Effect of Coronary Arterial Pressure on Coronary Stenosis Resistance

JEFFREY S. SCHWARTZ, M.D., PETER F. CARLYLE, B.S., AND JAY N. COHN, M.D.

SUMMARY  The effects of coronary pressure on coronary stenosis resistance were studied in 13 open-chest dogs. A noncircumferential stenosis was produced in the circumflex coronary artery by placing sutures into either side of the artery and invaginating a portion of the arterial wall by tying the sutures. Coronary pressure both proximal and distal to the stenosis and coronary flow were measured. Coronary pressure was lowered by 1) hemorrhage and 2) placing a snare proximal to the noncircumferential stenosis and tightening the snare. After hemorrhage, mean proximal coronary pressure fell from 100 ± 5 to 56 ± 6 mm Hg (p < 0.01) and resistance across the noncircumferential stenosis increased from 0.56 ± 0.13 to 1.3 ± 0.26 units (p < 0.05). After the snare was tightened, mean proximal coronary pressure fell from 110 ± 4 to 58 ± 4 mm Hg (p < 0.01) and resistance across the noncircumferential stenosis increased from 0.43 ± 0.05 to 1.1 ± 0.25 units (p < 0.02). In a series of experiments, coronary pressure was raised by inflating a balloon in the proximal aorta. After the balloon was inflated, mean proximal coronary pressure increased from 95 ± 7 to 129 ± 5 mm Hg (p < 0.01) and resistance across the noncircumferential stenosis decreased from 2.34 ± 0.56 to 2.05 ± 0.46 units (p < 0.05). These changes in stenosis resistance were consistent with passive narrowing and distension of the stenotic segment caused by the changes in coronary pressure. Alterations in coronary pressure may therefore affect the severity of a coronary stenosis.

CORONARY STENOSSES are frequently considered to be fixed in severity. However, some stenotic segments of coronary arteries apparently may change in caliber. For example, studies of patients with variant angina have shown that spasm may occur in the area of atherosclerotic narrowing, indicating that the stenotic segment is capable of active vasomotion.1,2 It has also been shown in patients with coronary atherosclerosis that vasodilators may cause an increase in the area of the stenotic segment, again suggesting that the stenotic area may be dynamic.3

If active vasomotion can change the caliber of a stenotic segment of a coronary artery, the stenotic segment may not be rigid. Therefore, the vessel might also passively change in caliber in response to changes in intraluminal pressure. Consequently, various maneuvers that change the caliber of the vessel could considerably alter the severity of the stenosis. If the coronary stenoses were severe, small changes in its cross-sectional area could result in large changes in resistance and flow across the stenosis.

In the present study we created a severe, noncircumferential stenosis in the circumflex coronary artery of open-chest dogs and examined the effects of alterations in perfusion pressure on the hemodynamics of this noncircumferential stenosis.

Methods

The studies were performed in open-chest dogs anesthetized with alpha chloralose (100 mg/kg) and morphine (2 mg/kg). The mean weight of the dogs was 30 ± 1 kg.

All dogs were pretreated with oral aspirin, 900 mg, to lessen the possibility of platelet aggregation in the area of the stenosis. This dose of 30 mg/kg was similar to that used by Folts in studies suggesting that aspirin prevents formation of platelet thrombi in dogs with severe coronary stenosis.4 Respiration was controlled with a Harvard volume respirator pump and a cuffed endotracheal tube. A left thoracotomy was performed.

The experimental preparation is shown in figure 1. The proximal portion of the left circumflex coronary artery was dissected free. Two PE50 catheters were placed into separate branches of the circumflex coronary artery so that coronary pressure at two points along the artery could be measured. All other visible branches between the two catheters were tied off. Statham P231D pressure transducers were used. Before each experiment, each transducer system was calibrated against the same series of test pressures. The catheters were then inserted into the circumflex artery through the separate branches as shown in figure 1. The two catheters in the circumflex artery were identical. During the course of the experiment, each transducer was attached to the same catheter while the catheter remained in the artery to be certain that the sensitivities of the two transducer systems remained equal. If there was any discrepancy, the calibration procedure was repeated. A PE200 catheter was placed in the aorta for pressure monitoring.

