Sequential QRS Vector Subtractions in Acute Myocardial Infarction in Humans

Time Course and Relationship to Serial Changes in Serum CK-MB Concentration

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SUMMARY We used an automated recording system and computer analysis to perform hourly QRS subtractions on ECG signals obtained with dipolar leads in 14 patients admitted within 6 hours of the onset of symptoms of acute myocardial infarction (AMI). The resulting changes in QRS time-voltage area were expressed as a difference vector (QRSMD) which was found to have a simple time course that was similar for infarcts in different locations and closely fit the equation:

$$\text{QRSMD}(t) = a \left(1 - e^{-\beta(t-t_0)}\right)$$

where $t_0$ is the time of admission, $t$ is the time of each measurement, $\beta$ is the exponential development rate, and $a$ is the asymptotic value for QRSMD. QRSMD changes rapidly and essentially linearly during the initial 10 hours and the changes were 90% complete at $13 \pm 2$ hours. When $a$ was computed from data obtained after hospital entry, it correlated poorly with infarct size estimated from CK-MB analysis. Extrapolations to correct for changes assumed to have occurred prior to entry did not significantly improve the correlation. The exponential development rate, $\beta$, and the initial growth rate, $a/\beta$, were also poor predictors of infarct size estimated by the CK-MB method. The QRSMD and the integral of serum CK-MB release had a similar time course, with the QRSMD changes preceding the changes in CK-MB concentration by approximately 10 hours. It is concluded that the QRS difference vector measured during the AMI has a characteristic time course that is independent of anatomical location and has similarities to the integrated CK-MB release course. However, the rate of change of QRSMD and various functions of the maximum QRS difference are poor predictors of infarct size as determined by the CK-MB method.

A RELIABLE, non-invasive method to measure both the rate that ischemic myocardium progresses to necrosis and the final size of the infarct would have obvious value in assessing interventions designed to modify the course of myocardial infarction. Electrocardiographic (ECG) methods to accomplish this goal have been the subject of intensive investigation because a quantitative relationship between the size of the infarct and the resulting ECG changes has been appreciated for many years (Myers et al., 1948). Whereas most of the recent work on ECG infarct sizing has used ECG maps that require a large number of electrodes and complicated data acquisition systems, there is experimental evidence that the ECG changes associated with infarction have a large dipolar component (Ideker et al., 1975; Mirvis et al., 1978). To quantify pre- and post-infarction ECG changes, waveform subtraction methods have been devised in which the difference between time-equivalent points or segments from two or more ECG signals are measured and displayed (Wickline and McNamara, 1978; Flowers et al., 1978). This form of analysis is applicable to ECG signals obtained from surface maps or other lead configurations. Studies in primates have demonstrated that subtraction methods applied to ECG signals from dipolar leads correlate exceedingly well with the physical size of experimentally induced myocardial infarctions (Wickline and McNamara, 1978) and that indices of infarct size derived from dipolar leads correlate well with those obtained from multi-electrode mapping procedures in animals (Flowers et al., 1978) and in human beings (Akiyama et al., 1975). If the ECG changes resulting from myocardial infarction are largely dipolar throughout the course of infarction,
it will be possible to use subtraction techniques on ECG's recorded with relatively simple orthogonal leads to extract the principal electrical components of the infarction. The purpose of this report is to describe the results of applying subtraction techniques to ECG signals obtained from orthogonal leads in order to measure the time course of electrical changes during acute myocardial infarction. We have related the ECG difference values to serial changes in the concentration of serum CK-MB and to estimates of infarct size made from CK-MB concentration kinetics.

Methods

Patients

Candidates for this study were patients admitted to the coronary care units of the VA Medical Center and the Vanderbilt University Hospital within 6 hours of onset of chest pain that was characteristic of acute myocardial infarction. Patients were excluded from study if they were hypotensive (systolic blood pressure less than 90 mm Hg) and had signs of systemic hypoperfusion. Patients were also excluded from study if the initial ECG showed left bundle branch block, and data from patients were not included in the analysis if the serum CK-MB did not change in a manner consistent with an acute myocardial infarction. Data from patients were not included if symptoms, ECG changes, or enzymatic changes suggestive of infarct extension occurred after the patient entered the study. Fourteen patients met criteria for inclusion. Their ages ranged from 45 to 71. Eight had an anterior myocardial infarction (anteroseptal, strictly anterior, or anterolateral), and six had an inferior myocardial infarction.

