ALTERATIONS in transmural blood flow and body surface ST segment abnormalities produced by ischemia in the circumflex and left anterior descending coronary arterial beds of the dog

DAVID M. MIRVIS, M.D., AND K. B. RAMANATHAN, M.D.

ABSTRACT  Previous studies have documented a quantitative relation between alterations in transmural myocardial blood flow and body surface electrocardiographic distributions during rapid atrial pacing after chronic occlusion of the left circumflex coronary artery (LCx). Because other studies have described functional differences between the left anterior descending (LAD) and the LCx perfusion beds, we tested the hypothesis that these two territories exhibit quantitative differences in their responses to demand-dependent myocardial ischemia. To do so, 25 sedated dogs were studied 3 weeks after implantation of an ameroid constrictor around the proximal LCx (15 dogs, group I) or the LAD (group II). Oxygen demand was increased by rapid atrial pacing at rates of 90 to 210 beats/min, myocardial blood flow was measured by serial injections of radiolabeled microspheres, and the electrocardiographic consequences were evaluated by isopotential body surface mapping. Endocardial flows and the endocardial/epicardial flow ratio fell to significantly lower levels during atrial pacing in the ischemic LAD bed than in the LCx perfusion zone. Electrocardiographic patterns indicative of subendocardial ischemia also developed with lesser abnormalities in endocardial/epicardial ratios as determined by logistic regression models, in the LAD than in the LCx bed. Thus the LAD bed is more susceptible to ischemia than the LCx region because of differences in collateral blood flow patterns. In addition, the intensity of the surface electrocardiographic potentials during ischemia was significantly greater, as measured by linear regression, after LAD than after LCx obstruction. These data thus demonstrate significant differences between the two cardiac regions as electrocardiographic potential sources during ischemia. Circulation 76, No. 3, 697–704, 1987.

THE UTILITY of the exercise stress test for detecting coronary artery disease is based on the production of transient subendocardial myocardial ischemia by increasing myocardial oxygen demand. As demonstrated in both clinical and animal studies, the increased demand produces alterations in regional myocardial blood flow\textsuperscript{1–3} and electrocardiographic patterns.\textsuperscript{4–9} These changes can then be detected by radionuclide imaging or electrocardiographic techniques.

Prior studies from this laboratory\textsuperscript{9} have demonstrated an explicit quantitative relationship between the degree of flow abnormality produced and the intensity of the resultant electrocardiographic effects. This was accomplished by means of rapid atrial pacing to increase demand in an animal preparation in which the circumflex artery was gradually but completely occluded by an implanted ameroid constrictor.

However, other data from several other sources suggest that the various perfusion territories of the heart may significantly differ from each other.\textsuperscript{10, 11} For example, occlusion of the left anterior descending artery (LAD) results in more necrosis than does similar obstruction of the left circumflex artery (LCx).\textsuperscript{11, 12} Because this finding relates to reduced collateral flow to the anterior bed\textsuperscript{10} and because such flow is a direct determinant of the response to pacing, we undertook these studies to test the hypothesis that the quantitative relations between blood supply and electrocardiographic changes are also different in the LAD and LCx beds.
Methods

Experimental preparation. Twenty-five adult mongrel dogs were included in this study. Each animal was subjected to a left thoracotomy, under sterile conditions, with a mixture of halothane, nitrous-oxide, and oxygen for anesthesia. A plastic cannula was inserted into the left atrium through its appendage, and a quadripolar plaque electrode was sutured to either the right or left atrial appendage.

In 15 animals (group I), the LCx proximal to any major ventricular branches, was dissected and an amiodar constrictor with an internal diameter of 2.77 mm was placed around the vessel. Some of the data derived from this group have been previously reported.9 In the remaining 10 dogs (group II), the LAD was exposed and a 2.5 mm internal diameter amiodar constrictor was placed around its proximal portion (below the septal artery but above major diagonal branches).

