Relationship Between Myocardial Infarct Size and Occluded Bed Size in the Dog: Difference Between Left Anterior Descending and Circumflex Coronary Artery Occlusions

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SUMMARY We compared myocardial infarct size produced by permanent occlusion of the middle left anterior descending (LAD) or circumflex (LCx) coronary artery in the anesthetized dog. The dogs were killed 3–10 days later, and the occluded coronary bed was visualized by postmortem arteriography. The outlines of the infarct and occluded bed were marked on tracings of weighed left ventricular (LV) rings and the size of the infarct and occluded bed was calculated by planimetry. For both arteries, infarct size and occluded bed size were linearly related to each other, but LAD infarcts were larger relative to occluded bed size (52.0% vs 32.3%, p < 0.05). A smaller occluded bed was necessary for the appearance of an infarct after LAD occlusion than after LCx occlusion (8.3% vs 18.5% of the left ventricle, p < 0.005). Reconstructed LV ring maps indicated a significantly wider margin of noninfarcted myocardium at the lateral edge of the occluded bed for LCx infarcts than for LAD infarcts. For dogs with similar occluded bed sizes in the range of 20–35% of the left ventricle, infarct size was considerably larger for LAD occlusion (15.9% vs 6.1% of the left ventricle, p < 0.001). In this subgroup, blood pressure and heart rate 10–20 minutes after occlusion were not significantly different for the two arteries, but collateral flow, measured with 9-μ radioactive microspheres, was approximately 50% lower after LAD occlusion. The relationship between the amount of myocardium with reduced blood flow and developed infarct size was similar for the two arteries. We conclude that occlusions of the middle LAD and LCx are not equivalent. For a given occluded bed size, LAD occlusions produce larger areas of infarction, apparently related to lower levels of collateral flow delivered to the occluded region.

ONE of the most popular animal models for the study of regional ischemia and infarction is the dog in which one of the major coronary arteries has been temporarily or permanently occluded. The anterior descending (LAD) and circumflex (LCx) branches of the left coronary artery are both used for this purpose and are considered more or less interchangeable. Which branch is used in a given laboratory appears to depend more on custom than on any scientific considerations.

Although more proximal occlusion of a coronary artery tends to result in a larger ischemic region and a larger completed infarct, a wide variation is found in infarct size, even with occlusion at a constant anatomic site.1, 2 This fact stems from the variability in coronary artery anatomy and pertains to both branches of the left coronary artery. The observed variability in infarct size, at least for LCx occlusions, can be accounted for in large measure by the size of the occluded coronary bed and the severity of ischemia within the occluded region.1, 2

No systematic comparison of LAD and LCx distribution infarcts has been undertaken. We therefore determined the intensity of ischemia and the size of developed infarct for dogs with permanent occlusion of one of these two coronary arteries.

Methods

Coronary Artery Occlusion
Forty-six mongrel dogs of either sex that weighed 40–56 pounds were anesthetized with i.v. sodium pentobarbital, 30 mg/kg, and ventilated with room air through a cuffed endotracheal tube. A left thoracotomy was performed aseptically and polyethylene catheters were placed in the left atrium and right common carotid artery. A short segment of either the LAD (22 dogs) or LCx (24 dogs) was dissected free just past the first or second major diagonal or marginal branches, and a 2-0 silk ligature was passed underneath. Because of the high mortality associated with proximal occlusions, a ligation site was chosen about one-third of the way along the epicardial course of the vessel. The selection of which artery to occlude was made before thoracotomy, independent of the coronary anatomy of the individual dog.

Lead II of the ECG and aortic pressure (Statham P23Db transducer) were monitored continuously on a direct-writing recorder. After abrupt permanent ligation of the coronary artery, the distal ends of the polyethylene tubes were externalized at the back of the neck and filled with heparinized saline. The thoracotomy was closed, air was evacuated from the left chest, and penicillin (1 million units) and streptomycin (1 g) were given intramuscularly. The dogs were returned to their cages after recovery from anesthesia. Thirty-two dogs survived 3–10 days and form the basis of this report. Of 14 3-day survivors with LCx occlusion, one died spontaneously (at 5 days) and 13 were sacrificed (three at 6 days, nine at 7 days, and one at 10 days). Of 18 3-day survivors with LAD occlusion, five died spontaneously (two at 3 days, two at 5 days and one at...
8 days) and 13 were sacrificed (one at 3 days, five at 4 days and seven at 7 days).