Data Acquisition and Analysis

After admission to the coronary care unit, electrodes were attached to the patient in the Frank orthogonal lead configuration. Electrode sites were marked with carbolfuchsin stain to ensure constancy of electrode positions. After appropriate calibration, ECG signals were recorded for 1 minute each hour for 48 to 72 hours with a system consisting of a Frank resistor network, three isolated ECG amplifiers, and a multi-channel FM magnetic tape recorder with a time-code generator. A timing device was used to automatically start and stop the recorder during the period of observation. Figure 1 shows analog ECG signals at three points during the course of an acute anterior myocardial infarction in one of the patients. The analog tape record, which consisted of hourly samples of X, Y, Z data and the measurement time, was digitized and analyzed by a computer program that segmented the ECG waveform into the desired components and labeled and measured ECG amplitudes and durations. Analog reconstructions of the digital data were available to check visually the accuracy of the analytical steps. Statistical routines eliminated complexes with measurements which lay outside two standard deviations of the mean for the group of complexes recorded during the hourly sampling. The average measurements were then computed for the set of XYZ data for each time interval.

To calculate spatial mean vector magnitudes, we integrated each QRS complex of the set of XYZ data from onset to the j point. The integrals, or time-voltage areas, of the set of QRS complexes recorded at admission to the CCU were the cartesian coordinates of the reference QRS area vector. QRS area vectors computed from data recorded later in the course of the AMI were compared to the reference vector to obtain the difference vector. As shown in Figure 2, the distance between the terminus of the admission QRS area vector, \( P_A \), and the terminus of the QRS area vector, \( P_D \), computed later during the course of the AMI was the magnitude of the difference vector, \( P_D \). The magnitude of \( P_D \) is mathematically defined as

\[
|\vec{P}_D| = \sqrt{AD_x^2 + AD_y^2 + AD_z^2} = QRS_{MD} \quad (1)
\]

where \( AD_x, AD_y, AD_z \) are the QRS area differences measured from their respective orthogonal leads. The magnitude of \( P_D \) is the magnitude of the difference vector for the QRS areas, hence the name QRS_{MD}. This calculation is equivalent to the area measurements used by Wickline and McNamara (1978).
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QRS AREA DIFFERENCES (AD)

\[ \text{QRS}_{MD} = \sqrt{AD_x^2 + AD_y^2 + AD_z^2} \]

**Figure 2** a The instantaneous area difference vector \( \overrightarrow{P_0} \) represents the vector change between an initial control QRS area vector \( \overrightarrow{P_A} \), and one recorded at a later time during the course of AMI. The angle \( \theta \) is measured in the plane determined by \( \overrightarrow{P_A} \) and \( \overrightarrow{P_B} \). b: The illustration shows an example of the three orthogonal area difference components between two QRS complexes.

Serum CK-MB Measurements, and Kinetic Analysis

In eight patients, blood samples were obtained at the time of admission to the CCU, at intervals of 4 hours for 16 hours after admission, then at 8-hour intervals for 32 hours, and then daily for the remaining 48 hours for a total of 11 specimens per subject. Infarct size was estimated in gram-equivalent units using the method described by Shell et al. (1971). A clearance constant (\( k_d \)) of 0.0015/min was used for the computations.

Statistics

Curve fitting was performed by the method of nonlinear least squares analysis (IMSL, 1977; Brown and Dennis, 1972). The data were shown to fit the curve of least squares by employing a \( \chi^2 \) "goodness-of-fit" test (Orear, 1958). In this test \( \chi^2 \) is defined as

\[ \chi^2 = \sum \frac{(E_i - F_i)^2}{\sigma_i^2} \]

where \( E_i \) is the value predicted by the curve of least squares, \( F_i \) is the observed mean value and \( \sigma_i^2 \) is the variance. We normalized and grouped the patient data as described in Results, then used the variances at each hour to compute a weighted average of variance which was used in the equation above. We also performed regression analysis of these data to determine the quality of fit. This was accomplished by pairing the observed values with the corresponding values predicted by the curve and then applying standard linear regression analysis. The significance of the correlation coefficient was determined by Student's t-test. The comparative analysis of QRSMD data and estimates of infarct size by CK-MB kinetics was performed using linear regression analysis.

