Surface Reflections of Cardiac Excitation and the Assessment of Infarct Volume in Dogs

A Comparison of Methods

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SUMMARY Ventricular depolarization was analyzed in intact dogs by simultaneously recording body surface potential maps, McFee axial vectorcardiograms, and a 5 x 4 lead precordial grid of QRS complexes. The purpose of this study was to compare the effectiveness of subtraction approaches, using the simultaneously acquired data. The totally closed chest approach avoided the problem of volume conductor alteration by thoracotomy. Infarct volume was calculated morphologically from measurements of serial ventricular sections. The maximal correlation with anatomic infarct size using the precordial QRS grid approach was 0.51, using cumulative difference data between 1 and 38 msec when the postinfarction grid was subtracted from the preinfarction grid. A correlation coefficient of 0.80 was achieved using the numerically integrated data between 1 and 31 msec from the vectorcardiogram, and the body surface potential map achieved a correlation coefficient above 0.88 when the electrical difference of msec 16 was used. These data suggest that estimates of infarct size from selected surface reflections of the activation process are feasible if some sort of preinfarction control data are available. Caution must be exercised to avoid inclusion of electrical effects late in the activation process which contain contamination by highly variable alterations in the excitation sequence due to delayed conduction or alteration in conduction pathway in or near the infarct zone.

DURING the past few years, a great deal has been written about the utilization of portions of the surface electrocardiogram to predict the size of myocardial infarction or to follow the sequels of experimental and therapeutic interventions.1-7 This study is a report on intact dogs in which simultaneous data were accumulated in the form of 142-lead body surface potential maps,8 McFee axial vectorcardiograms,9 and a 5 x 4 matrix grid of precordial QRS complexes before and after closed chest myocardial infarctions. Predictions of infarct size based upon subtraction techniques applied to each of these three sets of data were correlated with anatomic delineation of the volume of the infarctions. The purpose of the study was to compare the relative effectiveness of the three techniques, and to explore further and state the limitations of such approaches.

Methods

Ten dogs, representing a 76% survival rate of our infarction technique (see below), were used for the study. The dogs, all weighing between 20 and 30 kg, were anesthetized with sodium pentobarbital, 30 mg/kg, iv. After intubation, controlled respiration was established by means of a Harvard pump ventilator, using room air with tidal volumes calculated by a nomogram considering the size of the dog and instrument dead space. Normal arterial blood gas values were verified at the beginning of the experiments. Body surface electrical potentials were recorded on analog magnetic tape from each of 142 body surface sites. The effective frequency response of the system was between 0.2 and 3000 Hz. The McFee axial vectorcardiographic system for dogs was used with the approximate combining coefficients applied to the surface voltages after analog-to-digital conversion. A five-column, four-row precordial grid of QRS complexes also was obtained. Digitization was accomplished at a rate of 1000 samples/sec. The fiducial mark for digitizing, averaging, and time alignment of averaged data was obtained from a filtered, shaped, simultaneous control lead II as previously described.8 The onset of ventricular electrical activity was programmatically determined as the first of eight successive increases in the root mean square (RMS) value of the total surface (142-lead) electrocardiogram. The level of the signal for each electrode site during the quiescent period immediately prior to the onset of the QRS complex was accepted as the zero or reference level, and all potential values were programmatically adjusted to this baseline. With the help of a PDP-9 laboratory computer, the information was displayed as (1) a precordial grid of QRS complexes (Fig. 1), (2) three orthogonal vectorcardiographic leads (Fig. 2), and (3) body surface potential maps in isometric projection form at 1-msec intervals...
throughout the period of ventricular excitation (Fig. 3). It should be noted that, in Figures 1 and 2, a third-degree linear interpolation was employed to connect the data points of the QRS complexes for purposes of illustration only. The interpolated data points were not used for numerical analysis. Such data were obtained and recorded prior to and 1 week after the induction of coronary occlusion.

