Transmural Distribution of Myocardial Infarction: Difference Between the Right and Left Ventricles in a Canine Model

KEIZABURO OHZONO, SAMON KOYANAGI, YOSHITOSHI URABE, YASUHIKO HARASAWA, HITONOBU TOMOIKE, AND MOTOOMI NAKAMURA

SUMMARY The evolution of myocardial infarction 24 hours after ligating both the right coronary artery and the obtuse marginal branch of the left circumflex coronary artery was examined in 33 anesthetized dogs. Postmortem coronary angiography and a tracer microsphere technique were used to determine risk areas and their collateral blood flows, respectively. The mean weight of the risk areas was 11.3 ± 0.5 g (mean ± SEM) in the right ventricle and 10.5 ± 0.9 g in the left ventricle (NS). The weight of infarcted tissue was 5.7 ± 0.7 g in the right ventricle and 5.2 ± 0.9 g in the left ventricle (NS). In both ventricles, infarct weight was linearly related to risk area size, and the percent of risk area necrosis was inversely correlated with the extent of collateral flow at 24 hours of coronary ligation, defined as the mean myocardial blood flow inside the central risk area. Ratios of infarct to risk area between the subendocardial and subepicardial layers were 0.76 ± 0.06 and 0.28 ± 0.05 in the right and left ventricles, respectively (p < 0.01, between ventricles, n = 31), which coincided well with subendocardial-to-subepicardial-flow ratios at 24 hours, i.e., 0.86 ± 0.04 in the right ventricle and 0.32 ± 0.06 in the left ventricle (p < 0.01). The regional distribution of myocardial infarction correlated well with flow distribution inside the risk area; the slope of these relations was similar between the subendocardial and subepicardial in the right ventricle, whereas in the left ventricle it was larger in the subendocardium than in the subepicardium. Thus, in the dog, the inherent change in the regional distribution of coronary collateral blood flow is an important modifier in the evolution of myocardial infarction, especially in the left ventricle. (Circulation Research 1986;59:63-73)

KEY WORDS • risk area • myocardial necrosis • regional myocardial blood flow • collateral flow

We attempted to define whether there is any topological difference in the evolution of myocardial necrosis through different transmural layers between right and left ventricles, with reference to risk area and regional myocardial blood flow.

Materials and Methods

Experimental Model and Protocol

Fifty-one adult mongrel dogs of either sex (weight 16–29 kg) were anesthetized with sodium pentobarbital (25 mg/kg IV) and ventilated by room air and supplemental oxygen (2 l/min) via an endotracheal tube with a positive pressure respirator. A polyvinyl catheter was placed at the descending aorta through the carotid artery to monitor the aortic pressure and for reference blood sampling. The chest was opened in the left fourth intercostal space, and the heart was suspended in a pericardial cradle. The largest obtuse marginal branch of the left circumflex coronary artery as well as the main trunk of the right coronary artery (RCA) 2–3 cm distal to its orifice were dissected. These arteries were selected for obstruction because their perfusion areas are remote and comparable in size (Table 1).

Catheter-tip manometers (PC-370, Miller Instruments) were placed in the left ventricular (LV) and right ventricular (RV) cavities through the femoral artery and femoral vein, respectively. After a control
TABLE 1. Risk and Infarct Sizes in the Canine Right and Left Ventricles (n = 33)

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Total heart weight (g)</th>
<th>RV weight (g)</th>
<th>LV weight (g)</th>
<th>Risk region (g)</th>
<th>Infarct region (g)</th>
<th>Infarct/risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RV</td>
<td>LV</td>
<td>RV</td>
<td>LV</td>
<td></td>
</tr>
<tr>
<td>16-29</td>
<td>101±4</td>
<td>24±1</td>
<td>77±3</td>
<td>11.3±0.5</td>
<td>10.5±0.9</td>
<td>47.9±5.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.7±0.7</td>
<td>5.2±0.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>46.2±3.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SEM. RV = right ventricle; LV = left ventricle.

