Relationship between Blood Flow to Ischemic Regions and Extent of Myocardial Infarction

Serial Measurement of Blood Flow to Ischemic Regions in Dogs

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SUMMARY This study was designed to measure early sequential changes in blood flow to ischemic regions after acute coronary occlusion and to determine the relationship between blood flow and the extent of subsequent myocardial infarction. Initial studies were carried out on five dogs which verified using radioisotope-labeled microspheres, 7–10 μm in diameter, to measure changes in blood flow in small myocardial regions after acute coronary artery occlusions. Studies then were carried out on 11 awake dogs chronically prepared with indwelling catheters in the aorta and left atrium and occluders on the left circumflex coronary artery. Microspheres were injected via the left atrial catheter 45 seconds and 2, 6, and 24 hours after complete circumflex coronary occlusion. Six days later myocardial blood flow and the extent of histological infarction were determined for multiple samples from four transmural layers of the entire ischemic zone. Average blood flow to the circumflex region was $0.25 \pm 0.03$ (SE), $0.39 \pm 0.05$, $0.39 \pm 0.04$, and $0.53 \pm 0.07$ ml/min per g at 45 seconds, and 2, 6, and 24 hours, respectively. When samples from each transmural layer were grouped according to increasing ranges of blood flow, the extent of infarction in each layer was inversely related to blood flow. When samples in the same range of blood flow were compared, the extent of infarction in endocardial samples exceeded that in epicardial samples. These data indicate that the relationship between a given measurement of regional blood flow after acute coronary occlusion and the extent of subsequent myocardial infarction varies in different transmural layers and is a function of the time after occlusion that blood flow is measured.

UNDER BASAL conditions the myocardium extracts near-maximum amounts of oxygen from the arterial blood.\(^1\) Because the metabolism of the myocardium is predominantly aerobic and the capacity for anaerobic metabolism is limited during ischemia,\(^2,3\) the metabolic integrity of the myocardium is critically dependent on adequate blood flow. The heart is thus extremely vulnerable to disease processes or experimental interventions that reduce myocardial blood flow. It follows that blood flow to a region of ischemic myocardium should be a major determinant of the extent of injury or infarction. That blood flow to an ischemic region after acute coronary occlusion does in fact reduce the extent of myocardial injury is shown by the finding that the infarcted region is usually smaller than the area perfused by the occluded vessel.\(^4,6\)

However, a quantitative relationship between blood flow after acute coronary occlusion and the extent of subsequent myocardial infarction has not been established. Previous investigators have reported a wide range of flow values after acute coronary occlusion in experimental animals, depend-

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sodium thiamyl (30-40 mg/kg, iv) and ventilated with a respirator (Harvard model 607). A left thoracotomy was performed via the 4th left intercostal space. A polyvinyl chloride catheter with outer diameter (o.d.) of 3 mm was inserted via the left internal mammary artery into the arch of the aorta for the purpose of measuring aortic pressure and obtaining reference samples of arterial blood. The ventral pericardium was incised and a polyvinyl chloride catheter, 3 mm in o.d., was inserted into the left atrial chamber via the atrial appendage and secured with a purse-string suture for injection of radioactive microspheres and measurement of left atrial pressure. Both catheters were filled with heparin.

The left circumflex coronary artery was isolated and dissected 1-2 cm from its origin and a polyethylene loop snare-type occluder was positioned around it proximal to any branch. The catheters and occluder were tunneled to the base of the neck and placed in a subcutaneous pouch. The chest was closed, the pneumothorax was evacuated, and the dogs were taken off the respirator and allowed to breathe spontaneously.

Postoperatively, each dog was checked daily for signs of infection and trained to lie quietly on a laboratory table. A minimum period of 7 days was allowed for recovery from the operative procedure before study. At the time of study all dogs were free of fever or other signs of infection. Mean hematocrit was 44 ± 5.0 (sd); range, 38-52. The snare and catheters were exteriorized from the subcutaneous pouch, with 2% lidocaine for local anesthesia. The dogs were loosely restrained and studied while awake and resting quietly on their right sides. The laboratory was dimly illuminated and kept free of noise or other environmental conditions that might disturb the dog. Standard lead III of the electrocardiogram was recorded. Phasic aortic and left atrial blood pressures were measured with pressure transducers (Statham model P23Db). Data were recorded on an eight-channel direct-writing oscillograph (Hewlett-Packard model 8800) and an eight-channel magnetic tape recorder (Hewlett-Packard model 3917-A). After all recording instruments had been connected, a 45- to 60-minute period was allowed for the dog to adjust to the laboratory conditions.

