Effects of coronary occlusion on cardiac and body surface PQRST isoarea maps of dogs with abnormal activation simulating left bundle branch block

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ABSTRACT The possibility of detecting myocardial infarction in the presence of left bundle branch block by analysis of cardiac and body surface PQRST isoarea maps was studied in nine open-chest and six closed-chest dogs. Recordings were taken during supraventricular drive or right atrial plus right ventricular pacing in control periods and at intervals for up to 10 hr after left anterior descending coronary artery occlusion. Right ventricular pacing was used to simulate left bundle branch block. Myocardial infarction was documented with triphenyl tetrazolium staining. The PQRST areas during supraventricular drive and right atrial plus right ventricular pacing were highly correlated to each other both before and after coronary occlusion. The PQRST isoarea maps after coronary occlusion showed a strong pole overlying the ischemic area on the cardiac surface in open-chest animals and over the left anterior thorax in closed-chest animals. The PQRST pole was positive during the first 1 to 2 hr of occlusion and became negative after several hours. The findings demonstrate that localized abnormalities due to ischemia and infarction are manifest in body and cardiac surface PQRST isoarea maps of both supraventricular complexes and right ventricular paced complexes. The findings suggest that PQRST isoarea maps may aid in identification and localization of ischemic or infarcted myocardium in the setting of abnormal activation such as left bundle branch block.


Abnormalities of ventricular repolarization should be manifest in PQRST area distributions independent of ventricular activation sequence. The concept that the PQRST deflection area is independent of activation sequence and is a measure of inhomogeneity of ventricular repolarization was first introduced by Wilson et al. in 1934. The theoretical basis for the concept has been established and there is considerable experimental evidence to support it. In early clinical studies, the failure of PQRST areas to be independent of activation sequence could have been due in part to variations in cycle length or measurement error. In more recent studies on experimental animals, distributions of body surface PQRST areas for different activation sequences have been shown to be more similar than the distributions of QRS or ST-T areas. The small differences in measurements of PQRST for different activation sequences are probably due to electrotonic modulation of repolarization properties by activation sequence.

The clinical usefulness of PQRST isoarea maps has been demonstrated for a number of situations. However, the utility of PQRST isoarea maps for the
diagnosis of myocardial infarction has not been fully evaluated.\textsuperscript{17, 18} Myocardial infarction is associated with localized abnormalities of activation and repolarization and the latter abnormalities should be manifest in PQRST isoaREA maps regardless of the activation sequence. The purpose of this study was to examine the effects of coronary occlusion on cardiac and body surface PQRST isoaREA maps during supraventricular drive and right ventricular pacing. The results indicate that localized abnormalities of ischemia can be detected in PQRST isoaREA maps recorded during ventricular as well as supraventricular drives and suggest that PQRST isoaREA maps may be useful in the diagnosis of myocardial infarction in the setting of left bundle branch block. These findings are in agreement with a recent preliminary report on the use of PQRST mapping in the diagnosis of old myocardial infarction in patients with abnormal activation sequences.\textsuperscript{18}

**Methods**

Fifteen adult mongrel dogs weighing 15 to 28 kg were anesthetized with intravenous pentobarbital (30 mg/kg). A slow intravenous infusion (300 mg in 500 ml of saline) as well as additional bolus injections of pentobarbital were given as needed to maintain deep anesthesia. The trachea was cannulated and the animals were ventilated with room air and supplemental oxygen with a volume pump respirator. Arterial blood gases and pH were monitored and kept within the normal range. Arterial pressure was continuously monitored.

In nine of 15 dogs, the heart was exposed by a midsternal thoracotomy and suspended in a pericardial cradle. The sinus node was crushed and bipolar stimulating electrodes were attached to the right atrium and right ventricle. The heart was paced at a cycle length of 400 msec with 2 msec square-wave pulses at twice diastolic threshold voltage. The driving stimuli were applied to the atrium or simultaneously to the atrium and right ventricle to simulate left bundle branch block. Sixty-four silver wire unipolar electrodes attached to a nylon stocking that was stretched over the heart were used for recording cardiac surface maps. The open chest was covered with a plastic sheet to minimize temperature changes in the thoracic cavity. All recordings were obtained with the respirator held in end-expiration to minimize beat-to-beat variations in the electrograms. Each drive was maintained for at least 3 min before recording electrograms.

