive states and was more easily identified in high and severe hypertension. The depression in systolic flow and the augmentation of early diastolic flow provided a definitive change in pulsatile flow characteristics from that observed in dogs with normotensive myocardium. The systolic to diastolic flow ratio decreased little in moderate hypertension (33%) from that observed in the normotensive state; however, in high and severe hypertension we found a dramatic decrease in the ratio (9–15%) (Table 1).

Peak reactive hyperemic responses in dogs with right ventricular hypertension were obtained in the same manner as described for normal dogs. Heart rates, aortic pressures, and cardiac outputs remained similar to their resting control values (Table 2) for dogs 6–9. We observed a diminished amplitude of systolic blood flow in right ventricular hypertension (Fig. 3). The throttling was appreciably greater in severity with the higher levels of hypertension. This became most marked in severe hypertension with a depressed late systolic flow. Even in the latter state, which exhibited control retrograde flow, systolic flow remained essentially antegrade. In isometric relaxation blood flow accelerated rapidly and reached its highest peak in early diastole. The differential between suppressed systolic flow and augmented early diastolic flow distinguished peak reactive hyperemia of the right coronary artery in hypertension from the same response in normotension. Mean peak flow increased 305–435% (Table 2) and showed no relationship between augmentation capabilities and the degree of right ventricular hypertension. Systolic to diastolic flow ratios remained similar to the control values. At peak flow, the right coronary artery utilized a greater degree of cardiac output (3.9–6.2%) than during control. Although the range varied considerably, no established relationship of utilization fraction to right ventricular hypertension appeared.

Electrocardiograms from the hypertensive dogs at rest during hemodynamic studies showed right axis deviation greater than 100°; this suggested right ventricular hypertrophy. In dogs 6, 8, and 9, S-T segment changes implied subendocardial ischemia.

**PATHOLOGY**

Prestudy diagnoses were confirmed at postmortem examination, except in dogs 2 and 3. The experimental procedures after the control studies in dogs 2 and 3 modified their hearts and precluded confirmation of initial diagnoses. The remaining normotensive controls, except dog 4, exhibited a normal thorax. In dog 4 the thorax contained 125 ml of fluid; the free right ventricular wall was thin and showed endocardial injury. The injury was attributed to ventricular fibrillation and subsequent resuscitation during surgery. In dog 9 we found 325 ml of thoracic fluid and extensive pulmonary congestion at autopsy.

Hearts from hypertensive dogs were enlarged, with thickened right ventricular walls, particularly in the infundibular region. Infundibular enlargement appeared comparatively more pronounced in dogs with higher levels of right ventricular pressure. A summary of the ratio of the weight of the right ventricular wall to the septum plus the
left ventricular wall (Table 3) substantiated a significant increase in right wall mass in the dogs with hypertensive pulmonic stenosis. Poststenotic pulmonary artery dilatation was absent in these dogs. Valvular stenosis was accompanied by thickened cusps in three dogs; dog 7 had thin cusps with extremely deep sinuses, with marked peripheral fusion forming a restricted valvular lumen.

In the dogs with right ventricular hypertension there was histopathological evidence of peripheral coronary artery lesions that consisted of intimal proliferation, subintimal edema, and medial hypertrophy. Intramural arterial enlargement with possible wall damage (Anitschkow cells in the walls of some vessels) appeared in dogs 7 and 8. An infarct with marked fibrosis occurred in the free right ventricular wall of dog 9, associated with rupture of the wall of a large coronary artery. These findings were present primarily in the inner half of the right myocardial wall, and were most prominent subendocardially in dog 9.

**Discussion**

Pulsatile right coronary artery blood flow in the normotensive dog at rest differed in appearance from left coronary flow patterns. Although all normal systolic coronary flows at rest commenced with a sharply peaked overshoot, this peak usually represented the greatest flow amplitude only in the right coronary flow pattern. The immediate drop to a level of flow nearly equal in magnitude to diastolic flow characterized pulsatile right coronary artery blood flow. A quantitative consideration of this flow pattern substantiated the fact that a significant amount of pulsatile flow (systolic to diastolic ratio = 36%) perfused the right myocardium during systole. The high ratio represented a marked perfusion of the right myocardium during systole when compared to systolic flow to the left myocardium via the left circumflex, taking into consideration similar heart rates and coronary perfusion pressures. The left circumflex systolic to diastolic flow ratio was 13 ± 3.6% (SD) (n = 77 observations, eight dogs) (unpublished observations). An essentially flat early diastolic flow distinguished this part of the pulsatile right coronary flow from the main left, left circumflex, and anterior descending flow patterns. Pitt and Gregg demonstrated the presence of diastolic coves in the left circumflex flow pulse following P waves in the conscious dog with a surgically blocked atroventricular node. Even though a correlation between the P wave and a transiently marked depression in diastolic flow occurred in right coronary, main left circumflex, and to a lesser extent in the left anterior descendens flow patterns, no established proof for its origin exists. Previous studies, using electromagnetic flowmeters about the left circumflex artery, demonstrated flows of 30-45 ml/min 100 g for three conscious dogs and subsequent unpublished results from a similar experimental model from one of our laboratories showed a flow of 35 ± 7.0 (SD) ml/min 100 g (n = 30 observations, three dogs). Our results for right coronary flow, therefore, indicate that right and left myocardial blood flows per unit of tissue in the resting canine are of essentially the same magnitude. Gregg et al. showed that main left coronary blood flow used 2.6% of the cardiac output. We found that right coronary flow took approximately 0.5% of cardiac output. On this basis, right coronary flow would supply 16% of the total blood flow to the canine myocardium at rest.