In the excised heart, the left main coronary artery and the right coronary artery proximal to its ligated portion were cannulated and flushed with saline. A barium-gelatin mixture (BaSO₄ 42 g; gelatin 17 g; water 53 ml) was perfused simultaneously at a perfusion pressure of 120–140 mm Hg for 5 minutes at 37°C. The heart was then immersed in crushed ice for 5 minutes to harden the barium-gelatin mixture. The RV free wall was removed from the LV. The RV and LV were sliced parallel to the atrio-ventricular groove into 4 and 5 slices, respectively, of equal thickness (0.8–1.2 cm). Each slice was immediately incubated in 1% solution of triphenyl tetrazolium chloride (TTC), buffered in 0.2 mol/l Tris buffer to pH 7.8 at 20°C for 30 minutes and fixed in 20% formalin. At this temperature the barium-gelatin mixture was prevented from melting away from the myocardial slices. The infarct areas of both RV and LV were clearly defined by TTC staining (Figure 1). Stereoscopic radiograms (SRO-M40S, Sofron) of the slices were taken without magnification. The perfused area of the occluded artery, i.e., the area at risk was determined by two independent observers who followed the course of occluded and nonoccluded vessels with a stereoscopic viewer. The interobserver difference was negligible. When the difference was larger than 2 mm in width, the two observers discussed the matter and determined the area at risk. The tracings of the risk area and the infarct area in each slice were superimposed, and these

Measurement of Area at Risk and Infarct Size

hemodynamic recording, both the obtuse marginal and right coronary arteries were ligated. Thirty minutes after coronary ligation, the chest was closed and the dog allowed to recover in a cage. No treatment was given for the arrhythmias. Twenty-four hours after coronary ligation, the dog was reanesthetized with sodium pentobarbital (15–20 mg/kg IV), 5,000 units of heparin was infused, and the animal was sacrificed by administering 20 ml of saturated KCl intravenously. The heart was then excised.
areas were measured using a computerized planimeter (HIPAD Digitizer, Houston Instruments; Nova-01 minicomputer, Data General Co.). Then, the LV and RV were subdivided into three and two layers from the subendocardial to the subepicardial direction, respectively. These dividing lines were drawn as parallel as possible to the epicardial contour of each ventricle. The risk area and the infarct area were measured independently in each layer, in both the right and the left ventricles. The mass of each risk and infarct area was calculated by multiplying the percentage of the area by the weight of the ventricular slice.

Measurement of Regional Myocardial Blood Flow

Regional myocardial blood flow was measured in 11 of 51 dogs before, 5 minutes after, and 24 hours after coronary occlusion and after intravenous administration of dipyridamole (0.5–1.0 mg/kg). For this we used carbonized tracer microspheres, 8–11 μm in diameter labelled with γ-emitting nuclides: 141Ce, 113Sn, 46Sc (New England Nuclear), and 85Sr (3M Company) as described by Tomoike et al.18 For each measurement 0.5–1.0 ml of ten million microspheres was injected into the left atrium via the left atrial catheter. To calculate absolute values of regional myocardial blood flow, arterial blood was collected from the catheter at the descending aorta with a constant withdrawal rate of 6.17 ml/min. The collection was begun 10 seconds prior to injection of microspheres and continued for 120 seconds.

Myocardial samples were obtained from the following regions: 1) normally perfused region [LV — the region perfused by the left anterior descending coronary artery (LAD); RV — anterior portion of the RV free wall perfused by LAD and/or RCA proximal to the occluded site], 2) inner 5 mm of the risk region from the boundary (a), 3) outer 5 mm from the boundary of the risk region, and 4) center of the risk region (b). A whole risk region was a + b. Each region was subdivided into subendocardial (Endo), midwall (Mid), and subepicardial (Epi) layers in the LV (Figure 1), and into subendocardial (Endo), and subepicardial (Epi) layers in the RV. Sample weight in the subendocardial and subepicardial layers was 0.81 ± 0.06 and 1.11 ± 0.16 g in the LV (p < 0.01 between Endo and Epi) and 1.72 ± 0.27 and 1.75 ± 0.33 g, respectively, in the RV (not significant between layers).

The radioactivities of the myocardial and blood samples were measured using a Packard Autogamma Spectrometer. The data were corrected for background and Compton scattering, and regional myocardial blood flow was calculated according to Heymann et al17 using a PDP 11/44 computer: \[ Q_m = Q_r \left( \frac{C_m}{C_r} \right) \]
where \( Q_m \) = myocardial blood flow (ml/min), \( Q_r \) = reference blood flow (ml/min), \( C_m \) = counts/min in myocardium, and \( C_r \) = counts/min in reference blood. Myocardial blood flow (in milliliters per minute) was divided by the sample weight and expressed as milliliters per minute per gram. Collateral blood flow was defined as the regional myocardial blood flow to the center of the risk region, by which the involvement of the normal tissue was minimum, as shown in Figure 2.