In six closed-chest dogs, bipolar pacing catheters were placed, under fluoroscopic control, into the right atrium and ventricle via the femoral vein. The right atrium and right ventricle were paced with 2 msec square-wave pulses at twice threshold voltage. The cycle length of right ventricular pacing was regulated so it was slightly less than the spontaneous sinus cycle length. One hundred ninety-two stainless steel needle electrodes were placed subcutaneously for body surface mapping. Sixteen columns were uniformly spaced around the thoracic circumference and the 12 electrodes in each column were uniformly spaced between the levels of the upper abdomen and cervicothoracic junction. Under fluoroscopic control, a modified Judkins left coronary catheter was introduced through the left carotid artery into the left coronary artery and a No. 2F Fogarty catheter with an inflatable balloon on its tip was inserted into the left anterior descending artery through the guiding catheter.\textsuperscript{19} The balloon was placed just distal to the bifurcation of the first diagonal branch of the left anterior descending coronary artery. All recordings were obtained with the respirator held in end-expiration to minimize beat-to-beat variations in the electrocardiograms.

**Experimental protocol**

*Open-chest animals.* Data for control cardiac surface maps were recorded during right atrial pacing and during simultaneous right atrial and right ventricular pacing. The left anterior descending coronary artery was then permanently ligated. Antiarrhythmic agents were not administered. Electrograms were recorded during right atrial pacing and during simultaneous pacing from the right atrium and right ventricle 10 min, 30 min, and hourly for 4 to 6 hr after the coronary ligation. Two of nine dogs had ventricular fibrillation and died soon after coronary occlusion. Data from these two animals were not analyzed.

*Closed-chest animals.* Data for control body surface maps were recorded during spontaneous sinus rhythm and during simultaneous right atrial and right ventricular pacing before insertion of the Fogarty catheter into the left anterior descending artery. After placement, the Fogarty catheter balloon was gradually inflated with diluted contrast material until cylindrical deformity of the balloon was observed under fluoroscopy. Complete occlusion of the left anterior descending artery distal to the bifurcation of the first diagonal branch after inflation of the balloon was confirmed by injection of contrast material into the left coronary artery through the guiding catheter. Lidocaine was given by continuous intravenous infusion beginning 30 min before coronary occlusion. Electrocardiograms were recorded during spontaneous sinus rhythm and during simultaneous pacing of the right atrium and right ventricle 10 min, 30 min, and hourly for 8 to 10 hr after coronary occlusion.

**Triphenyl tetrazolium chloride (TTC) staining.** In seven open-chest and six closed-chest dogs the hearts were excised after the experiments and rinsed in saline. The ventricles were sliced parallel to the atrioventricular groove into 1 cm thick slices from apex to base. Each slice was incubated in a 1% solution of TTC buffered in 0.2M Tris buffer to pH 7.8 at 37°C for 5 min, then fixed in 10% buffered formalin and later photographed.\textsuperscript{19}

**Data acquisition and analysis.** Each cardiac or body surface electrode was referenced to a Wilson central terminal. Cardiac surface electrograms and body surface electrocardiograms were recorded simultaneously with a sampling interval of 1 msec. The characteristics of these systems have been previously described.\textsuperscript{13, 20} Data from simultaneously recorded complexes were digitized, gain and baseline were adjusted, and the data were stored on digital magnetic tape. A root-mean-square (rms) voltage vs time curve based on all leads was plotted to help identify the beginning and end of the QRS and end of T deflections that were manually selected from this curve. QRS, ST-T, and PQRST deflection areas were calculated by integrating each lead over the appropriate interval and were expressed in millivolts per millisecond. The QRS, ST-T, and PQRST isoaREA contours were separated by 100 mV·msec for cardiac surface maps and 10 mV·msec for body surface maps. During ventricular pacing, the atria were paced simultaneously with the ventricles so that P waves and QRS complexes were superimposed. During atrial stimulation, P wave areas were added to those of the QRS. By adding P wave areas to the QRS during atrial stimulation and simultaneously stimulating the atria during ventricular stimulation, P wave areas were common to records during the two activation sequences.

