Effects of Selectively Altering Collateral Driving Pressure on Regional Perfusion and Function in Occluded Coronary Bed in the Dog


To determine whether selectively altering the coronary perfusion pressure in the adjacent nonoccluded vessel has any influence on the occluded bed, the effects of alterations in the perfusion pressure of the left anterior descending coronary artery on the perfusion and function of the acutely occluded left circumflex coronary (LC) arterial bed were studied in 10 anesthetized open-chest dogs. Radiolabelled microsphere-assessed regional myocardial perfusion and endocardial excursion determined by twodimensional echocardiography were measured during control conditions prior to mid-LC occlusion with left anterior descending coronary arterial pressure (LADP) equal to aortic pressure (AoP) (Stage 0) and to 3 randomly performed postocclusion stages. At each postocclusion stage, the perfusion territory of the occluded LC bed (area at risk) was measured in vivo using myocardial contrast two-dimensional echocardiography. During Stage 1 (LADP = AoP), area at risk was 5.1 ± 0.9 cm² (± 1 SD) and transmural blood flow to the LC arterial bed decreased from 0.96 ± 0.50 ml/min/g (Stage 0) to 0.16 ± 0.12 ml/min/g (p < 0.01), while endocardial excursion decreased from 28.0 ± 9.0% to 2.0 ± 10.0% (p < 0.01). During Stage 2 (LADP < AoP), area at risk decreased to 4.4 ± 1.0 cm² compared with Stage 1 (p < 0.01), and transmural blood flow, endocardial:epicardial blood flow ratio, and endocardial excursion increased to 0.51 ± 0.39 ml/min/g, 0.64 ± 0.20, and 14 ± 6%, respectively (p < 0.01). In contrast, during Stage 3 (LADP > AoP), although the area at risk increased (5.6 ± 0.7 cm², p < 0.01) and transmural blood decreased (0.10 ± 0.10 ml/min/g, p < 0.01) compared with Stage 1, endocardial blood flow, endocardial:epicardial blood flow ratio, and endocardial excursion were unchanged (0.11 ± 0.16 ml/min/g, 0.52 ± 0.30, and 1.0 ± 4.0%, respectively). We conclude that significant lateral border zones exit during acute coronary ischemia, which can be influenced positively by selectively increasing the collateral driving pressure. In contrast, although the area at risk increases, when the collateral driving pressure is decreased, the endocardial blood flow and excursion in the area at risk do not further decrease. (Circulation Research 1987;61:77-85)
Materials and Methods

Animal Preparation

Ten mongrel dogs (23.0 ± 3.0 kg, x ± 1 SD) were anesthetized with 30 mg/kg of intravenous sodium pentobarbital (Abbott Laboratories, North Chicago, Ill.), intubated, and ventilated with a Harvard Apparatus Model 607 dual-phase control respirator pump (South Natick, Mass.). Additional anesthesia was given as needed during the experiment. A median sternotomy was performed, and the heart was suspended in a pericardial cradle.

After calibration with a mercury manometer, a 7F Millar Mikrotip PC-470 micromanometer-tipped catheter (Millar Instruments, Houston, Tex.) was introduced into the left ventricular cavity via the left ventricular apex to measure the left ventricular end-diastolic pressure (LVEDP). A 2F plastic cannula was placed into the ascending aorta via the right internal mammary artery to record the central aortic pressure (AoP). A similar catheter was placed in the left atrial appendage for injecting radiolabelled microspheres (Figure 1).

The left main coronary artery, the middle portion of the left circumflex coronary artery (LC), and a distal branch of the left anterior descending coronary artery (LAD) were carefully dissected free from surrounding tissues, and ties were placed loosely around them. A 20-cm-long, 22-gauge polyethylene catheter (Deseret Corporation, Sandy, Utah) was positioned in the distal branch of the LAD and secured there with a preplaced tie. This catheter was used to measure the LAD pressure (LADP). A similar catheter was introduced antegrade into the LC via a proximal branch, and its tip was positioned 1–2 mm distal to the prospective site of occlusion.