At 1-msec intervals, the voltages obtained from the precordial R wave grid obtained after infarction were subtracted from the preinfarction grid (Fig. 1) and the RMS value of these differences was retained for correlation with the morphological volume of infarcted tissue. In the case of the vectorcardiogram, the absolute difference vector \( \sqrt{\Delta X^2 + \Delta Y^2 + \Delta Z^2} \) (resulting from subtraction of corresponding instants in the three orthogonal XYZ waveforms after infarction from those of the control) was compared at each instant to the anatomically determined size of the infarcted zone (Fig. 2). In the case of the surface potential data, a difference map was obtained by subtracting each 1-msec map obtained after infarction from that obtained before infarction using a point-by-point subtraction of the chest voltages recorded after infarction from the corresponding voltages recorded before infarction (Fig. 3). The RMS value of the difference map was compared with the size of the myocardial infarction demonstrated anatomically.

The myocardial infarction was induced in every instance by a completely closed-chest technique. A Sones no. 7 or no. 7.5 catheter was advanced under fluoroscopic control through the right carotid artery and positioned at the bifurcation of the circumflex and the left anterior descending branch of the left coronary artery. A coronary arteriogram was performed to confirm position and then a 0.025-inch guide wire was passed through the catheter and positioned in the left anterior descending branch distal to the origin of the first diagonal. The catheter was removed and a sterilized metallic bead was placed over the guide wire. The catheter was then replaced on the guide and positioned in the left anterior descending branch distal to the origin of the first diagonal. The catheter was removed and a sterilized metallic bead was placed over the guide wire. The catheter was then replaced on the guide and was used to advance the bead to the proper position in the left anterior descending branch, after which the guide was removed. A coronary arteriogram was again obtained using renografin 76; this advanced the bead slightly further down the artery. Constant recording of multiple lead surface voltages allowed further confirmation of the infarction. After a stable state had been attained, the dog was allowed to return to the animal care facility and recover from anesthesia.

**Figure 1** A: QRS complexes recorded from five rows separated by 3 cm extending from below the clavicle to 6 cm above the xiphoid process, and from five columns extending from the mid sternal line to the left mid-axillary line. A = before infarction; B = after infarction; while C = instant by instant A-B, or the lost potentials of the zone of infarction. Calibration: 1 mV; 50 msec.
Seven days after infarction and after the second acquisition of the electrical information from the surface, the dog was quickly killed under anesthesia and the intact heart rapidly removed. In the first of six dogs, the hearts were immediately frozen with liquid nitrogen, sliced, and prepared for histochemical staining, using 40-μm thick subsections of each measured centimeter slice. Stains were applied for lactic and succinic dehydrogenase as well as hematoxylin and eosin staining and periodic acid-Schiff staining. After it was ascertained that at 7 days postinfarction we were able to determine the extent of the infarcted zone as well without the use of the special enzyme staining, the histological determinations were not continued in the remaining four dogs. Precise 1-cm thick slices of the heart were immediately photographed and then traced on ruled paper so that total surface area for each slice was determined. The surface areas accounted for by the ventricular cavities were subtracted from the total surface area. Similarly, the planimeterized area of the myocardial infarction was obtained for each slice. From these areas, estimates of volume of myocardium and of volume of infarction were cal-

**Figure 2** Orthogonal leads x, y, and z from the McFee axial vectorcardiogram which was obtained simultaneously from the same dog whose QRS grid is depicted in Figure 5 and whose body surface difference map is depicted in Figure 7. The first column represents the control recording prior to infarction, and the second column demonstrates the anterolateral infarction (resulting from the catheter-placed bead in the anterior descending branch of the left coronary artery). Column three shows the vectorcardiographic or dipolar approximation of the lost potentials of infarction (before minus after) in the first, second, and third rows, while the absolute magnitude or Pythagorean sum of this difference is represented by the waveform in the lower right. Calibration: 1 mV; 50 msec.

**Figure 3** Before, after, and before-minus-after infarction body surface potential map at 16 msec is illustrated. The top plane represents the 1-mV level, whereas the bottom plane in each figure represents the zero level. The extreme left and right borders of the maps represent the vertebral line, while the 11th grid column is the midthoracic line. The top row of each map is below the level of the clavicle, whereas the bottom row is 3 cm below the dog's xiphoid process. The bottom map depicts the difference between the first two, and may be interpreted as showing the surface effect of normal activation of only that portion of the myocardium that now lies within the infarction zone.
FIGURE 4  Diagrammatic representation of the morphological determination of infarction size from 1-cm thick ring sections from the whole heart. Infarct zone was identified from 40-μm thick sections which were stained for dehydrogenase enzymes, photography, and planimeterization (see text).

culated by Newton's method. The percentage of infarction was calculated and was expressed as a percentage of the total heart volume (Fig. 4).