During body surface mapping, the stimulating pulse during right atrial pacing often occurred during the preceding T wave because of the shorter cycle length in closed-chest animals in which the sinus node was not crushed. This made it difficult to
calculate the PQRST area. Therefore, PQRST isoarea maps taken during spontaneous sinus rhythm were used in analysis of body surface maps. There were only small differences between paced and unpaced cycle lengths.

PQRST isoarea maps were visually inspected for changes, and correlation coefficients and rms differences were calculated to quantify similarities between QRS, ST-T, and PQRST areas of the two activation sequences during each state. The mean ± 2 SDs of control cardiac surface PQRST areas recorded at each electrode site during atrial drive was calculated (n = 9). The mean ± 2 SDs of control body surface PQRST areas recorded at each electrode site during sinus rhythm was also calculated (n = 6). PQRST area values within 2 SDs of mean control values were regarded as within the normal range. PQRST area difference maps (occlusion-control) were constructed to show those electrode sites at which PQRST area values were above and below the normal range.

Results

The presence of myocardial ischemia after coronary occlusion was confirmed by the presence of QRS and ST-T changes in the cardiac surface electrograms or body surface electrocardiograms. In addition, after the experiments, sharply delineated areas of myocardial infarction were identified by lack of staining with TTC in all animals. Infarction involved the apical anterior one-third to three-quarters of the left ventricle and included portions of the anterior papillary muscle.

Cardiac surface maps. To determine the degree of similarity between maps taken during right atrial and right atrial plus right ventricular pacing, correlation coefficients and rms differences in cardiac surface QRS, ST-T, and PQRST areas for these two drives were calculated. Correlation coefficients for PQRST areas of right atrial and right atrial plus right ventricular drive were higher than for QRS and ST-T areas (the range of values for seven experiments was \( r = .93 \) to .96 for PQRST compared with .55 to .64 for QRS and .51 to .77 for ST-T). The rms differences of PQRST areas of right atrial and right atrial plus right ventricular drive were smaller than those for QRS and ST-T areas (the range of values for seven experiments was \( \text{rms} = 91 \) to 157 mV-msec for PQRST compared with 517 to 686 mV-msec for QRS and 542 to 656 mV-msec for ST-T).

Cardiac surface PQRST isoarea maps computed from data recorded from one dog during right atrial pacing and right atrial plus right ventricular pacing are shown in figure 1. The maps were recorded during the control period, 10 min after coronary occlusion, and 4 hr after coronary occlusion. Only the anterior view of the maps is illustrated because changes on the posterior surface after coronary occlusion were small. The PQRST isoarea maps during right atrial and right ventricular pacing were very similar to each other both before and after coronary occlusion. Ten minutes after coronary occlusion both PQRST isoarea maps had a maximum in the anteroapical region that corresponded to the distribution of the occluded left anterior descending artery. Four hours after coronary occlusion, both PQRST isoarea maps had a minimum in the anteroapical region. The intensity of the minimum at 4 hr was less than that of the maximum at 10 min but the poles had approximately the same distribution. The QRS and ST-T isoarea maps of ventricular paced complexes and right atrial paced complexes are not illustrated, but as would be expected, differed greatly from each other both before and after coronary occlusion.
Ddifference Map

10 min

4 hrs

> M+2SD

< M-2SD

**Figure 2.** Location of electrode sites at which PQRST area values were beyond 2 SDs of mean control values. Data were obtained from the same dog as in figure 1 during right ventricular pacing 10 min and 4 hr after coronary occlusion. Cardiac areas with abnormally high PQRST values and abnormally low PQRST values are indicated by hatched and shaded areas, respectively.