A Statham P2202 electromagnetic flowmeter was used. A 2.0- or 2.5-mm flow probe was placed on the circumflex artery proximal to the two catheters. Circumflex pressure was monitored while the flow probe was put in place. The size of the probe was chosen so

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From the Department of Medicine, Cardiovascular Division, University of Minnesota, Minneapolis, Minnesota.

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Address for correspondence: Jeffrey S. Schwartz, M.D., University of Minnesota, Department of Medicine, Box 258, Mayo Memorial Building, Minneapolis, Minnesota 55455.

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that it gave a good quality flow signal without changing circumflex arterial pressure distal to the probe. Zero flow, obtained by transient complete occlusion of the circumflex coronary artery, was checked frequently during the course of each experiment.

The probes were calibrated postmortem by cannulating the coronary artery proximal and distal to the probe, infusing blood through the artery at constant rates and performing timed collection of blood from the distal cannula.

A noncircumferential stenosis was produced in the section of the circumflex artery between the two PE50 catheters. Sutures were placed into both sides of the artery and a portion of the arterial wall was invaginated by tying the sutures. The stenosis was made severe enough so that a pressure gradient was present across the stenosis in the control state. At the end of each study a cast was made of the circumflex coronary artery by hand injection of RTV-11 silicone.

The hemodynamics of the stenotic coronary artery were studied when coronary perfusion pressure was lowered and raised. Coronary pressure was lowered by two methods: 1) In eight experiments in eight dogs, systemic and thus coronary pressure was lowered by controlled hemorrhage. Arterial blood was withdrawn from the femoral artery until aortic pressure had fallen by at least 25 mm Hg. 2) In 19 experiments in five dogs, a snare was placed distal to the flow probe but proximal to the noncircumferential stenosis (fig. 2). Coronary pressure in the artery distal to the snare, and thus in the region of the noncircumferential stenosis, was lowered by at least 20% by tightening the snare.

We determined by visual inspection that the snare did not distort the geometry of the stenosis or the artery in the area of the pressure catheters and the flow probe.

Five dogs were used for both hemorrhage and snare experiments. In each of these dogs, one hemorrhage experiment was done after the snare experiments were completed. The dog was then sacrificed. Three dogs were used only for hemorrhage experiments.

In 14 experiments in five additional dogs, coronary arterial pressure was raised. A #8F Foley catheter was placed into the thoracic aorta via the carotid artery. The catheter was advanced until inflating the balloon with 3–5 ml of saline caused a rise in proximal coronary arterial pressure. In these five dogs, the heart rate was controlled with atrial pacing to prevent a reflex decrease in heart rate when aortic pressure increased.

All measurements were recorded on a four-channel Hewlett Packard 7700 recorder at paper speeds of 1–25 mm per second. Mean resistance was calculated using the formula $R = (P_1 - P_2)/F$ and was expressed in resistance units (mm Hg/ml/min). $P_1 =$ mean proximal coronary pressure, $P_2 =$ mean distal coronary pressure and $F =$ mean circumflex coronary blood flow. All data are shown as mean ± SEM. Significance of the differences was determined by the paired $t$ test.

**Results**

In each study a cast was made of the noncircumferential stenosis. An example of such a cast is shown in figure 3. In each instance, the presence of a severe stenosis was confirmed. We did not quantitatively analyze the dimensions of the stenoses from these casts.
In eight experiments in eight dogs, coronary pressure was lowered by controlled hemorrhage. The results are shown in table 1. The mean fall in both aortic and proximal coronary pressure after hemorrhage was 44 mm Hg. The time required to reach this end point varied, but was usually within 30 minutes. Measurements were performed as soon as aortic and proximal coronary pressure had fallen by at least 25 mm Hg. The heart rate increased significantly from 97 ± 18 to 142 ± 10 beats/min. Flow through the circumflex coronary artery decreased significantly. The change in magnitude of the pressure gradient across the stenosis was not consistent, as it increased in four experiments and decreased in four experiments. However, as shown in table 1 and figure 4, hemorrhage resulted in a significant increase in the calculated resistance across the stenosis from 0.56 ± 0.13 to 1.30 ± 0.26 units (p < 0.05).

