Effects of Coronary Blood Flow and Perfusion Pressure on Left Ventricular Contractility in Dogs

By Ronald M. Abel, M.D., and Robert L. Reis, M.D.

ABSTRACT

The effects of changes in coronary blood flow and coronary artery pressure on left ventricular (LV) contractility were determined in 18 animals. Dogs on cardiopulmonary bypass provided isovolumetric LV contractions during controlled perfusion of the coronary circulation. Coronary venous efflux, myocardial oxygen consumption, peak LV pressure, LV dp/dt, and the force-velocity relations of the LV were determined at normal and at "supernormal" levels of flow and pressure. Coronary vasodilatation was obtained with nitroglycerine, permitting independent variation of flow and pressure. Augmenting flow by increasing pressure increased LV contractility, as reflected by increases in peak LV pressure, dp/dt max, peak wall tension, and maximal measured contractile element velocity. Increased contractility appeared to be primarily due to increased flow, rather than to pressure, as an increase in flow without an increase in pressure produced similar changes, and decreases in pressure at constant flow did not change maximal measured contractile element velocity or dp/dt max, although some decrease in peak LV pressure and wall tension did occur. These data suggest that coronary flow is an independent determinant of the contractile state of myocardium, and that an increase in flow in excess of that required to supply metabolic demands augments myocardial contractility.

ADDITIONAL KEY WORDS

myocardial contractility nitroglycerine coronary vascular resistance myocardial oxygen consumption contractile element velocity force-velocity relations inotropic state ventricular compliance
while the systemic circulation was maintained by cardiopulmonary bypass. Coronary vascular resistance was decreased by a coronary vasodilator, and the effects of changing coronary flow or pressure were then independently assessed.

**Methods**

Eighteen American foxhounds of either sex (average weight: 23.0 ± 3.0 kg) were anesthetized with 0.6 ml/kg of intravenous Dial (allobarbital 100 mg, urethane 400 mg, and monoethylurea 400 mg/ml). After endotracheal intubation, respirations were controlled with a positive-pressure ventilator supplying O2 at 16 cpm. A bilateral transternal thoracotomy was performed, the heart and great vessels exposed, and sodium heparin (3 mg/kg) was administered intravenously. Extracorporeal circulation was provided with a rotating disc oxygenator supplied with 98% oxygen and 2% carbon dioxide at 6 liter/min. The pump-oxygenator was primed with 2500 to 3000 ml of freshly heparinized, homologous blood of the same major blood groups as the experimental animals (A-negative). Minimally pulsatile blood flow was provided by totally occlusive roller pumps. The superior and inferior vena cavae were cannulated and all systemic venous return was drained into a reservoir. Oxygenated blood was returned to the animal by a roller pump through a cannula in a femoral artery. The main pulmonary artery was ligated and a multifenestrated cannula was inserted into the right atrium and ventricle through the right atrial appendage to collect all coronary venous efflux returning to the right side of the heart. A cannula was passed through the left subclavian artery and placed in the aortic root 1 cm above the aortic valve cusps; perfusion of the coronary arteries was provided by occluding the ascending aorta around the cannula with a tourniquet. Isovolumetric LV contractions were obtained by inserting a low compliance latex balloon attached to a metal cannula into the cavity of the LV through an apical stab wound. The cannula was connected to Statham P23Db pressure transducers by a 2-cm length of nylon catheter from which the full left ventricular pressure pulse and high sensitivity left ventricular pressure were recorded. The response of the pressure recording systems was uniform to ±2% to 20 cpm. To prevent herniation of the balloon into the left atrium and to allow drainage of coronary blood returning directly to the LV cavity (10), the mitral valve orifice was occluded with a fenestrated Teflon plug, secured in place by a purse-string suture placed in the mitral valve annulus. The sinoatrial node was crushed, and the heart rate controlled by electrical stimulation of the right atrium at 170 beats/min, a rate which obviated competitive pacing in all instances. Temperature was monitored by a thermistor placed in the inferior vena cava through the common femoral vein, and was maintained at 37 to 38°C by a heat exchanger in the extracorporeal circuit. Central aortic and aortic root pressures were recorded from polyethylene catheters placed through the right brachial artery and aortic root, respectively; LV dp/dt was obtained with an R-C differentiating circuit and was calibrated following each experiment with a triangle-wave generator.