Figure 2 shows the cardiac locations where PQRST areas recorded 10 min after coronary occlusion and 4 hr after coronary occlusion were beyond 2 SDs of mean control values. The map is from the same animal as in figure 1. Ten minutes after coronary occlusion, PQRST areas in the anteroapical region were significantly greater than control values, and 4 hr after coronary occlusion, PQRST areas in this region were significantly less than control values.

Average PQRST isoarea maps constructed from data recorded from seven animals during the control period and 10 min and 4 hr after coronary occlusion during simultaneous right atrial and right ventricular pacing are shown in figure 3. Because there was a high correlation and low rms error between maps during both activation sequences, only data averaged from electrograms recorded during simultaneous right atrial and right ventricular drive are presented. As in the maps from individual animals (figure 1), average control period PQRST areas on the anterior cardiac surface were positive and of low amplitude. Ten minutes after coronary occlusion, the positivity increased and there was a distinct maximum pole in the anteroapical region. Four hours after coronary occlusion, negative PQRST areas were distributed over a wide region of the anterior cardiac surface and a distinct minimum pole was located near the apex.

**Body surface PQRST isoarea maps.** Correlation coefficients for body surface PQRST areas of sinus complexes and right ventricular paced complexes before and after coronary occlusion were higher than correlation coefficients for QRS and ST-T areas (range of values for six experiments was $r = .91$ to .99 for PQRST compared with .61 to .84 for QRS and .11 to .57 for ST-T). The rms differences for body surface PQRST areas of sinus complexes and right ventricular paced complexes before and after coronary occlusion were smaller than those for QRS and ST-T areas (range of values for six experiments was $\text{rms} = 12$ to 15 mV·msec for PQRST compared with 57 to 65 mV·msec for QRS and 54 to 60 mV·msec for ST-T). Thus, there was close correlation between PQRST areas during right ventricular drive and supraventricular drive before and after coronary occlusion. The small average rms differences for PQRST areas during right ventricular compared with supraventricular drive is evidence for small quantitative differences compared with QRS and ST-T areas. The data demonstrate that PQRST map characteristics before and after coronary occlusion are relatively independent of drive site.

One dog's body surface PQRST isoarea maps computed from data recorded during spontaneous sinus rhythm and right ventricular pacing before and after coronary occlusion are shown in figure 4. There were only minor differences in PQRST isoarea maps during the two activation sequences before or after coronary occlusion. During the control period, there was a maximum pole over the anterior chest and a diffuse negative area over the upper chest and back during both sinus rhythm and right ventricular pacing. Ten minutes after coronary occlusion, PQRST area values over the left anterior chest increased markedly, while values over the right lateral chest and back decreased slightly. Ten hours after coronary occlusion, a mini-
coronary occlusion. The map characteristics shown in panel A are similar to those described above. The PQRST isoelectricity map during the control period showed a positive pole over the left anterior chest, and a diffuse negative area over the upper chest and the back. Ten minutes after coronary occlusion, the map showed greater positivity over the left anterior chest and more negative values over the right anterior chest and back. One hour after coronary occlusion, the amplitude of the positive region decreased. Four hours after coronary occlusion, PQRST values over the left anterior chest decreased further and there was some negativity over the anterior chest, and 8 hr after coronary occlusion, there was a minimum over the left anterior chest. Sites at which PQRST areas were beyond two standard deviations of mean control values are shown in panel B. Ten minutes after coronary occlusion, there was a large area over the anterior chest where the PQRST areas were greater than 2 SDs of mean control values, and a large area over the right anterior chest and back where PQRST areas were less than 2 SDs of mean control values. One hour after coronary occlusion, the area over the anterior chest with values above 2 SDs of control values was smaller. Four and eight hours after coronary occlusion, PQRST values over the anterior chest area were less than 2 SDs of control values and values over the right upper chest and back were greater than 2 SDs of control values.

