Correlation of Intramyocardial Electrocardiograms with Polarographic Oxygen and Contractility in the Nonischemic and Regionally Ischemic Left Ventricle

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We have previously shown that the epicardial-surface electrocardiogram is an inadequate index of localized myocardial ischemia. While striking changes of polarographic oxygen and contractility regularly occur a few seconds after coronary arterial branch occlusion, epicardial electrocardiographic changes are delayed and sometimes absent. Intramyocardial electrocardiographic studies, on the other hand, reveal that localized ischemia disturbs myocardial electrical activity at least as early as either oxygenation or contractility, and over a more extensive area.

We have developed a technique for amplification and recording of oxygen-reduction currents and electrocardiograms simultaneously from the same lead-point in the myocardium. This technique was combined with motion-picture records of muscle contraction and epicardial-surface color. Thus, simultaneous information about electrical activity, oxygenation, and contractility in locally altered myocardium and adjacent, undisturbed muscle became available. This makes possible, as we will show in the present paper, an assessment of the limitations of epicardial heart-body leads, which are still indispensable links between open-chest situations and the body-surface electrical phenomena of concern to the clinician. We consider such an assessment to be elementary for understanding the behavior of the heart muscle and the electrocardiogram in coronary heart disease.

Methods

In 28 dogs, weighing 15 to 23 Kg., the heart was exposed under morphine-Dial-urethane-pentobarbital anesthesia. A branch of the left anterior descending coronary artery was isolated. Eight to 10 glass-insulated platinum electrodes were inserted in the left ventricle as previously described. The construction of electrodes had been modified from those used in our earliest work. The relatively heavy shank was eliminated and the entire shaft was made of light glass fused to a 0.2-mm. platinum wire which was connected at a plastic-insulated junction to a very light lead wire (no. 42 copper enameled) insulated by polyethylene tubing (fig. 1). A white glass bead, cemented to the shaft at the level desired, acted as a depth stop and as a marker for cinematographic studies of muscle contraction. These electrodes were made the cathodes of an electrolytic circuit measuring changes in oxygen polarographically according to the method of Davies and Brink and Montgomery and Horwitz. The electrodes were also used as exploring lead-points for direct heart-body electrocardiograms. The platinum tips in the myocardium have an electrolytic capacitance of approximately 0.5 microfarad, which makes it possible to use them for simultaneous measurement of extracellular electrical activity. The reference electrode for both systems consisted of approximately two feet of 18 B&S-gauge pure silver wire immersed in a jar of physiological saline into which one of the hind limbs of the dog was also immersed. The myocardial oxygen-reduction currents, range \(10^{-7}\) to \(10^{-9}\) amperes, were amplified by means of a...
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special preamplifier. Modulation of the oxygen-reduction current by the myocardial electrocardiogram was largely eliminated by inserting a series resistor and a shunt capacitor at the input of the oxygen-reduction current preamplifier. The series resistor also allowed the electrode to follow the electrocardiogram so that the latter could be recorded separately via a capacitor and voltage preamplifier (Tectronic model 122). A circuit diagram of the apparatus is given in figure 2. The recorder was ordinarily a six-channel Brush direct-writing oscillograph with appropriate driver amplifiers. In some experiments, additional oxygen and electrocardiogram preamplifiers were added to the system.

Color motion pictures were synchronized with the electrical activity of the heart by including in the photographic field either an epicardial electrocardiogram (from a nonischemic surface) or a neon bulb triggered by the R wave of such a record. Special silver, silver-chloride intramyocardial electrodes were occasionally used with D.C. amplification to distinguish between the RS-T segment and baseline shifts which comprise the net RS-T segment displacement ordinarily recorded with an A.C. amplifier.

Our myocardial explorations were largely confined to depths of 3 mm. or more beneath the epicardial surface. Electrodes were difficult to maintain in position when inserted less deeply, and the records obtained from them tended to be unstable. After inserting the platinum electrodes, it was necessary to await the stabilization of the oxygen-reduction currents (initially large) and the electrocardiograms. R waves were at first absent; then, they might appear as notches on the ascending limbs of the monophasic ventricular complexes. After 30 to 45 minutes, the QRS configuration and net RS-T segment levels remained stable, the latter usually isoelectric, not infrequently somewhat elevated, occasionally very slightly depressed.

