Vectorcardiographic Quantification of Infarct Size in Baboons

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SUMMARY A vectorcardiographic method has been developed for determining the absolute size of myocardial infarcts in baboons resulting from coronary artery ligation. Spatial area (mvolt · msec) and voltage (mvolt) difference-vectors were obtained for 8 animals by measuring the voltage loss and temporal deviation from pre-to-postligation McFee scalar leads. The difference vectors were then correlated with the absolute infarct volumes, which were derived by histological assessment 10 days after ligation. Absolute lesion sizes ranged from approximately 2 cc to 14 cc, involving 10–30% of ventricular muscle mass. The correlation coefficient, r, for the area deviation index was 0.98 (SEE = ± 0.24 cc); and for the voltage deviation index, r = 0.92 (SEE = ± 0.51 cc). These results demonstrate that the severity of infarction can be accurately determined if prepathological vectorcardiograms are available.

NONINVASIVE QUANTIFICATION of absolute infarct size using electrophysiological data would be of considerable benefit in the management of patients with acute infarctions and in the assessment of experimental therapeutic interventions. Although epicardial QRS and ST-complex changes during infarction have been correlated with subjacent myocardial necrosis, the invasiveness of the recording technique precludes its eventual clinical implementation. Recent investigations of infarcts using extensive body surface maps indicate that surface potential recordings also contain a substantial amount of potentially quantifiable information. These studies suggest that necrosis in specific ventricular wall segments will produce characteristic alterations in maps of body surface potential. By subtracting postinfarction and control thoracic potentials point-for-point, a voltage difference map that represents the original electrical contribution of the necrotic segment to the control map can be derived. This method of “difference mapping” appears promising, but body surface recording in general is too cumbersome and extinguating to be clinically practicable at present.

The simple vectorcardiogram offers an alternative source of noninvasive electrical data for examining acute and chronic infarctions. The vectorcardiographic representation of myocardial electrical activity as an equivalent dipole has proven its utility in diagnosis and theoretical
The vectorcardiogram has also been shown to correlate well with the events of ventricular activation and the sequential development of body surface potentials. In addition, Selvester and co-workers have reported a quantitative technique for investigating myocardial infarction that entails a computer-modeled vectorcardiographic difference analysis. Thus, the vectorcardiogram provides a feasible source of quantitative electrical information that merits evaluation in an empirical application.

The rationale for the infarct sizing method proposed in this paper stems from the relationship between internal sources of electromotive force and their expression on the body surface. The process of myocardial activation generates a complex surface potential distribution which is reduced to three orthogonal components in the vectorcardiogram. Both the magnitude and the spatio-temporal orientation of these lead potentials depend on the area of the myocardial activation front remaining after the internal cancellation of opposing fronts. When a segment of muscle dies following myocardial infarction, it becomes electrically inert. A portion of the normal activation front is then lost for a period of time. During the time that the wavefront propagates around the infarcted region, the total area of uncancelled front will be affected, causing a deviation in lead potentials away from the infarcted segment. A "difference vector" can be computed to obtain a measure of the absolute electromotive force contributed by the infarcted area prior to necrosis. The magnitude and duration of this electrical loss depends on the loss of source strength, or muscle mass. In addition, if the normal myocardial activation sequence is known, the temporal character of the vector lead deviations can be correlated with infarct location to determine the regional influence of myocardial activity.

The vectorcardiographic sizing method proposed in this paper was validated empirically by correlating the observed surface potential losses with histologically measured infarct sizes in nine baboons. The technique is capable of estimating lesion size to within 2 cc of muscle mass and is amenable to clinical application. The data base consists exclusively of control vectorcardiograms taken prior to infarct inception and serial recordings taken during the acute and chronic stages of an infarction. Vectorcardiographic data may be easily obtained in a Cardiac Care Unit setting where the progression of myocardial damage is observed for an extended period of time. The proposed method incorporates the advantages of simple data collection and analysis, economy, and serial assessment of patient progress.

**Methods**

A group of 12 baboons (Papio anubis) was used in this study. The initial three animals served as controls in the evaluation of intrinsic methodological variability. Epicardial activation mapping was also done on these animals. The remaining nine animals constituted the experimental coronary artery ligation group.

**Experimental Procedure**

One week prior to the coronary ligation procedure, baboons of 15 kg average weight (table 1) were sedated with 1 mg/kg Sernylan (phenytoicline hydrochloride) and maintained with sodium pentothal as required. Animals were intubated and ventilated with a Harvard volume respirator. A left anterolateral thoracotomy was performed through the fourth intercostal space and a pericardial cradle was created to expose an arterial ligation site. A suture was passed around the selected artery and enclosed in a piece of rigid polyethylene catheter to form a snare. The snare was brought to the surface for subcutaneous implantation and the pericardium was closed loosely. The chest was closed meticulously in layers in an attempt to preserve volume conductor characteristics. Residual air and fluids were drained from the left hemithorax with lungs at full expansion using a flexible drainage catheter.

