Correlation of Regional Myocardial Blood Flow and Function with Myocardial Infarct Size During Acute Myocardial Ischemia in the Conscious Pig

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SUMMARY Regional myocardial function and blood flow were determined for 48 hours after permanent occlusion of the left circumflex coronary artery in conscious swine. Systolic wall thickening and end-diastolic wall thickness (EDWTh) were correlated with regional myocardial flow (RMBF) at 15 minutes, 24 and 48 hours after occlusion. Both regional function and blood flow were compared with the extent of myocardial necrosis (determined histologically) after 48 hours in functionally distinct zones. Group 1 (control zones) was characterized by increased systolic wall thickening, EDWTh, RMBF and had no necrosis. Group 2 (marginal zones) had depressed systolic wall thickening (35 ± 3% [mean ± SEM] of preocclusion level at 48 hours) and RMBF (64 ± 6% of preocclusion values), transiently decreased EDWTh and 46 ± 5% necrosis. In Group 3 (ischemic zones), all values were greatly reduced: systolic wall thickening was 3.6 ± 1.2%, EDWTh 76 ± 8% and RMBF 25 ± 9% of preocclusion values; necrosis was 90 ± 5%. Groups 2 and 3 had increased RMBF at 24 and 48 hours from that at 15 minutes after occlusion; however, in neither case was systolic wall thickening greater than that at 15 minutes after occlusion. We conclude that there is close correlation between RMBF, systolic wall thickening and the extent of necrosis present after 48 hours of coronary artery occlusion in the conscious swine; subsequent increases in RMBF to the marginal zone after occlusion are not accompanied by improved regional function.

TENNANT AND WIGGERS first demonstrated the loss of regional contractile function after coronary artery occlusion.1 More recently, the use of chronically implanted ultrasonic crystals has permitted the precise measurement of regional dimensions of the left ventricle in unanesthetized animals.2-4 These studies examined the effect of restricted regional blood flow upon regional myocardial function after coronary occlusion in the conscious dog. Rivas et al.5 studied the relationship between this reduced blood flow and the extent of the subsequent infarct in the canine myocardium.

Theroux and co-workers5-6 identified three functionally distinct zones in the acutely ischemic myocardium: a normal zone that showed increased function after coronary artery occlusion; an ischemic zone that showed immediate dyskinesis and later nonfunction; and a marginal zone that showed partially impaired function. This marginal zone may represent an area of salvageable myocardium and is therefore of considerable interest.

The dog heart, however, differs from the human heart in several respects that may affect the extrapolation of experimental data to man. The coronary artery...
anatomy has a different regional distribution in man than in dogs and the coronary collateral circulation is relatively large in the normal dog heart. Also, the ratio of heart weight to body weight is higher in dogs than in man. The pig, therefore, may be a more appropriate model of acute myocardial ischemia for comparison with man.

This study was designed to examine the relationship of regional myocardial blood flow (RMBF) and function in the functionally defined marginal zone of the left ventricle after permanent occlusion of the left circumflex coronary artery (LCCA) and to correlate changes in RMBF and regional myocardial function with the extent of histologically determined myocardial necrosis in each zone.

Methods

Experimental Model

Twenty-nine adult pigs (40–50 kg) had an anesthesia induced with ketamine (1 mg/kg, i.m.) and surital (20 mg/kg, i.v.). Anesthesia was maintained with a combination of 1% halothane with oxygen and i.v. succinylcholine (300 mg/l at 7 ml/min) and ventilation was maintained by a Bird Mark 4 respirator. A left lateral thoracotomy was performed in the fourth intercostal space; the pericardium was opened and the heart elevated. Silastic catheters were placed in the descending thoracic aorta to monitor systemic arterial pressure and to withdraw blood samples during microsphere injection, in the left ventricle via the apex to monitor left ventricular pressure and its first derivative (dP/dt), and in the left atrium for microsphere injection.