*This amplifier was originally designed for oxygen measurements in skin and myocardium by one of us (Mr. Peiree) under the support of USPH Grants 392(C) and 398(C4). A modification for use in blood, constructed under his supervision, was recently described by Polgar and Forster.10

Galvanometric measurements of oxygen-reduction currents can be combined with myocardial electrocardiograms from the same electrode, provided the input impedance is increased to the order of megohm. In this case, it is not necessary to shunt the galvanometer with a filter capacitor, because the slow speed of the instrument is sufficient to eliminate most of the electrocardiographic modulation.

Experimental Procedures

Once stable control configurations for myocardial electrocardiograms and levels of oxygen-reduction currents had developed, reversible localized or generalized alterations of myocardial function were produced, using techniques described previously. We discarded information from electrodes which did not return to control configurations between procedures. Localized changes consisted of maximal ischemia1 with release-recovery (occlusion of a medium-sized branch of the left anterior descending coronary artery for two to five minutes), and alteration of superficial myocardial layer behavior by local warming or cooling, and by topical procaine HCl (25 to 50 per cent) or KCl (5 per cent) solutions. Blood-pressure and heart-rate changes were negligible with these procedures. In four animals, two or three simultaneous records of myocardial oxygen and electrocardiograms were followed to permit comparison of the borders of ischemic areas with the centers. Generalized changes included the effects of inhalation of 100 per cent oxygen, hypoxia (10 per cent oxygen for 10 to 15 minutes), asphyxia (respirator turned off), and intravenous levarterenol. In four animals, D.C.-amplifier myocardial electrocardiographic studies of localized changes and of levarterenol effects were carried out. Insulation was used only in these animals. Most of the animals had been studied
Figure 2

Circuit for simultaneous recording of polarographic oxygen-reduction current and intramyocardial electrocardiogram from same electrode. See Methods and Discussion. In operation, the grounding of the dog and the connection to the dog via the silver reference electrode is completed before turning on the apparatus. (SW-5) is closed, and one minute later (SW-1) is closed and the polarizing voltage set by adjustment of the (4K) potentiometer. With (SW-6) open and (SW-4) set to desired sensitivity, the (20K zero adj.) potentiometer is so set that closure of zero test (SW-2) or (SW-3) produces minimum deflection of the (0-10V) output meter. Full-scale sensitivity is equal to 10V / feedback resistance selected by (SW-4). This circuit has worked satisfactorily with feedback resistance as high as 10^11 ohms.

Results

Control Records

An Rs, RS, or rS complex was present in myocardial electrocardiograms whenever the lead-point lay in the outer 9 mm. of the left-ventricular wall (estimated to be about two-thirds of its thickness in our dogs). There was a wide variability of RS-wave configurations (fig. 3), but Q waves preceding R waves were very rare and small. At greater depths than 10 to 12 mm., QS patterns were almost invariably found. Absolute values for the amplified and recorded oxygen-reduction currents ranged from 0.01 to 0.1 microamperes. They were unrelated to the depths of electrode insertion, and were similar to what we previously described for galvanometric determinations. Muscle temperatures in exposed hearts gradually fell 1 to 2 C. below left-ventricular blood temperature. The T wave became negative in the outer layers of the wall, and of small amplitude in the inner
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layers. Muscle-contraction variations resembled those previously described.1 2

Regional Ischemia

Central Zones

Within a few seconds of coronary occlusion, net RS-T segment elevation appeared in the myocardial electrocardiogram, and S-wave amplitude diminished (fig. 4). R-wave amplitude then increased, but a slight decrease usually preceded this. The first measurable changes in electrical activity were sometimes seen as early as the onset of muscle-contraction failure (late systolic bulge) and, not infrequently, preceded any fall of local oxygen. The rapidity and severity of myocardial electrocardiographic and oxygen changes were independent of the depth of electrode insertion, except that electrodes in the deeper layers showed little or no measurable abnormality of the R wave, if one were present. Decreased S-wave amplitude occurred at all depths. When occlusions were maintained, small Q waves not infrequently developed within 60 seconds, but since they were sometimes delayed as much as 30 to 60 minutes, they were not useful indices of early ischemic change. The order of appearance of the first measurable myocardial electrocardiographic and oxygen abnormalities after 25 seconds of coronary occlusion is shown in figure 5 (upper portion). After release of brief (2 to 5 minutes) occlusions, myocardial electrocardiograms and oxygen began to return toward normal in two to ten seconds (fig. 5, lower portion). The electrocardiograms regained control configurations within 10 to 30 seconds: concurrently with epicardial records, if these were abnormal.