An 8F catheter was introduced into the right femoral artery and advanced retrogradely into the descending aorta. This catheter was attached to a Dow Corning silastic tubing with a 3/16-inch i.d. (Midland, Mich.), which was connected to a Gregg cannula via a roller pump. A T-shaped plastic connector was placed at the middle of the silastic tubing from which arterial reference blood samples were withdrawn for radiolabelled microsphere determination of regional myocardial blood flow. The system was primed with a 0.9% solution of sodium chloride, and the Gregg cannula was introduced into the ascending aorta via the left common carotid artery. The roller pump was started at a flow rate of 100 ml/min. The tip of the Gregg cannula was carefully introduced into the left main coronary artery and firmly secured with a preplaced tie. Then, the roller pump was adjusted so that the pressure in the LAD was the same as obtained prior to insertion of the Gregg cannula. Gould Model #P231D fluid-filled transducers (Gould Instruments, Oxnard, Calif.) positioned at the level of the right atrium were used to measure pressures, and tracings were recorded on an Irex Continual multichannel recorder (Irex Medical Systems, Upper Saddle River, N.J.).

Two-Dimensional Echocardiographic Studies

Two-dimensional echocardiographic studies were performed using a commercially available mechanical sector scanning system with an Advanced Technology Mark III 5-MHz transducer (Seattle, Wash.). Images were recorded on videotape using a Panasonic NV8200 1/2-inch VHS recorder (Japan). The transducer was fixed at the midpapillary muscle level using a clamp affixed to the procedure table. The gain settings were optimized at the beginning of the study and kept constant throughout the recording period. A saline bath acted as an acoustic interface between the heart and the transducer.

A hand-agitated mixture of equal amounts of saline and Renografin-76 (diatrizoate meglumine and diatrizoate sodium, 18.5 g/50 ml; ER Squibb and Sons, Inc., Princeton, N.J.) was used for myocardial contrast echocardiography based on its ability to enhance myocardial echo intensity. This mixture contains mi-
Microbubbles similar in size to radiolabelled microspheres (12 ± 7 μm) that produce only transient hemodynamic and electrocardiographic alterations after intracoronary injection. Furthermore, no pathologic effects are noted in the myocardium, brain, and kidneys during postmortem examination 24 hours after injecting this mixture into these organs. To define risk area during each stage of the experiment, a bolus of 0.5 ml of this mixture was injected into the LC via the preplaced catheter.

The recorded images were analyzed on a Microsonics Easyview II off-line image analysis system (Indianapolis, Ind.). The video recordings initially were reviewed to select cycles in which the borders of risk areas were optimally defined. Selected cycles were transferred to a Sony SVM 1010 video disk system (Japan). A single observer outlined the edges of the risk areas using a hand-held digitizing device. Then, the area at risk was expressed in cm². The interobserver correlation and error using this method are 0.98 (p<0.001) and 0.37 cm², respectively, while the intraobserver correlation and error are 0.99 (p<0.0001) and 0.22 cm². Figure 2 shows examples of the area at risk during Stages 1 and 2 in 1 dog.

Because contrast agents produce functional and hemodynamic changes, albeit transient, wall motion analysis at each stage of the experiment was performed on echocardiographic images recorded just prior to contrast injection. End-diastolic and end-systolic endocardial outlines were digitized, and the junction of the right ventricular free wall and posterior left ventricular wall was identified. The center of the endocardial area for each frame and an average center of area of the 2 frames was then automatically defined by the computer. Systolic rotation of the heart was corrected by aligning the right ventricular free wall–posterior left ventricular wall junction in the 2 frames. Then, 16 equally spaced radii emanating from the average center of area and intersecting the endocardial outlines were constructed automatically by the computer. Endocardial systolic excursion was assessed along each radius using the following equation:

\[
\frac{\text{Endocardial excursion}}{\text{EDr} - \text{ESr}} \times 100
\]

where EDr and ESr are end-diastolic and end-systolic radial lengths, respectively. The circumferential endocardial extent of abnormal wall motion was determined using the following equation:

**Figure 2** Hemodynamic data and myocardial contrast echo-defined area at risk in dog with left circumflex coronary artery occlusion during A Stage 1, LADP = AoP; and B Stage 2, LADP > AoP. Area at risk is smaller in Stage 2 compared with Stage 1. AoP, aortic pressure, LADP, left anterior descending artery pressure, LVEDP, left ventricular end-diastolic pressure, EKG, electrocardiogram
\[ \% \text{ Circumferential extent of abnormal wall motion} = \frac{n}{16} \times 100 \]