The LCCA was carefully dissected free 3–5 cm from its origin and a hydraulic occluder was implanted to produce coronary artery occlusion at a later time. Three pairs of ultrasonic crystals were placed in the left ventricular wall to continuously measure wall thickness. One pair was placed across the anterior wall in a region perfused by the left anterior descending artery (LAD) to serve as a control (nonischemic) crystal. Another pair was placed at the base of the LCCA perfusion bed across the lateral left ventricular wall to measure wall thickness in a potentially necrotic zone. The third pair was positioned across the lateral midwall at the edge of the LCCA bed to monitor an ischemic, marginal zone. The subendocardial transducers were implanted by means of a small Teflon tube surrounding the lead wires. Crystals were held at the tip of the tube and advanced diagonally to a site close to the endocardium through a narrow tract created by an 18-gauge needle. Withdrawing the tubing left the transducer near the endocardium facing the epicardium. Epicardial transducers were sutured in place at a site where the ultrasonic signal was strongest. This technique allows crystal placement across the left ventricular free wall without damaging the intervening tissue. Wall thicknesses were approximately 10 mm; all crystal placements and wall thicknesses were confirmed at autopsy. After implantation of the crystals, the LCCA was temporarily occluded using the hydraulic cuff to confirm the proper positioning of the crystals and the closure of the occluder. All catheters, crystal wires and the occlusive cuff were exteriorized between the scapulae.

Aortic and left ventricular pressures were measured with Elema-Schönander transducers. Pressures were calculated using appropriate calibration factors. The ultrasonic technique for the measurement of ventricular wall thickness used a Schuessler and Associates ultrasonic dimension system (model 401), the calibration of which has been described. Measurements of left ventricular pressure, dP/dt, wall thickness and an ECG were recorded on an Elema-Schönander Mingograph 81 ink-jet recorder.

Regional Myocardial Function

Regional myocardial function was assessed by the continuous measurement of ventricular wall thickness. Peak negative dP/dt and peak positive dP/dt were used as indicators to determine end-systole and end-diastole for the wall thickness measurements. Left ventricular end-diastolic wall thickness (EDWTh) was measured just before the rapid increase of left ventricular pressure; left ventricular systolic thickness (ESWTh) was measured approximately 20 msec before peak negative dP/dt. Regional function was evaluated by monitoring ESWTh and the percentage of wall thickening during systole (%Th), which was defined as (ESWTh − EDWTh)/EDWTh × 100. Both %Th and ESWTh were expressed as a percentage of preocclusion control for that crystal.

Regional Myocardial Blood Flow

The tracer microsphere techniques used in this study are similar to those used previously and follow the guidelines of Heyman and co-workers. RMBF was determined by injecting carbonized microspheres (9 µm; 3M Co and New England Nuclear) labeled with one of the gamma-emitting nuclides 48Sc, 85Sr, 88Y, or 113Sn. The microspheres were suspended in 0.01% Tween solution (10% dextran) and placed in an ultrasonic bath. Before injection, the microspheres were agitated by direct contact with a vortex shaker to ensure proper dispersion. Absence of microsphere aggregation were verified by microscopic examination at the end of the experiment. Two milliliters of the microsphere solution were drawn into a 3-ml siliconized Wade-Hamilton gastight syringe with a Teflon plunger and immediately injected into the pig's left atrium over a 5-second period. The syringe and catheter were then flushed with 10 ml of sterile saline. Approximately 6 × 106 microspheres were injected into the left atrium with each measurement and the order of radioisotopes used was randomized throughout the protocol. A reference sample of arterial blood from the aortic catheter was
withdrawn at the rate of 7.5 ml/min beginning 10 seconds before microsphere injection and continued for 1.5 minutes after the injection was completed. Regional flow measurements were made before occlusion (control), and at 15 minutes, 24 and 48 hours after occlusion of the LCCA. Upon completion of the experiment, tissue samples for RMBF determinations were taken from each of the three functionally defined zones. Each transmural tissue block (about 1 g) contained endo- and epicardial crystal sites and all intervening tissue. These samples were placed in vials with formalin and analyzed for microsphere content using a Packard-Autogamma spectrometer (model 5912) equipped with a multichannel analyzer. Additional samples were taken from histologically distinct zones representing normal, marginal and necrotic tissue. Radioactivity per gram of tissue was calculated as previously described by using a Hewlett-Packard 9825A programmable calculator. Myocardial blood flow was then calculated by the withdrawal method using the arterial blood reference sample obtained from the aortic catheter. All RMBF values were expressed in ml/min/100 g.