In 19 experiments in five dogs, coronary perfusion pressure was lowered by tightening a snare proximally on the circumflex coronary artery. An example of the pressure and flow recordings from one of these experiments is shown in figure 5. The results of all 19 experiments are shown in table 2. The mean fall in prox-

**Figure 3.** Cast of a circumflex coronary artery with a noncircumferential stenosis.

**Figure 4.** Individual and group data for stenosis resistance in experiments in which coronary arterial pressure was lowered by hemorrhage. The values shown were obtained during a control period and after hemorrhage. Mean values are connected by the dashed line.

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**Table 1.** Hemodynamic Changes in Stenotic Coronary Arteries Before and After Hemorrhage

<table>
<thead>
<tr>
<th></th>
<th>Mean proximal pressure (mm Hg)</th>
<th>Mean distal pressure (mm Hg)</th>
<th>Mean gradient (mm Hg)</th>
<th>Mean coronary flow (ml/min)</th>
<th>Resistance across stenosis (mm Hg/ml/min)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100 ± 5</td>
<td>86 ± 7</td>
<td>14 ± 3</td>
<td>26 ± 2</td>
<td>0.56 ± 0.13</td>
<td>97 ± 18</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>56 ± 6</td>
<td>39 ± 5</td>
<td>17 ± 3</td>
<td>14 ± 2</td>
<td>1.30 ± 0.26</td>
<td>142 ± 10</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.01</td>
<td>NS</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.05</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

**Table 2.** Hemodynamic Changes in Stenotic Coronary Arteries Before and After Lowering Coronary Pressure by Tightening Proximal Snare

<table>
<thead>
<tr>
<th></th>
<th>Mean proximal pressure (mm Hg)</th>
<th>Mean distal pressure (mm Hg)</th>
<th>Mean gradient (mm Hg)</th>
<th>Mean coronary flow (ml/min)</th>
<th>Resistance across stenosis (mm Hg/ml/min)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>110 ± 4</td>
<td>100 ± 5</td>
<td>10 ± 2</td>
<td>23 ± 2</td>
<td>0.43 ± 0.05</td>
<td>90 ± 8</td>
</tr>
<tr>
<td>Snare tightening</td>
<td>58 ± 4</td>
<td>47 ± 4</td>
<td>11 ± 1</td>
<td>13 ± 2</td>
<td>1.10 ± 0.25</td>
<td>92 ± 8</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.01</td>
<td>NS</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.02</td>
<td>NS</td>
</tr>
</tbody>
</table>
imal coronary pressure was 52 mm Hg. The hemodynamic measurements were made at a mean time of 35 ± 5 seconds after the fall in proximal coronary pressure. There was no change in heart rate or aortic pressure in this series of experiments. Flow through the circumflex coronary artery decreased significantly and, again, there was no consistent change in the pressure gradient across the stenosis. However, as shown in table 2 and figure 6, after coronary pressure was lowered by tightening the snare, the calculated resistance across the stenosis increased from 0.43 ± 0.05 to 1.10 ± 0.25 units (p < 0.02).

The magnitude of the increase in stenosis resistance in the snare experiments was similar to that in the hemorrhage experiments (fig. 7).

In 14 experiments in five dogs, coronary perfusion pressure was raised by inflating a balloon in the thoracic aorta while the heart rate was controlled by atrial pacing. The results are shown in table 3. In some of these experiments, the aortic pressure catheter was distal to the balloon so that inflating the balloon caused a fall in measured aortic pressure. Therefore, the changes in proximal aortic pressure were not

**Figure 5.** Pressure and flow recordings in an experiment in which coronary pressure was lowered by tightening a snare proximally on the coronary artery. Recordings are shown during a control period and after the snare was tightened.

**Figure 6.** Individual and group data for stenosis resistance in experiments in which coronary arterial pressure was lowered by tightening a snare proximally on the coronary artery. The values shown were obtained during a control period and after the snare was tightened. Mean values are connected by the dashed line.