**Results**

Time Course of QRS Vector Differences

The time course of QRS vector magnitude differences (QRSMD) for two representative patients with acute myocardial infarction (AMI) is shown in Figure 3. Patient P0133 had an acute inferior myocardial infar-
dial infarction and the ECG recording was begun within 2 hours after the onset of chest pain. Patient P2354 had an acute anteroseptal myocardial infarction, and the ECG recording was started within 3 hours after the chest pain began. The respective volumes of the infarcts were estimated to be 33.8 g and 29.0 g from analysis of serum CK-MB concentrations. The combined mean and standard errors of data from 12 patients are presented in Figure 4a.

Figure 4b shows the data for the subgroup of five patients with inferior myocardial infarction and Figure 4c is for the seven patients with anterior myocardial infarction. Since the final magnitude of the difference vector varied between subjects, the combined data values in Figure 4 were determined by normalizing each data point from an individual patient by dividing it by the asymptotic value reached late in the course of that individual’s infarction, where the asymptotic value is the mean of the final 20 hours of data. The mean and standard errors from the groups were calculated after grouping the data into 4-hour intervals. This aided in smoothing the early fluctuations caused by the 4-hour spread in the admission time of individual patients and facilitated the comparison of the QRSMD with CK-MB data, since the CK-MB sampling interval was not constant and more ECG measurements were made than CK-MB determinations.

Mathematical Description of Time Course of QRS Changes

We have found that, irrespective of the location of the infarction, the time course of QRSMD data of individual patients and of combined QRSMD data closely fit the equation

\[ QRS_{MD}(t) = \alpha \left(1 - e^{-\beta(t-t_0)}\right) \]  

where \(t_0\) is the time of admission to the CCU after the onset of chest pain, \(t\) is the time of each measurement after the onset of chest pain, \(\beta\) is the exponential growth rate, and \(\alpha\) is the asymptotic value for the QRS vector magnitude difference. The correlation coefficients obtained from fitting the QRSMD data of patients P0133 and P2354 to Equation 2 are 0.97 and 0.93, respectively. The fit of the grouped data illustrated in Figure 4, a-c, to Equation 2 yielded correlation coefficients of 0.94 for all patients, 0.95 for patients with inferior myocardial infarctions, and 0.91 for patients with anterior myocardial infarctions. Table 1 summarizes the fits to Equation 2 for the various data. Note that the data of patients P0839 and P4857 fit Equation 2 poorly. In these two cases, the size of the infarct was small, causing a low signal-to-noise ratio.

By inspection of Figures 3 and 4, it is evident that the QRSMD changes rapidly and essentially linearly during the first 10 hours of AMI. Data obtained from patients P0133 and P2354 during the initial 10 hours of the AMI have been replotted in Figure 5, a and b, and the linearity of the changes with respect to time was tested by regression analysis. The correlation coefficients were 0.98 and 0.96, respectively. The mean time for which the QRSMD changes were 90% complete was calculated to be 13 ± 2 hours. Linear regression analysis was performed on the average normalized QRSMD data from a subgroup of eight patients whose electrocardiograms were recorded for 72 hours, and the rate of
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TABLE 1 Summary of the Fit of QRS_MD Data from Individual Patients to the Equation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Infarct location</th>
<th>( \omega ) (hours)</th>
<th>( \alpha ) (mV.sec)</th>
<th>( \beta ) (hours(^{-1}))</th>
<th>( r )</th>
<th>df</th>
<th>( \chi^2 ) (gm eq)</th>
<th>CK-MB ISE (gm eq)</th>
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<tbody>
<tr>
<td>P3777</td>
<td>Inferior</td>
<td>14.35</td>
<td>0.45</td>
<td>0.90</td>
<td>38</td>
<td>5</td>
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<tr>
<td>P4662</td>
<td>Inferior</td>
<td>35.57</td>
<td>0.24</td>
<td>0.93</td>
<td>14</td>
<td>4</td>
<td></td>
<td></td>
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<tr>
<td>P9190</td>
<td>Inferior</td>
<td>19.15</td>
<td>0.19</td>
<td>0.88</td>
<td>20</td>
<td>11.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P1144</td>
<td>Inferior</td>
<td>15.81</td>
<td>0.39</td>
<td>0.81</td>
<td>29</td>
<td>25.6</td>
<td></td>
<td></td>
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<tr>
<td>P8005</td>
<td>Inferior</td>
<td>41.77</td>
<td>0.13</td>
<td>0.87</td>
<td>51</td>
<td>20.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P839</td>
<td>Inferior</td>
<td>5.96</td>
<td>0.10</td>
<td>0.57</td>
<td>47</td>
<td>65.8</td>
<td></td>
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</tr>
<tr>
<td>P133</td>
<td>Inferior</td>
<td>27.86</td>
<td>0.19</td>
<td>0.97</td>
<td>38</td>
<td>2</td>
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<td></td>
</tr>
<tr>
<td>P2954</td>
<td>Inferior</td>
<td>23.13</td>
<td>0.10</td>
<td>0.93</td>
<td>57</td>
<td>9.9</td>
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<tr>
<td>P1223</td>
<td>Inferior</td>
<td>14.52</td>
<td>0.32</td>
<td>0.86</td>
<td>62</td>
<td>35.0</td>
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</tr>
<tr>
<td>P4875</td>
<td>Inferior</td>
<td>10.96</td>
<td>0.21</td>
<td>0.41</td>
<td>59</td>
<td>113.7</td>
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<td></td>
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<tr>
<td>P1199</td>
<td>Inferior</td>
<td>20.46</td>
<td>0.48</td>
<td>0.86</td>
<td>56</td>
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<tr>
<td>P6859</td>
<td>Inferior</td>
<td>28.11</td>
<td>0.16</td>
<td>0.70</td>
<td>28</td>
<td>14.4</td>
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<tr>
<td>P4294</td>
<td>Inferior</td>
<td>19.60</td>
<td>0.36</td>
<td>0.93</td>
<td>31</td>
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<tr>
<td>P9343</td>
<td>Inferior</td>
<td>5.75</td>
<td>0.54</td>
<td>0.82</td>
<td>36</td>
<td>40.9</td>
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<tr>
<td>Group</td>
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<td>1.0</td>
<td>0.18</td>
<td>0.94</td>
<td>18</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>Inferior</td>
<td>1.0</td>
<td>0.18</td>
<td>0.95</td>
<td>18</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>Inferior</td>
<td>1.0</td>
<td>0.19</td>
<td>0.91</td>
<td>18</td>
<td>3</td>
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</tr>
</tbody>
</table>