Measurement of Occluded Bed and Infarct Size

The size of the occluded coronary bed was measured in all dogs that survived 3 days and in eight of the 14 dogs that died early using a postmortem angiographic technique. The dogs were killed with an overdose of anesthetic, causing the hearts to arrest in diastole. Cannulas were placed in the origins of the right coronary artery, the LAD, and the LCx, and a barium sulfate gelatin mass was simultaneously injected at a controlled pressure of 160 mm Hg. The hearts were packed with gauze to maintain diastolic relationships, fixed in formalin and radiographed stereoscopically. Each heart was sliced into four to eight transverse sections 1.0–1.5 cm thick. Pairs of wire markers were placed at opposite points through the wall of the ventricle in each section and paired stereoscopic radiographs were made. Using the whole-heart images and the radiographs for each slice, an independent observer marked the boundaries of the occluded coronary bed by following the course of each major coronary branch from ring to ring and examining the patterns of interdigitation of terminal branches. Retrograde filling of the occluded bed by collaterals from the nonoccluded vessels allowed definition of the border between coronary branches. We have shown good interobserver reproducibility with this technique. The formalin-fixed heart slices were dissected free of the atria, right ventricle, large epicardial vessels and fat. Each slice was weighed and the top and bottom surfaces were traced on plastic transparencies to outline the left ventricle. Areas of infarction were identified by gross inspection and marked on each tracing. The margin of the infarct was marked by drawing an envelope around the outer margin of discoloration, recognizing that small amounts of apparently normal myocardium would necessarily be included. The tracing of each ring was superimposed on the corresponding radiograph, using the wire markers for alignment, to permit precise transfer of the marked boundaries of the occluded bed. Areas of left ventricle (whole ring), occluded coronary bed and infarct were measured by electronic planimetry for each ring, and the top and bottom surface areas were averaged for left ventricle and infarct. Masses of infarct and occluded coronary bed were calculated by multiplying the weight of each ring by the ratio of infarct and occluded bed area to the area of the corresponding whole ring.

To validate our gross morphologic method of measuring infarct size, 12 dogs underwent permanent occlusion of the middle LCx and were killed 3 days later. Infarct size was determined both grossly and histologically in each dog. The entire occluded bed and a liberal border of normal-looking myocardium were excised from each left ventricular ring and divided into multiple 1–2-g samples, each of which was weighed and embedded in paraffin. Sections were taken from the top, middle and bottom of each tissue block and stained with hematoxylin and eosin. Each section was examined microscopically and the percentage of necrosis visually estimated to the nearest 5%; estimates from the three levels in each block were averaged and multiplied by the sample weight to obtain the amount of necrosis in each sample. Infarct size for the whole heart was obtained by summing the amount of necrosis in each sample. Gross infarct size (ISG), expressed in grams, agreed closely with histologic infarct size (ISH) without systematic over- or underestimation: ISG = 1.35 (ISH) − 6.50 (r = 0.94).

Myocardial Blood Flow

Collateral flow to the occluded region was measured with 8–10-μ diameter radioactive microspheres in 15 of the 32 dogs surviving 3 days (eight LAD and seven LCx) and seven of the 14 early deaths (four LAD and three LCx). Measurements were made before ligation and 10–20 minutes after ligation, except for two dogs with LAD occlusion in which postocclusion flow measurements were not made until 32 and 59 minutes. For each flow measurement, 2–4 million spheres labeled with 141Ce, 46Sr, 99Nb or 45Sc were injected into the left atrium, followed by a 5-ml saline flush. Microspheres were obtained as 2 mCi of nuclide in 10 ml of 10% dextan, to which one drop of polysorbate 80 was added to minimize clumping. Microsphere vials were vigorously agitated on a mechanical mixer for 2–3 minutes before use. Starting just before injection and continuing for 2 minutes afterwards, a reference arterial blood sample was withdrawn by a Harvard pump at a constant rate of 2.17 ml/min.