**Figure 7.** Bar graph showing that the magnitude of the increase in resistance across the noncircumferential stenosis was similar after lowering coronary pressure with hemorrhage and after tightening a snare proximally on the coronary artery.
always assessed. Proximal coronary pressure increased an average of 34 mm Hg. The hemodynamic measurements were made at a mean time of 65 ± 8 seconds after the balloon was inflated. There was no change in heart rate. The pressure gradient across the stenosis increased significantly, as did the circumflex coronary blood flow. However, as shown in figure 8 and table 3, calculated hydraulic resistance across the noncircumferential stenosis decreased significantly from 2.34 ± 0.56 to 2.05 ± 0.46 units (p < 0.05).

### Table 3. Hemodynamic Changes in Stenotic Coronary Arteries Before and After Raising Coronary Pressure by Inflating Balloon in Proximal Aorta

<table>
<thead>
<tr>
<th></th>
<th>Mean proximal pressure (mm Hg)</th>
<th>Mean distal pressure (mm Hg)</th>
<th>Mean gradient (mm Hg)</th>
<th>Mean coronary flow (ml/min)</th>
<th>Resistance across stenosis (mm Hg/ml/min)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>95 ± 7</td>
<td>51 ± 6</td>
<td>44 ± 8</td>
<td>30 ± 4</td>
<td>2.34 ± 0.56</td>
<td>172 ± 9</td>
</tr>
<tr>
<td>Balloon inflated</td>
<td>129 ± 5</td>
<td>75 ± 8</td>
<td>54 ± 10</td>
<td>43 ± 7</td>
<td>2.05 ± 0.46</td>
<td>172 ± 9</td>
</tr>
</tbody>
</table>

Discussion

The purpose of this study was to evaluate the effects of changes in coronary arterial pressure on the resistance across a noncircumferential coronary stenosis. To calculate stenosis resistance, pressure across the stenosis was measured, as was flow through the stenotic artery. No attempt was made to evaluate changes in distal coronary bed resistance or left ventricular diastolic pressure because these variables could only influence stenosis resistance indirectly through their effects on coronary blood flow and distal coronary pressure.

In this study, interventions that lowered coronary arterial pressure resulted in an increase in calculated resistance across a noncircumferential stenosis, and an intervention that raised coronary pressure resulted in a decrease in stenosis resistance.

Previous investigators have shown that the calculated hydraulic resistance across a stenosis of fixed severity is not constant and therefore a change in resistance may not reflect a change in severity of a stenosis. These authors have shown that the calculated hydraulic resistance of an anatomically fixed stenosis depends on distal bed resistance and thus on flow. In their studies, as flow across a fixed stenosis increased, the pressure gradient increased more than flow. Therefore, calculated hydraulic resistance increased directly with flow. In our studies, however, when the coronary pressure was raised and flow increased, calculated resistance decreased, a change opposite from that which would be expected as a result of flow alone. Conversely, when pressure was lowered and flow fell, resistance increased, again a change opposite in direction from that which would be expected as a result of flow changes alone. Thus, these changes in resistance cannot be explained on the basis of changes in flow.

The changes in resistance in the present study, therefore, must be due to alterations in the geometry of the stenosis, perhaps caused by changes in coronary arterial pressure. Geometric factors that affect the pressure-flow characteristics of a stenosis include length, stenosis diameter, divergence angles and lumen roughness. Because each stenosis was used as its own control, it can be assumed that the length of each stenosis did not change as a result of the intervention.

Gould et al. showed that when flow through a coronary stenosis is increased, the epicardial artery distal
to the stenosis can dilate, resulting in a larger divergence angle at the distal end of the stenosis. This phenomenon could result in an increased pressure loss across the stenosis and therefore an increased calculated resistance across the stenosis. In our studies, the alterations in perfusion pressure could certainly have resulted in alterations in the caliber of the epicardial vessel adjacent to the stenosis. Raising the pressure would be expected to increase the caliber of the epicardial vessels. If the stenosis diameter remained constant, this increase would be expected to result in no change or an increase in calculated resistance across the stenosis. In fact, resistance fell. In the same way, a fall in coronary pressure may have decreased the caliber of the epicardial artery adjacent to the stenosis and would be expected to result in no change or a decrease in calculated resistance. In fact, resistance increased. It appears unlikely, therefore, that changes in the caliber of the epicardial artery adjacent to the stenosis were responsible for the changes in resistance that we found.