Limitations to accurately determining infarct size and blood flow in the acute infarct have been suggested by Jugdutt et al. and Reimer and Jennings. Using their methods, we avoided this problem by correcting the 15-minute and 24-hour flow values for microsphere loss using differences in flow values between the LAD and LCCA perfusion beds as a measure of combined tissue and apparent loss. The LAD/LCCA microsphere ratio was used in two ways. First, it was used to normalize blood flow at 15 minutes and 24 hours by multiplying the blood flow to the ischemic region by the ratio. The range of values for microsphere loss was 2–11% (mean 5.7 ± 0.4%). Thus, the 15-minute and 24-hour blood flow values were increased by multiplying by individual ratios ranging from 1.02–1.11. Microsphere loss was considered to be the same at both times. Similarly, infarct size was adjusted to account for overestimation due to tissue edema. The ratio of preocclusion blood flow to the LAD and LCCA perfusion beds was used to correct infarct size. This ratio (average 0.95) was multiplied by measured infarct size to reduced measured infarct size by 5.7 ± 0.4%.

**Experimental Protocol**

The pigs were allowed 2 weeks to recover from surgery. Control recordings of left ventricular pressure, dP/dt, %Th and an ECG were made; this was done twice during the week before and 1 hour before LCCA occlusion. A control dose of radioactive tracer microspheres was given 1 hour before the occlusion during simultaneous monitoring. The pigs were confined in a lidless box (2 × 4 feet) during monitoring to restrict their movement and allow access to catheter and wires from above. Before LCCA occlusion, the conscious pigs were given a 100-mg bolus of i.v. lidocaine and maintained on a 2-mg/min i.v. infusion for arrhythmia prophylaxis. Morphine sulfate (5 mg i.v. and 15 mg subcutaneously) was given for analgesia 30 minutes before occlusion. The LCCA was occluded by injecting a formalin-catalyzed gelatin solution into the evacuated hydraulic occluder. Inflation of the occlusive cuff occluded the artery and hardening of the gelatin made it permanent. The pigs were monitored continuously for 3 hours after the occlusion. Eight pigs that developed malignant arrhythmias were excluded from the study. A second dose of tracer microspheres was given 15 minutes after the occlusion when hemodynamic and regional function variables had stabilized. Regional function was monitored again after 12, 24 and 48 hours; injections of radioactive microspheres were only given at 24 and 48 hours. Forty-eight hours after LCCA occlusion, the pigs were sedated with surital and killed using potassium chloride.

**Histologic Determination of Myocardial Necrosis**

The pigs were autopsied and the hearts removed with the instrumentation intact. Hearts were fixed in 10% formalin for 48 hours and then sectioned into six cross sections 1 cm thick. Traces of each slice were made on a Plexiglas overlay to include the outline of the endocardial and epicardial surfaces of the left ventricle, location of the infarct and the locations of the three pairs of ultrasonic crystals. Infarct size was then calculated using an electronic digitizer (Graf Pen-3) to planimeter the area of infarct. Total infarct size, expressed as a percentage of left ventricular volume, was determined compiling infarct determinations from each of the six cross-sectional slices and correcting for edema by the method of Reimer and Jennings.