For regional myocardial blood flow measurements, tissue samples were taken serially through the occluded bed in each ring and in the center of the opposite nonischemic wall. All samples were divided into inner and outer halves and each was weighed. The majority of samples weighed 0.4–1.2 g, although the range across all hearts was 0.25–1.8 g. Within a given heart, sample sizes were more uniform. Samples from infarct border areas tended to be smaller than those from homogeneously injured infarct centers or nonischemic areas. Tissue samples were placed in vials containing formalin and counted for radioactivity along with the reference blood samples in a gamma scintillation counter (Packard model 5986) at energy windows adjusted to the peak emission for each nuclide used. Regional myocardial blood flow (F) was calculated using the formula: F = R × (Cm/Cr) (ml/min/g), where R = reference blood flow pump withdrawal rate, Cm = counts per gram in myocardial tissue sample, and Cr = counts in reference blood sample. Flows for corresponding regions in each ring were averaged to yield single values for the center and border of the occluded bed and nonischemic region. For the purposes of this study, the center ischemic region was defined as the central half of the occluded bed and the border ischemic region as the lateral one-quarter on either side. Rings showing necrosis on only one side were excluded from this analysis, as was the apical cap, except when infarcts were very small.

All flows were corrected for true and apparent mi-
crosphere loss.4-6 The preoccusion content of microspheres in each ischemic region, expressed relative to that in the nonischemic area, was used as a quantitative measure of the combined effects of microsphere loss, local edema, hemorrhage and inflammatory cell infiltrate.7 Inner flow values were corrected using subendocardial flows and outer flow values using subepicardial flows: \( F_c = F \times (P/A) \), where \( F_c \) = corrected flow, \( F \) = uncorrected flow, \( P \) = preoccusion flow in the region of interest, and \( A \) = preoccusion flow in a corresponding nonischemic region.

**Topographic Analysis of Infarcts**

The average spatial distribution of infarct within the occluded bed was determined by creating average ring-by-ring maps for the two coronary artery occlusion groups. For this purpose, dogs with small (≤ 10% of left ventricle) and large (> 10% of left ventricle) infarcts were analyzed separately. For each ring the center of the infarct on the endocardial surface was marked. Distances along the endocardium from the infarct center to the edges of the occluded bed and the edges of the infarct were measured to the nearest millimeter. At each of these points, the width of the myocardial ring was determined. The thickness of the infarct was measured at the infarct center and at points on the endocardial surface midway between the infarct center and each infarct edge. The length of the occluded bed along the epicardial surface was also measured. Corresponding measurements for each ring were then averaged to yield values used in creating the maps. Five rings were reconstructed in each dog; when only four rings were available, the basal ring was repeated, and when more than five rings were present, adjacent rings were averaged. All dogs were used for this analysis, except that data on three dogs was missing.

**Statistical Analysis**

The significance of differences between groups for hemodynamic and flow data, and for measurements of infarct, left ventricular, and occluded coronary bed masses was tested using unpaired t tests. Linear regression analysis was used to compare infarct size with occluded bed size, postocclusion flow and mass of ischemic myocardium. Differences in mortality rates were tested by chi-square analysis.

**Results**

Overall mortality over the first 10 days was similar after LCx and LAD occlusion (11 of 24 [45.8%] vs nine of 22 [40.9%], NS). More dogs with circumflex occlusion died within the first hour and first 2 days (20.8% vs 4.5% and 41.7% vs 18.2%, respectively), while more dogs with anterior descending occlusion died between the third and tenth day. None of these differences was statistically significant. Because of the uncertainty about whether infarcts had reached their fullest extent, dogs that died before the third day were excluded from analysis.