Mean systemic arterial pressure was maintained at 75 mm Hg (a level at which systemic blood flow averaged 75 to 125 ml·kg⁻¹·min⁻¹) and was kept constant by altering flow from the pump-oxygenator. Coronary blood flow was determined by timed collections of the coronary venous efflux and controlled by adjusting the flow rate through the catheter in the aortic root. MVo₂ was calculated from the equation:

\[
MVo_2 (\text{ml O}_2 \cdot \text{min}^{-1} \cdot 100 \text{ g LV}^{-1}) = \frac{\text{coronary arteriovenous O}_2 \text{ difference (ml O}_2 \cdot 100 \text{ ml blood}) \times \text{coronary blood flow (ml/min)}}{\text{LV weight (g)}} \times 100.
\]

The coronary arteriovenous oxygen difference was determined by manometric analysis of the oxygen content of samples of aortic and right ventricular blood (11). Coronary vascular resistance (CVR) was calculated from the equation:

\[
\text{CVR} = \frac{\text{coronary artery pressure (mm Hg)}}{\text{coronary blood flow (ml·min}^{-1} \cdot 100 \text{ g LV}^{-1})} \times 100,
\]

and expressed in resistance units (r.u.), and represented mean values under the experimental conditions of nonpulsatile coronary perfusion. Analog data were recorded on a multichannel direct-writing oscillograph. Force-velocity relations were calculated as previously described (12, 13). The ventricle was assumed to be a thick-walled sphere, and the total tangential force at
CORONARY BLOOD FLOW AND CONTRACTILITY

the endocardial equator was calculated from a modification of the Laplace relation (14), where

\[ F = \frac{P \cdot r^2}{r_0 - r_1} \times 1.36, \]

where \( F \) is force \((g \cdot wt/cm^2; g \cdot wt = 980 \text{ dynes})\), \( P \) is instantaneous LV pressure, \( r_0 \) is the internal (endocardial) ventricular radius \((cm)\), \( r_1 \) is the external (epicardial) radius \((cm)\), and 1.36 a conversion factor (15).

Since the ventricle was assumed to be spherical, \( r_0 \) and \( r_1 \) were solved from the equation:

\[ \text{Volume} = \frac{4}{3} \pi r^3. \]

The internal ventricular radius was determined from the volume of the LV balloon, and the external radius from the sum of the volumes of the LV balloon and the LV muscle mass (15, 16). The specific gravity of the LV muscle was assumed to be 1.0 (13, 15-17), and the LV muscle volume was, therefore, determined by its weight. Velocity of shortening of the contractile element \((v_{ce})\) was calculated from the equation:

\[ v_{ce} = \frac{2 \pi r}{\pi / 280}, \]

where \( v_{ce} \) is velocity of contractile element shortening \((cm/sec)\), \( P \) is LV pressure \((mm Hg)\), and \( r \) is the midventricular radius \((cm)\) (13). Force-velocity relations were determined by comparing the instantaneous relations between force and \( v_{ce} \) at 10-msec intervals during the course of single isovolumetric beats. \( v_{ce} \) was defined as the peak LV wall stress \((force)\) when \( v_{ce} \) was zero. Because of the difficulties in extrapolating the force-velocity curves to zero tension, no attempt was made to estimate \( V_{max} \). Changes in the contractile state were assessed by comparisons of the maximum measured velocity (max \( V_{ce} \)) (15, 18). The force at which comparisons were made for each individual animal was the lowest force common to all curves at which a corresponding \( V_{max} \) was determined. Statistical analyses were performed by comparing peak LV pressure, \( dp/dt \) max, \( MV_{O_{2}} \), \( F_o \), max \( V_{ce} \) and LVEDP determined after an intervention to those values obtained during the control state. Student's t-test for paired data using an equal variance model was employed, assigning a two-tailed significance level \((P \text{ value})\) to each \( t \)-ratio.

**Group 1: Effects of Increased Coronary Blood Flow and Increased Coronary Artery Pressure.**

After a stable period of cardiopulmonary bypass of 15 to 30 minutes, the intraventricular balloon was inflated with saline to a volume that produced a peak LV systolic pressure of approximately 100 mm Hg. The ascending aorta was occluded around the catheter in the aortic root and aortic root perfusion was initiated at a flow rate sufficient to maintain mean aortic root pressure \((coronary \text{ artery pressure})\) identical to mean central aortic pressure \((75 \text{ mm Hg})\). At this level of mean coronary artery pressure, average minute flow rates approximated normal flows for working canine hearts (1), and were taken as the "baseline" state of coronary flow. After an additional 5-minute period during which coronary venous efflux and LV pressure did not vary more than \( \pm 5\% \) from minute to minute, LV pressure, \( dp/dt \), and coronary flow were recorded and arterial and coronary venous blood samples obtained for oxygen content. The flow rate through the catheter in the aortic root was then increased so that mean aortic root pressure increased to 150 mm Hg; all measurements were then repeated in an identical manner.