Epicardial electrocardiographic disturbance was variable. Usually there was no change for at least 10 to 30 seconds. Large dogs (>20 Kg.) were likely to show the least abnormality; not infrequently, they showed none. When epicardial electrocardiographic changes did occur, they were limited to the center of the ischemic areas, never extending beyond the limits of surface cyanosis when this could be discerned.

Border Zones

Simultaneous, continuous records from more than one area during occlusion showed that altered myocardial electrical activity was the only unequivocal abnormality at the periphery of ischemic zones. Polarographic oxygen fell early, but stabilized at comparatively high levels. Muscle-contraction abnormalities were complex, as described previously.1 3 While abnormal electrical activity demarcated the outermost limits of measurable dysfunction, distinction of the borders of ischemic areas from the centers required simultaneous comparison of relative myocardial oxygen levels, since myocardial electrocardiograms changed early, consistently, and in a qualitatively similar fashion at centers and bor-
Figure 4
Polarographic oxygen and electrocardiogram from the same electrode during coronary occlusion and release. The fall in oxygen (upward on the record) begins almost at once and is fastest between 5 and 20 seconds. Myocardial electrocardiographic changes (net RS-T segment elevation, diminished S-wave amplitude, and slightly lessened R-wave amplitude) are present within 10 seconds. Return toward a normal electrocardiographic pattern is well advanced when oxygen overshoots control values, and is largely complete by 100 seconds (oxygen beginning to return toward control).

Localized Alterations of Ventricular Electrical Behavior Without Change of Myocardial Oxygen

Localized cooling (＞0.5 °C) immediately increased the negativity of T waves in the outer third of the left-ventricular wall, without otherwise changing the electrocardiogram. Local warming decreased the negativity of myocardial T waves or made them positive. The changes were limited to the outer myocardial layers immediately beneath the heated or cooled area of heart surface and to the local epicardial electrocardiogram, which re-

landers. Profound falls of oxygen occasionally occurred at electrodes considered to be well outside ischemic areas, but the electrocardiograms recorded from such electrodes provided decisive evidence of artifact. Net RS-T elevation due to local trauma appeared much sooner than the earliest ischemic changes, the electrical abnormality diminished instead of increasing with the passage of time, and the low oxygen levels did not rise following release of the coronary occlusion.
flected them best. Myocardial oxygen and contractility were not measurably altered. Electrocardiograms from lead-points 3 to 5 mm. beneath the surface did not change when potassium chloride solutions (1 to 5 per cent) or procaine HCl solutions (25 to 50 per cent) were applied to overlying portions of the exposed ventricular epicardium. As usual, there were striking reversible changes (net RS-T elevation and shallower S waves) in the local epicardial electrocardiogram. Both agents caused transient failure of local muscle contraction, but did not alter myocardial oxygen. Direct heart-body leads from the rest of the heart were unchanged by localized temperature or drug effects.

Changes of Myocardial Oxygen Without Electrocardiographic Change

Changes of the level of myocardial oxygen—reduction current associated with spontaneous heart rate (fig. 6, left half), and blood-pressure changes induced by inhalation of pure oxygen (fig. 6, right half) had little or no effect on the myocardial electrocardiogram recorded from the same electrode. This was also true of hypoxia (15 to 50 per cent fall of myocardial oxygen) and asphyxia (prior to the development of arrhythmias). Large increases or decreases of the oxygen-reduction currents recorded from nonischemic hearts were often associated with no electrocardiographic change at all. When changes did occur, their amplitude rarely exceeded 10 per cent of the total QRS complex.

D.C.-Amplifier Analysis of Myocardial Electrocardiographic Changes

The net RS-T elevation immediately consequent on insertion of an intramyocardial electrode was found to be the result of a large, downward, baseline shift and a smaller, upward, RS-T segment shift. The first ischemic myocardial electrocardiographic change was baseline depression at centers and borders. With short occlusions, this was often the only change, except for QRS-amplitude alteration (fig. 7). The degree of the baseline depression exceeded any subsequent RS-T elevation for the first 60 to 180 seconds of ischemia (fig. 8). The net RS-T segment changes produced by levarterenol in nonischemic, ischemic, or hypoxic heart muscle were found to consist of a negative RS-T segment shift frequently combined with elevation of the baseline. These changes were much better seen in epicardial heart-body leads than in myocardial leads. We sometimes recorded such changes in the outer layers of the wall, but have failed to find them in the deeper layers.