**Occluded Bed and Infarct Size**

Despite coronary ligation at a fairly constant anatomic site, a wide range of occluded bed sizes and infarct sizes were found for both vessels (table 1). For the particular ligation sites used, the mean occluded bed size was significantly larger for LCx occlusion (29.3 ± 2.0% vs 22.3 ± 1.5% of the left ventricle, \( p < 0.01 \)). The mean infarct size was not significantly different for the two arteries when expressed in absolute terms or as a percentage of the left ventricle. However, expressed as a percentage of occluded bed size, occlusion of the LAD produced larger infarcts (52.0 ± 6.0% vs 32.3 ± 6.4%, \( p < 0.05 \)).

Occluded bed size and infarct size were linearly related to each other for both vessels, and the slopes of the linear regressions were similar (fig. 1). The LAD regression line was shifted to the left, indicating larger infarcts for a given occluded bed size. The horizontal axis intercept was significantly smaller for LAD occlusion (8.3% vs 18.5% of the left ventricle, \( p < 0.005 \)), indicating that a smaller occluded bed size was required for infarction to occur. In dogs that died before the third day, occluded bed size was similar to that in dogs that lived longer. In four dogs with LAD occlusion that died early, occluded bed size ranged from 21.5-26.3% of the left ventricle, while in four with LCx occlusion, the range was 25.8-34.1%

Because of wide variation found in occluded bed size and the tendency for LCx occlusions to produce larger occluded beds, further analysis was performed on the dogs that had comparable occluded bed sizes of 20-35% of the left ventricle. This subgroup included 10 dogs with LCx occlusion and 10 with LAD. This middle range of occluded bed size represents the area of overlap between the two arteries (fig. 1). Of seven dogs in which the occluded bed constituted < 20% of left ventricle, all were in the LAD group, while four of five dogs with occluded bed > 35% were in the LCx group. The average occluded bed size was similar for the two arteries (25.2 ± 0.9% of the left ventricle for

**Table 1. Occluded Bed and Infarct Sizes**

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<th>LCx (n = 14)</th>
<th>LAD (n = 18)</th>
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<tr>
<td>Infarct mass (g)</td>
<td>9.3 ± 2.3 (1.7-28.9)</td>
<td>11.6 ± 1.7 (0-23.5)</td>
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<tr>
<td>Occluded bed mass (g)</td>
<td>26.5 ± 1.8 (17.1-41.9)</td>
<td>21.5 ± 1.5* (12.7-36.5)</td>
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<tr>
<td>LV mass (g)</td>
<td>91.4 ± 3.5 (73.2-116.0)</td>
<td>98.2 ± 3.7 (74.8-133.3)</td>
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<tr>
<td>Infarct/LV (%)</td>
<td>10.4 ± 2.5 (1.7-27.8)</td>
<td>12.0 ± 1.7 (0-25.5)</td>
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<tr>
<td>Occluded bed/LV (%)</td>
<td>29.3 ± 2.0 (21.4-47.1)</td>
<td>22.3 ± 1.5* (12.4-39.5)</td>
</tr>
<tr>
<td>Infarct/occluded bed (%)</td>
<td>32.3 ± 6.4 (7.0-69.1)</td>
<td>52.0 ± 6.0* (9.0-93.6)</td>
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Values are mean ± SEM (range in parentheses).

*p < 0.05 vs LCx.

*p < 0.01 vs LCx.

Abbreviations: LV = left ventricle; LCx = left circumflex coronary artery; LAD = left anterior descending coronary artery.
the LCx and 24.4 ± 1.2% for the LAD). However, infarct size was considerably larger for LAD occlusion (15.9 ± 1.2% vs 6.1 ± 1.8% of the left ventricle, p < 0.001; 67.6 ± 5.0% vs 24.1 ± 7.0% of the occluded bed, p < 0.001) (fig. 2).