**Group 2: Effects of Increased Coronary Blood Flow at Constant Coronary Artery Pressure.**

In eight of the dogs, after the above measurements were obtained, glyceryl trinitrate U.S.P. \((hypodermic)\) dissolved in physiologic saline \((600 \text{ mg/ml})\) was infused into the catheter perfusing the aortic root. The infusion rate varied from 25 to 50 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \) from animal to animal, but was kept constant for each individual dog. Mean aortic root pressure was set at 75 mm Hg by increasing the flow through the catheter in the aortic root, and after a 5-minute period during which coronary flow and LV pressure did not vary more than \( \pm 5\% \) from minute to minute, LV pressure, \( dp/dt \) and coronary flow were recorded and arterial and coronary venous blood samples obtained. Flow through the catheter in the aortic root was then increased until mean aortic root pressure increased to 150 mm Hg and the measurements were repeated.

**Group 3: Effects of Decreased Coronary Artery Pressure at Constant Coronary Blood Flow.**

In the remaining 10 dogs, after the assessments described in group 1 were obtained,
flow through the aortic root catheter was set at the original flow rate when mean aortic root pressure was 75 mm Hg. Glyceryl trinitrate was infused as described in group 2, but flow through the catheter perfusing the aortic root was maintained constant, and aortic root pressure was allowed to fall in response to decreased coronary vascular resistance. After measurements were obtained, flow through the catheter perfusing the aortic root was increased to the flow rate observed before the drug was given when aortic root pressure was 150 mm Hg. Flow was maintained constant at this level and repeat measurements were obtained.

Group 4.—To establish that myocardial ischemia was not present during the baseline assessments at a coronary pressure of 75 mm Hg, several additional studies were performed under experimental conditions identical to those present in the previous groups. In six dogs, after a 10-minute period during which coronary venous efflux did not vary more than ±5%, arterial and coronary venous blood was simultaneously sampled and lactate content determined by the method of Marbach and Weil (19). The lactate extraction ratio was calculated as:

\[
\frac{\text{arterial lactate (mg/100 ml)} - \text{coronary venous lactate (mg/100 ml)}}{\text{arterial lactate (mg/100 ml)}} \times 100,
\]

and expressed as percent lactate extracted.

In each animal postischemic hyperemia was then evaluated by occluding the ascending aorta for 60 seconds and measuring coronary venous efflux at 1-minute intervals after unclamping, until coronary flow returned to preoclusion levels. In five of the animals, lactate determinations were also performed 1 minute after aortic unclamping.

In four additional animals, the myocardial contractile state was assessed over a wider range of coronary pressures and flows. The effects on the contractile state of coronary artery pressures ranging from 45 to 175 mm Hg were determined. Furthermore, by increasing intraventricular balloon volume from 15 to 30 ml in 5-ml increments, a range of peak LV pressures at different coronary pressures (ranging from 45 to 175 mm Hg) were determined. Baseline assessments were also made in an additional two dogs in which mean coronary pressure was maintained at 150 mm Hg, a level clearly higher than peak LV pressures. Glyceryl trinitrate was then administered and mean coronary pressure maintained at 150 mm Hg by increasing flow and the measurements repeated.

Results

Group 1: Effects of Increased Coronary Blood Flow and Increased Coronary Artery Pressure.—At a mean aortic root pressure of 75 mm Hg, coronary flow averaged 94.3 ± 8.4 ml/100 g LV • min⁻¹ (±SE); after aortic root pressure was increased to 150 mm Hg, coronary flow averaged 228 ± 15.4 (P < .001). Calculated coronary vascular resistance decreased from 84.1 ± 5.7 (±SE) resistance units at a perfusion pressure of 75 mm Hg to 73.9 ± 5.5 at a perfusion pressure of 150 mm Hg (P < .05). When aortic root pressure was increased to 150 mm Hg, coronary venous oxygen content increased, coronary arteriovenous oxygen difference decreased, but significant increases in MVo₂ resulted because of higher flow rates.