Wall thicknesses at each of the three crystal sites were measured to confirm the ultrasonically determined measurements; misplaced crystals were eliminated from the study. Thin sections of tissue between the crystal pairs were taken from the tissue blocks previously used for the microsphere determination and prepared for histologic examination. Each block was embedded in paraffin and three transmural histologic sections were obtained. The extent of tissue necrosis between the crystal pairs was determined using a point-counting technique. The amount of fibrosis and necrosis caused by the implantation procedure was determined and was not included in the measurement (usually 1 mm). Necrosis was expressed as a percentage of the tissue volume between the crystals and represents the average of the three sections examined.

**Statistical Analysis**

Comparison of regional function was done using two-way analysis of variance and hemodynamic and blood flow measurements were compared using paired- or mean t tests. Correlation between regional function and blood flow, blood flow and necrosis, or function and necrosis was done using linear regression analysis. The probability was considered to be
statistically significant if less than 0.05. All values are expressed as mean ± SEM.

Results

Eight of the 29 pigs in this study had ventricular fibrillation after LCCA occlusion, eight had either nonfunctional or misplaced crystals, two were excluded due to fever and one had an inoperative occlusive cuff. Of the 10 pigs in which complete serial studies were obtained, the infarct size was 12.1 ± 1.5% of the left ventricular mass. Figure 1 shows a characteristic infarct and the location of the marginal zone crystals in relation to it.

The hemodynamic variables measured before and during the 48-hour occlusion are presented in table 1. Only heart rate was significantly changed by occlusion of the LCCA. Heart rate was significantly increased at 15 minutes after the occlusion and remained elevated at 24 hours, when it reached a peak of 137 ± 8 beats/min (12% above control).

Regional myocardial zones were categorized into three groups based on their functional response during the initial 15 minutes of coronary artery occlusion as done previously by Theroux et al.2 Group 1 included zones with initial hyperfunction or no change of regional function. This group contained exclusively crystal pairs implanted in control regions of the LAD perfusion bed. Group 2 included zones with a moderate decrease of function (%Th of 25–40% of preocclusion levels at 15 minutes after LCCA occlusion). This group included crystal pairs implanted across the lateral midwall at the edge of the LCCA perfusion bed (marginal zone). Group 3 included zones with a rapid decrease in function (%Th less than 5% of preocclusion levels at 15 minutes). These crystals were positioned at the base of the LCCA perfusion bed (ischemic zone) (fig. 2).

Regional Myocardial Function

We used %Th to assess regional myocardial function (table 2, fig. 3). The %Th for all crystal sites before LCCA occlusion was 23 ± 3% (n = 28). Thickening after occlusion has been normalized for each crystal to the %Th before the occlusion. In group 1 crystals (n = 8), %Th increased to 123 ± 16% at 15 minutes after the occlusion and remained elevated throughout the 48-hour study.

In group 2 (n = 9), %Th decreased at 15 minutes to 37 ± 6% of the preocclusion value and remained depressed for 48 hours. In group 3 (n = 11), %Th decreased quickly to 5 ± 1% at 15 minutes. Function further deteriorated to paradoxical thinning at 12 hours after occlusion and at 48 hours, %Th was still absent. The three groups were significantly different (p < 0.05).

Regional End-diastolic Wall Thickness

Changes in end-diastolic wall thickness are presented in table 2 and figure 4. The absolute wall thicknesses for all 28 zones before LCCA occlusion was 10 ± 1 mm. In group 1, EDWTh was increased (111 ± 10% of control) at 15 minutes after the occlusion and remained significantly thicker than control for 48 hours. In group 2, EDWTh initially thinned slightly, but was statistically the same as control at 48 hours.

<table>
<thead>
<tr>
<th>TABLE 1. Hemodynamics After Occlusion of the Left Circumflex Coronary Artery</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>HR (beats/ min)</td>
</tr>
<tr>
<td>AMP (mm Hg)</td>
</tr>
<tr>
<td>LVP (mm Hg)</td>
</tr>
<tr>
<td>LV dP/dt (mm Hg/sec)</td>
</tr>
</tbody>
</table>

Values are mean ± SEM (n = 10).
*p < 0.05 compared with control.