Because of possible differences in measured infarct size related to differences in time of death or sacrifice, these data were further analyzed for dogs that died 5–7 days after ligation (nine dogs with LCx occlusion and five with LAD occlusion). Infarct size continued to be significantly greater with LAD occlusion (16.8 ± 2.5% vs 6.4 ± 2.0% of the left ventricle, p < 0.01; 66.6 ± 6.2% vs 25.1 ± 7.7% of the occluded bed, p < 0.005).

In the dogs in which the occluded bed was 20–35% of left ventricle, hemodynamic measurements made under anesthesia at the time of flow measurements failed to show any significant differences between dogs with LCx and those with LAD occlusion (table 2). In the same group, regional myocardial flow measurements 10–20 minutes after occlusion were available in five dogs with LCx and six dogs with LAD occlusion. Collateral flow to the occluded bed was significantly lower in dogs with LAD occlusion (table 3). The differences averaged 30–60% and reached statistical significance in the subepicardial portion of both center and border zones. In the center zone subepicardium, the mean flow was 52.6% of that in the opposite nonischemic wall during LCx occlusion, compared with 23.4% during LAD occlusion (p < 0.02).

In dogs that died before the third day, collateral flow was available in seven and was within the range of flows among dogs that lived longer. Flow in the center zone subepicardium was 17.5–37.6% of the nonischemic flow in four dogs in the LAD group that died early and 13.9–43.5% in three dogs in the LCx group that died early. When these dogs were included with the 3-

<table>
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<th>Table 2. Hemodynamic Values After Coronary Occlusion</th>
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<td>Systolic arterial pressure (mm Hg)</td>
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<tr>
<td>LCx occlusion (n = 10)</td>
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<td>LAD occlusion (n = 10)</td>
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Abbreviations: LCx = left circumflex coronary artery; LAD = left anterior descending coronary artery.
decrease in infarct size for further increases in flow (infarct/left ventricle [I/LV] (%) = 33.5 - 0.87 (flow) + 0.006 (flow)^2; r = 0.93). In this analysis, dogs with LCx and LAD occlusion appear to be intermixed, suggesting a similar relationship between flow and infarct size for the two vessels.

The mass of ‘ischemic’ myocardium was determined for each dog by summing the weights of tissue samples with postocclusion flow ≤ 50% of flow in the nonischemic region (separately determined for subendocardial and subepicardial layers); this was called the ‘functional risk region.’ In all cases, this functional risk region was less than the anatomic occluded bed size, averaging 42% of the occluded bed. The mean functional risk region, as a percentage of left ventricle, was larger after LAD occlusion (14.4 ± 1.7% vs 10.0 ± 1.5%; t = 1.93, p < 0.10).

Figure 4 shows the relation between infarct size and functional risk region size. In contrast to figure 1, the data appear to constitute a single population in which infarct size increases linearly with functional risk region size. The horizontal axis intercept is close to zero, in contrast to figure 1, in which the horizontal axis intercept was 8.3% of left ventricle for LAD occlusion and 18.5% for LCx occlusion. The relationship between infarct size (I/LV) and functional risk region size (R/LV) was similar for LAD and LCx occlusions when each was determined separately (LAD: I/LV = 0.95 R/LV + 2.25 [r = 0.91]; LCx: I/LV = 1.11 R/LV - 5.27 [r = 0.93]).

**Topographic Analysis of Infarcts**

The spatial relationship of infarct and occluded bed was examined for the two different arteries by reconstructing ring-by-ring maps representing average infarcts and occluded beds (fig. 5). With LCx occlusions, some myocardium perfused by the occluded artery was present in all five rings, but with LAD occlusions, the basal one or two rings did not contain any myocardium at jeopardy. This resulted in a general pattern of more extensive infarction at the base with LCx occlusion and at the apex with LAD occlusion. With both vessels, noninfarcted myocardium was located within the occluded bed and the amount of

**Figure 3.** Relation between collateral flow 10–20 minutes after coronary occlusion and infarct size. Dogs with left anterior descending (LAD) and circumflex (LCx) occlusions appeared to have a similar decrease in infarct size with increasing flow.