Intraventricular balloon volume (LVEDV)

and expressed as percent lactate extracted.
TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>CAP (75 mm Hg)</th>
<th>CAP (150 mm Hg)</th>
<th>Maxa difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBP (ml \cdot 100 g LV⁻¹ \cdot min⁻¹)</td>
<td>94.3 ± 8.6*</td>
<td>752.3 ± 15.4</td>
<td>139.9 ± 11.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CVR (resistance units)</td>
<td>54.1 ± 5.7</td>
<td>73.9 ± 5.5</td>
<td>-10.3 ± 4.3</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>LV EDP (mm Hg)</td>
<td>11.3 ± 1.6</td>
<td>10.9 ± 1.5</td>
<td>0.4 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Peak isovolumetric LV pressure (mm Hg)</td>
<td>118.2 ± 4.6</td>
<td>153.7 ± 5.7</td>
<td>36.4 ± 4.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>dp/dt max (mm Hg/sec)</td>
<td>1450 ± 108</td>
<td>2000 ± 155</td>
<td>580 ± 80</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>V max (cm/sec)</td>
<td>66.1 ± 3.1</td>
<td>85.6 ± 3.1</td>
<td>19.5 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Max V co (cm/sec)</td>
<td>17.2 ± 1.2</td>
<td>22.0 ± 1.4</td>
<td>4.8 ± 0.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MVO₂ (ml O₂ \cdot 100 g LV⁻¹ \cdot min⁻¹)</td>
<td>8.87 ± 0.59</td>
<td>12.06 ± 0.95</td>
<td>3.19 ± 0.00</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CBP = coronary blood flow; CVR = coronary vascular resistance; CAP = coronary artery pressure; MVO₂ = myocardial oxygen consumption; LV EDP = left ventricular end-diastolic pressure; Max V co = maximal measured velocity of contractile element.

*Mean values for 18 dogs ± SE. fOne g-wt = 980 dynes.

respectively. Peak systolic isovolumetric pressure, dp/dt max, F o, max V co, and MVO₂ were increased significantly after the drug when flow was increased compared to those values observed at identical coronary artery pressures before the drug. The force-velocity curves inscribed in each animal after glyceryl trinitrate were shifted upwards and to the

AUGMENTED CORONARY PRESSURE WITH FLOW

Representative force-velocity curves from a dog in which the effects of augmented coronary flow (CBF) at constant coronary pressure (CAP) were assessed. Left: curves inscribed at a pressure of 75 mm Hg and after it was increased to 150 mm Hg, simultaneously increasing coronary flow. Middle: curves inscribed when pressure was maintained constant at 75 mm Hg before and after nitroglycerine. (Coronary flow is increased after nitroglycerine). Right: curves inscribed when pressure was maintained constant at 150 mm Hg before and after nitroglycerine.

One gram weight = 980 dynes.
Representative force-velocity curves from a dog in which the effects of decreased pressure at constant flow were assessed. Left: curves inscribed at a coronary pressure of 70 mm Hg and after it was increased to 156 mm Hg. Middle: curves inscribed with constant flow at a pressure of 70 mm Hg and 135 mm Hg (before and after nitroglycerine). Right: curves inscribed with constant flow at a pressure of 156 mm Hg and 135 mm Hg. Abbreviations as in Figure 1.

Group 3: Effects of Decreased Coronary Artery Pressure at Constant Coronary Blood Flow.—After glyceryl trinitrate, coronary pressure decreased an average of 19.3 ± 2.2 mm Hg when flow was maintained at that present before the drug at a pressure of 75 mm Hg, and a 22.3 ± 3.7 mm Hg decrease was observed when flow was maintained at that present before the drug at a pressure of 150 mm Hg, reflecting an average decrease in coronary vascular resistance of 21.9 ± 4.4 r.u. and 13.1 ± 3.5 r.u., respectively. No significant changes in LVEDP accompanied the decreases in coronary pressure. When flow was maintained at that present before the drug at a pressure of 75 mm Hg, although no significant changes in resting tension occurred after the drug, significant decreases in peak systolic LV pressure and hence F<sub>s</sub> were observed at the considerably lower coronary perfusion pressures present after giving glyceryl trinitrate. No significant changes were apparent, however, in either MVO<sub>2</sub>, dp/dt max, or max V<sub>c</sub>. When flow was maintained at that present before the drug at a pressure of 150 mm Hg, no significant changes in peak LV systolic pressure, dp/dt max, F<sub>s</sub>, max V<sub>c</sub>, or MVO<sub>2</sub> were apparent at the decreased coronary pressures present following glyceryl trinitrate. Representative force-velocity curves inscribed in an animal from this group are reproduced in Figure 2 and the data from all the animals are summarized in Table 3.