Having allowed seven days for the electrical effects of the thoracotomy to stabilize, the baboon was again sedated and shaved to expose all surface electrode sites. Arterial and venous catheters were inserted for blood sampling, pressure monitoring, and drug administration. The animal was intubated and then positioned on a supportive mesh hammock to permit easy access to all electrode sites. While on the hammock, the snare was carefully isolated by removing several stitches from the previous skin closure. Baseline vectorcardiograms were then recorded prior to ligation.

Following the baseline recordings, a bolus of lidocaine (50 mg) was injected for control of arrhythmias. The snare was then tightened and clamped externally. Standard ECG leads were monitored for ST-segment elevation to ensure arterial occlusion. After a brief period of surveillance for fibrillation, the snare was secured in the occluded position, replaced subcutaneously, and the skin incision was closed. In three animals, however, the snare was eventually released within 3 hours of initial occlusion, allowing coronary reperfusion to occur.

All animals, with the exception of I (table 1), had acute recordings of vectorcardiographic data taken serially. Animal I was returned to his cage after a brief period of observation and no acute recordings were done during the 6-hour period following arterial ligation. Upon completion of recording, all animals were returned to their enclosures and allowed to recover. Approximately 10 days after ligation, chronic recordings were obtained. Data sets for the 1 hour, 3 hour, 6 hour and chronic periods were analyzed as detailed below. The animal was then sacrificed using concentrated potassium chloride. The heart was excised and fixed in a formalin solution for histological processing. This 10-day interval allowed sufficient time for the electrical stabilization of the injury and for the replacement of necrotic tissue by a collagenous matrix.

**Histological Evaluation of Infarct Size**

For each excised heart, nine transverse slices of equal thickness were made along the major axis of the left ventricle. Tissue sections from the middle of each slice were mounted on slides and stained with hematoxylin-eosin and Gomori tri-chrome stains (fig. 1a). In general, the infarcts manifested a central area of complete fibrosis, which was surrounded by areas of patchy fibrosis intermingled with normal tissue (fig. 1b). The discrete boundaries of the damaged tissue permitted easy differentiation of central necrotic segments, patchy-necrotic segments, and normal tissue.

The slides were placed in a photographic enlarger and the sections were traced on paper. Areas of central necrosis and patchy necrosis were outlined for each section. Significant
Table 1. Compiled Data for Individual Animals

<table>
<thead>
<tr>
<th>Animal</th>
<th>Wt (kg)</th>
<th>Ligation site</th>
<th>Ligation duration (hrs)</th>
<th>Infarct location</th>
<th>Infarct volume* (cm³)</th>
<th>Chronic area deviation† (mvolts/msec)</th>
<th>Chronic voltage deviation† (mvolts)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Circumflex</td>
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<td>Postero-septal</td>
<td>2.48</td>
<td>0.73</td>
<td>3.21</td>
</tr>
<tr>
<td>C</td>
<td>14.1</td>
<td>LAD</td>
<td>Chronic</td>
<td>Antero-septal</td>
<td>6.93</td>
<td>0.00</td>
<td>6.93</td>
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<td>D</td>
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<td>0.52</td>
<td>13.22</td>
</tr>
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</table>

*I = Tissue volume demonstrating complete necrosis; P = 40% of tissue volume demonstrating patchy necrosis; Total = I + P.
†dx, dy, and dz = area or voltage difference between pre-ligation and chronic recordings in X, Y, and Z; dsSpatial = (dx² + dy² + dz²)².

Abbreviations: LAD = left anterior descending coronary artery.

Surface vectorcardiographic data was collected from ten locations on the thorax and extremities with subsequently played and photographed. A scanning speed of 9.6 m/sec. was employed to optimize the display of the desirable features of the QRS complex without excluding the baseline. The data was manually digitized and displayed on the oscilloscope screen. The resulting waveforms were then used to analyze the time intervals and amplitudes of the cardiac complexes.

The absolute volume of infarcted tissue for each animal was determined by multiplying the percentage of normal myocardium that was measured on the tracing of each heart by the total volume of normal myocardium. The volume of each heart was determined by integrating the area of each section. The volume of normal myocardium, the percentage of normal myocardium, and the volume of infarcted tissue were then used to calculate the absolute volume of infarcted tissue for each animal.

