Dissociation Between Regional Myocardial Dysfunction and ECG Changes During Ischemia in the Conscious Dog

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SUMMARY The relations between regional ventricular function and regional and surface ECGs were studied in eight conscious dogs during complete and partial coronary obstructions. Wall thickness and local ECGs were measured using an implanted sonomicrometer, and 11 subcutaneous electrodes were implanted in a modified McFee vectorcardiographic array. Complete obstruction of the circumflex coronary artery (using a hydraulic occluder) produced regional hypokinesia after 15 seconds and regional dyskinesia at 1 minute. Significant ECG changes occurred first in the surface vectorcardiogram, ST segments changed at 30 seconds and mean epicardial and endocardial ECG ST segments increased after 1 minute. During mild partial coronary stenosis that produced stable reductions of systolic wall thickening (%ΔWT) of less than 25% of control, no ST-segment changes occurred in the surface vectorcardiogram during the 10-minute study period, although ST segments increased significantly in the endocardial and epicardial ECG. With moderate coronary stenoses that produced immediate 25–48% reductions of %ΔWT (average reduction 36 ± 4%), significant mean ST displacements occurred after 2 minutes in the endocardial ECG, after 3 minutes in the epicardial ECG and after 4 minutes in the surface vectorcardiogram. With coronary stenoses that produced more than 50% reduction of %ΔWT (average reduction 69 ± 2%), mean endocardial ST-segment changes were noted after 2 minutes, and changes in both the mean epicardial ECG and the surface vectorcardiogram occurred after 3 minutes. Thus, during mild coronary stenosis, regional myocardial dysfunction can occur without surface ECG changes, while during moderate coronary stenosis, it occurs before endocardial ST-segment changes and precedes surface ECG alterations by several minutes. The surface ECG was slightly more sensitive than the local ECG during complete coronary occlusion and less sensitive during partial coronary obstruction. We conclude that regional contractile abnormalities provide a more sensitive indicator of ischemia than electrocardiographic ST-segment changes.

REGIONAL VENTRICULAR dysfunction and ST-segment displacement on the ECG are valuable indicators of myocardial ischemia. However, ST-segment displacement on the body surface ECG is not specific for ischemia, and both false-negative and false-positive ECG findings during exercise testing for detecting coronary artery disease have been reported. In the experimental setting, regional wall function dynamics are highly sensitive to local ischemia both at rest and during exercise in the conscious dog; in clinical studies, simultaneous recordings of ventricular function using radionuclide angiographic techniques and ECG recordings during exercise have suggested superiority of mechanical over electrical events for the detection of temporary myocardial ischemia. Nevertheless, the exercise test with ECG recordings is still the most popular and economical screening test for coronary artery disease in man, and further understanding of the relations between electrical and mechanical events during ischemia is needed. Smith et al., using open-chest dogs, reported that endocardial ST-segment elevation may be a more sensitive index of ischemia than depression of myocardial contractile function, but the surface ECG was not recorded.

We developed a preparation in the conscious dog to allow measurements of the surface ECG simultaneously with the local electrogram and an independent detector of ischemia, regional myocardial function. This animal model was used to study electromechanical relations during ischemia produced by complete and partial coronary artery obstructions.

Methods

Eight adult mongrel dogs weighing 20–30 kg (mean 26 kg) were anesthetized with sodium pentobarbital (30 mg/kg). Under sterile conditions, a left thoracotomy was performed in the fifth left intercostal space, the left circumflex coronary artery was dissected free near its origin and a hydraulic occluder made from polyvinyl tubing was positioned around it. A pair of miniature ultrasonic crystals implanted in the endocardium and epicardium of an area to be rendered ischemic near the base of the posterior papillary muscle was used to measure wall thickness, as previously described. Unipolar endocardial and epicardial electrograms were monitored from the implanted piezoelectric crystals. The signals were taken from the output side of the pinger isolation transformer and the input side of the receiver isolation...
transformer. The pinger spike was rejected by a filter and the signal was amplified 20-fold; the preamplifier output drove the amplifier of a Brush forced-ink recorder. The preamplifier had a single-pole high-pass filter with a response of 0.2 Hz and a three-pole low-pass filter with a response of 70 Hz. The input impedance was approximately 70 kΩ. The remote reference electrode for the unipolar electrograms was located on the lower part of the left rear leg.