Group 4.—Lactate extraction was observed in each animal at a coronary pressure of 75 mm Hg under experimental conditions identical to those present in the previous groups. Arterial lactate concentration averaged 40.7 ±
### TABLE 2

**Group S: Effects of Increased Coronary Blood Flow at Constant Coronary Artery Pressure**

<table>
<thead>
<tr>
<th>Coronary artery pressure</th>
<th>Before TNG*</th>
<th>After TNG*</th>
<th>Mean difference</th>
<th>P value</th>
<th>Before TNG*</th>
<th>After TNG*</th>
<th>Mean difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CBF</strong> (ml • 100 g LV⁻¹ • min⁻¹)</td>
<td>95.1 ± 10.1</td>
<td>128.4 ± 16.1</td>
<td>33.3 ± 5.8</td>
<td>&lt;.001</td>
<td>235.4 ± 22.2</td>
<td>119.4 ± 27.3</td>
<td>94.0 ± 15.9</td>
<td>&lt;.005</td>
</tr>
<tr>
<td><strong>CVR</strong></td>
<td>8.3 ± 6.9</td>
<td>6.1 ± 6.0</td>
<td>−22.2 ± 2.0</td>
<td>&lt;.001</td>
<td>69.7 ± 6.3</td>
<td>48.2 ± 4.1</td>
<td>−21.6 ± 4.6</td>
<td>&lt;.005</td>
</tr>
<tr>
<td><strong>LVEDP</strong></td>
<td>15.6 ± 1.8</td>
<td>15.5 ± 2.0</td>
<td>−0.1 ± 0.9</td>
<td>NS</td>
<td>15.1 ± 1.8</td>
<td>15.9 ± 2.2</td>
<td>0.8 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Peak isovolumetric LV pressure</td>
<td>128.1 ± 9.6</td>
<td>128.5 ± 9.7</td>
<td>0.4 ± 3.3</td>
<td>&lt;.025</td>
<td>161.1 ± 9.3</td>
<td>172.0 ± 10.4</td>
<td>11.9 ± 2.5</td>
<td>&lt;.005</td>
</tr>
<tr>
<td><strong>dp/dt max</strong></td>
<td>1668 ± 155</td>
<td>1807 ± 206</td>
<td>239 ± 54</td>
<td>&lt;.005</td>
<td>2302 ± 274</td>
<td>2547 ± 291</td>
<td>245 ± 90</td>
<td>&lt;.005</td>
</tr>
<tr>
<td><strong>Fe</strong></td>
<td>60.1 ± 6.5</td>
<td>76.3 ± 9.9</td>
<td>7.2 ± 2.0</td>
<td>&lt;.02</td>
<td>90.1 ± 6.8</td>
<td>99.5 ± 7.4</td>
<td>9.4 ± 2.3</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Max VOT</td>
<td>15.7 ± 1.7</td>
<td>18.9 ± 1.9</td>
<td>3.2 ± 0.4</td>
<td>&lt;.001</td>
<td>22.3 ± 1.8</td>
<td>24.9 ± 2.3</td>
<td>2.6 ± 0.9</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>MVoj</td>
<td>9.3 ± 1.3</td>
<td>11.3 ± 1.24</td>
<td>1.97 ± 0.46</td>
<td>&lt;.005</td>
<td>12.9 ± 1.65</td>
<td>15.8 ± 1.32</td>
<td>2.9 ± 0.63</td>
<td>&lt;.005</td>
</tr>
</tbody>
</table>

Units and abbreviations as in Table 1.
*TNG = glyceryl trinitrate.