For the region of the ventricular wall that was necrotic, the necessary correction for the ventricular wall thickness based on the adjusted thickness extended to normal dimensions. In these cases, the corrections for the necrotic and non-necrotic portions were manually determined to normal dimensions. The thickness of the ventricular wall was assumed for necrotic tissue, while the thickness of the non-necrotic tissue was applied uniformly to the non-necrotic tissue volumes in order to produce the uninfarcted size estimates.
FIGURE 1. A) Mesial transverse section of heart showing upper limits of anteroseptal, transmural infarct in animal A (see table 1). B) Representative photomicrograph of patchy (P), normal (N), and necrotic (I) regions.

data were also simultaneously recorded on a Gould Brush Recorder at 125 mm/sec.

Data Analysis

Slides made of the photographed waveforms were projected and drawn on tracing paper with timing and voltage calibration signals. The pre-ligation vector lead recordings served as control data for comparison with each successive postligation data set. The stable PQ segment was used to draw a baseline across the QRS portion of all waveforms. Each set of post-ligation tracings was then superimposed over the corresponding preligation control tracings by matching the two baselines. The initial deflection of the QRS was used as a fiducial point to match the tracings temporarily. A data set overlay is included for reference (fig. 2).

The deviations of X, Y, and Z post-ligation waveforms from control waveforms were traced as area differences for each time period (fig. 3). The area difference tracings were planimetered and converted to millivolt • millisecond units (or units of area under lead waveforms) by applying the voltage and timing calibration factors. Since two waveforms had been recorded for each X, Y, and Z lead at a given time period, the area differences (mV • msec) were averaged. The magnitude of the spatial vector “area deviation” was then computed by squaring the averaged X, Y, and Z lead area differences, summing, and taking the square root. These spatial vector area deviation data were then correlated with the histologically determined infarct size.

Wave amplitude differences, or simple voltage alterations, between control and post-ligation complexes were also examined as parameters of infarction (fig. 3). The maximum positive and negative voltage deflections of each lead were determined for each time period. The control waveforms were compared with all subsequent serial recordings and voltage differences were obtained. The magnitude of the spatial vector “voltage deviation” was then computed and correlated with infarct size.

Both independent and paired t-tests were employed to

FIGURE 2. Superimposed waveform tracings for 2 animals. The solid line represents the preligation vectorcardiogram and the broken line represents the chronically recorded data. A) Antero-septal infarction: animal E. B) Postero-lateral and diaphragmatic infarction: animal B.
assess the differences between appropriate groups of data as indicated in the Results. Regression analyses of vectorcardiographic deviations on infarct sizes were performed, and the Pearson correlation coefficients (r) were calculated. Unbiased estimates of the r values (r0) were obtained by applying Hotelling’s transform for correlation coefficients in small samples.26 Confidence and tolerance hyperbolae were also determined to provide 95% estimate intervals for predictions of infarct size.26

**Epicardial Activation Sequence**

Epicardial activation mapping was performed in three animals to determine regional cardiac influences on the control and postinfarction vectorcardiogram. A unipolar exploring electrode was used to record epicardial electrograms since the analysis of unipolar complexes has been shown to yield activation timing results identical to bipolar complex analysis.27 Limb lead I was recorded simultaneously as a timing reference.

Forty to 50 epicardial points were mapped. Activation at a particular grid point was assumed to occur at the peak of the intrinsic deflection in the recorded complex. Waveforms lacking a sharp intrinsic deflection were excluded from analysis. Activation times were located at appropriate points on a diagram of the heart drawn from in situ photographs. Isochrones were then constructed to depict the spatio-temporal progression of the depolarizing wave across the epicardium. The individual vectorcardiograms were time-normalized with epicardial activations by matching the timing reference for both sets of data. The correlation between myocardial activation and vectorcardiographic deflection is reported in the Results.

**Evaluation of Technique**

Several potential sources of confounding error were examined prior to formulating the experimental ligation protocol. These variables included the reproducibility of electrode placement in the McFee vector system; the accuracy of recording and calibration procedures; and the electrical effects of thoracotomy and pericardiotomy. The assessment of these variables and the findings are presented in the Results.

**Results**

**Evaluation of Methods**

The effect of electrode placement errors on McFee X, Y and Z leads was determined in two normal animals. All electrodes were removed from the chest and repositioned several times without the aid of the silastic locating template. Electrodes were also randomly placed within a distance of ± 2 cm of their preferred position to determine the “worst case” estimates of repositioning error. Where attempts were made to reposition electrodes accurately, waveform deviations were negligible. The maximum error associated with deliberate misplacements was 3.24 mV·ms for spatial
vector area deviation and 0.24 mvolt for spatial vector voltage deviation. The X lead was found to be the most sensitive to placement errors, with Z less sensitive, and Y nearly insensitive. Waveform photography and oscillographic display produced negligible variations in duplicate control waveform recordings.