Surface ECGs were obtained by implanting 11 subcutaneous stainless-steel wire electrodes in a modified McFee vectorcardiographic (VCG) array.13, 14 These leads were recorded using a modified commercial VCG system (Hewlett Packard/Sanborn Model 1507A Vector programmer and Model 760-6A Visoscope). The plug-in lead selector card was replaced with an active mixing network designed to give the McFee weighting to the respective leads.* This circuit was designed to have a single-pole high-pass filter response of 0.3 Hz and a three-pole low-pass filter response of 70 Hz. The output of this plug-in card drove the HI1507A circuit.

The pericardium was left open, the chest was closed, and the hydraulic occluder tube and all wires were tunneled to the back of the dog and brought through the skin between the scapulae.

Protocol

The dogs were conscious and had recovered completely when the experiments were performed, at least 7 days after the operation. Each dog was resting quietly on its right side on the floor. Control recordings of wall thickness, endocardial ECG, epicardial ECG and surface VCG leads X, Y and Z were made for at least 10 minutes. Using a syringe, the hydraulic occluder was then rapidly and forcefully inflated with water to produce complete occlusion of the circumflex artery. As soon as regional akinesis or dyskinesis was accompanied by detectable regional and surface ST-segment changes (usually after 1.5 minutes), the hydraulic occluder was deflated. On separate days in each dog, the hydraulic occluder was gradually inflated with water to produce stable regional hypokinesia for 10 minutes or until ECG changes became evident. Our initial objective was to create mild hypokinesia, which required careful manipulation of the hydraulic occluder to create mild dysfunction (less than 25% reduction in wall thickening). The difficulty of creating stable mild dysfunction without ECG changes for 10 minutes in the conscious dog (e.g., slight movement of the dog could markedly affect the relative severity of a given stenosis due to changes in heart rate), was such that we could produce this condition in only three of the eight dogs. Another time, the hydraulic occluder was inflated to produce more than 25% and less than 50% reduction in systolic wall thickening (moderate dysfunction); with these more severe degrees of stenosis, ECG changes appeared earlier and stable conditions of less than 5 minutes were required. A third time, the cuff was inflated to create more than a 50% decrease in wall thickening (severe dysfunction). On these two occasions, stable hypokinesia was obtained in six of the eight dogs.

The experiment was terminated 14–28 days postoperatively. At postmortem examination in each dog, the crystals were in proper alignment: The inner crystal of the wall thickness pair was in the inner one-third of the left ventricular wall, and the external crystal was well fixed to the epicardium. The circumflex coronary artery was widely patent in all dogs, and there was no macroscopic evidence of myocardial infarction in the area supplied by this vessel.

Data Analysis

All variables were recorded simultaneously on an eight-channel Brush forced-ink recorder. ST-segment changes in the endocardial, epicardial and surface ECG recordings were measured 0.04 second after the J junction, with the PR segment as the isoelectric line. On the endocardial and epicardial ECGs, ST elevation was calculated as the change (in mV) from the control ST-segment level. The surface ST-segment changes were calculated as the sum of ST-segment elevations or depressions (in mV) in VCG leads X, Y and Z relative to control. Regional systolic wall thickening (%ΔWT) was calculated as end-systolic wall thickness minus the end-diastolic wall thickness (measured at the time of maximal deflection of the QRS complex of the endocardial ECG) divided by the end-diastolic wall thickness.13 End-systolic wall thickness was measured as the maximum wall thickening during ventricular ejection. In 100 observations from five other dogs in which ventricular pressure was measured, end-ejection on the ventricular pressure tracing just before peak negative dP/dt was followed the termination of the T wave of the endocardial ECG by 50 ± 20 msec (SD). Therefore, maximum systolic shortening was identified as the maximum positive excursion on the wall thickness tracing that followed the termination of the endocardial T wave by approximately that interval.