Pacing wires and catheter tubing were tracked to the back of the neck and buried in a subcutaneous pocket. The chest was closed in layers, air was evacuated, and the animals were allowed to recover. Acetromazine was administered as an agesic and broad-spectrum antibiotics were prescribed.

Experimental protocol. Electrocardiographic recordings and blood flow measurements were made 3 weeks after surgery when complete vascular obstruction was expected9 and when all the animals were ambulatory. They were brought to the laboratory and sedated with Innovar-Vet (1 to 2 ml im) and pentobarbital (7 mg/kg iv), intubated, and respired with oxygen-enriched air. Buried tubing and pacing wires were exteriorized, a large-bore catheter was passed into the abdominal aorta through a femoral artery for blood withdrawal and arterial pressure monitoring, and a second catheter was inserted into a femoral vein for drug administration. Arterial blood gases were monitored intermittently to ensure adequate ventilation.

A total of 88 chloridized silver electrodes were then placed. Four were on the limbs to form the standard limb leads and to determine the Wilson central terminal voltage. The remaining 84 were affixed to the anterior and posterior chest, extending from the level of the clavicles to below the inferior rib margins. Animals were then positioned in an upright posture with a support sling.

Potentials from each of the electrodes were then recorded as detailed below during spontaneous sinus rhythm after a 30 min stabilization period. An initial bolus of 3 to 4 million radiolabeled (46Sc, 152Gd, 117Sn, 103Ru, or 57Co) microspheres was injected through the left atrial catheter and flushed with 5 ml of warmed saline. Spheres were 9 ± 1 μm in diameter, suspended in 10% dextran with added polysorbate 80, and mechanically and ultrasonically agitated before injection. Blood was withdrawn from the aortic cannula via a calibrated pump at a rate of 8.0 ml/min beginning 30 sec before microsphere injection and continuing for 2 min.

Atrial pacing was next initiated at 90 beats/min, with pulses 2 msec in duration and 50% above diastolic threshold in amplitude. Pacing rather than exercise was used to augment oxygen demand because of the excessive electrical noise generated by motor-driven exercise devices. Rate was incremented every 4 min by 20 beats/min until a maximum rate of 210 beats/min was reached. Atropine (1 to 2 mg iv) was administered at a rate of 170 beats/min to ensure one-to-one atrioventricular conduction.

Electrocardiographic signals were recorded during the last minute of pacing at each heart rate. Additional doses of microspheres were administered at rates of 150, 170, 190, and 210 beats/min. At the completion of the protocol, animals were killed by potassium chloride injection and their hearts were rapidly excised for determination of perfusion beds and measurement of myocardial blood flow.

Electrocardiographic recording techniques. Potentials from the 88 electrodes were amplified by low-noise, differential (electrode vs Wilson central terminal potential) amplifiers with computer-controlled gains of 1000 to 16,000 and a bandpass (−3 dB) of 0.04 to 1500 Hz. Analog signals were converted to digital form at a rate of 500 Hz/channel, with all channels being sampled simultaneously.

Fourteen seconds of data were acquired at each pacing rate. Linear baseline drift was corrected and PQRS waves in each lead that were similar in form were averaged to reduce random noise, as previously detailed.9 The onset of the P wave, the QRS complex, and the ST-T interval were then chosen manually from plots of three relatively orthogonal leads, and potentials during a 10 msec portion of the PR segment were averaged for use as a zero-potential reference level.

Body surface isopotential maps were then constructed (figures 1 and 2, panels A to C) at 4 msec intervals throughout the ST-T wave. At high rates, the pacing artifact and P wave of one cycle became superimposed on the ST segment of the preceding waveform9; only portions of the ST segment before this overlap were examined. The quadripolar pacing electrode configuration generated smaller stimulus artifacts than would a standard bipolar pattern.