**Figure 4.** Relation between mass of ischemic myocardium 10–20 minutes after coronary occlusion (functional risk zone) and infarct size. Functional risk zone was defined as myocardium with flow ≤ 50% of simultaneous nonischemic region flow. A similar linear relation was found for left anterior descending (LAD) and circumflex (LCx) occlusions (compare with figure 1).
spared tissue was much greater for small infarcts (\(<=10\% \text{ of left ventricle}\)) than for large infarcts (\(>10\% \text{ of left ventricle}\)). The amount of sparing at the lateral edges of the occluded bed was greater for LCx than for LAD occlusions (fig. 5). This was true for both large and small infarcts, although the difference was more impressive with smaller infarcts. With large LAD infarcts, virtually no lateral sparing could be identified, especially in the apical rings. The noninfarcted lateral margins averaged 1.4 \(\pm\) 1.5 mm (\(\pm\) sp) for large LAD infarcts and 3.2 \(\pm\) 1.6 mm for large LCx infarcts \((p < 0.02)\). These distances represented 4.3% and 7.1% respectively, of the width of the occluded bed along the endocardium on each side. For small infarcts, the noninfarcted margins averaged 3.8 \(\pm\) 2.4 mm for LAD and 7.7 \(\pm\) 2.3 mm for LCx occlusions \((p < 0.005)\). These distances constituted 19.9% and 31.7% of the occluded bed width on each side.

### Discussion

The major finding of this study was that occlusion of the LAD produced a more extensive myocardial infarction than LCx occlusion for moderate-sized occluded regions measuring 20–35% of the left ventricle. LAD occlusions were associated with more extensive and severe reductions in regional myocardial blood flow without significant differences in heart rate or blood pressure. When infarct size was expressed relative to the mass of ischemic tissue in each heart, the difference between the two arteries was no longer apparent (fig. 4). Thus, it appears that LAD infarcts were relatively larger because of the more severe myocardial ischemia produced, and that the relationship between flow deprivation and necrosis was similar for LCx and LAD occlusions.

A number of methodologic points concerning this study require discussion. Infarct size was determined by a gross morphologic technique, which could be criticized as being insufficiently precise. However, in a separate validation study in 12 dogs, our method gave results comparable to those obtained by detailed histologic examination of the left ventricle, without systematic under- or overestimation of infarct size \((\text{IS}_0 = 1.35 (\text{IS}_m) - 6.50; r = 0.94)\). The magnitude of the infarct size difference found between LAD and LCx occlusions is too large to be explained by our use of gross morphologic measurements. Similarly, we have had considerable experience measuring occluded bed size from postmortem angiograms and have reported a reproducibility of 2% in basal rings and 5% in apical rings. The "functional risk zone," on the other hand, was determined by adding the weights of tissue samples with reduced postocclusion flow, and its accuracy is therefore limited by the size of the samples, particularly at the margins of the occluded bed. For most hearts, these samples were in the range of 0.4–1.0 g. An additional problem is that samples taken from both sides of the occluded bed margin almost certainly contained a mixture of ischemic and nonischemic myocardium. The border dividing vascular beds has been shown to be complex in shape with much interdigitation of the microvasculature. Since our method only defines an "average" border on a macroscopic level, significant mixture of ischemic and nonischemic tissue is expected. Using the mean flow values from table 3, samples could be classified as ischemic even if they contained as much as 36–46% of nonischemic myocardium, and nonischemic even with 54–64% of ischemic tissue. Because the first error tends to overestimate the functional risk zone and the second error to underesti-
mate it, and because both errors occur randomly, the measured size of the functional risk zone should be approximately correct. This is supported by the relationship between infarct size and functional risk zone, which shows zero infarction at a functional risk zone size very close to zero (fig. 4).