All data from ECGs and wall thickness tracings were averaged over 10 consecutive beats at paper speeds of 50 mm/sec. Statistical analysis was conducted by analysis of variance with repeated measures. When statistical significance was established with analysis of variance, Dunnett’s test was used to determine which groups were significantly different from control measurements.18 The level of statistical significance was p < 0.05, and the data are presented as the mean ± SEM.

Results

Coronary Occlusion

During complete coronary occlusions, regional ventricular hypokinesia was recorded in all eight dogs within 15 seconds. The mean %ΔWT decreased significantly (p < 0.01), from 23.6 ± 1.6% (mean ± SEM)
at control to 15.6 ± 1.6% 15 seconds after the hydraulic occluder was inflated. One minute after complete coronary occlusion, the mean %ΔWT decreased further, to −0.8 ± 1.4%, indicating regional dyskinesia (figs. 1 and 2). The first significant electrocardiographic ST changes occurred in the surface VCG 30 seconds after complete occlusion, and the mean sum of the VCG ST segments changed from control by 0.3 ± 0.1 mV (p < 0.01) (figs. 1 and 2). Significant epicardial ST changes occurred 30 seconds later, and the mean epicardial ST segments were increased at 1 minute by 0.38 ± 0.1 mV from control (p < 0.01) (figs. 1 and 2), while significant endocardial ST-segment changes occurred at 1.5 minutes, the mean endocardial ST segments increasing by 0.94 ± 0.18 mV from control (p < 0.01) (figs. 1 and 2). During complete coronary occlusions, the endocardial and epicardial ECGs both showed ST-segment elevations in each dog, but only VCG lead Z showed ST elevation; VCG lead X showed ST-segment depression in most dogs (table 1).

Moderate and Mild Coronary Stenosis

When moderate partial coronary stenosis was produced in six dogs by partially inflating the hydraulic occluder to produce a rapid 25–48% reduction of regional ventricular function (average 36 ± 4%) (figs. 3A and 4), there were no significant changes in the surface ECG for 5 minutes in one dog, for 4 minutes in three dogs and for 2 minutes in two dogs. The mean surface ST segments changed significantly 4 minutes after partial stenosis, by 0.31 ± 0.10 mV (p < 0.01) (fig. 3A). The Z lead of the surface VCG showed ST elevation in most of the dogs (table 2). The endocardial and epicardial ST-segment changes preceded any changes in the surface ST segments. The mean endocardial ST segments were increased significantly at 2 minutes (p < 0.01) by 1.00 ± 0.29 mV, and the mean epicardial ST segments were increased significantly at 3 minutes (p < 0.01) by 0.72 ± 0.29 (figs. 3A and 4).

In three dogs, mild-to-moderate coronary stenosis without ST-segment changes in the surface VCG leads was maintained for 10 minutes (fig. 5). The reduction in %ΔWT was less than 25% of control (average 17 ± 2%). Each of the three dogs showed significant ST-segment elevation in both the endocardial and epicardial ECGs; the average endocardial ST segments increased by 2.5 ± 0.9 mV and the average epicardial segments increased by 1.2 ± 0.7 mV.

Severe Coronary Stenosis

When more severe coronary stenosis was produced to decrease regional function by more than 50% of control (average reduction 69 ± 2%), endocardial ST-segment elevation preceded epicardial and surface ST-segment changes by 1 minute (figs. 3B and 6). The endocardial ST segment increased significantly (p < 0.01), by 1.75 ± 0.48 mV, 2 minutes after the stenosis was produced, and the epicardial ST segments and surface ST segments changed significantly, by 1.77 ± 0.58 mV and 0.52 ± 0.10 mV, respectively, at 3 minutes (figs. 3B and 6).