Isopotential difference maps (figures 1 and 2, panel D) were also computed by subtraction of voltages sensed at each torso location at one rate from those registered from the same site and at the same point in the cardiac cycle at a second heart rate. The resultant pattern depicted the electrical field generated by the intervention, i.e., increased heart rate, while controlling for biological variability in baseline potential distributions.10,9

Perfusion bed and myocardial blood flow measurements. Complete occlusion of the constricted vessel was verified visually in all cases. Excised hearts were first perfused with colored dyes to define the ischemic and nonischemic vascular beds. The aortic root was perfused with red monastral dye, and the vessel obstructed by the amiodar device was perfused with a blue pigment. The latter was accomplished by cannulating the LCx (group I) or the LAD (group II) immediately distal to the occlusion. Perfusion of both the aorta and the affected coronary artery was performed at equal pressures of 100 mm Hg for a minimum of 2 min. Hearts were then placed in buffered formalin for approximately 48 hr.

After fixation, hearts were sliced parallel to the base into pieces 8 mm thick. These were photographed for subsequent delineation of size of the perfusion bed by computerized planimetry of stained areas.

Full-thickness samples from the center of the ischemic (blue-stained) region and from the opposite ventricular wall (nonischemic zone) were cut from each of two midlevel slices. These were then subdivided into endocardial, midwall, and epicardial thirds. Each piece was then weighed, and radioactivity was measured in a computerized scintillation counter; software routines corrected for background radiation and overlap of the spectra of the five isotopes. Arterial blood samples withdrawn with each microsphere injection were similarly counted.

Myocardial blood flow (ml/min/g) in each sample was then calculated by the standard formula

\[ Q_{m} = Q_{C}/C_{m} W_{m} \]

where \( Q_{m} \) is myocardial blood flow, \( Q_{C} \) is reference sample flow rate (8.0 ml/min), \( C_{m} \) is counts per minute in myocardial tissue sample, \( C_{s} \) is counts per minute in reference blood sample, and \( W_{m} \) is tissue sample weight in grams. Flows in the two slices, which were consistently within 10% of each other, were averaged and the ratio of endocardial to epicardial (endo/epi) flow was calculated.

Map analysis. By previously detailed methods,8,9 body surface isopotential maps depicting the spatial distribution 40 msec into the ST segment were classified into “normal” or

698 CIRCULATION
FIGURE 1. Body surface isopotential maps constructed from one animal of group 1, 3 weeks after implantation of an ameroid constrictor around the LCx. Patterns (symbols detailed in the text) depict the spatial distribution of voltages sensed 40 msec in to the ST segment during atrial pacing at rates of 90 (A), 150 (B), and 190 (C) beats/min. The isopotential difference map displayed in panel D was constructed after subtraction of voltages of panel A from those of panel C. Contour lines are drawn at 0, 10, 20, 40, 100, 200, and 400 µV levels. Abnormal negative areas in the difference map are shaded.

FIGURE 2. Isopotential maps, similar to those shown in figure 1, during atrial pacing after ameroid constriction of the left anterior descending artery. A, Atrial pacing at 90 beats/min; B, 150 beats/min; C, 190 beats/min; D, subtraction map. Contour lines are drawn at the same intervals as in figure 1.
“ischemic” subgroups. Examples of the process are shown in figures 1 and 2 for maps from animals in groups I and II, respectively.

In each frame, the plus and minus signs mark electrode locations, with the sign corresponding to the polarity of the sensed voltage. The center of the map is along the sternum and the right and left edges lie on the left and right paravertebral zones, respectively. Contour lines connect sites at equal potential relative to the Wilson central terminal. The zero isopotential lines are overdrawn for emphasis, and negative potential zones are cross-hatched. Intensities of the most positive (“maximum”) and the most negative (“minimum”) potentials are listed in each panel.

Distributions in figure 1 were constructed from voltages sensed 40 msec into the ST segment from one animal after ameroid constriction of the LCX. At a paced rate of 90 beats/min (panel A), positive potentials were sensed over the anterior torso. Increasing the rate to 150 beats/min (panel B) did not alter this basic topography, although the intensity of both the anterior maximum and the posterior minimum increased. When the stimulation frequency was further increased to 190 beats/min (panel C), a abrupt change in the isopotential pattern developed. Now, abnormal negative potentials were recorded over the inferior anterior and posterior chest, with positive voltages being registered on the superior torso. Negative potentials over the inferior chest correspond to ST segment depression in scalar unipolar leads from this area.