Discussion

No other combined study of myocardial contractility, electrical activity, and oxygenation is known to us. For myocardial electrocardiograms in nonischemic dog hearts, Prinzmetal et al. reported in 1953 that R waves were present for not more than a few millimeters beneath the ventricular surface. In subsequent reports, the data of this group differ less from the findings of others as has been summarized elsewhere. There is general agreement that
significant Q waves are not found in the outer third to half of the normal canine left ventricular wall, and that R waves are absent in the inner third. We have found greater variability of R-wave amplitude at different sites and levels of electrode insertion than has been generally reported, irrespective of the variability that is introduced by the nature of the contact between the heart and the body. For studies concerned only with changes in myocardial function, the wide variability of control behavior at different sites causes no difficulty. As in previous work, we have not attempted to interpret absolute values.

Studies of ischemic hearts by other groups have been limited almost completely to large ischemic areas. Kennamer et al. reported that coronary occlusion produced less net RS-T elevation in the inner than in the outer layers of the left ventricle. Conrad et al. found that R waves frequently disappeared in the deeper layers of the wall, and attributed this to a change of electrical activity of ischemic origin. We have not been able to confirm these two sets of observations for small or medium-sized ischemic areas. The myocardial electrocardiographic studies of Rakita et al., in general agreement with ours, have been discussed elsewhere. Durrer's group studied ischemic areas massive enough to show early, extensive, epicardial electrocardiographic abnormality and found net RS-T segment elevation greatest in the outer myocardial layers soon after coronary occlusion, but later greatest in the subendocardial layers. They recorded RS-T segment depression in the ventricular cavity.
opposite the endocardial surface of the ischemic area, but not at the borders of such areas. The extent of exposure of the heart was not specified. The form of the ischemic QRS disturbances in direct heart-body leads from ventricular surface or wall resembled those we have described, but the much greater size of the ischemic areas studied makes difficult a comparison of these studies with ours. So far, we have found no discrepant electrocardiographic reports that cannot be explained by differences in size of area studied, or by variations in the nature of the heart-body contact areas for open-chest preparations. No other group has reported D.C.-amplifier intramyocardial electrocardiographic data. This study shows them to be useful as an intermittent analytic procedure; but, so far, myocardial D.C. electrocardiograms have provided no information that epicardial D.C.-amplifier records, in retrospect, could not have provided.

Husni and Simeon reported that following coronary occlusion, myocardial temperature fell contemporaneously with an early profound fall of myocardial oxygen. They used small-caliber oxygen electrodes and an undescribed amplification system. The temperature findings are not discrepant with our own observation that no fall occurs for 15 to 30 seconds in medium-sized ischemic areas, since in exposed hearts, cooling would be faster for larger areas. Myocardial pH declined, as others have noted. Reynolds et al. after coronary ligation in semiclosed-chest dogs, noted (as we had) that the direction of ischemic T-wave abnormality was opposite to what could be accounted for by the unchanged or lower local temperatures. They demonstrated accelerated recovery of excitability (shortened effective refractory period) soon after ligation. This could account for local T-wave positivity.

In any study of oxygen-reduction currents,
Comparison of RS-T segment and baseline deviation in myocardial electrocardiograms following coronary occlusion: 4 dogs and 8 ischemia episodes. Control baseline and RS-T segment levels are taken at zero for all electrodes. See text and compare with epicardial electrocardiographic D.C. response, illustrated elsewhere.† Dog no. 177 showed electrical alternans of the RS-T segment during the third minute of one ischemic period. It is necessary to bear in mind that some interaction of polarographic information and myocardial electrocardiographic information is unavoidable, owing to the high capacitance of the platinum cathode, which introduces modulation currents into the oxygen-reduction-current record as a result of alternating potentials in the surrounding tissues. *Just after insertion of an electrode, when a wide monophasic electrocardiogram is produced, it is possible to misinterpret distorted records of this sort as reflecting myocardial contraction.