Discussion

In this study, we used a conscious dog model to avoid the adverse effects of anesthesia and acute operative changes, which can alter normal physiologic responses.19, 20 This model also permitted measurement of body surface ECGs using a VCG system recorded simultaneously with local electrical and

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**FIGURE 1.** Effects of complete coronary occlusion on percent systolic wall thickening (%ΔWT), elevation from control of endocardial ST segments (ΔST ENDO ECG), epicardial ST segments (ΔST EPI ECG), the sum of ST-segment displacements from control in the vectorcardiographic leads X, Y, and Z (ΣΔST VCG) and heart rate (HR). Negative values for %ΔWT represent regional dyskinesia.
Figure 2. Representative tracing of regional wall thickness, endocardial and epicardial ECGs and McFee vectorcardiographic (VCG) leads at control and during complete coronary occlusion in one dog. After 30 seconds of complete coronary occlusion, endocardial and epicardial ST segments were unchanged, whereas ST segments were clearly depressed relative to control in VCG lead X, depressed in VCG lead Y and elevated in VCG lead Z. There appeared to be slight depression in the X-lead ST segment at 15 seconds. The vertical arrows indicate end-systolic thickness.
# Table 1. ST-segment Elevation or Depression at Control and 1.5 Minutes After Complete Coronary Occlusion in the Endocardial and Epicardial Electrocardiograms and the Surface Vectorcardiographic Leads

<table>
<thead>
<tr>
<th>Dog</th>
<th>Endocardial (mV)</th>
<th>Epicardial (mV)</th>
<th>Y (mV)</th>
<th>Z (mV)</th>
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<td>5.5</td>
<td>0.5</td>
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<td>8</td>
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<td>Complete coronary occlusion (1.5 min)</td>
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# Table 2. ST-segment Elevation or Depression at Control and 4 Minutes After Partial Coronary Occlusion to Produce Less Than 50% Reduction of Systolic Wall Thickening

<table>
<thead>
<tr>
<th>Dog</th>
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<th>Epicardial (mV)</th>
<th>X (mV)</th>
<th>Y (mV)</th>
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*Surface ST-segment changes occurred only in the fifth minute after partial coronary occlusion.
mechanical events. This modified McFee VCG array has been shown to be more stable than other ECG/VCG systems in chronically instrumented animals. Exercise-induced ST-segment shifts using VCG leads have been shown to be as sensitive for detecting ischemia as those recorded on the standard ECG leads. Because spatial changes rather than localized changes in proximity to electrodes are assessed, the VCG approach should be unmatched for sensitivity, except perhaps by precordial ECG mapping.

During complete and partial coronary occlusions, wall function was always more sensitive to reduction of coronary blood flow than either regional or surface electrocardiographic ST-segment changes. In fact, mild regional dysfunction was maintained for as long as 10 minutes without any surface ECG changes; moderate regional dysfunction could be maintained for 3–5 minutes before surface ECG changes occurred and for 1–3 minutes before regional ECG changes occurred. Dysfunction did reflect ischemia, as indicated by recent studies in our laboratory showing a close correlation between reductions in regional myocardial blood flow measured by the microsphere technique and decreases in regional systolic wall thickening. The occurrence of endocardial ST-segment elevation before epicardial ST elevation during partial coronary stenosis is consistent with previous findings.