The interobserver and intraobserver errors in our laboratory for defining the circumferential extent of abnormal wall motion using this method are 3.6 and 2.4%, respectively.\(^{14}\)

**Measurement of Regional Myocardial Blood Flow**

Myocardial blood flow was measured at each stage of the experiment by injecting approximately \(4.5 \times 10^6\) radiolabelled microspheres (10–15 \(\mu\)m, New England Nuclear Corp., North Billerica, Mass.) into the left atrium. Prior to injection, the microspheres were mixed thoroughly using a mechanical agitating device (Model 11-550-G, Vortex Genie, Scientific Industries Inc., Bohemia, N.Y.). Reference arterial blood sample collection was begun just prior to microsphere injection from the T connection of the silastic tubing (see above) using a Critikon Model 911 Holter pump (Tampa, Fla.) and was continued for a total of 2 minutes. The radiolabelled spheres were injected in the following order: \(^{113}\)Sn, \(^{103}\)Ru, \(^{95}\)Nb, and \(^{46}\)Sc. Generally, microspheres injected into the left atrium enter the myocardium during the first-pass transit via the coronary circulation.\(^{15}\) In our model, however, as the left main coronary artery was cannulated, the microspheres first traveled to the femoral artery and entered the heart via the Gregg cannula connected to the femoral artery via silastic tubing (Figure 1). Arterial reference samples were drawn from this tubing at the end of the experiment, an 18-gauge, 3-inch-long needle was passed through the heart such that it traversed the anterior and posterior walls of the left ventricle at the level corresponding to the short-axis echocardiographic recordings. The heart was then removed from the thorax, and the atria, great vessels, epicardial fat, and right ventricular free wall were discarded. The left ventricle was cut on either side of the needle in a breadloaf manner to obtain a 1-cm-thick slice corresponding to the echocardiographic short axis level. Starting with the right ventricular free wall–left ventricular posterior wall junction, the myocardial slices were cut into 16 equal wedge-shaped pieces that approximated the 16 radii used for analyzing endocardial excursion (Figure 3). Then, each piece was cut into endocardial and epicardial segments. After weighing them, these 32 myocardial segments and the reference blood samples were counted in a well counter (Auto-Gamma Scintillation Spectometer Model 5986 Packard Corporation, Downers Grove, Ill.) to obtain a minimal count of 10,000 for each isotope. The different energy windows for counting were \(^{113}\)Sn, 275–450 KeV; \(^{103}\)Ru, 460–600 KeV; \(^{95}\)Nb, 610–800 KeV; and \(^{46}\)Sc, 805–1,205 KeV. A computer program was used to correct for activity spilling from one window to another and for measuring blood flow in ml/min/gm in each of the myocardial samples using the following equation: \(Q_m = (C_m \times Q_r)/C_r\), where \(Q_m = \text{myocardial blood flow (ml/min)}, C_m = \text{tissue counts (counts/min)}, Q_r = \text{withdrawal rate of arterial sample (ml/min)}, \) and \(C_r = \text{counts in the reference arterial sample}.\) Flow per gram of tissue was calculated by dividing the blood flow by sample weight. Transmural flow was calculated by dividing the total flow (ml/min) to the epicardial and endocardial segments by the combined weight of the two segments.

**Protocol**

In the baseline stage prior to coronary occlusion (Stage 0), the roller pump was adjusted such that LADP equalled AoP. Microspheres were injected into the left atrium, reference arterial blood samples were collected, and two-dimensional echocardiographic images were obtained prior to and following the injection of contrast. Ten minutes were allowed after the occlusion of the midportion of the LC; then Stages 1, 2, and 3 were performed in a random order, and all measurements were repeated in each stage. Five minutes were allowed for hemodynamic equilibration between stages. In Stage 1, LADP was maintained at the same level as AoP using the roller pump; in Stage 2, LADP was increased to about 1.5 times AoP; and in Stage 3, LADP was lowered to about half of AoP. At the end of these 3 stages, a needle was passed through the heart at the level of the echocardiographic recordings, and the animal was killed.