Substantial extraneous waveform variations occurred as a result of thoracotomy. In two of three animals observed for thoracotomy effects, significant waveform changes were noticed immediately after chest closure. General features of these changes included slightly diminished QRS potentials (although wave morphologies were unaffected), and T-wave inversion. After a period of one week, the QRS potentials had assumed normal magnitudes. The apparent stabilization of these alterations at one week permitted the recording of new postsurgical, pre-infarction baseline vectorcardiograms.

**Normal Electrical Activity**

Normal McFee QRS waves displayed a characteristic preponderance of anterior, inferior, and leftward forces. The average spatial vector voltage magnitude was 0.98 mV oriented in the left lower anterior octant at 53° below the horizontal and at 32° clockwise from the left. The control QRS durations ranged from 41 to 70 msec, with a mean value of 54 msec and a standard deviation (sd) of ±8.1 msec.

Activation maps done on all three baboons revealed a similar sequence of epicardial depolarization in each heart. Initial activity on the anterior right ventricular surface at 10 msec was correlated with posterior (Z), rightward (X), and superior (Y) vector forces. During the mid-phase (10–25 msec), left ventricular activity appeared simultaneously at the anterior and posterior paraseptal borders, with apical depolarization following shortly thereafter. Corroborating anterior (Z), leftward (X), and inferior (Y) forces predominated throughout this period. During the terminal phase (25–45 msec), posterolateral depolarization occurred as the activation wave closed out at the left lateral margin. Anterior and inferior forces declined rapidly while leftward forces dissipated gradually.

**Histological Alterations**

Individual animal data pertaining to the gross and microscopic characteristics of the induced infarctions are summarized in table 1. The majority of ligatures were placed below the first diagonal branch of the left anterior descending artery (LAD), approximately halfway between apex and base. Ligation at this site resulted in necrosis of mesial and apical septal regions, with anterior extension around the left free wall. In several cases, necrosis also extended paraseptally around the posterior free wall. The apex was circumferentially infarcted in most instances. The lower anterior free wall of the right ventricle was variably affected, but the infarcted volume was negligible in comparison with the total left ventricular involvement. The transverse mesial section in figure 1a (animal A) represents a typical small anteroseptal infarct.

In contrast to the usual distal LAD ligature placement, animal B was ligated on a marginal circumflex branch. The resulting infarct was located in the mesial and apical sections of the posterolateral free wall. Diaphragmatic extension was observed, along with minor anterior apical extension. The septum and right ventricle were not affected.

Absolute infarct volumes ranged from 2.62 cc to 13.22 cc, corresponding to a 10–30% destruction of left ventricular muscle mass. All infarcts were transmural and rectangular in configuration, with necrosis being equally and randomly dispersed in endocardial and epicardial regions. No instances of subepicardial preservation were observed. Areas of patchy necrosis bordered the central zone of complete necrosis (fig. 1b) and accounted for 17.8% (±13.5%, sD) of the absolute infarct volume in the total population. The three reperfused animals suffered a greater amount of patchy necrotic damage (26.8% ±15.2%) than did the six chronically ligated animals (13.2% ±11.1%). The difference was not statistically significant, however.

**Vector Waveform Alterations**

Deviations in area and voltage from control to chronic 10-day recordings are listed in table 1 for individual leads. Spatial vector deviation data are also included, since it constitutes the basis for subsequent regression analyses.

No gross conduction defects, peri-infarction blocks, or intra-infarction blocks were observed in any animal after ligation. Postligation waveform durations were not significantly different from the controls in a paired t-test. This conformity of onset and offset times for individual pre- and post-ligation waveforms permitted accurate superposition of all complexes for deviation analysis.

The vectorcardiographic alterations diagrammed in figure 2a are typical for animals with anteroseptal infarctions. The most profound changes occurred in the Z lead. A decrease in the magnitude and duration of R waves was invariably observed, implying a loss of anterior forces. Late alterations in the QRS occurred only in animals A and H, suggesting that terminal posterior activity remained intact in most cases. Y lead alterations consisted primarily of diminished R waves, implying a loss of inferior forces. The X lead usually demonstrated initial flattening of Q waves and increases in R wave magnitude, indicating an early loss of rightward forces. Mid-phase changes in the X lead varied considerably and consisted of increased R wave magnitudes in some cases and diminished magnitudes in others.