The \( P \) value for all fits is < 0.001. Abbreviations: \( r \) - correlation coefficient; CK-MB ISE = CK-MB infarct size estimate; df = degrees of freedom; gm eq = gram equivalent units.

Relationship of the Time Course of QRS_MD to Changes in Serum CK-MB Concentration

The relationship between QRS_MD and CK-MB concentration was examined by comparing the data from 10 patients with both QRS_MD and serum CK-MB measurements. The normalized QRS_MD curve and the integral of serum CK-MB release are shown in Figure 6 using the 4-hour grouping of the data. It is evident that the integral of CK-MB release has a time course similar to that of the QRS_MD. The correlation coefficients obtained from fitting Equation 2 to the QRS_MD and CK-MB data are 0.92 and 0.96, respectively. The mean time for the QRS_MD to reach 90% of its final value was found to be 13 ± 2 hours. The mean time for the integral of CK-MB release to reach the 90% value was 24 ± 4 hours. Thus the QRS_MD changes precede the changes in CK-MB concentration by approximately 11 hours and, because of the similarity in the shape of the two curves, the QRS_MD may be considered to predict the shape of the CK-MB release curve.

The relationship between the asymptotic value of QRS_MD and the infarct size estimated from CK-MB concentration kinetics was assessed by plotting \( a \) for individual patients vs. CK-MB size in gram equivalents. There was a poor correlation \([ r = -0.02, not significant (NS) ]\) between the two parameters. However, since QRS_MD increases rapidly during the early hours of infarction, important changes may take place in the period between the onset of ischemic injury or necrosis and the first ECG recording. The omission of early changes would tend to...
to underestimate the infarct size. Since QRSMD has a well-defined time course, we attempted to correct for the missing early data by extrapolating the post-admission curves back in time to the onset of symptoms.

One approach was to use Equation 2 to derive a correction term, $a \beta t_0$, for the changes that had occurred prior to entry (see Appendix for details). The corrected asymptotic values of QRSMD, $\alpha + a \beta t_0$, then were correlated with CK-MB estimates of infarct size, but the correlation was not significantly improved ($r = 0.31$, NS) (Table 2). We also investigated another method for correcting the curve for pre-admission changes by making a linear fit to the first 10 hours of data. This determines the intercept, $i$, of QRSMD at $t = 0$, which was added to $\alpha$ and correlated with the CK-MB estimate. This correction did not improve the correlation ($r = 0.35$, NS).