---

**Figure 3** Diagrammatic representation of the method of data analysis for comparison of regional myocardial function from in vivo-derived two-dimensional echocardiograms and regional myocardial blood flow determined using postmortem tissue specimens.
**Data Analysis**

Echocardiographic and blood flow data in the same short-axis cross-section of the heart were compared. Since a two-dimensional cross-section represents approximately 1-cm thickness of the heart, blood flows were calculated in a 1-cm-thick slice corresponding to the echocardiographic images. For spatial registration of data, the myocardial slice was divided into 16 equal parts, with the first segment starting at the junction of the right ventricular free wall and left ventricular posterior wall (Figure 3). Blood flows and endocardial excursion in the same 16 segments were compared. To determine if flow within the most ischemic zone was affected by altering the collateral driving pressure, the endocardial segment demonstrating the least blood flow at Stage 1 was identified as representing the central ischemic zone. Then, flows in this zone were compared at different stages.

All data were expressed as $x \pm 1$ SD. For each of the 4 stages, the sizes of the risk areas, percent of endocardial excursion within the hypoperfused zone, circumferential extent of abnormal wall motion; transmural, endocardial, and epicardial blood flow measurements, and AoP, LADP, and LVEDP were compared using analysis of variance with repeated measures. A difference in means between individual groups was considered significant at a $p$ value of <0.01 after implementing the Bonferroni correction for multiple comparisons.

**Results**

**Hemodynamic Data**

Prior to LC occlusion (Stage 0), AoP was similar to LADP (see Table 1). During Stage 1 (postocclusion), LADP and AoP were similar and comparable with preocclusion values, while LVEDP was significantly higher than the preocclusion values ($p<0.01$). During Stage 2, LADP was significantly higher than AoP ($p<0.01$) but LVEDP was not different from that at Stage 1. During Stage 3, LADP was significantly lower than AoP, while LVEDP remained unchanged compared to Stages 1 and 2. Therefore, there were no significant changes in AoP and LVEDP during the 3 postocclusion stages.

**Myocardial Blood Flow**

Within the prospective area at risk, endocardial and epicardial flows were equal and endocardial:epicardial blood flow ratio was near unity during Stage 0 (preocclusion, LADP = AoP) (see Table 2). During Stage 1 (postocclusion, LADP = AoP), transmural, endocardial, and epicardial blood flows and endocardial:epicardial blood flow ratio were significantly less ($p<0.01$) compared with preocclusion values. During Stage 2 (postocclusion, LADP > AoP), transmural, endocardial, and epicardial flows and endocardial:epicardial blood flow ratio within the area at risk were significantly higher ($p<0.01$) compared with the values at Stage 1. During Stage 3 (postocclusion, LADP < AoP), the transmural and epicardial blood flows were less ($p<0.01$) compared with Stages 1 and 2, but the endocardial blood flow and endocardial:epicardial blood flow ratio were significantly less only compared with Stage 2 and were not different from those at Stage 1.

The blood flow in each animal within the endocardial segment that showed the least blood flow at Stage 1 was examined, and this area was designated as the central ischemic zone (CIZ). Blood flow within this area was significantly higher ($p<0.01$) during Stage 2 (postocclusion, LADP > AoP) compared with Stage 1 (postocclusion, LADP = AoP) and Stage 3 (postocclusion, LADP < AoP), while the values were not significantly different between Stages 1 and 3.

**Endocardial Excursion**

Endocardial excursion was significantly less in all postocclusion stages compared to baseline (Stage 0) (see Table 3). It was significantly less in Stage 1 (postocclusion, LADP = AoP) and Stage 3 (postocclusion, LADP < AoP) compared with Stage 2 (postocclusion, LADP > AoP) and was comparable in Stages 1 and 3.