One animal, B, manifested a different pattern of waveform deviations as a consequence of posterolateral and diaphragmatic infarction (fig. 2b). The Y lead was most profoundly disturbed in this case, implying a major loss of inferior forces. The Z and X leads showed moderate changes, suggesting the loss of mid-phase anterior and lateral forces. The augmentation of late leftward force (see X lead, fig. 2b) seemed incongruous with the expected affects of this lesion, but was probably related to the specific activation sequence disruption in this particular case.

The regional electrical effects of these lesions can be demonstrated by correlating the vector waveform alterations (fig. 2) with the epicardial activation sequence. The initial and mid-phase anterior losses in the Z lead were associated with septal inactivity, implying that the majority of anterior positivity was generated by the septum. Mid-phase inferior vector losses in the Y lead were associated with apical inactivity, especially in the case of posterolateral and diaphragmatic infarction (fig. 2b, D), implying...
that apical and diaphragmatic areas were responsible for inferior positivity. Early rightward losses in the X lead were attributable to septal necrosis, while mid-phase leftward losses were associated with apical and left free wall activity. These findings are in general agreement with previous work on the contribution of discrete ventricular wall elements to surface potentials.4 7 17 23

Sizing Criteria

Figure 4 represents the regression of infarct size on chronic spatial vector area deviations for eight of the nine animals studied. The X-on-Y regression format is presented in order to facilitate the use of the graph in predictions of lesion size. Animal H was not included in the derivation of optimum area of voltage deviation criteria (figs. 4 and 5). In the scatter plots of chronic deviation data (figs. 6 and 7), point H was significantly removed from the linear relationship that obtained for the remainder of the group (P < 0.05 by single point aberration analysis).26 Persistent ST segment elevation was observed in this case, resulting in a vertical displacement of the postligation offset point. No temporal offset was noted, however, as both control and postligation durations were equivalent. The complete results of the correlation and regression analyses for the study population of nine animals are reported in figures 6 and 7 for comparison.

The chronic spatial vector area deviation correlated well with histologically determined infarct size (r = 0.98; r95 = 0.97). The standard error of estimate for the regression sample of eight animals was ±0.24 cc. The slope and intercept of the regression line were 0.47 and -1.71 cc respectively.

Since the predictive value of this regression analysis depends on the level of certainty with which infarct sizes can be estimated, 95% confidence and 95% tolerance hyperbolas were calculated. The confidence interval provides the limits on the estimation of average infarct size for a group of animals that have equivalent spatial vector area deviation measurements. The tolerance interval provides the limits on the estimation of individual infarct size for a single animal at any given spatial vector area deviation. Inspection of the tolerance hyperbola reveals that a prediction of infarct size could be made for 95% of new infarct cases, using the area deviation data, with a potential error of ±2 cc or less across the range of infarct sizes.

The chronic spatial vector voltage deviation magnitude also correlated well with infarct size (r = 0.92; r95 = 0.89). Figure 5 represents the regression analysis for eight animals. The standard error of estimate for the sample was ±0.51 cc. The slope and intercept of the regression lines were 8.35 and -1.48 cc respectively. Ninety-five percent confidence and tolerance hyperbolas were calculated as before for N = 8. The resultant tolerance interval indicates that a prediction of infarct size could be made for 95% of new infarct cases, using the voltage deviation data, with an error of ±4 cc or less across the range. The individual voltage and area deviations were also significantly associated for the eight animals analyzed (r = 0.94).

Figures 6 and 7 illustrate the instability of the spatial vector area and voltage deviation parameters from the 6-hour to the chronic recording period. Vectorcardiographic deviations for the two time periods are plotted against the true independent variable in this study, ultimate infarct size. The scatter plots are paired for all animals except I, since no acute recordings were done in this case.

For the entire group of nine animals, the chronically recorded area deviations (fig. 6) correlated well with infarct size (r = 0.91; r95 = 0.88). The standard error of estimate for the regression line was ±1.06 mV • msec; and the slope and intercept were 2.09 and 4.78 mV • msec respectively. The 6-hour area deviations for eight animals also correlated significantly with infarct size (r = 0.72). The standard estimate error for the regression line was ±1.82 mV • msec, with slope and intercept of 1.78 and 2.58 mvolt • msec.

The plot of voltage deviations for the two time periods (fig. 7) manifested an analogous superiority of chronic data over 6-hour data as an index of ultimate infarct size. Voltage deviations, though, were less associated with infarct size.

![Figure 4](https://example.com/figure4.png)  
**Figure 4.** Regression of infarct size on spatial vector area deviation for N = 8. The correlation coefficient, r, was significant at P < 0.005. Ninety-five percent tolerance and confidence hyperbolae are depicted, along with the line equation, for use in infarct size predictions. S.E.E. = standard error of the estimate.