We excluded dogs that died during the first 2 days because of uncertainty as to whether the infarct had reached its full extent. Because more of these exclusions came from the LCx group, and because it might reasonably be supposed that these dogs had the largest occluded bed sizes and lowest collateral flows, it is at least theoretically possible that our conclusions were affected. A number of considerations, however, suggest that this did not occur. In the first place, occluded bed size was not larger in the excluded dogs that died early. This confirms our previous finding and suggests that in this model, there is no simple relation between size of ischemic region and early death. Second, our results indicate that the finding of larger LAD infarcts for a given occluded region holds over a broad range of occluded bed sizes, at least up to 35% of the left ventricle (fig. 1), and that even with small beds, LAD infarcts occur more readily. Third, spatial analysis indicated that for both large and small occluded beds, LAD infarcts were relatively larger, with less sparing of tissue within the boundaries of the occluded bed (fig. 5). Finally, collateral flow in dogs that died early was within the range of those that lived longer, and a difference between LAD and LCx occlusions was still present when the early deaths were included.

Although many previous studies have involved occlusion of a coronary artery and measurement of subsequent infarct size, the methods and models used have varied considerably, and only one has directly compared the LAD and LCx arteries using similar methods. Bishop et al. reported no difference, but did not measure the region at jeopardy. As in our study, dogs with LCx occlusion may have had larger occluded beds and smaller infarct/occluded bed ratios. In the handful of studies in which the region at jeopardy was measured, permanent occlusion of the circumflex artery produced infarct sizes of 23–76% of the jeopardized zone, compared to 56–75% after LAD occlusion. Direct comparison of results for the two arteries is difficult because some studies used conscious and others anesthetized dogs, survival ranged from 6 hours to 1 week after coronary occlusion, methods of infarct sizing varied, and the site of occlusion along the length of the coronary artery was not comparable. Probably most importantly, the method for defining the region at jeopardy varied substantially. Some studies measured anatomic occluded bed size using postmortem intracoronary injections of dye or radiographic contrast material. Others identified a smaller area of ischemia (functional risk zone) inside the anatomic occluded bed using epicardial ST-segment mapping, radiolabeled microspheres and autoradiography, or injection of dye into the left atrium just before sacrifice. The anatomic risk region theoretically represents the largest infarction that could occur under the worst conditions, while the functional risk region is probably a more accurate estimate of the myocardium truly at jeopardy under ordinary circumstances. As defined by dye or microspheres, the functional risk zone comprises only about 50% of anatomic occluded bed size.

Our finding of relatively larger infarcts after LAD occlusion was due to the presence of lower collateral blood flow. Many studies have measured collateral flow after occlusion of a coronary artery, but because of differences in experimental conditions, timing of postocclusion flow measurements, and sites of arterial occlusion, it is virtually impossible to derive a meaningful comparison between the two arteries from these reports. An exception is the recent report by Reimer and colleagues, who compared collateral flow directly during transient occlusion of the proximal LAD or LCx. Occluded bed size, measured by postmortem intracoronary dye perfusion, was >30% of the left ventricle for all dogs and averaged 37% for the LCx and 36% for the LAD. Collateral flow was severely and similarly reduced with both occlusions, averaging 0.12 ml/min/g for the LCx and 0.16 ml/min/g for the LAD (NS). In our study, the difference in infarct size and collateral flow between the two arteries occurred in dogs with occluded beds of moderate size (20–35% of the left ventricle). Although there were not many dogs with occluded beds >30%, figure 1 suggests that there may have been no difference between the two arteries for large occluded beds (>30%). Wusten et al. also directly compared collateral flow after LAD or LCx coronary artery occlusion in anesthetized beagle dogs. Regional flow in the center of the ischemic region was 31.5% of control after LAD occlusion and 18.5% after LCx occlusion, but the difference was attributed to a larger occluded bed in the case of the LCx artery, causing available flow to be distributed over a larger area of myocardium. We and others have also found that collateral flow is inversely related to occluded bed size.

We can only speculate on the reason for the difference in flows during LAD and LCx occlusion. Perhaps the most attractive explanation relates to possible differences in intramyocardial forces inhibiting collateral inflow. The anterior wall, by virtue of greater thinness at the apex, would be expected to develop a higher level of regional wall tension than the posterior wall. In addition, the LAD perfusion bed is completely surrounded by contracting nonischemic left ventricular myocardium, while a portion of the LCx bed is fixed to the noncontractile atrioventricular ring. The importance of extravascular forces was emphasized by Schaper, who showed that collateral flow in the isolated empty beating heart was fourfold greater than flow in the heart beating in situ at the same perfusion pressure.