Regional myocardial blood flow was determined by injecting carbonized microspheres 7-10 μm in diameter and labeled with gamma-emitting nuclides 44Sc, 85Sr, 141Ce, and 51Cr. The microspheres were obtained as 1 mCi of each nuclide in 10 ml of 10% dextran and 0.05% of polysorbate 80 (3M Co.). This stock solution was diluted in 10% dextran so that 1.5 ml, the volume injected, contained approximately 4 × 10⁶ microspheres. Before each injection, the microspheres were mixed by alternate agitation for at least 15 seconds.

Immediately after the injection the heart was removed, weighed, and placed in 10% buffered formalin for a 3-day period to facilitate sectioning. The lumen of the proximal circumflex coronary artery was carefully examined to verify the presence of a total occlusion by the snare. The great vessels, atria, right ventricle, large epicardial blood vessels, and visible epicardial fat were dissected from the left ventricle. The average weight of the left ventricle was 107 ± 7 g. The left ventricle was then sectioned, from base to apex, into four transverse sections of equal thickness, as previously reported and illustrated in Figure 1. The two central sections were divided into six circumferential regions, i.e., anterior, septal, posterior, posterior papillary muscle, lateral, and anterior papillary muscle. The blue-stained area in the two central sections corresponded to the posterior,
where $Q_m = \frac{Q_r C_m}{C_r}$, $Q_r$ = reference flow (ml/min), $C_m$ = counts/min in myocardium, and $C_r$ = counts/min in reference blood flow. Myocardial blood flow (ml/min) was divided by the sample weight and expressed as ml/min per g.

After the blood flow measurements had been obtained, samples were prepared for histological section by recombinning the four tissue samples from each circumferential region in the precut transmural sequence. Histological sections were obtained from each region containing the four samples and stained with hematoxylin and eosin. Thus, the extent of myocardial infarction was determined in each of approximately 32 tissue samples weighing 1–2 g from each dog studied. A minimum of two sections was taken at different depths in each tissue block and the average extent of infarction was determined. The percentage of infarcted myocardium in each rectangular tissue sample was determined with the use of grid markers inked on the side using a millimeter ruler so that the tissue section was divided evenly into 12.5–25% regions.

Each histological section was analyzed by two independent observers. The extent of infarction in each sample represents the average reading. If the extent of infarction determined by the two reviewers differed by more than 10% for a given sample, the histological section was re-reviewed and an average value calculated. This degree of observer variability occurred for approximately 5% of the readings. Infarcted myocardium was characterized by partial or complete cellular dissolution, extensive inflammatory cell infiltrate, and loss of normal cell architecture. Thus, 6 days postinfarction intact and infarcted myocardial tissues were clearly delineated and easily analyzed by use of routine hematoxylin and eosin stains. By this procedure blood flow and the extent of myocardial infarction were determined for multiple small samples of the entire region subjected to ischemia.

Student's $t$-test for paired data was used to compare sequential changes in blood flow. The coefficients of correlation were calculated by standard regression analysis.

Results

Table 1A lists the average $\pm$ SEM of the measurements of blood flow obtained after left circumflex coronary occlusion by simultaneous injection of the four isotopes. The average difference $\pm$ SEM of these blood flow measurements is given in Table 1B. Blood flow to nonischemic layers, i.e., the anterior region, varied from 1.36 ± 0.10 to 1.66 ± 0.11 ml/min per g, with the mean blood flow difference between simultaneously measured flows ranging from 0.09 ± 0.02 to 0.12 ± 0.03 ml/min per g. Blood flow to the ischemic regions represented by the posterior, lateral, and posterior papillary muscle regions varied from 0.02 ± 0.01 to 0.56 ± 0.12 ml/min per g. Blood flow differences between simultaneously measured flows were small in the ischemic region, ranging from 0.01 ± 0.001 (SEM) at lowest flow rates to 0.06 ± 0.02 ml/min per g at highest flow rates. Thus, the variability in the distribution of the microspheres that occurred during ischemia resulted in only small differences in the computed blood flow. Changes in blood flow of 0.10 to 0.014 ml/min per g (mean difference ± 2 SEM), respectively, would represent statistically significant differences in regions with blood flow values ranging from 0.50 to 0.10 ml/min per g. This degree of variability was observed when
Table 1: Blood Flow Measurements after Left Circumflex Coronary Artery Occlusion Using Four Isotopes Injected Simultaneously