### TABLE 3

**Group S: Effects of Decreased Coronary Artery Pressure at Constant Coronary Blood Flow**

<table>
<thead>
<tr>
<th>Coronary artery pressure</th>
<th>Before TNG*</th>
<th>After TNG*</th>
<th>Mean difference</th>
<th>P value</th>
<th>Before TNG*</th>
<th>After TNG*</th>
<th>Mean difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAP</strong> (mm Hg)</td>
<td>74.0 ± 0.0</td>
<td>54.7 ± 2.9</td>
<td>−19.3 ± 2.2</td>
<td>&lt;.001</td>
<td>156.0 ± 2.0</td>
<td>137.7 ± 4.5</td>
<td>−18.3 ± 4.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>CVR</strong></td>
<td>86.9 ± 5.4</td>
<td>64.9 ± 4.0</td>
<td>−21.9 ± 4.4</td>
<td>&lt;.005</td>
<td>80.1 ± 8.3</td>
<td>67.0 ± 5.2</td>
<td>−13.1 ± 3.5</td>
<td>&lt;.005</td>
</tr>
<tr>
<td><strong>LVEDP</strong></td>
<td>9.1 ± 2.0</td>
<td>9.3 ± 2.0</td>
<td>0.2 ± 1.0</td>
<td>NS</td>
<td>8.9 ± 1.8</td>
<td>9.0 ± 1.7</td>
<td>0.2 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>Peak LVP</td>
<td>114.6 ± 4.6</td>
<td>105.0 ± 5.0</td>
<td>−9.6 ± 3.8</td>
<td>&lt;.05</td>
<td>150.0 ± 7.8</td>
<td>148.1 ± 7.8</td>
<td>−1.9 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td><strong>dp/dt max</strong></td>
<td>1279 ± 103</td>
<td>1223 ± 121</td>
<td>−56 ± 33</td>
<td>NS</td>
<td>1929 ± 188</td>
<td>1909 ± 203</td>
<td>−20 ± 95</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Fe</strong></td>
<td>66.2 ± 2.9</td>
<td>59.2 ± 1.9</td>
<td>−6.0 ± 2.5</td>
<td>&lt;.05</td>
<td>85.0 ± 3.7</td>
<td>83.6 ± 3.4</td>
<td>−1.4 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Max VOT</td>
<td>17.7 ± 1.7</td>
<td>16.4 ± 1.8</td>
<td>−1.3 ± 0.8</td>
<td>NS</td>
<td>22.4 ± 1.8</td>
<td>22.7 ± 1.9</td>
<td>0.3 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>MVoj</td>
<td>8.12 ± 0.29</td>
<td>9.99 ± 0.36</td>
<td>−0.88 ± 0.24</td>
<td>&lt;.01</td>
<td>11.20 ± 0.24</td>
<td>12.46 ± 0.91</td>
<td>1.20 ± 1.70</td>
<td>NS</td>
</tr>
</tbody>
</table>

Units and abbreviations as in Table 1.
*TNG = glyceryl trinitrate.
4.5 mg/100 ml (mean ± se) and coronary venous lactate concentration averaged 33.1 ± 3.5 mg/100 ml. The mean lactate extraction was 18.3 ± 1.3% (P < 0.002). Coronary blood flow increased from 102.5 ± 5.7 ml/min to 169.7 ± 9.7 ml/min (P < 0.01) 1 minute following aortic unclamping at which time lactate production was present. As mean coronary pressure was increased from 45 to 175 mm Hg, peak systolic isovolumetric LV pressure progressively increased, and in no animal did the responses reach a plateau except at extremely high perfusion pressures (Fig. 3). Peak systolic isovolumetric left ventricular pressure also progressively increased in every dog as the intraventricular balloon volume was sequentially increased (Fig. 4).

In both dogs in which coronary pressure was maintained at 150 mm Hg, peak systolic left ventricular pressure, dp/dt max, and max V_{max} increased following glyceryl trinitrate. Peak systolic LV pressure was 102 mm Hg in one dog and 90 mm Hg in the other before and 118 and 109 mm Hg, respectively, after glyceryl trinitrate; dp/dt max was 2000 and 1880 mm Hg/sec before and 2210 and 2090 mm Hg/sec after; max V_{max} was 18.9 and 17.4 cm/sec before and 22.0 and 20.2 cm/sec after the drug.

**Discussion**

The maximum velocity of shortening (V_{max}) is considered to be an index of the...
inherent contractile state, but the difficulties in its determination by extrapolation may invalidate its use. In the present studies, therefore, the contractile state was assessed by determining the maximum measured velocity (max $V_{ce}$) and comparisons were made in the same animal at identical wall tensions. Under these circumstances, it seems reasonable to assume that changes in max $V_{ce}$ reflect alterations in the inherent contractile state. When coronary flow and pressure were increased, myocardial contractility as assessed by these methods was augmented, and these findings are in agreement with those of previous investigators (20, 21). The present studies suggest, however, that flow rather than pressure is the major determinant of these changes since max $V_{ce}$ increased when flow increased at constant pressure, but no change in max $V_{ce}$ was apparent when pressure decreased at constant flow.