![Figure 5](https://example.com/figure5.png)  
**Figure 5.** Regression of infarct size on spatial vector voltage deviation for N = 8. The correlation was significant at P < 0.01. Other items described in figure 4.
than were area deviations. For the nine animal group, the
chronically recorded voltage deviations also demonstrated a
high coefficient of correlation \( r = 0.85; r_0 = 0.81 \). The
regression line had a standard error of estimate of \( \pm 0.08 \)
mv, with slope and regression of 0.10 and 0.33 mv. The
6-hour data was not strongly correlated with infarct size
\( r = 0.38 \). The standard estimate error for this regression
line was \( \pm 0.10 \) mv, with slope and intercept of 0.03 and
0.66 mv. The individual voltage and area deviations
(chronic) were also significantly associated in the nine
animal group \( r = 0.95 \).

Infarct Evolution

Figure 8 shows the serial alteration of spatial vector
cardioelectric magnitudes for the nine study animals. Both acute
and chronic spatial voltage deviations are represented as
differences from the control data. Again, animal I (circled)
was not followed acutely and no serial deviations are plotted. The dashed lines in the figure denote the onset of reperfusion for animals A, B, and D (onset time listed in
table 1).

The majority of the ultimate voltage deviation in each
animal appears to have occurred after one hour of arterial
occlusion. Between 1 and 6 hours, infarct progression
generally caused further vector waveform deviations. Sub-
stantial variations in waveforms were also observed after the
6-hour period, although the trend associated with these late
changes was related to the duration of ligation. The
chronically ligated animals showed a mean voltage deviation
increase of 43% from the 6-hour to chronic recordings. Area
deviations (fig. 6) also increased by an average of 75%, even
though one animal, G, showed a 10% decline. These late
changes demonstrate that substantial losses of electrical ac-
tivity can occur during the recovery phase in animals with
permanent coronary arterial occlusion.

In contrast, the mean voltage deviation for the three
reperfused animals declined by 16% over the recuperative
period. Area deviations (fig. 7) also declined, though A showed a 5% increase. These minor late vector-
cardioelectric changes reflect the ultimate recovery of some
electrical activity in the animals B and D due to early reper-
fusion. For animal A, the reperfusion after 3 hours resulted in
small, equivocal vectorcardioelectric changes, suggesting
at least the limitation of infarct size by this later intervention. The difference between the two trends of waveform
cardioelectric evolution in reperfused and nonreperfused animals
was statistically significant in an independent t-test ($P < 0.05$).

Animal H was excluded from the regression analyses due to the presence of potentially confounding ST-segment elevations in the 10-day follow-up recordings. Although the QRS offset was vertically displaced from the baseline by the ST shift, the aberration in this case may have derived from the effects of the injury potential on the terminal QRS morphology. It is possible that an unobserved extension of the infarct occurred after 6 hours as a result of thrombus formation in septal branches of the LAD proximal to the ligation site, causing the large increments in voltage and area deviations seen in figures 6–8. Similar infarct extensions may also have occurred in C and E. Other animals showed much smaller waveform shifts after the 6-hour period.

A complete serial assessment of spatial vector area deviation data was not performed, due to the sensitivity of the area deviation analysis to acute isoelectric baseline shifts or ST-segment elevations. Injury currents usually developed immediately upon arterial occlusion and increased in magnitude to peak values within one hour of ligation. Therefore, the ST-segment elevations declined to minimum values at 3 hours, and usually had disappeared by 6 hours. The uncertain location of true isoelectric baselines did not permit the accurate superposition of 1 and 3-hour postligation and control waveforms, in order to compare morphological aberrations and derive genuine point-to-point changes. The simple spatial vector voltage analysis was less sensitive to these baseline shifts, at least in terms of obtaining a well-described index of change. By defining the stable PQ segment of each lead as the baseline, total waveheight differences could be measured without devoting the scrupulous attention to baseline shifts that was required for overlaying the vector tracings. Fortunately, the disappearance of ST-segment elevations by 6 hours permitted the calculation of 6-hour spatial vector area deviation data (fig. 6).

Discussion

Much recent criticism has been directed against the fundamental assumption in vectorcardiography that the heart's electrical activity can be represented as a single dipolar source of electromotive force. According to various reports, the single, fixed dipole could theoretically account for 85–95% of the electrical information measured on the body surface. The residual, non-dipolar information is due to the heart actually behaving as a distributed source of potential located eccentrically in a finite, inhomogeneous volume conductor.