**Figure 2.** Changes in regional myocardial blood flow after dipyridamole (0.5–1.0 mg/kg) at 24 hours of coronary occlusion in 11 dogs. RV = right ventricle; LV = left ventricle; MBF = myocardial blood flow; NS = not significant. See text.
There was no decrease in ratio of preocclusion counts of microspheres in the risk to normal areas such as 1.09 ± 0.05 in the LV and 0.93 ± 0.10 in the RV. Thus, the correction for microsphere loss was not performed. Such a nonsignificant microsphere loss may be explained by a rather small size of myocardial infarction due to a branch occlusion and a rather large number of microspheres injected in the present study.

Statistical Analysis

All values are presented as means ± SEM. Analysis of variance was applied to assess myocardial blood flow in relation to time course and ventricles (RV and LV). When analysis of variance demonstrated a statistically significant result (p < 0.05), a Bonferroni’s t test was used to identify the subgroup differences. For paired data, Student’s t test was used. Regression lines and associated correlation coefficients were computed by the least squares method. The level of statistical significance was p < 0.05.

Results

Eighteen of 51 dogs died, 3 from ventricular fibrillation within 5 minutes, 7 between 30 minutes and 3 hours, and 8 between 4 and 24 hours after coronary occlusion. Thirty-three dogs survived until the end of the study, and these were used for the following analysis.

Hemodynamics

Hemodynamic variables before and after coronary ligation are summarized in Table 2. Right ventricular systolic pressure decreased from 25 ± 2 mm Hg before coronary ligation to 20 ± 2 mm Hg 30 minutes after and 24 ± 1 mm Hg 24 hours after coronary occlusion. Reduction of systolic pressure during 30 minutes was statistically significant. Heart rate increased markedly (p < 0.01), and ventricular arrhythmia along with slight increases in left ventricular end-diastolic pressure was noted in every dog 24 hours after coronary occlusion. Mean aortic pressure, left ventricular systolic pressure, and right ventricular end-diastolic pressure did not change significantly after coronary ligation.

Regional Myocardial Blood Flow

Five minutes after coronary occlusion, regional myocardial blood flow to the purely necrotic area decreased from 0.67 ± 0.03 to 0.06 ± 0.03 ml/min/g in the RV and from 1.47 ± 0.09 to 0.19 ± 0.03 ml/min/g in the LV (Table 3). The blood flow to the total risk or central risk areas was also decreased but was greater (p < 0.05) than that at the purely necrotic site in either RV or LV, as shown in Table 3. Between 5 minutes and 24 hours after coronary occlusion, transmural myocardial blood flow toward the total or central risk area did not change significantly in either the RV or the LV, whereas that to the purely necrotic area of the LV decreased significantly from 0.19 ± 0.03 to 0.01 ± 0.01 ml/min/g (p < 0.01).

Dipyridamole, a potent coronary vasodilator, was used to evaluate changes in regional blood flow across the anatomical borderline of the risk area 24 hours after coronary ligation (Figure 2). Regional myocardial blood flow of the area 5 mm outside the risk area increased from 0.87 ± 0.10 to 2.99 ± 0.38 ml/min/g (p < 0.01) and from 1.09 ± 0.13 to 2.55 ± 0.34 ml/min/g (p < 0.01) after dipyridamole in the RV and LV, respectively, which were larger (p < 0.01) than the increases in regional flow of the area 5 mm inside the risk area, ie, from 0.52 ± 0.08 to 0.96 ± 0.15 ml/min/g (p < 0.05) and from 0.70 ± 0.10 to 1.04 ± 0.12 ml/min/g (p < 0.05) in the RV and LV, respectively. Regional myocardial blood flow was unchanged in both the purely necrotic and central risk areas. Accordingly, despite a sharp change in regional myocardial blood flow across the borderline after dipyridamole (Figure 2), regional flow toward the central risk area was considered as a collateral flow in the risk area in the following analysis.