In a previous study where a similar model was used, we demonstrated that when area at risk is less than 50% of the myocardium in the short-axis slice being examined, endocardial excursion of $<10\%$ correlates well with contrast echo-defined area at risk. Therefore, the circumferential endocardial extent of abnormal wall motion was examined using this criterion. There

<table>
<thead>
<tr>
<th>Table 1. Hemodynamic Data (Mean ± SD) During 4 Experiment Stages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean arterial pressure (AoP)</strong> (mm Hg)</td>
</tr>
<tr>
<td>Preocclusion</td>
</tr>
<tr>
<td>Stage 0 (LADP = AoP)</td>
</tr>
<tr>
<td>Stage 1 (LADP = AoP)</td>
</tr>
<tr>
<td>Stage 2 (LADP &gt; AoP)</td>
</tr>
<tr>
<td>Stage 3 (LADP &lt; AoP)</td>
</tr>
</tbody>
</table>
was no abnormal wall motion at Stage 0. The circumferential endocardial extent of abnormal wall motion was less at Stage 2 (postocclusion, LADP > AoP) compared with Stage 1 (postocclusion, LADP = AoP). During Stage 3, the entire left ventricle demonstrated abnormal wall motion.

**Area at Risk**

During Stage 2 (postocclusion, LADP > AoP), area at risk measured by myocardial contrast echocardiography was significantly less ($p < 0.01$) compared with Stage 1 (postocclusion, LADP = AoP). Area at risk was significantly larger in Stage 3 (postocclusion, LADP < AoP) compared with Stages 1 and 2.

**Discussion**

The present study demonstrates that following acute coronary occlusion in the anesthetized, open-chest dog, regional blood flow and function improve significantly when the perfusion pressure in the nonoccluded vessel is increased selectively above the aortic pressure. In addition, the size of the occluded bed (area at risk) also decreases. In contrast, when perfusion pressure in the nonoccluded vessel is decreased to levels below the aortic pressure, the size of the area at risk increases; however, endocardial blood flow and excursion remain unchanged. Therefore, these data support the existence of sizable lateral border zones immediately following acute coronary occlusion that can be influenced by the collateral driving pressure. These data also illustrate the maximal benefit that can be obtained acutely by increasing collateral blood flow in the absence of any changes in the loading conditions of the left ventricle. Finally, this study demonstrates that myocardial contrast two-dimensional echocardiography can be used for studying in vivo the dynamic changes in the perfusion beds of coronary vessels.

**Critique of Our Methods**

Because change in afterload and preload significantly influence endocardial motion, we selected a model in which we could selectively alter coronary perfusion pressure without affecting the loading conditions of the heart. In this manner, we hoped to study the 'pure' effects of alterations in collateral driving pressure on the area at risk. In our experiments, LVEDP, AoP, and heart rate did not change significantly in the postocclusion stages despite significant alterations in the collateral driving pressure. Therefore, we believe that changes in regional perfusion and function within the occluded bed in this study are related only to changes in the collateral driving pressure. To what degree a continuous rather than pulsatile blood flow affected our results is difficult to determine. Because the aim of the present study was to measure alterations within the ischemic bed, other hemodynamic variables, such as...

Table 2. Myocardial Blood Flow (Mean ± 1 SD) During 4 Experiment Stages

<table>
<thead>
<tr>
<th></th>
<th>Endocardial</th>
<th>Epicardial</th>
<th>Transmural</th>
<th>Endocardial:epicardial ratio</th>
<th>CIZ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preocclusion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0 (LADP = AoP)</td>
<td>0.96 ± 0.50</td>
<td>0.95 ± 0.40</td>
<td>0.96 ± 0.40</td>
<td>0.98 ± 0.20</td>
<td>0.93 ± 0.56</td>
</tr>
<tr>
<td><strong>Postocclusion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1 (LADP = AoP)</td>
<td>0.16 ± 0.12</td>
<td>0.30 ± 0.19</td>
<td>0.24 ± 0.14</td>
<td>0.50 ± 0.20</td>
<td>0.09 ± 0.07</td>
</tr>
<tr>
<td>Stage 2 (LADP &gt; AoP)</td>
<td>0.51 ± 0.39</td>
<td>0.82 ± 0.62</td>
<td>0.65 ± 0.41</td>
<td>0.64 ± 0.20</td>
<td>0.24 ± 0.14</td>
</tr>
<tr>
<td>Stage 3 (LADP &lt; AoP)</td>
<td>0.11 ± 0.16</td>
<td>0.18 ± 0.20</td>
<td>0.10 ± 0.10</td>
<td>0.52 ± 0.30</td>
<td>0.05 ± 0.05</td>
</tr>
</tbody>
</table>

CIZ, central ischemic zone (defined as endocardial segment demonstrating least flow in Stage 1 (postocclusion with LADP = AoP)). LADP, left anterior descending artery pressure. AoP, central aortic pressure.