The relative sensitivity of electrical and contractile events in ischemia has been studied only in open-chest animals in which changes in the local electrogram were compared with alterations of regional function. Using a preparation in which the left anterior descending artery was cannulated and coronary blood flow through the cannula was progressively altered with a screw clamp, Smith et al. concluded that endocardial ST-segment elevation may be slightly more sensitive to ischemia than depression of regional contractile function. Our results, on the other hand, indicate that regional function is more sensitive than the intramyocardial or surface ECG in detecting ischemia. The difference in findings may be due in part to differences in experimental preparations, including the location of the ischemic area (left anterior descending vs cir-
Figure 4. Representative tracings from one dog of partial coronary stenosis to produce less than 50% reduction of systolic wall thickening (\%\Delta WT) maintained at a relatively stable state for 4 minutes. ST-segment changes in the regional ECG precede those on surface ECG, and both are preceded by regional dysfunction. VCG = vectorcardiogram.
cumflex artery), measurement of regional function (midwall segment shortening vs overall wall thickening), presence of anesthesia and surgical trauma, and different timing of the measurements. Also, in the study of Smith et al., the location of the endocardial ECG lead did not correspond precisely to the area in which segmental shortening was measured, and because subendocardial ischemia precedes the development of transmural ischemia during progressive reductions in coronary perfusion pressure, endocardial ST-segment changes could occur before alterations in midwall segment shortening. Consequently, comparisons between the results of our study and those of Smith et al. are difficult.

During complete coronary occlusions, surface ECG ST-segment changes occurred rapidly (30 seconds) and, on the average, slightly preceded the development of epicardial and endocardial ST-segment changes, which became significant 30–60 seconds later. The reason for the relatively more sensitive detection of complete occlusion by the surface leads, compared with the greater sensitivity of the intramyocardial leads for detecting partial stenosis, is not entirely clear, but may relate to differences in the location of electrodes and in the size of the ischemic zone, as well as to the intensity of the current of injury at the boundary between ischemic and nonischemic tissue. Based on solid-angle theory, it might be expected that production of a large ischemic area by coronary occlusion would result in relatively more marked ST-segment changes in the body surface leads, with less marked changes in the local electrograms. However, because partial coronary artery stenosis produces an area of ischemia that is predominantly intramural or in the subendocardial region and involves a smaller ischemic area than with complete occlusion, the body surface leads would subtend this smaller angle; or, if the zone were intramural, these leads might even be electrically silent for injury. Intramyocardial leads, which reflect local intensity of the injury and subtend a relatively large angle of the injured area, however, might be expected to detect such ischemia.

The high sensitivity of surface ST-segment changes for detecting complete coronary occlusion produced by coronary spasm has been noted clinically. The present study may mimic the effects of coronary spasm to some degree, because the reduction of coronary blood flow was not preceded by an increase in myocardial oxygen demands, and the surface ECG leads corresponding to the occluded coronary artery usually showed ST-segment elevation. During spontaneous coronary spasm, hemodynamic changes of decreased left ventricular dP/dt and increased ventricular end-diastolic pressure often precede ECG changes, suggesting, as observed in this study, that regional myocardial dysfunction is the earliest event.
Our findings carry implications for stress testing in the detection of latent coronary artery stenosis. With mild coronary stenosis or during stress of relatively short duration, ST-segment displacement could be absent or delayed for many minutes. On the other hand, regional contractile dysfunction could allow detection of regional ischemia under these conditions. Therefore, further refinement of noninvasive analysis of regional wall motion during exercise by radionuclide\textsuperscript{7} and echocardiographic\textsuperscript{30-32} techniques should enhance the sensitivity and specificity of stress testing for the detection of latent coronary disease.
Acknowledgment

We are grateful to Mark Miller for engineering assistance, Daniel McKown and Michael McKown for technical assistance, Elizabeth A. Gilpin for the statistical analysis, and Rosemary Montoya for the secretarial work.

References

Dissociation between regional myocardial dysfunction and ECG changes during ischemia in the conscious dog.
A Battler, V F Froelicher, K P Gallagher, W S Kemper and J Ross

_Circulation_. 1980;62:735-744
doi: 10.1161/01.CIR.62.4.735

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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