One consequence of such theoretical caveats has been the abatement of research into the prospective quantitative applications of vectorcardiography and the devotion of greater effort to the refinement of diagnostic criteria. Nevertheless, the fact that body surface signals include non-dipolar components does not exclude the possibility of developing accurate quantitative criteria. The results of this study clearly demonstrate that the proposed vectorcardiographic method can reliably estimate infarct size in a primate model. The empirical validity of this vectorial infarct analysis in baboons also suggests its potential clinical utility in humans.

Two related vectorcardiographic indices of infarction were examined in this study. The spatial vector area deviation index was obtained by integrating timing and voltage alterations in McFee scalar leads. The corresponding voltage deviation index was obtained by measuring maximum lead waveheight differences. The chronically measured area deviation magnitudes (fig. 4) correlated better with infarct size than did the voltage deviation magnitudes (fig. 5). The area deviation data, with its narrower tolerance limits, also proved to be a more reliable estimator of infarct size than the voltage deviation data.

The inclusion of timing data in the area deviation index (mV·msec) significantly improved the estimate by accounting for the protracted morphological differences between superimposed control and chronic waveforms (fig. 2). These prolonged lead departures resulted from infarct extension throughout several ventricular regions that had previously energized at different times during depolarization. In cases of antero-septal infarcts for example, post-ligation lead deflections approximated their pre-ligation courses only after 25–30 msec, the time required for completion of normal antero-septal activation. This direct temporal relationship of vector lead aberration to activation sequence and infarct location was elucidated in the Results.

The voltage deviation index (mV) was evaluated at a single instant, and reflected only the electrical status of cardiac elements normally active at that time. It seems fortuitous that the voltage deviation correlated so well with infarct size. Flowers et al. have also reported a good correlation between canine heart size and voltage losses in body surface maps at the 16 msec period of depolarization. The success of these two similar indices may have been due to the preponderance of anteroseptal infarctions in both studies. Such lesions would consistently have affected early cardiac activity and predisposed to favorable correlations between early voltage difference measurements and infarct size. However, the sensitivity of both voltage and area deviation indices to the posterolateral, diaphragmatic infarction in B (table 1) suggests that this technique is applicable to a broader range of infarcts than just anteroseptal lesions.

These vectorcardiographic parameters can also be used to assess relative changes in the status of infarction. In the graph of serial voltage deviation data (fig. 8), a general tendency for reperfused animals to recover some of their initial potential losses was observed. In contrast, chronically ligated animals tended to incur further losses in potential. Although the individual changes in potential after the 6-hour period were highly variable, especially for the chronic ligations, the difference between these two trends was statistically significant. It was not possible to quantitate the effect of coronary reperfusion on infarct size, but the efficacy of early intervention was implied by the observed vectorcardiographic recovery.

Infarct size was associated more closely with chronically recorded waveform alterations than with 6-hour alterations, as evidenced by the regression analyses. Inspection of figures 6–8 reveals that the waveform alterations were not stable enough at the 6-hour post-ligation period to represent the ultimate infarct size. In the case of chronically ligated animals, some of the additional waveform variation may have been caused by infarct extension during the recuperative period (H, for example). In reperfused animals, the recovery of potential may have resulted from the eventual salvage of some injured myocardium.
Since vectorcardiograms were recorded only acutely and at 10 days postligation, the exact course of waveform stabilization was not ascertained. Thus, the most propitious time for recording "chronic" waveform alterations was not determined. The apparent rapidity of infarct evolution in these animals indicates that an estimate of infarct size would be possible well within the 10-day "waiting period" of this study. The 6-hour period, however, represents the lower time limit for reliable predictions of lesion size using the proposed technique.

As previously mentioned, the vectorcardiogram presents a very condensed and simplified picture of myocardial electrical activity. Because the distribution of potential on the body surface is variously dipolar, multipolar, and multi-peaked at times,24-37 the vectorial representation might exclude significant information, making the analysis susceptible to unquantifiable sources of error. The significance of these confounding factors is mitigated by the calculation of difference vectors which incorporate only the non-dipolar contribution of the infarcted area into the sizing analysis. Thus, the single dipole source assumption need be accurate only for the infarct region. In view of the small standard errors encountered in these results (figs. 4 and 5), any distortions caused by multipolarity or multiple peaks could not have seriously affected the correlation between infarct size and vectorcardiographic alterations.

Another potential source of error involves the expectation of greater thoracic variability in humans than in these study animals. Since multipolar distortion is primarily a product of torso inhomogeneity,38 this error may be more significant in clinical applications. The occurrence of substantial torso variability may necessitate the calibration of the vector lead system to fit each individual patient, since vector lead strengths are fundamentally determined by the conductive properties of the chest. Failure to equilibrate the leads could result in the incorrect estimation of infarct size. Therefore, the three orthogonal McFee leads must be adjusted to equal sensitivity in each direction to ensure the accurate computation of spatial vector voltage and area deviations.