Correlations then were established between the anatomically determined relative volume of infarction and each of the estimates of electrical loss, both in terms of instantaneous values (i.e., for a given millisecond after onset of ventricular activation) and for cumulative values during the activation process.

In the case of the cumulative estimates, in order to specify the highest correlation values for serial summations, we first determined the RMS value at 1 msec and correlated this with the size of the infarct zone. Then sequential summations, millisecond by millisecond, were correlated to include, finally, data from the earliest through the latest instants of ventricular activation. This was followed by systematically truncating millisecond after millisecond from the beginning of activation, and then from both the beginning and the end, to determine an optimum time span for correlation with the anatomic estimate, e.g., to explore the possibility that perhaps better cumulative correlations existed in mid QRS.

Results

Before infarction, duration of ventricular activation was 46.6 ± 2.95 msec and after infarction was 48.3 ± 2.87. This lengthening, although not dramatic, occurred in 8 out of 10 dogs and appeared to be confined to the last one-fourth to one-half of activation.

Figure 5 demonstrates for each dog the best instantaneous correlation between the morphologically determined infarct size and the electrical estimate of infarct effect which was determined to be at 16 msec in the body surface potential difference map.

Figure 6 demonstrates the single instants of correlation from the precordial R wave difference grid, the vectorcardiogram (VCG) difference determinations, and the body surface difference maps. Note that the best correlation (r = 0.88) was found in the difference map at 16 msec, while the VCG correlated relatively well (r = 0.70) at 18 msec. The precordial grid was considerably less successful in predicting infarct size with a maximal instantaneous correlation coefficient of 0.5 at 38 msec.

As indicated in Methods, an interval scan was applied to all of the instantaneous data with the idea of achieving an optimal electrical value cumulative over time. The best cumulative correlation,
using body surface difference map data, was achieved by summation of difference RMS values from msec 1–31, \( r = 0.85 \). The optimal cumulative vectorcardiographic difference was more impressive \( r = 0.80 \) when msec 1 through 31 were summed than was any instantaneous vectorcardiographic determination. Data from the precordial grid, when summed throughout the QRS, gave their optimal correlation with the inclusive time span from msec 1 through 38, with a correlation coefficient of 0.51 (Fig. 7).

**Discussion**

**Limitations Related to Method**

Caution must be observed in interpreting these data because (1) the sample size is small, (2) the recording and data-handling techniques are highly specific, (3) each dog served as its own control, and (4) comparison was facilitated by averaging to reduce signal noise and by avoiding such interventions as opening the chest.

Consider, for example, the correlation value of 0.88 between the 16-msec RMS potentials of the difference map and the anatomic volume of infarction: for a 10-membered sample, the 95% confidence limits are 0.56 and 0.97.\(^1\) The range of 95% confidence level overlaps that for the peak cumulative VCG correlation value (0.34 to 0.90). The 95% confidence range for the peak precordial grid correlation of 0.51 is worse (−0.18 to 0.86) because it includes the possibility of no correlation. However, the millisecond by millisecond serial estimates of correlation (Figs. 6 and 7) show continuity and consistency in time, and this suggests to us that an increase in sample size will probably cause reduction in the confidence range about points very near those already observed, rather than drastic shifts of the correlation value within the present range.

Additional correlation analysis was performed, using the rank correlation coefficient of Spearman which, for a sample size of 10, should be 0.65 for the 95% confidence level or 0.79 for the 99% confidence level. The smallest values of the rank correlation coefficient obtained throughout the QRS complex and the instantaneous body surface map, vectorcardiogram, and precordial grid were 0.90, 0.90, and 0.85 for the respective cumulative body surface map, VCG, and precordial grid; no value dropped below 0.85. Thus it can be stated that there was significant concordance with anatomic volume of infarction for both the cumulative vectorcardiographic data and the instantaneous surface potential map data at the 99% level. Demonstration of
clear correlative superiority of map with regard to VCG obviously requires additional data.