The relationship between CK-MB infarct size estimates and parameters of the rate of change of QRSMD was also investigated. The term $\beta$ from Equation 2 is the exponential growth rate of QRSMD and determines the shape of the curve of QRSMD as a function of time. Regression analysis of $\beta$ vs. CK-MB infarct size yielded a correlation coefficient of 0.22 (NS). Expansion of the exponential of Equation 2 indicates that the product $a \beta$ describes the initial linear growth of the QRSMD curve (see Appendix). The correlation coefficient of QRSMD vs. CK-MB infarct size was 0.39 (NS). The product $a \beta$, in contrast to $\beta$, can be measured early in the course of the AMI, as shown in Table 3. In this table, $a \beta$ is determined from the initial three to six data points and ranged from 1.1 to 5.0 in ten patients.

The initial growth rate $a \beta$ may provide prognostic information early in the AMI, as illustrated by the following example. Patient P0329 died 10 hours after the onset of chest pain and 4 hours after ECG recordings were begun. The time course of QRSMD has been superimposed on the composite (non-normalized) curve obtained from the 14 patients who survived AMI (Fig. 7). The initial growth rate $a \beta$ for this patient was 7.0 and the mean for the surviving group was 2.1 ± 0.3. By inspection of Figure 7, it is evident that QRSMD was increasing rapidly during the 4 hours that preceded his death. Post-mortem examination of the patient revealed an extensive AMI which involved the anterior wall and septum.

### Discussion

It is generally recognized that cardiac excitation cannot be completely explained in terms of a simple dipole model, and research in electrocardiography in recent years has been dominated by efforts to apply surface mapping techniques to clinical situations (Muller et al., 1975). However, it does not...
necessarily follow that the electrical changes associated with AMI are as complex as excitation of the entire heart, and it has not been demonstrated that elaborate lead systems are required to provide valid quantitative information regarding the infarction. The voltage changes obtained by subtracting serial orthogonal ECG measurements will describe the dipole moment of the myocardial infarction within the accuracy of the lead system. It follows, from Brody (1962), that the components of this dipole moment will be determined by the area of the infarcted region as projected on each of the three coordinate planes. Thus, the dipole moment is determined directly by the size of the infarct. The quadrupole and higher moments of the infarcted myocardium must be determined by subtraction techniques applied to data from the appropriate lead system. However, these moments will be determined more by the location and shape of the affected area than by its size. Published data indicate that electrical changes associated with regional myocardial injury are largely dipolar (Mirvis et al., 1978). Ideker et al. (1975) showed that over 99% of the electrical changes associated with an epicardial burn in an isolated rabbit heart could be accounted for with a single dipole. McLaughlin et al. (1974) computed surface potential differences for a controlled infarction in dogs. Examination of the resulting ECG shows that they generally have one main peak and one main trough, indicating that they are predominantly dipolar. If the ECG changes associated with infarction are, in fact, primarily dipolar, translation of the difference dipole moment to terms that relate to infarct size will be greatly simplified.

Putting these theoretical considerations aside, there is strong experimental evidence suggesting that there is a quantitative relationship between difference vectors and infarct size. Nelson (1978) made difference measurements from orthogonal leads during infarction in young pigs and concluded that the difference vector was a useful quantity for studying infarctions. Wickline and McNamara (1978) computed spatial area (mV-msec) and voltage (mV) QRS difference vectors using the McFee lead system during controlled myocardial infarctions in eight baboons; difference vectors then were correlated with infarct volumes measured directly. The correlation coefficients of the QRS area and QRS voltage differences were 0.98 and 0.92, respectively. Although Flowers et al. (1978) have pointed out the inadequacy of the dipolar model of cardiac excitation, they recently compared the effectiveness of different subtraction approaches to estimate infarct size. Using simultaneously acquired data from orthogonal leads, ECG data from a 20-lead anterior grid, and 142-lead body surface potential maps to estimate the volume of anterior infarcts in dogs, they found that the 18-msec QRS difference vectors from orthogonal lead data correlated highly with infarct volume \( r = 0.70 \), and integration of the QRS data between 1 and 31 msec from the vectorcardiogram achieved a correlation coefficient of 0.80. Whereas the vector correlation was not as strong as for data obtained with the 142-lead map \( r = 0.88 \), the orthogonal lead data correlated better with infarct size than did QRS data from the 20-lead anterior grid in the presence of anterior infarction \( r = 0.80 \) vs. \( r = 0.51 \), respectively.