Average PQRST isoelectricity maps constructed from data recorded during right ventricular pacing before and after coronary occlusion are shown in figure 6. The average maps are similar to the maps from individual animals (figures 4 and 5). Maps recorded 10 min after coronary occlusion have a maximum over the left anterior chest and a negative area over the right anterior chest. Maps recorded 8 hr after coronary occlusion have a minimum over the anterior chest and an area of positivity over the lower anterior chest and back. Average maps constructed from data recorded during sinus rhythm were very similar to these maps.

**Discussion**

It is difficult to diagnose anterior myocardial infarction in the presence of left bundle branch block by 12-lead electrocardiography. Various electrocardiographic criteria for the diagnosis of anterior myocardial infarction in the presence of left bundle branch block have been proposed, such as initial notching of the R wave in leads I, aVL, and V5-6, notching of the upstroke of the S wave in leads V2-4, RS configuration in V5-6, and abnormal Q waves and ST elevation in I, aVL, and the precordial leads. However, the sensi-
FIGURE 4. Body surface PQRST isoarea maps of sinus and right ventricular paced complexes during the control period and 10 min and 10 hr after coronary occlusion. Isoarea contours are separated by 10 mV·msec. Electrode locations and area polarities are indicated by plus and minus signs. RV pacing = right ventricular pacing.

The correlation coefficients for PQRST areas recorded during the different activation sequences were much greater than those for QRS or ST-T areas both before and after coronary occlusion. Since the correlation coefficient may be high even when the error about the regression curve is high, the rms difference in the area values between maps, which is a measure of the error about the regression curve, was also calculated. The rms difference in PQRST areas was less than the differences for QRS and ST-T areas. Thus, the high correlation coefficients and the small rms differences in the PQRST areas during the two activation sequences both before and after coronary occlusion indicate greater similarity between PQRST areas as compared with QRS and ST-T areas.

Cardiac surface maps recorded before coronary occlusion showed low-amplitude, positive PQRST areas over the entire cardiac surface. The uniformity in PQRST area values over the cardiac surface is consistent with ventricular recovery properties being relatively homogeneous in the normal heart. Body surface maps taken before coronary occlusion showed a positive PQRST area over the anterior and lower chest, with a maximum located over the left anterior chest. Negative areas were located over the upper chest and back. These distributions were similar during supraventricular and right ventricular drive. The distributions of positive and negative areas in PQRST isoarea body surface maps are in agreement with previous reports.\(^\text{13, 14}\)
FIGURE 5. Body surface PQRST isoarea maps (A) and difference maps (B) of right ventricular paced complexes during the control period and 10 min, 1 hr, 4 hr, and 8 hr after coronary occlusion. Isoarea contours are separated by 10 mV·msec. On difference maps, PQRST values above and below 2 SDs of the mean are indicated by hatched and shaded areas, respectively. RV pacing = right ventricular pacing.
In the first 1 to 2 hr after coronary occlusion, PQRST area values increased and exceeded the upper limit of the normal range over the anteroapical site of the left ventricle in cardiac surface maps or the left anterior chest in body surface maps, regardless of activation sequence. Abnormally high PQRST areas corresponded to increased QRS amplitude and ST segment elevation in individual cardiac surface electrograms and body surface electrocardiograms in the acute phase of ischemia. Over the next several hours, PQRST area values over the anteroapical site or the anterior chest gradually decreased below the lower limit of the normal range. Abnormally low PQRST areas corresponded to T wave inversion and the evolution of Q waves after an hour of coronary occlusion. On the cardiac surface maps, PQRST abnormalities occurred primarily in the anteroapical region corresponding to the location of the infarct. On body surface maps immediately after coronary occlusion, PQRST area values over the back decreased as PQRST area values over the left anterior chest increased. After several hours of coronary occlusion, PQRST area values over the right anterior chest and back increased, while PQRST area values over the left anterior chest decreased.

Changes in PQRST areas during ischemia could be due to changes in the QRS due to loss of excitable myocardium, ST-T changes due to shifts in resting membrane potential of injured myocardial cells, or changes in action potential duration and amplitude. Because we did not use direct-current recordings, the actual shift in voltage potential during the cardiac cycle could not be determined. Rather, the baseline was set on the TP segment for supraventricular complexes and just before the stimulating pulse for ventricular complexes. Setting the baseline on the TP segment could have resulted in greater apparent ST elevation in the acute phases of ischemia and could have contributed to the positivity in PQRST areas seen in the first hour of coronary occlusion.