Successful comparison of potentials at the 16th msec after onset of ventricular activation before and after infarction depends on careful attention to technique. Were all of the earliest activated portions of the ventricle included in the infarction, the proper fiducial mark after infarction would not be found. The sites of infarction in this study were not so placed as to be likely to have removed the original onset marker. Given comparable onsets, precise timing and digitization are necessary to assure subtraction of comparable instants after onset. Furthermore, similar results may have been obtained had the sampling interval been every 2nd millisecond instead of every millisecond, but some detail would have been lost because of loss of instantaneous peaks of correlation or because of blurring of the calculation of cumulative effect.

The intent of the study deserves emphasis: it is a testing of the hypothesis that infarct volume predicts quantitative change in surface potential. Care was taken to remove other variables. Each dog served as its own control, and the intervention of thoracotomy was proscribed. Such steps severely limit extrapolation to clinical contexts: the patient with acute myocardial infarction is not likely to have adequate preinfarction control data; the patient undergoing coronary bypass surgery cannot escape thoracotomy.

However, we are presently evaluating the limits of applicability of using the ranges of a normal population data base as the clinical counterpart to preinfarction map data.

**Comparison of Formats for Potential Recording and Display**

It appears that not only was the best average instant of correlation in the body surface difference map at 16 msec and in the vectorcardiogram at 18 msec, the best single instant of correlation for these procedures in each of the dogs was within that temporal range. The consistency of the finding is exciting, but not altogether unexpected. In considering the sequence of ventricular activation in the dog, it is within this time zone that the activation wavefront is at its maximum and is just prior to the time of explosive epicardial breakthrough. It might be expected, then, that a better approximation of the lost potentials represented by the infarction zone could be achieved by subtraction techniques applied at these instants, assuming that the normal time of excitation of the zone that later became infarcted was within that time frame. Ideally, the estimation of infarct size by subtraction techniques permits probing of the anatomic extent of the in-

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**Figure 7** The time course of the best of the cumulative sequences of correlation is shown. For example, along the abscissa at the numeral 5, the electrical estimates of infarction size represent the sums of instantaneous estimates from msec 1 through 5 for the BSM, the VCG, and the QRS grid. Note the maximal correlation with integration of msec 1 through 31 of the difference map ($r = 0.85$). This was slightly below the instantaneous correlation demonstrated at 16 msec. The VCG, however, with integration between 1 and 31 msec ($r = 0.80$), performed better compared to its best instantaneous correlation of 0.7 illustrated in Figure 6.
farct zone by the “phantom” wave of activation. Subtraction "removes" all of the wavefront outside the infarct zone. Thus, the better the correlation between the “difference” surface potential and the “difference” internal wavefront, the better the correlation to be expected between the difference potential and infarct extent. The VCG is an approximation of the dipolar content of surface potential. Because of this, and the fact that the myocardium in the immediately limited region of infarction is a geometrically simpler generator than the whole ventricular mass (more readily representable as a dipolar electrical source), the RMS values of the difference between the preinfarction and postinfarction VCG at 18 msec offered a respectable correlation of 0.70. The cumulative correlation increased to 0.80 when msec 1 through 31 were considered in total. This suggested that a succession of dipolar estimates was better than a single isolated estimate. The body surface difference map, however, performed significantly better both in terms of the correlation of an instantaneous difference map at 16 msec and the correlation of the cumulative difference maps between 1 and 31 msec. The zone of infarction is certainly not totally dipolar, is often irregular and divided, and is large enough to contain an extended curving shell or wavefront. In these instances in particular, the irregular boundaries of the infarct zone and the separation of the loci or origin of the potentials of infarction found more complete representation in the surface map potential distributions than in the vectorcardiogram. The body surface map data resulted in a higher correlation in each individual dog as well as higher mean correlation with the anatomically determined size of infarction.

Why did the VCG improve as a result of summing the volumes of the difference maps several instants in time, while the instantaneous difference map demonstrated better correlation than the summed difference map? We suspect it is related to the basic mathematical differences of the techniques of the VCG and the body surface map. In the former technique, with an ideal vectorcardiographic system, one would expect each instant throughout the three orthogonal leads to be a good estimate of the dipolar component of the wavefront in the infarct zone, and these estimates would thereby be improved by being added together. In the case of the surface difference map, the instant during which the wavefront most nearly filled the entire infarct zone should give the best surface expression of infarction. Adding other instants could only cancel portions of this estimate and would thus only lead to deterioration of correlation on either side of this “ideal” instant (Fig. 6).