Abbreviations: HR = heart rate; AMP = aortic mean pressure; LV dP/dt = maximal rate of rise of LV pressure; LVP = peak left ventricular pressure.
hours. In group 3, however, EDWTh was significantly thinner at 15 minutes (80 ± 13%) and remained that way throughout the study.

**Regional Myocardial Blood Flow**

Transmural blood flow measurements for the three functional groups are presented in table 3 and figure 5. Blood flow for all zones averaged 0.67 ± 0.05 ml/min/g before the LCCA occlusion (including the correction factor of 5.1% to account for microsphere loss). Group 1 showed a small but significant increase in blood flow at 15 minutes and increased further to 142 ± 12% of control at 24 hours. Group 2 showed a decrease in blood flow to 64 ± 6% of control at 15 minutes, but flow was significantly increased at 24 and 48 hours compared with the level at 15 minutes. In group 3, blood flow was greatly decreased (12 ± 5%) at 15 minutes postocclusion. A small but significant increase in flow was observed at 24 and 48 hours. Tissue from the center of the infarct (determined histologically at the end of the experiment) showed almost no blood flow at 15 minutes and little change throughout the 48 hours.

**Regional Myocardial Necrosis**

The extent of myocardial necrosis between the crystals for the 3 groups at 48 hours after occlusion is presented in table 3. The small amount of necrosis (1%) found in group 1 probably represents damage secondary to implantation of the crystals, although the small fibrous rings surrounding the crystal sites (usually about 1 mm thick) were not included in these measurements. In contrast, the center of the infarct had more than 98% necrotic tissue. In group 2 zones, necrosis (46 ± 5%) was present in a heterogeneous area, with interdigitating areas of necrosis and viable tissue.

**Correlation of Systolic Wall Thickening, Regional Myocardial Blood Flow and Myocardial Necrosis**

The relationship between RMBF and %Th 48 hours after LCCA occlusion is shown in figure 6. At this

**Table 2. Systolic Wall Thickening and End-diastolic Wall Thickness**

<table>
<thead>
<tr>
<th>%Th</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>1 hr</th>
<th>2 hrs</th>
<th>3 hrs</th>
<th>12 hrs</th>
<th>24 hrs</th>
<th>48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 (n = 8)</td>
<td>123*</td>
<td>109</td>
<td>110</td>
<td>116*</td>
<td>113</td>
<td>96</td>
<td>108</td>
<td>112*</td>
<td>116*</td>
</tr>
<tr>
<td>± 12</td>
<td>± 10</td>
<td>± 15</td>
<td>± 10</td>
<td>± 15</td>
<td>± 12</td>
<td>± 17</td>
<td>± 10</td>
<td>± 14</td>
<td></td>
</tr>
<tr>
<td>G2 (n = 9)</td>
<td>37†</td>
<td>45†</td>
<td>37†</td>
<td>39†</td>
<td>31†</td>
<td>26†</td>
<td>19†</td>
<td>35†</td>
<td></td>
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<td>± 6</td>
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<td>± 7</td>
<td>± 5</td>
<td>± 9</td>
<td>± 4</td>
<td>± 7</td>
<td>± 6</td>
<td>± 4</td>
<td></td>
</tr>
<tr>
<td>G3 (n = 11)</td>
<td>4.5†</td>
<td>6.6†</td>
<td>6.6†</td>
<td>3.7†</td>
<td>0.9†</td>
<td>1.9†</td>
<td>-3.2†</td>
<td>3.0†</td>
<td>3.6†</td>
</tr>
<tr>
<td>± 1†</td>
<td>± 0.4†</td>
<td>± 4†</td>
<td>± 2†</td>
<td>± 1.7†</td>
<td>± 3.2†</td>
<td>0.03†</td>
<td>± 2.6†</td>
<td>± 12†</td>
<td></td>
</tr>
<tr>
<td>EDWTh</td>
<td>G1 (n = 8)</td>
<td>111</td>
<td>110</td>
<td>132*</td>
<td>108*</td>
<td>103</td>
<td>111*</td>
<td>101</td>
<td>114*</td>
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<tr>
<td>± 10*</td>
<td>± 13</td>
<td>± 21</td>
<td>± 11</td>
<td>± 10</td>
<td>± 11</td>
<td>± 11</td>
<td>± 11</td>
<td>± 10</td>
<td></td>
</tr>
<tr>
<td>G2 (n = 9)</td>
<td>94.3†</td>
<td>96.4†</td>
<td>90.6†</td>
<td>97.2†</td>
<td>96.0†</td>
<td>97.1†</td>
<td>94.4†</td>
<td>95.7†</td>
<td>102.3†</td>
</tr>
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<td>± 2.1</td>
<td>± 1.7</td>
<td>± 2.8</td>
<td>± 3.0</td>
<td>± 2.7</td>
<td>± 3.2</td>
<td>± 4.0</td>
<td>± 3.0</td>
<td>± 2.6</td>
<td></td>
</tr>
<tr>
<td>G3 (n = 11)</td>
<td>80†</td>
<td>77†</td>
<td>81†</td>
<td>79†</td>
<td>82†</td>
<td>86†</td>
<td>78†</td>
<td>76†</td>
<td></td>
</tr>
<tr>
<td>± 13</td>
<td>± 18</td>
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<td>± 11</td>
<td>± 3</td>
<td>± 8</td>
<td>± 8</td>
<td></td>
</tr>
</tbody>
</table>