The limitations of infarct sizing based on subtractions of ECG signals from orthogonal leads are similar to those associated with other electrocardiographic methods used to estimate infarct size. Erroneous estimations of infarct size and rate of development could be caused by occurrence of conduction defects during the infarction; the amplitude of the QRS could also be affected by hemodynamic factors such as ventricular volume changes (Brody effect) (Nelson et al., 1972) and thoracic conductivity variations. Methods of infarct sizing based on the assumption of dipolarity have the theoretical limitation that if two or more AMI coexist, the dipolar contribution of each AMI may combine in a manner that could produce misleading information about the total volume of infarcted tissue. Despite these limitations, our studies indicate that QRS changes develop with a characteristic time course that is independent of the anatomical location of the AMI, and the time course can be described mathematically by Equation 2. There is a strong relationship between the time course of QRS difference changes and the integral of CK-MB release, with the mean QRSMD changes preceding the mean CK-MB curve by 11 hours. However, the rate of change of QRSMD and measurements that are a function of the maximum QRSMD did not accurately predict the infarct size as determined by the CK-MB method. In the experimental studies in which a strong correlation between QRSMD and the physical size of the infarct was observed (Wickline and McNamara, 1978; Flowers et al., 1978), the methods employed differ from those used in the present study in that the exact time of the occlusion was known in the animal studies, and pre-infarction ECG data were available for the subtraction process.

The QRS complex changes rapidly during the first 10 hours after AMI and substantial changes in ventricular activation could have occurred prior to the first ECG recording in some of the patients included in our study. Although the changes in the QRS difference vector were essentially linear during the first 10 hours after the recordings were begun, extrapolating the post-admission curves back in time to the onset of symptoms did not significantly improve the correlation between the QRS difference vector and estimates of infarct size by the CK-MB method. The missing early data could have altered the slope of QRSMD change and be a source of error, or inaccuracies in timing the onset of the infarction may have made the extrapolations invalid. Moreover, in this study the difference vector
analysis was not carried beyond 72 hours after the infarction. It is possible that changes in QRSMD could continue to evolve very slowly during the first week after myocardial infarction and that measurements taken 1–2 weeks after infarction might be more representative of the QRS changes due to myocardial necrosis. The decision to end the analysis at 72 hours was based on the observation in a subgroup of the patients that the rate of change of QRS approached zero after 48 hours.

It has been noted that manifestations of injury current appear on the body surface during the QRS in acute myocardial infarction (Taccardi, 1967; Mirvis, 1980), and this may be a confounding variable in our investigation of the relationship of depolarization changes to the physical size of the infarct. The methods used in our study may be especially vulnerable to QRS distortion from injury current because the initial reference QRS data are obtained early in the infarction when the manifestations of injury current are near their peak, and because the QRS data during the subsequent 48 hours may be influenced by the injury current to a degree that will be different for different patients. In published studies using animals, the reference QRS data obtained prior to infarction would of course have no component attributable to injury current; measurements made 7–10 days after occlusion should have negligible QRS distortion due to injury currents.

Whereas we have demonstrated that QRSMD develops with a well-defined time course that is strongly predictive of the time course of cumulative CK-MB release and that the initial rate of development of QRSMD may have prognostic value, we have not detected any significant correlation between QRSMD and CK-MB estimates of infarct size.

Appendix A

The time course of QRSMD data closely fits Equation 2, which we present again here for convenience.

\[
\text{QRSMD}(t) = a(1 - e^{-\beta(t - t_0)}).
\]

We are interested in examining the behavior of QRSMD(t) in the neighborhood of \(t = t_0\). In this neighborhood we may linearize Equation A.1 by making a Taylor expansion about the point \(t_0\). Carrying this procedure out, we obtain

\[
\text{QRSMD}(t) \simeq a\beta t - a\beta t_0
\]

(A.2)

where we have neglected the smaller terms of higher order in \(\beta(t - t_0)\). We see that A.2 is the equation of a straight line and that the slope is given by \(a\beta\), hence the name the "initial linear growth rate" of QRSMD at \(t = t_0\). Recalling that the early QRSMD data is highly linear (see Fig. 4), we then can use Equation A.2 to extrapolate back in time to \(t = 0\) where we find the intercept of QRSMD to be \(-a\beta t_0\). Therefore, the complete change in QRSMD from \(t = 0\) to \(t = \infty\) is given by the sum of the pre-admission and post-admission changes, i.e., \(a + a\beta t_0\).

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doi: 10.1161/01.RES.49.4.1055

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