<table>
<thead>
<tr>
<th>Circumferential regions</th>
<th>Anterior</th>
<th>Posterior</th>
<th>Posterior papillary</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Average flow (ml/min per g ± SEM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Layer 1</td>
<td>1.36 ± 0.10</td>
<td>0.56 ± 0.12</td>
<td>0.26 ± 0.06</td>
<td>0.28 ± 0.06</td>
</tr>
<tr>
<td>Layer 2</td>
<td>1.62 ± 0.10</td>
<td>0.56 ± 0.15</td>
<td>0.09 ± 0.02</td>
<td>0.11 ± 0.02</td>
</tr>
<tr>
<td>Layer 3</td>
<td>1.66 ± 0.11</td>
<td>0.53 ± 0.14</td>
<td>0.04 ± 0.01</td>
<td>0.06 ± 0.01</td>
</tr>
<tr>
<td>Layer 4</td>
<td>1.55 ± 0.10</td>
<td>0.46 ± 0.10</td>
<td>0.02 ± 0.01</td>
<td>0.09 ± 0.02</td>
</tr>
<tr>
<td>B. Average of flow differences (ml/min per g ± SEM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Layer 1</td>
<td>0.12 ± 0.03</td>
<td>0.04 ± 0.01</td>
<td>0.03 ± 0.005</td>
<td>0.01 ± 0.001</td>
</tr>
<tr>
<td>Layer 2</td>
<td>0.12 ± 0.03</td>
<td>0.03 ± 0.01</td>
<td>0.01 ± 0.003</td>
<td>0.01 ± 0.005</td>
</tr>
<tr>
<td>Layer 3</td>
<td>0.10 ± 0.03</td>
<td>0.06 ± 0.02</td>
<td>0.01 ± 0.003</td>
<td>0.01 ± 0.002</td>
</tr>
<tr>
<td>Layer 4</td>
<td>0.09 ± 0.02</td>
<td>0.04 ± 0.01</td>
<td>0.01 ± 0.002</td>
<td>0.01 ± 0.002</td>
</tr>
</tbody>
</table>

Myocardial blood flow values obtained when four different isotopes were injected 30 seconds after left circumflex coronary artery occlusion. Measurements in part A represent average blood flow values ± SEM. Data in part B represent the average of the differences in blood flow ± SEM between the simultaneous blood flow measurements.

Table 2: Hemodynamic Measurements

<table>
<thead>
<tr>
<th>Heart rate (beats/min)</th>
<th>Mean aortic pressure (mm Hg)</th>
<th>Mean left atrial pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cont 45 sec 2 hr 6 hr 24 hr</td>
<td>Cont 45 sec 2 hr 6 hr 24 hr</td>
<td>Cont 45 sec 2 hr 6 hr 24 hr</td>
</tr>
<tr>
<td>86 ±5 124 ±5 127 ±4 128 ±8 185 ±11</td>
<td>99 ±3 100 ±3 103 ±3 94 ±3 84 ±3</td>
<td>4 ±1 6 ±1 7 ±1 7 ±1 5 ±1</td>
</tr>
<tr>
<td>SEM</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>= NS</td>
</tr>
</tbody>
</table>
Significant transmural differences in the extent of myocardial infarction were present with progressive increments in infarction in layers 1, 2, and 3. Blood flows and percent of myocardial infarction in layers 3 and 4 were not significantly different. Thus, the transmural distribution of blood flow changes in flows were comparable in each layer. The percent myocardial infarction in endocardial samples exceeded the percent of infarction in epicardial samples, indicating that the relationship between blood flow and the extent of myocardial infarction varied in different transmural layers of the myocardium. The standard error of each mean value for infarction in a given range of flow is a measure of the variability of the relationship between blood flow and the extent of myocardial infarction. The mean myocardial infarction values ± 2 SEM should predict with 95% confidence limits similar degrees of myocardial infarction in a different group of dogs subjected to comparable experimental conditions. The average standard error of the percent infarction values was ±8%, ±7%, ±6%, and ±7% at 45 seconds and 2, 6, and 24 hours postocclusion. \( P \) values compare the blood flow values at each interval with the preceding value. \( P > 0.05 = \text{NS} \) (not significant).