Values for EDWTh and %Th are given as a percentage of control (mean ± SEM).

Abbreviations: G1 = group 1; G2 = group 2; G3 = group 3; %Th = percentage of systolic wall thickening; EDWTh = end-diastolic wall thickness.

* p < 0.05 compared with control.
† p < 0.05 compared with group 1.
‡ p < 0.05 compared with group 2.

**FIGURE 2. Wall thickness tracings obtained from three regional zones (A, B and C) before and after coronary occlusion for 48 hours. These zones represent groups 1 (C), 2 (B) and 3 (A) functional responses. In traces A and B, after coronary occlusion there is marked functional deterioration. Aneurysmal thinning occurs in A, while there is a hyperkinetic response in C, the nonischemic zone. The aneurysmal thinning in A decreases slightly after 48 hours of coronary occlusion. The functional deterioration in B remains unchanged during the course of coronary occlusion. LVP = left ventricular pressure; dP/dt = rate of left ventricular pressure change.**
time, RMBF and %Th had a linear relationship ($y = 0.93x - 16.7, r = 0.81$). A linear relationship was observed at 15 minutes and 24 hours ($r = 0.63$ and $r = 0.71$, respectively). Although there is a good correlation ($r = 0.81$) between blood flow and function at 48 hours in group 2 zones, the reduction in function in these marginal crystals was always greater than the reduction in flow.

Figure 7 shows the relationship between %Th and the percentage of viable myocardium ($100 - \%$ necrosis) present in the tissue between the crystals at 48 hours after occlusion. At 15 minutes and 24 hours, %Th also correlated positively with tissue viability at 48 hours; however, the correlation was not as good ($r = 0.69$ and 0.64, respectively).

The relationship between RMBF and the percentage of viable myocardium at 48 hours was defined as $y = 1.3 \times -9.0$ ($r = 0.93$) (fig. 8). Significant correlation was also observed at 15 minutes ($r = 0.67$) and 24 hours ($r = 0.74$).