Transmural distribution of myocardial blood flow inside the risk area differed between the right and left ventricles, both at 5 minutes and 24 hours after coronary occlusion (Table 3). The subendocardial to subepicardial flow ratio in the central risk area of the RV was reduced slightly from 1.19 ± 0.06 before coronary occlusion to 0.85 ± 0.05 at 5 minutes and, significantly, to 0.69 ± 0.06 at 24 hours (p < 0.01). This ratio in the LV decreased remarkably from 1.29 ± 0.08 before occlusion to 0.51 ± 0.09 at 5 minutes (p < 0.01 vs before occlusion) and 0.09 ± 0.02 at 24

| Table 2. Hemodynamic Changes Before and After Coronary Occlusion in Dogs |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Heart rate      | Mean aortic     | LV pressure     | LV end-diastolic | RV pressure     | RV end-diastolic |
|                                | (beats/min)     | pressure         | (mm Hg)         | pressure         | (mm Hg)         | pressure         |
| Preocclusion                   | 135 ± 6         | 107 ± 5          | 118 ± 5         | 1.1 ± 0.9        | 25 ± 2          | 1.7 ± 0.8        |
| Postocclusion                  |                 |                 |                 |                 |                 |                 |
| 5 min                          | 129 ± 7         | 98 ± 5           | 110 ± 6         | 1.4 ± 0.8        | 21 ± 2          | 2.1 ± 0.8        |
| 30 min                         | 128 ± 8         | 97 ± 8           | 108 ± 8         | 0.9 ± 0.8        | 20 ± 2*         | 2.4 ± 0.7        |
| 24 hr†                         | 177 ± 7†        | 93 ± 5           | 105 ± 5         | 3.2 ± 0.7*       | 24 ± 1          | 2.8 ± 1.0        |

Values are means ± SEM. LV = left ventricle; RV = right ventricle.

†p < 0.05.  
†Almost all heart beats were of ventricular origin.  
*p < 0.01 between pre- and postocclusive periods.
TABLE 3. Regional Myocardial Blood Flow (ml/min/g) Before and After Coronary Occlusion

<table>
<thead>
<tr>
<th></th>
<th>Preocclusion</th>
<th>Postocclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5 min</td>
</tr>
<tr>
<td>RV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control area</td>
<td>Trans</td>
<td>0.97±0.17</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>1.03±0.19</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>0.90±0.17</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.17±0.12</td>
</tr>
<tr>
<td>Area at risk (total)</td>
<td>Trans</td>
<td>0.79±0.09</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>0.81±0.08</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>0.78±0.11</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.10±0.08</td>
</tr>
<tr>
<td>Area at risk (central)</td>
<td>Trans</td>
<td>0.76±0.07</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>0.81±0.07</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>0.72±0.09</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.19±0.06</td>
</tr>
<tr>
<td>Necrotic sample (n = 27)</td>
<td></td>
<td>0.67±0.03</td>
</tr>
<tr>
<td>LV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control area</td>
<td>Trans</td>
<td>1.23±0.17</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>1.30±0.16</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>1.15±0.17</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.18±0.05</td>
</tr>
<tr>
<td>Area at risk (total)</td>
<td>Trans</td>
<td>1.30±0.19‡</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>1.45±0.21‡</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>1.19±0.18‡</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.22±0.05</td>
</tr>
<tr>
<td>Area at risk (central)</td>
<td>Trans</td>
<td>1.35±0.18‡</td>
</tr>
<tr>
<td></td>
<td>Endo</td>
<td>1.52±0.20‡</td>
</tr>
<tr>
<td></td>
<td>Epi</td>
<td>1.22±0.19‡</td>
</tr>
<tr>
<td></td>
<td>Endo/Epi</td>
<td>1.29±0.08</td>
</tr>
<tr>
<td>Necrotic sample (n = 21)</td>
<td></td>
<td>1.47±0.09</td>
</tr>
</tbody>
</table>

Values are means ± SEM. RV = right ventricle; LV = left ventricle; Trans = transmural; Endo = endocardial layer; Epi = epicardial layer.

*p < 0.01 compared with before coronary occlusion.

†p < 0.05 compared with right ventricle.

‡p < 0.01 compared with right ventricle.

hours of coronary occlusion (p < 0.01 vs 5 minutes) (Table 3).

Infarct Size and Collateral Flow in the Right and Left Ventrices

With TTC staining, the infarcted myocardium was clearly detectable from the surrounding normal tissue, as shown in Figure 1. The mean infarct size and the ratio of the infarct size to the risk area (IS:RA) were not significantly different between occlusions of these two vessels, as shown in Table 1. There was a linear relationship between infarct size and risk area for both vessels (Figure 3). The infarct area was always located inside the risk area, in both the RV and the LV.