In peak reactive hyperemia of the right coronary bed, systolic flow was augmented to the same degree as diastolic flow. There was no marked systolic-diastolic differential in amplitude, as seen in the peak hyperemic response of the left coronary beds. The capability of the right coronary bed to dilate, using flow at rest as the reference, was less (peak hyperemic flow was 130-430% greater than flow at rest) than Olsson and Gregg observed for the left circumflex bed (peak hyperemic flow was 300-700% greater than flow at rest).

Central aortic blood pressure greatly exceeded right ventricular pressure throughout the myocardial cycle in the normotensive state. This indicated that extravascular tension factors exerted a minimal restraining influence on right coronary blood flow. Therefore, peripheral vessel tone would serve as the major impedance factor to right coronary flow in systole as well as diastole. The equal amplitudes of peak flow in systole (discounting the initial spike) and early diastole substantiated these premises.

In relating normal canine right coronary flow flow to human coronary flow dynamics, functional differences in anatomical distribution must be understood. The canine right coronary artery supplies the free right wall whereas the human right coronary supplies varying amounts of left myocardial tissue. Left myocardial contraction in the human, therefore, would impede the right coronary systolic flow proportionately, depending on the amount of left myocardium being perfused.

Donald and Essex totally compromised resting canine right ventricular function by occlusion of the right coronary artery for extended periods and showed little effect on cardiac output. Brooks et al. found right coronary blood flow essential for maintenance of cardiac output when they partially occluded the pulmonary arteries. Reduction of coronary flow led to decompensation at a lower systolic pressure. Part of our study considered the effects of pulmonic stenosis on right coronary blood flow in the state of stable hypertrophy. Except for phasic flow studies in subaortic stenosis and aortic insufficiency, knowledge of phasic coronary blood flow differences in valvular disease states with and without ventricular hypertension remains limited.
A reduction in systolic flow and an increase in early diastolic flow characterized the difference in pulsatile right coronary flow in dogs with right ventricular hypertension, from the pattern described for the normotensive dog. Whereas throttling of right coronary flow occurred in the latter part of systole in right heart hypertension, the greatest restriction of flow in dogs with subaortic stenosis was found early in systole. The differences in these observations may be explained by the temporal relationships of coronary perfusion pressure and intramyocardial tension. Neither this study nor that of Pyle et al.22 offers proof for this conclusion. Dog 7 had a coronary perfusion pressure nearly equal to right ventricular pressure, the same pressure relationship observed in the normal left myocardium. The resting and peak hyperemic flows in dog 7 appeared similar to the respective left coronary flow patterns of normotensive dogs.10,17 The stroke systolic to diastolic flow ratio (13.6%) for dog 7 fitted well within the range for the left circumflex flow ratio described earlier.

Although resting coronary flows per unit of right myocardium (Table 1) in the dogs with right ventricular hypertension showed only slight differences from the normotensive dogs, the distribution of blood within the myocardium probably differed, particularly with markedly elevated right ventricular pressures. Electrocardiographic recordings and observations made post mortem, particularly for those dogs with high and severe hypertension, suggested reduced blood flow to the inner layers of the right myocardium. Flickinger and Patterson12 observed myocardial lesions and/or changes in intramural coronary arteries in a small number of dogs with pulmonic stenosis; one dog with myocardial fibrosis had severe hypertension. Peak reactive hyperemia augmented flow to the same degree in dogs with pulmonic stenosis as in normotensive dogs. Right coronary systolic flow, during peak hyperemia in right ventricular hypertension, was attenuated to nearly the same degree as at rest. The capability of the right coronary artery to dilate in dogs with pulmonic stenosis was considerably less than that observed in the left circumflex bed of normal dogs17 or dogs with subaortic stenosis.22

In hypertrophied human hearts, superficial coronary artery elongation, an increase in cross-sectional area, and acute angulation of major branches represents large vessel compensatory factors facilitating reduced impedance to coronary blood flow. In this study we observed larger right coronary artery diameters in hypertrophied right hearts than in the normal hearts of dogs of comparable size. In conclusion, this study illustrates a nearly constant amplitude of canine right coronary blood flow throughout one cardiac cycle, except for diastasis at rest and during reactive hyperemia in the normotensive state. Also, we found that right coronary systolic flow was proportionately significantly greater than left coronary systolic flow. In pulmonic stenosis we observed an attenuation of right coronary systolic flow at rest and during peak reactive hyperemia with normal aortic perfusion pressures. The amount of systolic flow reduction was inversely related to the level of elevated right ventricular systolic pressure.

**Addendum**

The opportunity to study two additional dogs with pulmonic stenosis (right ventricular pressures of 40/3.6 mm Hg and 51/4.9 mm Hg) occurred, using an open-chest procedure with Dial urethane (CIBA) anesthesia (0.6 ml/kg). The reduced duration of diastole with high heart rates (133 and 171 beats/min) and attenuation in late systolic flow, intermediate in form between the normotensive and moderately hypertensive dogs, represented the only differences in right coronary flow pattern in these dogs. After a 10-second occlusion right coronary flow was augmented from 280% to 480% of control. In the dog with a right ventricular systolic pressure of 51 mm Hg the peak hyperemic flow pattern resembled that for moderate hypertension (Fig. 3), whereas the hyperemic pattern of the other dog appeared similar to its control except that systolic and diastolic flows were augmented.

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**References**

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

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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 Eds 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 multifiber 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
Phasic right coronary artery blood flow in conscious dogs with normal and elevated right ventricular pressures.

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