**Discussion**

We used conscious pigs to examine the relationship between regional myocardial function, blood flow and necrosis after acute coronary artery occlusion because of the similarity of the pig's coronary artery anatomy and collateral circulation to man's. Unlike the dog, pigs have few coronary artery anastomoses, which facilitates the production of myocardial infarcts by occluding a distal portion of a coronary artery. Pigs are susceptible to ventricular fibrillation, but by the appropriate use of antiarrhythmic agents prophylactically, we could produce stable preparations with infarcts as large as 20% of the left ventricular mass. In the 10 pigs reported here, the occlusion of the distal section of the LCCA resulted in infarcts (mean of 12% of the left ventricular mass) involving more than two-thirds of the ventricular wall thickness. These infarcts caused neither global left ventricular malfunction nor hemodynamic instability.

**Figure 3.** Wall thickening (%Th) before and after 48 hours of coronary occlusion. Group 1 (G1) zones had less than 1% necrosis. Group 2 (G2) zones averaged 46% necrosis and group 3 (G3) zones averaged 90% necrosis. In G1 zones, a hyperkinetic response occurs after coronary occlusion while moderate and severe functional loss is seen in G2 and G3 zones. There is a slight return of function in G2 zones after 48 hours of coronary occlusion. In G3 zones, function remains depressed, although there is a slight stiffening after 12 hours of coronary occlusion. Values are mean ± SEM. *p < 0.05 compared with preocclusion value. #p < 0.05 compared with values 12 hours after coronary occlusion.

**Figure 4.** End-diastolic wall thickness (EDWTh) expressed as percentage of preocclusion values (100%) in the three zones defined in figure 3. In G1 zones the wall thickens slightly throughout the observation period. In G2 zones there is wall thinning that disappears by 48 hours. In G3 zones there is severe thinning throughout the occlusion period. Values are means ± SEM. *p < 0.05 compared with preocclusion value. #p < 0.05 compared with values 12 hours after coronary occlusion.
TABLE 3. Regional Myocardial Blood Flow and Extent of Myocardial Necrosis

<table>
<thead>
<tr>
<th>Myocardial region</th>
<th>Myocardial necrosis (%)</th>
<th>15 min</th>
<th>24 hrs</th>
<th>48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n = 8)</td>
<td>1.0 ± 0.2</td>
<td>110 ± 9</td>
<td>142 ± 12*</td>
<td>114 ± 17</td>
</tr>
<tr>
<td>Group 2 (n = 9)</td>
<td>46.0 ± 5</td>
<td>64 ± 6*</td>
<td>91 ± 11†</td>
<td>81 ± 3*</td>
</tr>
<tr>
<td>Group 3 (n = 11)</td>
<td>90.0 ± 5</td>
<td>12 ± 5*</td>
<td>24 ± 10†</td>
<td>25 ± 9†</td>
</tr>
<tr>
<td>Infarct (n = 10)</td>
<td>97.0 ± 2</td>
<td>5 ± 1*</td>
<td>7 ± 2*</td>
<td>6 ± 2*</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
*p < 0.05 compared with preocclusion value within group.
†p < 0.05 compared with 15-minute value within group.

Such hemodynamic stability, despite regional dysfunction, may be explained by the hyperfunction observed in group 1. This compensatory increase in %Th has been reported in both the conscious dog and open-chest pig. Theraux and co-workers associated increased function in the nonischemic zones with an increased resting fiber length, indicating a reliance on the Frank-Starling mechanism. However, our findings in conscious pigs associated an increased %Th with an increased EDWTh (equivalent to a decreased resting fiber length). The increased RMBF to the hyperfunctioning zones undoubtedly contributes to the increased EDWTh, as may an enhanced sympathetic outflow that accompanies an acute coronary artery occlusion. Increased RMBF can contribute to an increased EDWTh; Gaasch and Bernard showed the tissue volume increases as blood flow increases. Hemodynamic stability can be maintained in the face of acute coronary artery occlusion by using a variety of methods.