**Discussion**

Myocardial ischemia does not result in homogeneous infarction of the ischemic zone. The ischemic zone contains...
varying amounts of reversibly and irreversibly injured myocardium for a variable period of time after the onset of ischemia. The anatomical criteria for recognition of irreversible, as compared to reversible, cell injury early after ischemia remain controversial. For this reason, in the present study the extent of infarction was determined 6 days after coronary occlusion so that intact and infarcted myocardium could be clearly delineated by routine histological sections. The boundary between viable and infarcted myocardium is irregular and characterized by intermingling of patches of intact and infarcted myocardium. Because of the heterogeneous nature of infarction in the ischemic regions, it was anticipated that selected sampling may not accurately reflect the extent of infarction in a given myocardial region in which blood flow was measured. Thus, the relationship between blood flow and the extent of myocardial infarction was determined by measuring blood flow and the extent of histological infarction in multiple small samples from separate transmural layers of the entire ischemic zone.

Initial studies were carried out to determine the precision of the microsphere technique for measuring blood flow in small myocardial samples under conditions of reduced flow rates. Buckberg et al. observed that if the number of microspheres in simultaneously collected reference blood samples fell below 400, the random variability in the number of microspheres in certain myocardial samples would be less than 400. To determine whether prohibitively high measurement variability would occur when tissue samples contained less than 400 microspheres. It was anticipated that, in the present study, during ischemia the number of microspheres in certain myocardial samples would be less than 400. To determine whether prohibitively high measurement variability would occur at low flow rates using the microsphere technique, the four microsphere used for...
blood flow measurements were injected simultaneously after left circumflex coronary artery occlusion. The average differences ± SEM between simultaneously measured flows provide an index of the variability of the microsphere technique for measuring blood flow in small ventricular samples and define the change in blood flow which may be detected by this technique. Although the reduced delivery of microspheres to the myocardial region during ischemia resulted in an increased variability of measurement, expressed as percentage differences, such variability resulted in only small differences in the simultaneously measured volumes of blood flow. These data indicate that the microsphere technique can be employed to reliably measure small changes in blood flow to ischemic regions.

Estimates of blood flow after acute coronary occlusion have varied considerably, depending on the measurement technique and conditions of the experiment. An early technique used for surgical preparations quantified the volume of blood flowing retrograde distal to a proximally occluded artery. Retrograde flow after acute occlusion represented approximately 10% of preocclusion flow values. Levy et al. using 42Rb clearance techniques, reported that flow to the ischemic region ranged from 22% to 67% of the flow to nonischemic areas. Rees and Redding using the 133Xe clearance technique in anesthetized dogs reported that flow to ischemic regions coincident with significant increases in heart rate from 86 ± 5 to 124 ± 4 beats/min. Blood flow to the circumflex region 45 seconds after circumflex occlusion averaged 0.25 ± 0.03 ml/min per g but was quite variable in different dogs, ranging from 0.12 to 0.52 ml/min per g.

The time course of early changes in ischemic flow after acute occlusion has not been clearly defined previously. Early increments, as well as initial values of ischemic flow, appear to be critically dependent on the conditions of the experiment as well as the technique used to estimate ischemic blood flow. Investigators studying anesthetized open-chest dogs have generally reported no significant increase in flow to the ischemic region in the initial hours after acute occlusion. In intact dogs which were "lightly anesthetized," Rees and Redding observed that 133Xe clearance in an ischemic region increased by approximately 20% within 1-2 hours after occlusion and then decreased between 2 and 6 hours. Pasyk et al. using 133Xe clearance in awake resting dogs, observed progressive increases in clearance rates beginning after occlusion. Clearance rates were equal to or in excess of preocclusion values 20 to 31 hours after occlusion. In the present study, significant increments in blood flow to the ischemic region occurred between 45 seconds and 2 hours and between 6 and 24 hours after occlusion. Blood flow increased by an average of approximately 100% during the 24 hours after occlusion.