The experiments in this study were based on the premise that the repolarization abnormalities associated with ischemia or infarction would be reflected as local changes in PQRST isoarea maps independent of activation sequence. The ventricular gradient concept, as proposed by Wilson et al. and later mathematically analyzed in greater detail, established that the PQRST area is independent of activation sequence and reflects inhomogeneity of action potential area. Lux et al. reported that the variability in the PQRST area for different activation sequences was consistently less than the variability in either the QRS or the ST-T area. Burgess et al. also found evidence that PQRST areas are largely independent of drive site. Other studies have reported differences in PQRST areas ranging from small to large with different activation sequences. The electrotonic modulation of repolarization that occurs with varied activation sequences has been reported as one of the potential causes for these differences. Thus, PQRST area is largely, but not exclusively, independent of ventricular activation sequence. In addition, PQRST area distribution is related to the magnitude and distribution of repolarization abnormalities. Burgess et al. studied the relationship between PQRST areas from cardiac surface maps and the size and severity of alteration of recovery properties induced by local warming. In that study, the PQRST isoarea map patterns were related closely to...
the size and severity of thermally induced changes in recovery properties. Abildskov et al.\textsuperscript{10} found that PQRST areas were highly correlated with changes in refractory period over multiple activation sequences. The present study demonstrated that localized abnormalities due to ischemia and/or myocardial infarction were also relatively independent of activation sequence and were evident in PQRST isoarea maps of both supraventricular complexes and paced complexes simulating left bundle branch block.

There are some limitations of the present study. First, right ventricular pacing only simulated left bundle branch block and produced no real conduction abnormalities. However, body surface electrocardiograms showed changes typical of left bundle branch block. These included abnormally wide QRS duration for dogs,\textsuperscript{15} QS or rS patterns in the right precordial leads, and rsR' patterns or monophasic R waves with notches or slurs in the left precordial leads. Second, left bundle branch block is commonly associated with conditions other than or in addition to myocardial infarction, such as valvular disease, ventricular hypertrophy, cardiomyopathy, and ischemic heart disease.\textsuperscript{33} Since, in the present study, left bundle branch block was simulated and not associated with other abnormalities, the results are not directly applicable to the clinical setting. Third, repolarization properties are affected by many factors, including drugs, electrolytes, and neural activity. Since alterations in the PQRST distribution are caused by differences in repolarization properties, factors that produce global changes in repolarization may not alter the PQRST distribution. On the other hand, factors that produce regional changes in repolarization, such as neural activation, should also change the PQRST distribution. Thus, evidence of localized abnormalities of repolarization in PQRST distributions may not be specific for ischemia or infarction. However, this is also true of ST-T abnormalities in 12-lead electrocardiograms in patients with normal conduction. As with any diagnostic test, abnormalities in PQRST isoarea maps will need to be interpreted in terms of the clinical setting. Further clinical studies will be required to establish the sensitivity and specificity of this method.

The low variability of PQRST areas over multiple activation sequences has been established in normal canine myocardium. Although conduction velocity is a major determinant of electrotonic modulation of repolarization by activation sequence,\textsuperscript{34} the present study indicates that large electrophysiologic abnormalities due to ischemia are apparent in PQRST maps in spite of possible enhanced electrotonic effects of activation sequence on repolarization. These findings are consistent with a recent preliminary report by Ikeda et al.\textsuperscript{18} in which localized body surface PQRST isoarea map abnormalities were found in patients with prior myocardial infarction and abnormal ventricular activation.

In conclusion, this study demonstrates that PQRST isoarea maps show regional abnormalities associated with myocardial infarction during supraventricular drive and abnormal ventricular activation simulating left bundle branch block. This study suggests the feasibility of the use of PQRST isoarea maps to diagnose anterior myocardial infarction in the setting of left bundle branch block.

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