An analogous sequence after constriction of the LAD is illustrated in figure 2. At rates of 90 (panel A) and 150 (panel B) beat/min, a normal pattern similar to that of figure 1, A and B, was seen; positive potentials overlay the anterior torso. Increasing the paced rate to 190 beats/min (panel C) again created an abnormal pattern, with negative voltages detected over the anterior thorax.

As previously described, patterns such as those in panels A and B of figures 1 and 2 were considered “normal,” whereas that in panel C of each figure was considered “abnormal,” the new anterior negativity reflecting subendocardial ischemia provoked by increased oxygen demand. Based on these standards, maps constructed from voltages sensed 40 msec into the ST segment at each paced rate were examined and classified into either of two subsets — “normal” or “ischemic.” This was performed by viewing maps in a random order without knowledge of the animal group, heart rate, or blood flow.

This approach, based on the ability of the isopotential map to depict spatial as well as intensity and temporal information, permits a dichotomous or binary classification scheme. This, in turn, obviates the problems of defining an abnormal test based on an arbitrary or statistically determined quantitative level of ST segment depression that may vary from lead to lead. Previous studies have demonstrated that classification is identical when performed with data recorded at different instants during the ST segment.

**Statistical analysis.** Data are presented as mean ± SD. Differences in rate and flow variables between ischemic and nonischemic perfusion beds and between the animal groups were evaluated by analysis of variance methods, relying on a 95% confidence level.

The relation between the electrocardiographic patterns and flow variables was determined with linear and logistic regression models. In the latter, the coded isopotential map pattern (“normal” or “ischemic”) was the dependent variable and the endo/epi flow ratio, reflecting the transmural blood flow distribution, was entered as the independent variable.

**Results**

**Blood flow responses.** Changes in myocardial blood flow produced by atrial pacing were quantified in the nonischemic (LAD bed in group I and LCX bed in group II) and ischemic (LCX bed in group I and LAD in group II) perfusion territories. Results are tabulated in table 1 and displayed in figure 3.

**Nonischemic bed.** Blood flow to both the endocardial and the epicardial thirds of the nonischemic wall increased progressively as heart rate was increased from 90 to 210 beats/min. The endo/epi ratio remained near unity. Flow changes were equivalent in the two experimental groups.

**Ischemic bed.** Flows in the epicardial third of the ischemic wall increased progressively as rate was increased from 90 to 210 beats/min. The resultant outer-wall flows were significantly lower (p < .05) in the ischemic bed than in the nonischemic bed at rates of 170 beats/min and higher, although the differences were

| TABLE 1 |
| Myocardial blood flow responses (ml/min/g) to rapid atrial pacing in dogs with ameroid constriction of the LCX or LAD |

<table>
<thead>
<tr>
<th>Group/rate (beats/min)</th>
<th>Nonischemic bed</th>
<th>Ischemic bed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endo Epi</td>
<td>Endo Epi</td>
</tr>
<tr>
<td>Group I (LCX ameroi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>0.99 ± 0.09</td>
<td>0.97 ± 0.06</td>
</tr>
<tr>
<td>150</td>
<td>1.21 ± 0.10</td>
<td>1.23 ± 0.08</td>
</tr>
<tr>
<td>170</td>
<td>1.30 ± 0.08</td>
<td>1.27 ± 0.10</td>
</tr>
<tr>
<td>190</td>
<td>1.42 ± 0.09</td>
<td>1.44 ± 0.09</td>
</tr>
<tr>
<td>210</td>
<td>1.51 ± 0.10</td>
<td>1.49 ± 0.07</td>
</tr>
<tr>
<td>Group II (LAD ameroi)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>0.86 ± 0.09</td>
<td>0.95 ± 0.11</td>
</tr>
<tr>
<td>150</td>
<td>1.17 ± 0.10</td>
<td>1.20 ± 0.12</td>
</tr>
<tr>
<td>170</td>
<td>1.29 ± 0.07</td>
<td>1.32 ± 0.08</td>
</tr>
<tr>
<td>190</td>
<td>1.40 ± 0.04</td>
<td>1.43 ± 0.07</td>
</tr>
<tr>
<td>210</td>
<td>1.46 ± 0.15</td>
<td>1.53 ± 0.06</td>
</tr>
</tbody>
</table>