In the present study, blood flow was not distributed evenly throughout the ischemic region. There were significant transmural gradients of flow in most regions, with flow decreasing from epicardium to endocardium. Transmural flow gradients were highest in the more ischemic regions. Numerous studies have documented that a variety of interventions which limit coronary flow, reduce coronary perfusion pressure, increase intraventricular pressure, or stimulate the distal vasculature when flow is limited proximally may result in uneven distribution of transmural blood flow gradients.

The microsphere technique has proved to be easily adapted to chronic studies. In previous studies in this laboratory on dogs prepared in a manner similar to that of the present study, mean blood flow measured for multiple small left ventricular samples using 7- to 10-μm microspheres was approximately 0.80 ± 0.06 ml/min per g during quiet resting conditions. In the present study, mean flow in the region supplied by the anterior descending coronary artery was 1.18 ± 0.10 ml/min per g 45 seconds after left circumflex occlusion. Thus, it is likely that acute coronary occlusion resulted in significant increases in blood flow to the nonischemic regions coincident with significant increases in heart rate from 86 ± 5 to 124 ± 4 beats/min. Blood flow to the circumflex region 45 seconds after circumflex occlusion averaged 0.25 ± 0.03 ml/min per g but was quite variable in different dogs, ranging from 0.12 to 0.52 ml/min per g.

FIGURE 2 The percent myocardial infarction ± SEM in myocardial samples from transmural layers 1, 2, and 3 plus 4 are plotted as a function of myocardial blood flow 45 seconds after coronary occlusion. These data are presented in tabular form in Table 5.

FIGURE 3 The percent myocardial infarction ± SEM in myocardial samples from transmural layers 1, 2, and 3 plus 4 are plotted as a function of myocardial blood flow 2 hours after coronary occlusion. These data are presented in tabular form in Table 5.
flow with disproportionate endocardial underperfusion. Moir and DeBra,24 using 82Rb clearance methods, and Griggs and Nakamura,25 using clearance of iodoantipyrene,1211, observed disproportionate underperfusion of the endocardial region when coronary perfusion pressure or coronary blood flow had been reduced. Becker et al.13 using 15-μm radioactive microspheres, observed an endocardial-epicardial (endo/epi) ratio of radioactivity of 0.76 ± 0.30 in the ischemic region after complete coronary artery occlusion. Buckberg et al.27 observed that ischemia-induced vasodilation in the presence of a proximal flow-limiting obstruction resulted in redistribution of myocardial blood flow so that selective subendocardial underperfusion occurred independently of changes in either heart rate or aortic or ventricular pressure.

Although previous experimental and clinical studies have demonstrated that the endocardial as compared to epicardial regions demonstrate greater infarction,182829 the relationship between blood flow and the distribution and extent of myocardial necrosis has not been defined. In the present study, blood flow measurements correlated significantly with the subsequent extent of myocardial infarction. Since the area of infarction averaged only 52% (range, 12–84%) of the area perfused by the occluded left circumflex coronary artery, residual inflow after occlusion afforded protection for a considerable but highly variable amount of ischemic myocardium. The extent of infarction was greatest in endocardial layers 3 and 4, with decreasing amounts of infarction in layers 2 and 1. Thus, the transmural distribution of infarction was inversely related to the transmural distribution of blood flow. Infarction in different dogs differed by the degree of extension into layers 1, 2, and 3. The extent of infarction was greatest in rings 1, 2, and 3, with variable extension in ring 4. Infarction was greatest in the posterior papillary region of rings 2 and 3 and lateral posterior segment of ring 1, intermediate in the lateral segment of rings 2 and 3, and least in the posterior segments of rings 2, 3, and 4 and in the medial posterior segment of ring 1. Histological sections of multiple small myocardial samples from the entire ischemic zone demonstrated that the distribution of infarction was not homogeneous. The boundary zone between noninfarcted and infarcted myocardium was extremely variable. Extension of infarction into layers 1 and 2 did not require total infarction of layers 3 and 4.