Table 3. Wall Motion and Area at Risk (Mean ± 1 SD) During 4 Experiment Stages

<table>
<thead>
<tr>
<th></th>
<th>Area at risk (cm²)</th>
<th>Circumferential extent of abnormal wall motion</th>
<th>% Endocardial excursion within area at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preocclusion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0 (LADP = AoP)</td>
<td>0</td>
<td>0</td>
<td>0.28 ± 0.09</td>
</tr>
<tr>
<td><strong>Postocclusion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1 (LADP = AoP)</td>
<td>5.1 ± 0.9</td>
<td>0.33 ± 0.07</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td>$p &lt; 0.01$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 2 (LADP &gt; AoP)</td>
<td>4.4 ± 1.0</td>
<td>0.11 ± 0.13</td>
<td>0.14 ± 0.06</td>
</tr>
<tr>
<td>$p &lt; 0.01$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3 (LADP &lt; AoP)</td>
<td>5.6 ± 0.7</td>
<td>*</td>
<td>0.01 ± 0.04</td>
</tr>
</tbody>
</table>

LADP, left anterior descending artery pressure. AoP, central aortic pressure.

*Entire circumference of the LV demonstrated abnormal wall motion.
collateral driving pressure and area at risk

In the present study, no measurements between 10 minutes and 6 hours following acute coronary occlusion were made within the first 10 minutes of coronary occlusion, and experiments lasted for only 35 minutes after coronary occlusion. Therefore, it is very unlikely that regional dysfunction within the ischemic bed could have been affected by the duration of coronary occlusion, especially when the loading conditions of the left ventricle remained constant. Furthermore, different stages of the experiment were performed in a random order, thus precluding any influence of time-related alterations in regional function on our results.

While regional function was not measured in the nonischemic zone, obvious changes in regional function were noted within this zone (increased function in Stage 2 and decreased function in Stage 3). Although it is possible that function in the normally perfused zone could have affected function within the border zones of the ischemic bed due to a tethering effect, it is highly unlikely to have affected function within the center of the ischemic bed. We, therefore, believe that changes in function within the ischemic bed were causally related to change in flow within the bed.

It is always difficult to obtain precise registration between data obtained in vivo and those obtained postmortem due to ambiguity in the three-dimensional orientations of the parts of the heart under examination. However, reasonable registration was accomplished by passing a needle through the level where the echocardiographic transducer had been fixed throughout the experiment and slicing the heart at that level. In addition, the internal landmarks of the heart (such as papillary muscles and right ventricular free wall–posterior left ventricular wall junction) were verified in the echocardiographic and postmortem data. Spatial registration between regional flow and function data was accomplished by dividing both the echocardiographic and postmortem myocardial short-axis sections into 16 equal segments, starting from the right ventricular free wall–posterior left ventricular wall junction, and comparing blood flow and wall motion data within the same segments.

**Effect of Increasing Collateral Driving Pressure**

While the effects of selectively increasing the collateral driving pressure on regional perfusion and function within the area at risk has not been studied previously, the effects of systemic hypertension on infarct size have been described. Using epicardial ST segment mapping and myocardial creatine phosphokinase activity, Maroko et al demonstrated a beneficial effect of acute systemic hypertension induced by methoxamine on ischemic myocardial injury in dogs. The same group of investigators, in a more recent preliminary report, have also demonstrated a significant decrease in infarct size in dogs made hypertensive following acute coronary occlusion compared with dogs with normal blood pressure. Bache also noted an increase in myocardial blood flow to the central and border zones within the ischemic bed when systemic hypertension was induced with intravenous phenylephrine. Similar results were obtained by Roan et al.