*p < .05 vs epicardial flow in same bed; †p < .05 vs nonischemic bed flow.
Endocardial flows rose in both groups I and II at lower rates but fell at the higher pacing frequencies. At rates of 150 beats/min and above endocardial flows were significantly lower than in corresponding epicardial samples and lower than those in the endocardial portions of nonischemic vascular beds. At rates of 170 and 190 beats/min, endocardial flow in the ischemic LAD was significantly lower than that in the ischemic LCx perfusion territory (figure 3, middle panel).

As expected from the above data, the endo/epi ratio fell significantly in both ischemic beds at higher heart rates. Mean values fell from near unity at rates of 90 beats/min to under 0.50 at rates of 210 beats/min. As illustrated in figure 3, bottom panel, ratios were significantly lower in the LAD (group I) than in the LCx (group II) perfusion territory at rates of 170 and 190 beats/min.

Perfusion bed sizes were measured by computerized planimetry and expressed as percent of the left ventricle. The LCx bed included 34.7 ± 4.02% of the left ventricle and the LAD bed measured 29.6 ± 5.53%. These sizes were not significantly different. Mean arterial pressures and rate-pressure products at each paced rate were equivalent in the two experimental groups (p > .1).

Electrocardiographic effects. Isopotential patterns 40 msec into the ST segment at each paced rate were categorized as normal or as ischemic as described above.

In group I after LCx constriction, 12 of the 15 dogs developed ischemic ST segment patterns at rates of 170 to 210 beats/min. Twenty-three of 72 technically adequate flow-ECG pairs (31.9%) were classified as ischemic, with peak negative potentials in subtraction maps (ischemic map minus map at 90 beats/min) of 299 to 617 μV (456.63 ± 92.42).

In the ten cases in group II studied after ameroid constriction of the LAD, ischemic ST patterns emerged in eight as rates of 150 to 210 beats/min. Of 50 data sets examined, 20 (40.0%) map patterns were ischemic, with a peak negative potential in isopotential difference maps of 447 to 825 μV (644.75 ± 108.76). Neither the frequency of abnormal maps nor the rate at development of abnormal patterns was different in the two groups.

Flow-ECG correlations. The relationships between the described changes in myocardial blood flow and body surface electrocardiographic patterns were examined in two ways, as described in Methods.

First, logistic regression modeling was used to determine whether a statistically significant relation existed between the endo/epi flow ratio and the recording of a normal or ischemic isopotential pattern.

For both LAD and LCx occlusions, the relationship was highly significant (p < .05). Plots showing the probability of registering a normal map at flow ratios of 0.4 to 1.00 are shown in figure 4 for both groups. The curve for the LAD cohort lies to the right of that for the LCx group; the two plots are significantly different from each other (t test, p < .05). Thus, for a given endo/epi ratio, a normal map was less likely to be observed after LAD occlusion than after LCx obstruction. Ratios at which a normal map could be expected with a 50% probability were 0.65 and 0.74 for LCx and LAD obstruction, respectively.

A similar analysis was performed with absolute endocardial flows (ml/min/g) rather than the endo/epi
ratio. Results likewise demonstrated that an abnormal map would occur (with a 50% probability) at a higher endocardial flow in the LAD than in the LCx perfusion bed (p < .05). When epicardial flow was used, logistic plots were colinear.

Second, the relationship between the intensities of the peak negative potential in the isopotential difference maps (constructed by subtracting patterns at a paced rate of 90 beats/min from that at each paced rate with an ischemic pattern) and the corresponding endo/epi ratio was determined by linear regression methods. Resulting plots are shown in figure 5.

