Vulnerability to ventricular arrhythmia: assessment by mapping of body surface potential

MARTIN J. GARDNER, M.D., TERRENCE J. MONTAGUE, M.D., C. SUSAN ARMSTRONG, M.Sc., B. MILAN HORACEK, PH.D., AND ELDON R. SMITH, M.D.*

ABSTRACT It is now well established that the vulnerability of the ventricular myocardium to repetitive dysrhythm increases in the presence of greater than normal disparity of local recovery times. Local recovery is reflected in the electrocardiographic waveform as an area of the ventricular deflection (QRST time integral), and thus disparate ventricular recovery may be manifested in the body surface distribution of this quality. To assess this possibility, we obtained simultaneous 120-lead electrocardiograms from both the anterior and posterior torso in 140 subjects (ages 8 to 75) grouped as follows: group A, 97 normal subjects; group B, 16 patients resuscitated from ventricular fibrillation or sustained ventricular tachycardia; and group C, 27 patients 6 to 12 months after myocardial infarction but without clinically significant arrhythmia. In each subject, the QRST integral was evaluated for each lead and isointegral contour maps were plotted. A score was assigned to each map, based on the number of extrema; each maximum or minimum scored one point, with the exception of simultaneously occurring anterior and posterior minima on the right shoulder (frequently occurring in normal subjects), which scored together only one point. All but one group A subject had dipolar QRST integral maps (mean ± SD score 2.11 ± 0.2). Conversely, 10 of 16 (62.5%) group B patients had scores of 3 or more (mean 3.16 ± 1.08; p < .01 vs group A). Group C patients had intermediate values, with eight of 27 (29.6%) scoring 3 or more (mean 2.46 ± 0.83); this was less than in group B (p < .01), but more (p < .05) than in group A. Thus, patients with repetitive ventricular arrhythmia tend to have multipolar distributions on QRST integral maps, possibly reflecting dispersion of underlying properties of ventricular recovery. These results suggest that body surface potential mapping may provide a noninvasive means to detect substrate for life-threatening arrhythmias.


RECURRENT sustained ventricular tachycardia and ventricular fibrillation are major factors in the morbidity and mortality of patients with heart disease. The most frequent underlying cause of these arrhythmias is chronic ischemic heart disease, particularly previous myocardial infarction. Symptomatic ventricular tachycardia/fibrillation also occurs in the acute stages of myocardial infarction and may be found in patients with a variety of other disorders, including prolonged QT interval syndrome, and even on occasion in structurally normal hearts. In an effort to reduce the incidence of sudden cardiac death, a number of investiga-tive approaches have been designed to quantitate the risk of recurrent ventricular tachycardia/fibrillation in individual patients. Approaches have included investigation of clinical profiles of patients,1,2 exercise testing,3,4 prolonged electrocardiographic (ECG) monitoring,5,6 radionuclide evaluation of left ventricular function,7,8 delineation of underlying coronary artery disease,4,11 and programmed ventricular stimulation studies.12-14 With the possible exception of the latter invasive method, to date there is no reliable way to assess the risk of malignant ventricular arrhythmias either in individuals or in populations of patients.

While abnormalities of the ventricular depolarization/repolarization process have been considered essential prerequisites for the onset of ventricular repetitive arrhythmias, the precise electrophysiologic substrate for these arrhythmias has defied assessment by standard ECG techniques. Berbari et al.,15 using a special high-resolution technique, detected low-level (microvolt range) ECG signals during the ST segment
in experimental canine myocardial infarction. They postulated that the signal originated in the very small mass of excitable tissue with marked delay in activation. In the intervening years, the recording of late potentials at the body surface became a challenge that was successfully met by several groups of investigators.16–19 The careful preoperative and intraoperative mapping studies of Josephson et al.20,21 in patients with recurrent ventricular tachycardia provided convincing direct evidence that areas of delayed depolarization exist in humans, and moreover, that the late activity could also be detected during sinus rhythm.