The relationship between blood flow and extent of infarction was examined further by grouping the samples for each transmural layer according to blood flow ranges. Within each transmural layer there was an inverse relationship between blood flow and the extent of infarction. Thus, the distribution of flow between rings, circumferential regions within a ring, and transmural layers conformed to the distribution of myocardial infarction as described above. When myocardial samples in the same blood flow ranges in each transmural layer were compared, the extent of infarction was greater in endocardial as compared to epicardial samples. The relationship between blood flow at a given interval after acute coronary artery occlusion and the extent of subsequent myocardial infarction varied in different transmural layers. There are at least two possible explanations for the disproportionate extent of endocardial infarction. As blood flow increased to the ischemic region (Table 5), the number of samples in the low blood flow ranges decreased and the number in the high blood flow ranges increased. There was a greater tendency for samples in the epicardial layers, as compared to samples in the endocardial layers, to shift to higher blood flow ranges, indicating that the increments in blood flow to the ischemic region were preferentially delivered to the epicardial layers. For example, 45 seconds after occlusion there were 44 samples in layer 1 and 66 samples in layer 4 in the flow ranges of 0–0.35 ml/min per g, whereas 24 hours after occlusion, eight samples in layer 1 and 46 samples in layer 4 remained in these flow ranges. Although disproportionate endocardial infarction was still apparent when samples were grouped 24 hours after occlusion, the differences between endocardial and epicardial infarction for comparable blood flow ranges were less striking.

Alternatively, it is possible that factors operating independently of blood flow may have contributed to the disproportionate endocardial infarction. Griggs et al.30 observed that coronary artery occlusion resulted in significant transmural metabolic gradients with concentrations of lactate and pyruvate increasing from outer to inner wall and adenosine triphosphate decreasing from outer to inner wall. The possibility that the transmural metabolic gradients may have resulted from transmural gradients in wall stress as well as blood flow was discussed by these investigators. Although the factors that contribute to the apparent disproportionate endocardial infarction have not been clearly delineated, these data indicate that the transmural location of the myocardial samples is an important determinant of the relationship between blood flow after acute coronary occlusion and the extent of subsequent infarct.

The relationship between measurements of blood flow early after acute coronary artery occlusion and the extent of subsequent myocardial infarction in samples grouped according to blood flow ranges and transmural layers should provide reference data that can be used to evaluate interventions which alter the extent of infarction (Table 5, Figs. 2 and 3). The mean percent infarction ± 2 SEM should predict with 95% confidence limits a similar amount of infarction in a different group of dogs subjected to the same experimental conditions. The standard error of each percent infarct value in a given flow range is a measure of the variability of the relationship between blood flow and subsequent infarction. The standard error of each infarct value thus determines the minimum change in infarct size that can be detected in a given flow range and layer. In future studies designed to evaluate the effects of a given intervention on infarct size, the protocol used in the present study will be followed. Blood flow will be measured 45 seconds and 2, 6, and 24 hours after occlusion. The intervention to be evaluated could be initiated after the 45-second, 2-hour, or 6-hour blood flow measurement. The blood flow data obtained before the intervention can be used to predict the expected amount of infarction, using the data provided in the present study. The...
Regional flow and myocardial infarction

Blood flow measurements obtained after initiation of the intervention can be compared to the blood flow data observed in the present study. Thus, any alteration in the extent of infarction can be related to changes in blood flow.

Studies by Jennings and Reimer on anesthetized animals indicate that infarction begins first in the papillary muscle areas of the endocardium. As the duration of the occlusion was increased, the initial infarct area progressively increased and involved varying amounts of the epicardium. 

The extent of infarction can be related to changes in blood flow observed in the present study. Thus, any alteration in the relationship between blood flow and the extent of infarction can be compared to the blood flow data obtained after initiation of the intervention and determination of the distribution of infarction, interventions which influence the generation of wall tension, such as increases and decreases in aortic pressure, may be expected to alter ischemic injury to a greater extent in the endocardium. It is possible that certain interventions will alter the extent of infarction coincidently with changes in blood flow whereas other interventions will alter infarction coincidentally with increases or decreases in blood flow to the ischemic region.

By permitting measurement of blood flow at intervals after acute coronary occlusion and determination of the relationship between blood flow and the extent of infarction in separate transmural layers rather than in the total region of ischemia, this model should provide (1) a sensitive technique for evaluating interventions that reduce or extend infarction, (2) data concerning the mechanism whereby infarction occurs coincidently with alterations in blood flow and infarction occurred coincidentally with alterations in blood flow. The model employs an awake dog and thus avoids the variables introduced by general anesthesia and acute surgery.

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