Figure 5. Regional myocardial blood flow expressed as percent of control preocclusion values (100%) in the three zones defined in figure 3. In G1 zones there is an increase in blood flow at all times after coronary occlusion. In G2 zones there is an immediate decrease in flow 15 minutes after coronary occlusion, but a slight increase occurs 24 hours after coronary occlusion. In G3 zones there is a severe decrease in blood flow 15 minutes after coronary occlusion, which persists throughout the 48 hours. Values are means ± SEM. *p < 0.05 compared with preocclusion value. #p < 0.05 compared with values 15 minutes after coronary occlusion.

Figure 6. Regional myocardial function (%Th) measured 48 hours after occlusion is plotted as a function of regional myocardial blood flow. The correlation was r = 0.81 (n = 28, p < 0.001). The regression line and its 95% confidence limits are shown.
of mechanisms, the importance of each depending on the experimental preparation.

Of particular interest is the functional behavior of group 2 because of the possibility that an area of partial ischemia may be salvageable if perfusion can be restored. The tissue surrounding the wall thickness crystals of group 2 probably contains tissue perfused by either the LCCA or LAD coronary arteries. Therefore, the reduced %Th after occlusion of the LCCA is probably the result of the net effect of two distinct populations of myocardial cells, one ischemic and the other normal. This idea is supported by the observation that although RMBF was significantly improved in group 2 at 24 and 48 hours, %Th was unchanged. The border zone consists of areas of both necrotic and normal cells and it is not known whether the increased RMBF in group 2 at 24 and 48 hours is due to increased blood flow to the normal cells (as suggested by the increased RMBF in group 1) or to the development of collateral flow to the necrotic areas. In either case, improvement of flow to the zone as a whole did not result in improved regional function. Because we terminated experiments at 48 hours, we do not know if improved regional function occurred in the partially ischemic zones after several weeks, as described by Theroux et al.2 in the dog. Two opposing factors may contribute to such changes. They are tethering of the partially ischemic zones by the necrotic tissue, which would limit functional improvement, and hypofunction of the tissue adjacent to the infarct2 secondary to increased tissue perfusion from an increase in collateral circulation. Because these opposing factors may operate simultaneously, it is difficult to quantify their independent contribution to the observed functional changes.

Previous studies in conscious dogs and open-chest pigs have shown that small reductions in RMBF have profound effects on systolic wall thickening.19, 21 Our
data confirm those findings. Increases in RMBF should not be considered to improve regional function. Stowe and associates found that increasing blood flow to the LAD to a rate 50% above control had little effect on regional contractile indexes in the open-chest pigs. Thus, the increased RMBF observed in group 1 is probably secondary to some other compensatory mechanism causing enhanced %Th.

The linear correlation between RMBF and the extent of myocardial necrosis is similar to that observed previously. Irvin and Cobb reported a close correlation between RMBF measured 15 minutes after coronary artery occlusion and the extent of myocardial necrosis present 48 hours later. The importance of RMBF on the eventual viability of the myocardium soon after coronary occlusion in our model is evident, because subsequent increases in RMBF to ischemic zones is not accompanied by an increased %Th. One might expect, therefore, a close correlation between RMBF at 15 minutes after occlusion and the percentage of viable tissue at 48 hours. A positive correlation was observed at both 15 minutes and 24 hours, but with lower correlation coefficients than that observed at 48 hours. We attribute this to the error associated with the measurements made at 15 minutes and 24 hours caused by microsphere loss despite the use of the correction factor suggested by Jugdutt et al. The RMBF measured at 48 hours avoids this error.

This study was designed to determine the interrelationships of regional myocardial function, regional myocardial blood flow and the extent of myocardial necrosis in an animal model with a limited coronary collateral circulation. The results show significant correlation between all three variables throughout the 48 hour study, yet give evidence for compensatory mechanisms for maintaining global ventricular function that may effect one variable independently. We also observed that the return of flow to zones with a severe reduction in function does not always enhance tissue viability. In these zones, the increase in collateral flow may represent revascularization in necrotic myocardium undergoing organization and eventual scar formation.

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