A second possibility relates to the dependence of collateral vascular resistance on the direction of flow. Scheel et al. showed that in dogs with native collaterals, resistance to flow from the circumflex to the LAD artery was 16% higher than resistance in the opposite direction (p < 0.10). With amiodar occlusion of the
LCx artery from 1 or 3 months, the difference became more pronounced. In addition, resistance from the right coronary artery to the LAD was 66% higher than resistance from the right coronary artery to the LCx (statistics not given). These differences are at least directionally consistent with our finding of higher collateral flow after LCx occlusion.

A third possibility is that the LCx artery could receive larger or more numerous collaterals from the other coronary arteries, particularly the right coronary artery. These interconnections would most likely be located in the posterior septal region, the posterior atrioventricular groove or across the atrioventricular junction. Gregg et al. found that the right coronary artery in the dog contributed 7% of chronic collateral flow to the LAD bed, compared with 19% to the LCx bed. Conversely, the right coronary artery received 22% of its collateral flow from the LAD and 75% from the LCx. Clinical studies in man have also suggested a greater propensity for collateralization from the right coronary artery to the LCx than to the LAD. In the study of Fuster et al., more patients with inferior than anterior wall coronary obstruction had angiographically visible collateral vessels, and exercise stress data showed that only the inferior wall collaterals protected against ischemia. Similarly, in the study of Eng et al., relative collateral protection was more common in inferior or lateral wall segments than anterior segments assessed by thallium-201 perfusion imaging.

The results of this study provide further information about the spatial distribution of myocardium located within the occluded bed but surviving infarction. Most of the surviving myocardium was located in the epicardial portion of the occluded bed, but significant amounts were also present laterally in epicardial and midwall layers (fig. 5). This distribution of surviving tissue coincides with the known distribution of collateral flow within the occluded region, i.e., highest in the peripheral and epicardial portions and lowest in the central endocardial zone. Although there is a general agreement that the spared lateral zone, or "border zone," may be quite wide in the epicardial layer, its width in endocardial and midwall layers has been disputed. Our data indicate that large LAD infarcts have virtually no identifiable lateral border zone at the endocardial surface, while large LCx infarcts have a small zone averaging 3.2 mm in width. In contrast, small infarcts tend to have considerable lateral sparing, with the lateral border zone wider for LCx than for LAD infarcts. In general, we have found that the width of the lateral spared zone is inversely related to the fraction of the occluded bed infarcted. Using techniques similar to ours, Koyangi et al. found that after permanent LCx occlusion, the width of the lateral border zone at the endocardium was less than 3 mm in 77% of slices, although in some slices the width was as great as 10 mm. It is difficult to directly compare these results to ours, since the lateral border zone measurements were not specifically related to infarct size; however, our results are probably similar because in Koyangi's study, 10 of the 14 dogs with more than trivial infarction had > 10% left ventricular necrosis. Using a method that examines the width of the lateral border zone microscopically, Factor et al. reported endocardial widths of only 30–50 μm. However, these studies used proximal LAD occlusion, and the results are therefore probably comparable to ours. For defining a precise lateral zone width, the method of Factor et al. is undoubtedly more accurate than ours, since we can delineate only average edges for the infarct and occluded bed, when in reality both are highly irregular and convoluted.

Our results may have implications for experimental studies of infarct size limitation in the dog. After coronary artery occlusion, the greatest potential for myocardial salvage is probably in ischemic regions with only moderately reduced blood flow. In contrast, regions that have severe reductions in flow are likely to be beyond help. Since LCx occlusion causes less severe ischemia and smaller infarcts for moderate occluded bed sizes, LCx occlusion might be a more sensitive model than LAD occlusion for uncovering the beneficial effect of a new therapy. Further studies are clearly required to explore this issue and determine the importance of this potential problem.

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