The most likely explanation for our findings appears to be a change in the area of the stenosis itself. Because these stenoses were quite severe, small changes in their cross-sectional area would be expected to have marked effects on resistance. The stenoses were produced so as to involve only part of the circumference of the vessel. Therefore, the passive vasomotor capability of the stenotic segment should have been retained. A fall in pressure in the stenotic segment would thus be expected to result in passive narrowing of the stenotic segment and an increase in large vessel resistance, whereas an increase in pressure might be expected to cause passive distension of the stenosis and a decrease in resistance.

Coronary pressure was lowered by two methods. The heart rate increased in the hemorrhage experiments but not in the snare experiments. In the hemorrhage experiments, a reflex increase in sympathetic nervous system activity could have had a direct effect on coronary artery caliber. In the snare experiments, however, there was no evidence of increased adrenergic discharge. Nevertheless, in both the hemorrhage and the snare experiments, the magnitude of the increase in resistance across the noncircumferential stenosis was similar. The most likely explanation is that both interventions caused a significant fall in coronary pressure, which led to passive narrowing of the stenotic segment.

We have recently shown that dilation of the distal coronary bed in the presence of a critical stenosis causes a decrease in distal coronary pressure and an increase in stenosis resistance. Therefore, in our previous study and in this study, an intervention that lowers pressure in the distal coronary artery, and therefore could be assumed to lower pressure in the stenotic segment, results in an increase in stenosis resistance.

Another factor that may have affected the stenosis resistance in our study is blood viscosity. In the hemorrhage experiments, the hematocrit could have decreased and affected blood viscosity. Although we did not measure hematocrit before and after hemorrhage, the time from onset of hemorrhage to the recording of hemodynamic measurements was brief, allowing little time for a fall in hematocrit. In addition, changes in hematocrit should not have occurred in the snare experiments, and the magnitude of the resistance changes in the hemorrhage and snare experiments was similar, suggesting that any effect of hematocrit on the hemorrhage experiments was small.

The apparent viscosity of blood also varies with tube dimensions and velocity of flow, both of which may have changed as a result of the interventions in this study. However, since we could not compare the results obtained with blood with those that might be obtained with a more homogeneous fluid, we cannot assess the effects of the anomalous viscosity of blood on the changes in resistance that we found.

Another variable that may have affected resistance to flow is lumen roughness. Resistance to flow may be higher for rough lumen tubes than for equivalent smooth tubes. In this study, we could not assess the effects of possible changes in lumen roughness before and after each intervention.

Two methodologic limitations of this study should be mentioned. We were careful to choose a flow probe that fit properly at the beginning of each study. However, in studies in which perfusion pressure fell, there could have been passive narrowing of the vessel under the flow probe, which could have altered the fit of the probe. Analysis of the flow tracings after each intervention showed that no artifact appeared in the phasic flow signal. However, aside from this observation, we cannot be certain that there were not subtle changes in the fit of the probe.

Second, the configuration of the stenosis we produced was artificial and therefore differed from a naturally occurring lesion. The hemodynamics of such an artificial lesion in open-chest dogs cannot be extrapolated directly to the hemodynamics of a human coronary stenosis. However, there is evidence that stenotic segments of coronary arteries in patients are capable of vasomotion, and the stenoses in this study were produced in such a way that they also should have been capable of vasomotion.

Logan has shown that a fall in perfusion pressure in isolated human coronary arteries perfused at steady pressure with isotonic glycerol saline can also result in an increase in resistance across the stenosis. In his study, the effect was seen in arteries with eccentric stenosis, in which only part of the arterial wall was involved, and not in those with concentric stenoses, in which the wall was completely rigidified. He stated that the increase in resistance in arteries with eccentric stenosis was consistent with an elastic arterial wall. Although Logan's studies were done at steady pressure with isolated segments of arteries and not in an intact coronary system, they do show that passive changes are possible in human coronary stenoses.

Coronary pressure is a major determinant of adequate transmural myocardial perfusion. In clinical situations in which coronary pressure falls, such as
hemorrhage, myocardial ischemia may occur.\textsuperscript{16} The present study, by showing an increase in stenosis resistance as coronary pressure falls, provides an additional possible mechanism by which a fall in coronary pressure may result in decreased myocardial blood flow.

References
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J S Schwartz, P F Carlyle and J N Cohn

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