Computed regression equations for both groups were highly significant, signifying a direct relation between the magnitude of the flow and the electrocardiographic abnormalities produced by pacing. Although the slopes of the two regression equations were not significantly different from each other, the y axis intercept for group II animals after constriction of the LAD was significantly (p < .05) greater than that for group I after LCx obstruction. Thus, for a given endo/epi ratio, more intense negative body surface potentials would be expected after LAD than after LCx occlusion.

Discussion

This study was based on two sets of previously reported data. First, prior reports from this laboratory identified a quantitative relationship between transmural myocardial blood flow during atrial pacing in dogs with chronic LCx occlusion and body surface isopotential maps during the ST segment. Statistical modeling demonstrated that a flow ratio of or less than 0.67 was required to yield, with a probability exceeding 50%, an abnormal potential pattern indicative of subendocardial ischemia. Furthermore, the magnitude of the abnormal surface potentials was inversely correlated to the endo/epi flow ratio.

Second, several lines of experimental and clinical evidence suggest functional differences between the various perfusion beds in the dog. For example, Becker et al. reported that acute occlusion of the LAD in the anesthetized dog produces more extensive infarction than does obstruction of the LCx. This finding is related to observations by Scheel et al. that stimulated collateral blood flow to the LAD bed is lower than that to the LCx territory. A similar spatial pattern has also been reported in the conscious dog.

Clinical studies have also suggested differences between the two perfusion territories. False-negative exercise tests are less common in patients with isolated LAD disease than with LCx or right coronary artery lesions and development of marked ST depression is more common with LAD disease. The latter has also been observed in the animal preparation used in this study.

Methodologic considerations. Because of these reports, we sought to test the hypothesis that pacing-induced
ischemia is more severe in the LAD bed. To do so, we used an animal preparation in which chronic ameroid constriction produces gradual but complete anterograde obstruction\textsuperscript{1-3} but without producing significant necrosis\textsuperscript{18} because of the rapid development of collateral flow from all other perfusion beds.\textsuperscript{2, 10} Although specific tests for infarction were not done, all animals had normal resting ECGs and no gross evidence of necrosis at postmortem sectioning.

Myocardial blood flow is normal at rest,\textsuperscript{2, 9} but ischemia develops during periods of increased demand produced by either exercise or by rapid atrial pacing.\textsuperscript{1-3, 9} This in turn reverses the normal transmural gradient of ventricular recovery properties\textsuperscript{19} to generate body surface ST segment abnormalities that are very similar to those observed during exercise stress tests in patients with significant coronary artery obstruction.\textsuperscript{5} Although animals in groups I and II were studied sequentially rather than simultaneously, methods used for both were identical.

**Effects of pacing.** Qualitative blood flow responses to rapid atrial pacing in both groups were as anticipated. In the nonischemic bed, both epicardial and endocardial flows increased progressively with increased demand, without transmural redistribution. The changes in group II after LAD were more severe than in group I after LCx obstruction. As shown in table 1 and in figure 3, endocardial flow and the endo/epi ratio in the LAD bed was lower at midrange rates than in the LCx bed. Thus endocardial coronary vascular reserve is more limited than epicardial reserve\textsuperscript{20} and is more limiting in the anterior than in the LCx arterial system.

It is known, however, that pacing and ischemia do not produce maximal vasodilation of existing collateral channels\textsuperscript{21-2}, reasons for incomplete vasodilation are unknown but might differ quantitatively in the two regions if, for example, sympathetic innervation were responsible.