Despite similar results on regional blood flow, our results on endocardial excursion are not similar to those reported previously when systemic hypertension is induced. Levken and Kiel noted complete normalization of wall motion within the ischemic zone while...
we noted only partial recovery. These authors noted recovery only when area at risk was less than 20% of the entire left ventricle. Although we measured area at risk only at the midpapillary muscle level in our experiments, our risk areas were unlikely to be significantly larger than 20% of the left ventricle in most of the dogs. Roan et al.,25 on the other hand, noted a decrease in wall thickening using sonomicrometry during systemic hypertension despite increased myocardial blood flow and improved myocardial oxygen demand ratio as assessed by mass spectrometry. Because these authors made their first set of measurements 1 hour after starting the phenylephrine infusion, it is possible that a partial infarct6 or stunned myocardium,1 or both, could have resulted in a lack of improvement in function. In contrast, the collateral driving pressure was selectively increased and our measurements were made within 35 minutes of LC occlusion, at which time it is unlikely that infarction of any significance could have occurred within the ischemic bed.

Another unique aspect of our present study compared with previous studies is that the dynamic changes within the area at risk induced by changes in the collateral driving pressure were measured in vivo. Because in our studies using myocardial contrast echocardiography, the area at risk always appears to be transmural, any changes in the size of risk areas implies changes in the lateral borders rather than the transmural extent of the risk areas. Our results, therefore, support the presence of significant lateral border zones in the acutely ischemic bed, which can be influenced by changes in collateral driving pressure. Our results may, on superficial examination, appear contrary to the observations of Factor et al.,11 who reported that the lateral border zones are negligible in size. However, these authors measured the border zones within fully developed (24-hour) infarcts, at which time the cells within these areas may have ‘declared’ themselves into necrotic or normal tissue with very little intervening ischemic tissue. In our model, all changes were made acutely, and the total duration of coronary occlusion was about 35 minutes.

Effects of Decreasing Collateral Driving Pressure

Despite an increase in the size of the area at risk and a decrease in transmural blood flow, endocardial blood flow and motion were no worse at Stage 3 (postocclusion, LADP < AoP) compared with Stage 1 (postocclusion, LADP = AoP). This would be expected. Flow in the endocardial bed diminishes more than in the epicardium following coronary occlusion, which is related to both a greater abundance of collaterals and less postischemic wall stress in the epicardial region. Therefore, because the endocardial bed is not as dependent on collateral blood flow during normotensive ischemia as the epicardial bed, a further deterioration of endocardial flow does not occur with a reduction in collateral driving pressure. Similarly, as endocardial motion is dependent on endocardial flow,27 a further worsening of wall motion is also not seen.

Possible Clinical Implications

Although our studies, as yet, may not have direct clinical implications, this appears to be a promising area for further research. Because antegrade flow can rarely be immediately established after acute coronary thrombosis, any means of enhancing regional flow within the ischemic bed until antegrade flow is reestablished will improve chances of tissue viability. Similarly, any method of increasing regional function within the ischemic bed will result in stabilizing global left ventricular function and decreasing further ischemia. At present, the closest clinical situation to our model of selectively increasing collateral driving pressure is intraaortic balloon counter-pulsation. However, it remains controversial whether increased blood flow has a significant role in the improvement of left ventricular function using this technique.28-30 The major difference between our model and intraaortic balloon counter-pulsation may be that the aortic pressure using this technique is not increased to the same levels as the coronary perfusion pressure in the nonoccluded vessel in our model. Finally, in our model, the nonoccluded vessel was normal, and we increased the collateral driving pressure within minutes of coronary occlusion. Whether similar results can be obtained where the nonoccluded vessel itself has a critical stenosis and the collateral driving pressure is increased at variable periods following coronary occlusion remains to be demonstrated.

Acknowledgment

The authors are grateful to Drs. George A. Beller and Joseph A. Gascho for their helpful critique and review of this manuscript.

References

Collateral Driving Pressure and Area at Risk

Kaul et al

vivo determination of total left ventricular "area at risk." J Am Coll Cardiol 1984;4:1272-1282


KEY WORDS • area at risk • collateral driving pressure
Effects of selectively altering collateral driving pressure on regional perfusion and function in occluded coronary bed in the dog.
S Kaul, N G Pandian, J L Guerrero, L D Gillam, R D Okada and A E Weyman

Circ Res. 1987;61:77-85
doi: 10.1161/01.RES.61.1.77

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 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/61/1/77

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/