The relationship between necrotic area (percent of the risk size; y) and transmural collateral flow (x) 24 hours after coronary occlusion was inversely related in the LV and RV (Figure 4). The slope of the relationship was steeper in the RV than in the LV and the x-axis intercept was lower in the RV than in the LV. The correlation coefficients between necrotic area and collateral flow remained unchanged between 5 minutes and 24 hours of occlusion in the RV (-0.87 vs -0.75), but increased from -0.47 to -0.78 during 24 hours in the LV. Thus, data in Figure 4 and the following analysis represent data obtained 24 hours after coronary ligation.

Regional Differences in Distribution of Myocardial Necrosis in the RV and LV

In the LV, the subepicardial layer tended to be salvaged in most dogs, as shown in Figure 1. On the other hand, myocardial necrosis in the right ventricle was distributed rather homogeneously from the subendocardium to the subepicardium, showing transmural necrosis (7 of 33 dogs, as represented in Figure 5A) or
FIGURE 3. Relation between weight of infarcted and risk areas. The line labelled by $y = x$ is the line of identity, and the other line is the regression line. The standard error of estimate is shown by dotted lines. Two coronary arteries (obtuse marginal branch and right coronary artery) were ligated at a fairly constant anatomic site. The mean size of the risk area was similar between the RCA and the obtuse marginal branch; $11.3 \pm 0.5$ g and $10.3 \pm 0.9$ g, respectively; however, the size of the risk area was more variable in the case of occlusion of the obtuse marginal branch than in that of the RCA occlusion ($p < 0.05$). RV = right ventricle; LV = left ventricle. Each point represents data from respective dogs.

scattered small islands of necrosis, as represented in Figures 5B and 5C.

The relationship between infarct size and risk area for the subendocardial and the subepicardial layers in the RV and LV is shown in Figure 6. In the RV, data from the subepicardial layers and subendocardial layers are distributed between the x axis and a line of identity ($y = x$) of an infarct–risk relation, and there is no significant difference in variance between these layers; but in the LV, data from the subendocardial layers are grouped along the line of identity and data from the subepicardial layers are scattered randomly.

The infarct size, expressed as a ratio of the risk area (IS:RA), in the subendocardial and subepicardial layers was markedly different between the RV and LV (Figure 7). IS:RA of the subendocardial layer was $0.53 \pm 0.05$ ($n = 33$) and was slightly higher than that of the subepicardial layer ($0.40 \pm 0.05; p < 0.05$) in the RV, whereas in the LV, IS:RA was markedly higher in the subendocardial ($0.71 \pm 0.04$) than in the subepicardial layer ($0.21 \pm 0.04; p < 0.01$). The ratios of subepicardial IS:RA to subendocardial IS:RA in the RV and LV were $0.76 \pm 0.06$ and $0.28 \pm 0.05$, respectively ($n = 31, p < 0.01$ between ventricles).

Regional Difference in the Relationship Between Infarct Size and Collateral Blood Flow

Figure 8 shows the relationship between regional myocardial blood flow in the central risk area (collater-
al blood flow; x) 24 hours after coronary ligation and the percentage of myocardial necrosis to the risk region (IS:RA; y) in the subendocardial and subepicardial layers. In the RV, a slight rightward shift of the relationship between IS:RA and collateral blood flow was noted in the subepicardial layer, whereas in the LV, the infarcted area was always larger in the subendocardial than in the subepicardial layer, along with a markedly reduced slope of this relationship in the subepicardial layer.

Discussion

Comparing infarct size between right and left ventricular free walls, which was of a similar size in the risk area, we found that 1) there was an obvious difference in the transmural evolution of myocardial infarction between the right and left ventricles, and 2) this difference was explained by the difference in transmural distribution of regional myocardial blood flow in the right and left ventricles.

We determined risk areas by means of postmortem stereoscopic coronary arteriography. This procedure provides an "anatomical" risk region supplied by the occluded coronary artery. In the present study, ligating a rather small branch of the coronary artery, we confirmed a statistically significant correlation between the transmural infarct size and the risk area, in both RV and LV. To explain the difference of the risk–infarct relation between the RV and LV, the regional relation between infarct size and risk area...
from the subendo- to the subepicardium, was examined. Data from either the subendocardial or the subepicardial layers of the RV were distributed randomly between the x axis and the line of identity. In the LV, data from the subendocardial layer were practically linear, while data from the subepicardial layer were scattered, in a manner similar to that in the RV. Such a marked difference in the regional distribution of myocardial necrosis between the RV and LV suggests that the risk area, per se, is not a sole determinant of infarct size, especially in case of branch occlusion (Figure 6). Thus, variation in infarct size in relation to risk area size was examined, using as a parameter the collateral blood flow to the risk area.