Equal lead sensitivity was assumed in this study. Precise lead equilibration may not have been necessary though, since all baboon chests were remarkably similar in configuration, and since the predominant electrical alterations appeared in the McFee lead most sensitive to antero-septal infarcts, the Z lead. However, the lateral and diaphragmatic infarct in B, which produced its most prominent vectorcardiographic alterations in the Y lead (table 1), still conformed closely to the graphed regression line. Thus, the McFee lead system appeared to be equally sensitive to these two infarct types in baboons.

Extraneous, noninfarctional aberrations in the vector recordings can also lead to significant errors in the prediction of lesion size. Although conduction defects, such as peri-infarctional blocks, did not occur in these baboons, they may be more prevalent in humans.39 The criteria presented in this report are not capable of distinguishing between primary alteration by necrosis and secondary alteration by abnormal conduction and, therefore, would incorporate these extraneous deviations as estimate errors. The simultaneous occurrence of multiple infarcts might also present a problem, especially if they are located in wall elements that normally cancel during activation. The presence of a previous infarct, however, should not reduce the sensitivity of this analysis since the electrical deficit attributable to the chronic lesion would appear in both pre- and post-ligation recordings but not in the difference vectors. Persistent ST-segment elevation, due to infarct extension or aneurysm, would also affect the post-ligation QRS morphology in an unpredictable manner.

The most serious obstacle to the clinical implementation of this technique resides in the practical necessity for pre-infarctional vectorcardiograms, in order to obtain the most accurate and reliable estimate of infarct size. In the absence of individual control recordings, averaged normals might be substituted for the comparative analysis.18 The use of compiled normals as controls would reduce the resolution of the sizing estimate due to the variance in the averaged normal vectorcardiograms. To emphasize this point, if the averaged normal data for baboon vectorcardiograms had been used as control recordings, an infarct size of 8 cc could have produced vectorcardiographic alterations that fell within the 95% range of variability for the compiled normal waveforms.

The suitability of these graphs (figs. 4 and 5) for estimating infarct size in human patients is a matter of speculation. It is likely that a similar empirical study on a human population will be required to develop new regression equations, or to verify these. Much work remains to be done in this area, and we hope this report will serve to stimulate further empirical investigation into the potential of quantitative aspects of vectorcardiography.

References
Cardiovascular Complications during Exercise Training of Cardiac Patients

WILLIAM L. HASKELL, PH.D.

SUMMARY The occurrence of major cardiovascular complications during exercise training of cardiac patients in 30 cardiac rehabilitation programs in North America was determined by questionnaire. These programs conducted medically supervised cardiac exercise classes in 103 locations and reported information on 13,570 participants who accumulated a total of 1,629,634 patient hours of supervised exercise. Cardiovascular complications were reported as nonfatal or fatal and included cardiac arrest, myocardial infarction and other. A total of 50 cardiac arrests were observed during exercise, 42 of which were successfully resuscitated while eight were fatal. Seven myocardial infarctions were reported; five were nonfatal and two were fatal. Four other fatalities were reported due to acute cardiopulmonary disorders. The average complication rate for all programs was one nonfatal and one fatal event every 34,673 and 116,402 patient hours of participation, respectively. Complication rates are lower in programs which continuously monitor the electrocardiogram during exercise and are lower when only the experience since 1970 is evaluated. These data support the recommendation that medically prescribed and supervised exercise can be performed reasonably safely by medically selected cardiac patients.

AS PART OF A PROGRAM of comprehensive cardiac rehabilitation, coronary artery disease patients frequently are recommended a program of increased physical activity. The primary reasons given for encouraging cardiac patients to exercise include enhancement of cardiovascular function, improvement of psychological status and a reduction in the recurrence of clinical manifestations including cardiac arrest, myocardial infarction and sudden death.1 Exercise recommendations are made even though the specific benefits derived from an increase in physical activity by cardiac patients have not been established definitively nor has the relative safety of such participation been defined adequately. Data from various studies have consistently demonstrated an improved physical working capacity as the result of exercise training by selected cardiac patients due to changes in skeletal muscle and peripheral circulation with little apparent change in intrinsic myocardial performance.2 3 Generally these changes in work capacity are reflected in a slower heart rate at any submaximal workload and the ability to perform a higher workload before the onset of myocardial ischemia.2 Whether or not exercise training improves myocardial oxygen delivery still is an open question, but available results suggest that enhanced coronary blood
Vectorcardiographic quantification of infarct size in baboons.
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