The oxygen record by the electrocardiogram, the measurement of the oxygen-reduction current necessarily involves shunting of the electrode, producing a reduced electrocardiographic time constant. The circuit values used are a compromise between conflicting requirements. The speed of response of the oxygen preamplifier with filter (time constant about 0.35 second) is sufficiently slow to remove most of the electrocardiographic modulation, while still permitting the rapid changes in myocardial oxygen with coronary occlusion or release to be followed satisfactorily. Very rapid changes in the myocardial oxygen-reduction currents, such as differences during a cardiac cycle, cannot be followed because of the electrical activity of the myocardium and the limited frequency response of the amplification system which is necessitated by this activity. Possibly, if a reference electrode could be so located relative to the exploring electrode that both would be subject to the same potential variations, phasic changes of oxygen could be followed. The 1.2-megohm resistor at the input of the oxygen-reduction current preamplifier reduces shunting of the electrode capacitance sufficiently to permit simultaneous electrocardiographic recording at a time constant of about 0.6 second via a separate preamplifier coupled by a capacitor to the same electrode, but at the same time, it holds the mean potential of the electrode close to 0.6 volt, with respect to the reference electrode. An increase in the decoupling resistor would have increased the electrocardiographic time constant, but permitted too great a change in electrode polarization voltage with changes in oxygen-reduction currents.

Each of the three basic indices of local myocardial function—myocardial electrocardiogram, polarographic oxygen, and cinemographic muscle-motion records—provides unique information, can show changes when the others do not, and may be essential for interpreting the changes they do show. No single index suffices for studying the consequences of coronary occlusions, even under
stable systemic circulatory conditions. Myocardial electrocardiograms are indispensable for demarcating the extent of ischemic areas, for determining the earliest changes of electrical activity, and for excluding changes outside the ischemic zone. Continuous oxygen-reduction current records prevent confusion of local traumatic artifacts with early myocardial ischemic changes in the electrocardiogram. The initial rate of fall and the relative level of the oxygen-current plateau are reflections of residual or collateral circulation. Motion-picture records of ischemic situations provide visual estimates of contractility and vein color changes, as well as material for more precise analysis from any segment of the experimental field. Muscle contraction is the last abnormality of function to be restored to normal with release of occlusion, and the manner in which it recovers from ischemia differs strikingly from its response to levarterenol under both ischemic and nonischemic conditions. These studies reveal certain limitations of epicardial electrocardiograms for the study of exposed hearts. The absence of epicardial heart-body lead changes is no guarantee that profound disorders of tissue electrical activity, oxygenation, or contractility are absent in the heart wall beneath. Only with massive localized ischemia can one expect the epicardial electrocardiogram to reflect the severity of physiological disturbance. Even then, its use as an isolated index may lead to underestimation of the extent of any ischemic area. Epicardial heart-body leads, however, must be retained as one of the essential indices of experimental ischemic dysfunction for at least two reasons. Provided that the occluded coronary vessel is of moderate size, the "sweep" technique permits comparison of baseline and RS-T segment levels in ischemic and control muscle over long periods of observation. This cannot be done with silver intramyocardial electrodes because of electrode drift. The myocardial effects of small doses of levarterenol and other physiological catechol amines are best seen in epicardial heart-body leads, although superficially placed myocardial lead-points can provide similar information.

Summary
A new technique for simultaneous amplification and recording of intramyocardial oxygen-reduction currents and electrocardiographic voltages from the tips of platinum oxygen electrodes was combined with cinematographic muscle contraction records from exposed dog hearts. The picture of localized ischemia produced by occlusion of medium-sized coronary arterial branches was compared, under stable systemic circulatory conditions, with the changes of myocardial oxygenation, electrical activity, and contractility, separately or together. Myocardial electrocardiographic abnormality appeared as early as disturbances of local oxygen and contraction at the centers of ischemic areas; at the borders, only the myocardial electrocardiogram was unequivocally abnormal. The epicardial electrocardiogram could be normal despite severe, acute disturbance of electrical activity in the underlying myocardium, and was not useful for the study of small ischemic areas, the onset of ischemia, or the borders of any ischemic area. No single index of myocardial function was dependable for following the course and estimating the extent of regional ischemic dysfunction, or for distinguishing it from traumatic or nonischemic myocardial disturbances. The most complete description of the sequence of ischemic events was derived from the analysis of changes in local myocardial electrical activity. For this, however, it was necessary to interpret and compare direct heart-body electrocardiograms from myocardial and epicardial sites inside and outside an ischemic area, with attention to simultaneous records of myocardial oxygen and local contraction. Such a combination of indices is considered essential for adequate description and differentiation of any localized myocardial change in a working, blood-perfused heart.

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References


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