To assess independently the effects of changing coronary flow or pressure on myocardial contractility, nitroglycerine was used to alter coronary vascular resistance. Implicit in these comparisons is the assumption that nitroglycerine has no inherent effect on the contractile state of myocardium. In this regard, it is of importance that Zelis et al. (unpublished observation) noted that nitroglycerine had no effect on the contractile state of the isolated cat papillary muscle. In the present studies either an increase or no change in contractility was observed after similar doses of nitroglycerine depending on whether coronary pressure or flow were maintained constant.

Resting tension or diastolic fiber length as assessed by LVEDP was unchanged throughout the range of coronary blood flows and coronary artery pressures employed in the present study and, therefore, no consistent changes in left ventricular compliance were noted. This excludes the Frank-Starling relationship from consideration of possible mechanisms for the alterations in ventricular function observed. In addition, alterations in diastolic fiber stretch should not change the inherent contractile state and, therefore, could not explain the changes in max $V_{ce}$ (22). The small decreases in peak LVP and $P_{o}$ observed when coronary artery pressure decreased to relatively low levels, however, most probably are related to the Frank-Starling mechanism.

These data showing the lack of influence of changes in coronary artery perfusion on LV diastolic pressure-volume relations are consistent with the findings of Buckley et al. (23) and Arnold et al. (24). Salisbury and co-workers (25), however, noted a decrease in LVEDP when mean coronary artery perfusion pressure was decreased from 130 mm Hg to 30 mm Hg and suggested that alterations in coronary artery pressure and flow affect LV diastolic compliance. Since these workers also noted large decreases in peak systolic LV pressure when coronary perfusion was reduced to these very low levels, it is possible that the changes in ventricular compliance which they observed may have been influenced by myocardial hypoxia.

To obviate the possibility that the myocardium may have been ischemic during the control assessments (i.e., at coronary pressure of 75 mm Hg), evaluations were carried out at coronary flows which were clearly far above basal values expected for coronary flow for working hearts (1), and even under these circumstances, increased coronary flow increased contractility. Additional confirmation that myocardial ischemia was not present during the control assessments at a mean coronary pressure of 75 mm Hg was provided by the measurements of lactate. In addition, the experiments in which contractility increased during varying LV volume and developed systolic pressure that changed over a wide range of coronary pressure and flow suggest that underperfusion did not occur. The increased contractility that resulted from an increase in coronary flow, therefore, does not merely reflect the expected changes that would occur if flow were increased to an initially ischemic myocardium (26, 27), but suggests that coronary flow itself is an independent determinant of the contractile state. Confirmation of this phenomenon under conditions of greatly elevated coronary pressure

*Circulation Research, Vol. XXVII, December 1970*
(150 mm Hg) compared to peak systolic intracavitary pressures of 100 mm Hg suggests that these effects are not dependent upon the theoretical underperfusion that may occur at peak developed LV pressures at or slightly higher than mean coronary perfusion pressures. Specific regions may well have been transiently underperfused during instantaneous phases of the cardiac cycle (particularly subendocardial layers) during baseline studies even though lactate extraction was demonstrable in every instance, since this latter means of assessment of myocardial oxygen availability reflects only the total muscle mass. The present experimental design could not determine the significance, if any, of regional underperfusion, however.

The mechanism by which augmentation of coronary flow increases the contractile state is not clear. It has been suggested that increased flow may open latent capillary beds, thereby better irrigating portions of the myocardium, and perhaps more completely removing metabolites having deleterious influences on contractility (5, 28). It is also possible that alterations in coronary flow may alter the release or metabolism of catecholamines or other substances. Further studies are needed to investigate these possibilities.

References
CORONARY BLOOD FLOW AND CONTRACTILITY


Effects of Coronary Blood Flow and Perfusion Pressure on Left Ventricular Contractility in Dogs

RONALD M. ABEL and ROBERT L. REIS

Circ Res. 1970;27:961-971
doi: 10.1161/01.RES.27.6.961

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/27/6/961

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/