We defined collateral flow as the regional flow to the risk area. As the inclusion of normal tissue in sampling the risk area is inevitable due to the presence of islands or peninsulas along the border zone,23,24 the

![Figure 4](image1)

**Figure 4.** Relation between percent of necrosis of the risk area and transmural collateral flow in percent of non-ischemic flow 24 hours after coronary ligation. Right ventricle (RV): $y = -2.1x + 97.8 (r = -0.77)$. Left ventricle (LV): $y = -0.6x + 62.0 (r = -0.77)$. The standard error of estimate is shown by dotted lines.

![Figure 5](image2)

**Figure 5.** Triphenyl tetrazolium chloride staining of transmural sections of the right ventricle. A. Transmural necrosis. B and C. Small islands of necrosis. Myocardial necrosis is shown by the unstained area.
physiological appropriateness of our risk determination was examined by changes in regional flow across the boundary of the risk region, after administration of dipyridamole. A statistically significant increase in flow, preferentially outside the risk area, suggests that demarcation of the risk area by a postmortem angiogram was appropriate physiologically. To further minimize the involvement of normal tissue, we defined collateral flow as the regional flow to the central risk area.

Regional myocardial blood flow to ischemic regions 2 hours after acute coronary occlusion was 0.39 ± 0.05 ml/min/g in studies of Rivas et al,25 in which a purely ischemic sample of the left circumflex coronary artery was confirmed by staining with Evans blue dye. Similar results were repeatedly observed in studies on anesthetized as well as conscious animals.6-8 In the present study, regional myocardial blood flow to the purely necrotic myocardium was 0.01 ± 0.01 and 0.05 ± 0.03 ml/min/g in the RV and LV, values similar to those reported by Jugdutt et al and Nakamura et al.6-7 However, the mean regional myocardial blood flow to the whole risk area 5 minutes after coronary occlusion was larger (0.27 ± 0.05 ml/min/g in the RV and 0.62 ± 0.08 ml/min/g in the LV) than that in the necrotic myocardium. This discrepancy may have derived from inclusion of the well-perfused tissue via collateral channels or involvement of normal tissue. The latter was minimized when the central risk area was taken as a sample.

During 24 hours, collateral blood flow in the RV risk area was practically unchanged while collateral flow in the LV risk area tended to decrease from 0.58 ± 0.10 to 0.42 ± 0.09 ml/min/g (NS) and the endo:epi flow ratio decreased further from 0.51 ± 0.09 at 5 minutes to 0.09 ± 0.02 at 24 hours (p < 0.01). This phenomena is explained by 1) disruption of the microvasculature in the region of severe ischemia,26 27 2) a redistribution of collateral blood flow from the necrotic to the salvaged myocardium,28 as suggested by an increase in epicardial flow inside the risk area during 24 hours, and 3) the ischemia-induced vasoconstriction along the border of the ischemic zone.29 Unlike the coronary circulation in humans and pigs, there is a left coronary dominance in dogs. This difference may alter the amount of collateral flow but would not modify the distribution of flow within the wall. The present difference in regional myocardial blood flow between the RV and LV risk areas after coronary occlusion and nonsignificant change in correlation coefficients between necrotic size and collateral flow in the RV during 24 hours indicated the early determination of the infarct size in case of right coronary artery ligation. This evidence also suggests the rather lesser contribution of the "wave-front phenomena"31 in the RV.

An inverse correlation between regional collateral flow and infarct size inside the risk area was evident in the case of both ventricles. Accordingly, transmural flow distribution after abrupt coronary ligation may explain the variations in infarct size, relating to the risk area. The relationship between collateral flow and infarct size were similar in the subendocardial and subepicardial halves of the RV and the subendocardial layer in the LV. In the LV a marked difference in tissue derangements between the subendo- and subepicardial layers for a given reduction of coronary blood flow coincided well with a redistribution of collateral blood flow from the necrotic to the salvaged epicardium,
Ohzono et al. Myocardial Infarction in Right and Left Ventricle

P < 0.001

Endo Epi

RV LV

FIGURE 7. The infarct size expressed as a percentage of the risk area (IS:RA) transmurally in right and left ventricles. Each line represents one slice and shows the transmural distribution of IS:RA of each risk area. A marked transmural gradient of infarction was noted in the left ventricle (LV) and is rather negligible in the right ventricle (RV).