This regional difference is consonant with the finding that collateral vascular resistance to the LAD region is higher and flows lower than those to the LCx bed.\textsuperscript{10} This, in turn, may reflect innate anatomic variation or regional hemodynamic factors, such as increased intramural wall stress in the anterior heart that may collapse potential collateral pathways.\textsuperscript{24} The observation that it is the endocardial rather than the epicardial flows that are different is consistent with the predilection for subendocardial ischemia with either increased demand\textsuperscript{1-3} or reduced supply.\textsuperscript{4}

**Electrocardiographic correlations.** As described for flow responses, the electrocardiographic consequences of rapid atrial pacing were qualitatively similar in the two groups. In each, a highly significant relation was documented between the presence (figure 4) and the intensity (figure 5) of an abnormal or ischemic map pattern and magnitude of the changes in blood flow. The differences in the ischemic patterns reflect the differences in the positions of the ischemic flow within the torso, as previously detailed.\textsuperscript{6}

Such relationships are predictable from the solid angle theorem\textsuperscript{25} and from equivalent generator models.\textsuperscript{26} In each formulation, the electrocardiographic potential recorded by a remote electrode is proportional to the intensity of current flux across the boundary between normal and ischemic tissue as well as the size of the boundary and to other biophysical variables. Strength of both systolic and diastolic injury currents\textsuperscript{7, 25} would be expected to increase as the magnitude of flow defect increased. It would thus be anticipated that in the clinical setting the magnitude of ST segment depression during an exercise test would reflect not only the number of vessels diseased, as is commonly considered,\textsuperscript{27} but also the level of ischemia within those regions.

Study of these relationships between the two vascular beds, however, demonstrated two new findings. First, the logistic regression modeling suggests that ischemic ST segment patterns develop with less aberration of transmural flow in the LAD bed than in the LCx territory. The logistic plot (figure 4) for the LAD bed lies to the right of that for the circumflex bed, indicating that, for the same endo/epi ratio, the probability of detecting ST segment abnormalities was greater in the former than in the latter. The level at which an abnormal map might be expected in over 50% of cases increased from 0.65 to 0.74. The mechanism for this effect is unknown but is apparently not related to differences in bed size.\textsuperscript{9} One possibility relates to the regional differences in \(
\alpha \)-adrenergic innervation; stimulation of the right stellate ganglion produces vasconstriction only in the LAD bed\textsuperscript{28} that may persist to control flow despite development of ischemia.\textsuperscript{22, 23, 2} An analogous finding of more severe reductions in ventricular function with LAD than with LCx ischemia has recently been reported.\textsuperscript{20}

Second, for a given endo/epi ratio, the intensity of the abnormal body surface negative potentials was greater for LAD than for LCx obstructions. This is demonstrated in figure 5, in which the regression line between endo/epi ratio and the intensity of negativity in isopotential difference maps is higher for LAD than for LCx regions. This effect is probably related to the more eccentric position of the LAD bed within the chest, reducing the distance from the ischemic zone to
the recording electrodes. As noted above, perfusion bed sizes were equivalent.

Implications. The findings of this study thus support the hypothesis that the two vascular beds respond to demand-dependent ischemia in quantitatively different ways. Not only does subendocardial ischemia result from lesser degrees of increased demand in the LAD than in the LCx bed, but an ischemic ST segment pattern is more likely to be observed for a given degree of ischemia or transmural flow redistribution and the intensity of the abnormality is expected to be greater.

These data may be directly related to two common and important clinical findings. The lesser degree of ischemia required to produce an electrocardiographic abnormality may explain the lower incidence of false-negative exercise stress tests in patients with single-vessel LAD disease than with other lesion locations.14–16 Second, the steeper slope of the relation between flow aberration and intensity of ST segment depression would explain the observed greater degree of ST segment depression with anterior lesions.17 Thus these experimental data may have direct clinical relevance.

References
8. Mirvis DM: Ability of standard ECG parameters to detect the body surface isopotential abnormalities of pacing induced myocardial ischemia in the dog. J Electrocardiol 18: 77, 1985
Alterations in transmural blood flow and body surface ST segment abnormalities produced by ischemia in the circumflex and left anterior descending coronary arterial beds of the dog.
D M Mirvis and K B Ramanathan

Circulation. 1987;76:697-704
doi: 10.1161/01.CIR.76.3.697

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/76/3/697

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation 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 is online at:
http://circ.ahajournals.org/subscriptions/