The limitation of the precordial QRS grid probably is a limitation imposed by a combination of lack of orthogonality or uniqueness of information and the further constraint of a relatively small number of sampling sites.

Relationship between This Study and Clinical Observations

For practical purposes, each of these methods is limited to circumstances of sinus rhythm or excitation originating ideally from above the bifurcation of the bundle branches and without gross degrees of proximal conduction blocks, especially those involving the left bundle branch. If the sequence of the initial one-fourth to one-half of ventricular activation is drastically altered (exclusive of alterations specifically resulting from loss of muscle mass), the techniques become difficult to apply. Furthermore, as the last fourth to half of the activation sequence is approached, temporal dyssynchrony from relative delays (whether from slowed conduction, spotty transmission, or rerouting) becomes increasingly more manifest. Such mid and late alterations of the sequence of ventricular activation, although extremely helpful in making the diagnosis of myocardial infarction with surface maps,13-15 or even in suspecting subtle rearrangements of ventricular activation secondary to coronary artery disease, become distinctly not helpful in estimating precise volume of infarcted muscle.

We conclude then, that, in circumstances of endocardial to epicardial excitation with pacemaker control beginning above the bifurcation of the bundle branches, subtraction techniques applied to various forms of surface potential data can yield some correlation and, with certain techniques, very good correlation with anatomic infarct size when infarctions in this specific location are tested. Furthermore, the simpler, easier to apply vectorcardiographic system offers correlation less impressive than the surface potential difference map, but nevertheless quite good, and the ease of application is a distinct asset. We further conclude that it is desirable to enhance the vectorcardiographic estimate by summing during the first two-thirds of ventricular activation, but the surface map estimate is maximally effective at the instant just prior to epicardial breakthrough and is not improved by temporal summation.

References

Effects of a Cardiac Glycoside on Regional Function, Blood Flow, and Electrograms in Conscious Dogs with Myocardial Ischemia

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SUMMARY We studied the effects of coronary occlusion and of subsequent ouabain administration on regional myocardial function, flow, and electrograms in 14 conscious dogs. Coronary occlusion resulted in a graded loss of regional function as reflected by measurements of segment length (SL), velocity of SL shortening and myocardial "work" from the normal to severely ischemic zones, along with graded flow (radioactive microsphere technique) reductions and graded elevation of the regional S-T segment. Ouabain, 20 µg/kg, improved function in the normal zone, in which stroke shortening rose by 0.23 ± 0.07 mm (mean ± SE) and "work" rose by 30.2 ± 9.5 mm Hg·mm. In moderately ischemic segments, stroke shortening rose by 0.60 ± 0.05 mm and "work" rose by 58.1 ± 6.1 mm Hg·mm. In the majority of severely ischemic segments, stroke shortening and "work" also increased; the average effect in all severely ischemic segments was an increase in stroke shortening of 0.35 ± 0.10 mm and in "work" of 31.5 ± 9.9 mm Hg·mm. In addition, ouabain reduced S-T elevation by 0.90 ± 0.20 mV in moderately ischemic zones and by 3.14 ± 0.35 mV in severely ischemic zones, and increased flow by 28 ± 6% and 46 ± 9% in moderately and severely ischemic zones, respectively. All these changes were significant, P < 0.01. Thus, ouabain caused an improvement in perfusion of ischemic tissue, which was associated with significant enhancement of stroke shortening and "work." Most strikingly, ouabain returned normal systolic shortening to 10 severely ischemic segments which previously were akinetic.

THE POSITIVE inotropic effects of cardiac glycosides in normal and failing nonischemic hearts are well established,1-15 whereas their action on the acutely ischemic myocardium remains controversial.6-15 It could be hypothesized that in the ischemic setting the increase in myocardial oxygen demands induced by cardiac glycosides would be deleterious. This point of view gains support from several studies in which overall cardiac function, assessed pri-

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