In the present study and in that of Hirzel et al., this phenomena suggests a tissue sparing effect in the case of left coronary artery occlusion. A transmural difference in flow distribution in the normal LV can be related to a difference in myocardial oxygen consumption between layers. Weiss et al. noted that regional myocardial oxygen consumption was 20% higher in the subendocardial layer than in the subepicardial layer in the normal dog circulation. However, Weiss later reported that the regional oxygen consumption was markedly reduced in both the subendo- and subepicardial layers of the LV and that there were no differences between those layers after coronary occlusion. Thus, the role of regional oxygen consumption in determining susceptibility to myocardial ischemia after coronary ligation remained unanswered. The tissue pressure gradient may well become a dominant determinant of flow redistribution when the peripheral coronary pressure of the collateral channels is decreased by coronary ligation.

In the RV, relative subendocardial underperfusion, but not so severe as in case of the LV, appeared in the central risk area 24 hours after coronary ligation. This resulted in a leftward shift of the relation between collateral flow and percent of necrosis in the subendocardial layer (Figure 8). Subendocardial underperfusion was also noted in case of right ventricular systolic hypertension and right ventricular hypertrophy. Accordingly, the subendocardial region of the right ventricle is also prone to be underperfused, as

FIGURE 8. Relation between collateral blood flow (percent of control flow at 24 hours of coronary ligation) and percent of infarct to risk size in subendocardial (closed circles) and subepicardial (open circles) layers in right (RV) and left ventricles (LV). Note that the slope of the relationship is steeper for the subendocardium than for the subepicardium in the left, but not in the right ventricle. RV subendocardial layer: \( Y = -2.19x + 93.2; r = -0.708, n = 20. \) RV subepicardial layer: \( Y = -1.89x + 101.4; r = -0.829, n = 20. \) LV subendocardial layer: \( Y = -1.92x + 89.4; r = -0.668, n = 19. \) LV subepicardial layer: \( Y = -0.83x + 32.5; r = -0.631, n = 19. \) Insets show regional myocardial blood flow in milliliters per minute per gram in the subendocardial (endo) and subepicardial (epi) layers examined 24 hours after coronary ligation.
in the case of the LV. We noted the relatively lower flow level in the right ventricle, with regard to the x-axis intercept in Figures 4 and 8. This phenomena cannot be explained by the pattern of transmural flow distribution. Urabe et al showed a lower level of critical perfusion pressure in the right coronary artery in determining regional myocardial function, which accords well with the present results. The lower level of critical coronary flow in the right ventricle may also be explained by 1) a thinner wall and lower intracavitary pressure in the right ventricle and 2) a lower level of oxygen consumption. These are inherent characteristics.

In summary: Our study shows the close topological relation between regional myocardial blood flow and myocardial necrosis inside the risk area. Although collateral blood flow is a major determinant in salvaging tissue in case of myocardial ischemia, the unique difference in transmural distribution of regional myocardial flow or myocardial necrosis after coronary occlusion in the LV suggests a tissue sparing, i.e., sacrificing the injured myocardium to maintain a viable epicardium. The rather low level of critical flow in case of occlusion of the right coronary artery may explain the nonsignificant effects of right coronary artery narrowing on ventricular performance as seen clinically.

Acknowledgments
We thank M. Morì and R. Sato for technical assistance, M. Ohara for comments on the manuscript, and N. Misaka and T. Hirokawa for secretarial services.

References
1. Reimer KA, Jennings RB: The “wavefront phenomena” of myocardial ischemic cell death. II. Transmural progression of necrosis within the framework of ischemic bed size (myocardium at risk) and collateral flow. Lab Invest 1979;40:633–644
Transmural distribution of myocardial infarction: difference between the right and left ventricles in a canine model.

K Ohzono, S Koyanagi, Y Urabe, Y Harasawa, H Tomoike and M Nakamura

Circ Res. 1986;59:63-73
doi: 10.1161/01.RES.59.1.63

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1986 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/59/1/63

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/