It is probable, as well, that abnormalities in ventricular repolarization play at least as important a role in the genesis of ventricular arrhythmias as does the delayed depolarization.22 The importance of the magnitude of the ST segment displacement associated with acute myocardial infarction in predicting the occurrence of malignant ventricular arrhythmias has been appreciated for a long time.23,24 It is also recognized that the abnormal QT lengthening, apparently reflecting a prolonged repolarization process, can be occasionally demonstrated in patients with ventricular arrhythmias.25

Perhaps the most important electrophysiologic characteristic of cardiac states with increased vulnerability to repetitive arrhythmia found to date is a greater than normal disparity of recovery times.26–30 Abildskov et al.31 were the original proponents of the idea that the body surface manifestation of the disparity of repolarization could be detected and used as a noninvasive indicator of the increased risk of life-threatening arrhythmias. Moreover, they provided direct evidence linking QRST deflection area with ventricular recovery properties32 and suggested that the derived quantity of QRST area was a promising indicator of risk. The idea of an area of ventricular deflection on the electrocardiogram was introduced in 1934 by Wilson et al.33 as the “ventricular gradient”; they reasoned that the quantity was independent of activation sequence and that it reflected only repolarization properties. Abildskov and his colleagues34–38 have shown that QRST integrals of arbitrary unipolar ECG leads reflect local repolarization properties of ventricular myocardium. Therefore, multiple-lead QRST integral values displayed as body surface isointegral maps might provide a comparison of local repolarization properties from adjacent myocardial areas. A heterogeneity of such repolarization properties might then be demonstrated in patients with ventricular arrhythmias as a multipolar distribution of QRST integrals. The present study tests this hypothesis in patients with repetitive ventricular arrhythmias, normal subjects, and in patients with underlying ischemic heart disease but no clinically significant arrhythmias.

**Methods**

**Patient population.** One hundred and forty subjects were studied (table 1). Group A consisted of 97 normal control subjects, group B (table 2) of 16 patients who had maps recorded in close temporal proximity to an episode of ventricular fibrillation or sustained ventricular tachycardia requiring cardioversion, and group C of 27 patients who underwent body surface potential mapping 6 to 12 months after uncomplicated myocardial infarction.

Group A subjects had no evidence of heart disease on history, physical examination, 12-lead electrocardiogram, or echocardiogram.

As outlined in table 2, seven group B patients were resuscitated from ventricular fibrillation and nine had documented sustained ventricular tachycardia requiring cardioversion. Thirteen of the group B patients had underlying ischemic heart disease and four had evidence of long QT interval syndrome. Of the 13 with ischemic heart disease, five had sustained a recent acute myocardial infarction, whereas the remainder had chronic disease; three of the latter had clinical evidence of ventricular aneurysm.

Group C patients had no evidence of significant ventricular arrhythmias. All had a stable course after acute myocardial infarction; 15 had an anterior and 12 an inferior site of myocardial damage.

**Body surface potential mapping.** All patients underwent a session of body surface potential mapping. Acquisition and processing of ECG data were as follows.39 Digitized ECG signals were recorded simultaneously from 117 torso and three limb electrodes with the use of Wilson’s central terminal as reference and at a sampling rate of 500 samples/second/channel. The ECG signals were then processed off-line on a Xerox Sigma 5 computer. Selective averaging of 15 continuous seconds of recorded PQRS-T complexes was performed for each lead; artifacts and ectopic beats were rejected and the average complex was constructed from “similar” complexes, with the UP interval as baseline. Individual leads were visually edited for waveform appearance and baseline drift and invalid leads were rejected and interpolated from surrounding lead values.

The time instants of QRS onset and offset and T wave offset were identified from edited Frank X, Y, and Z leads. The QRS time integral was calculated for each lead as the algebraic sum of all potentials from the time instant of QRS onset to QRS offset, multiplied by the sampling interval. This represented the net area under the QRS curve with the UP interval baseline taken as zero potential (figure 1). The ST-T time integral was similarly calculated from the time instant of QRS offset to the T wave offset and the QRST time integral was the algebraic sum

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Population</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Description</th>
<th>Mean age (yr)</th>
<th>Sex (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>97</td>
<td>Normal subjects</td>
<td>29.8/22–49</td>
<td>59/38</td>
</tr>
<tr>
<td>B</td>
<td>16</td>
<td>Patients with VT/VF</td>
<td>55.4/8–75</td>
<td>14/2</td>
</tr>
<tr>
<td>C</td>
<td>27</td>
<td>Patients with MI</td>
<td>52.4/32–67</td>
<td>26/1</td>
</tr>
</tbody>
</table>

VT/VF = ventricular tachycardia/fibrillation; MI = myocardial infarction.
TABLE 2

Group B patients

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age (yr) and sex</th>
<th>Arrhythmia</th>
<th>Cause</th>
<th>Medication</th>
<th>Event-BSPM (days)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>58, M</td>
<td>VT</td>
<td>IHD, LVA</td>
<td>Lidocaine</td>
<td>1</td>
</tr>
<tr>
<td>B2</td>
<td>71, M</td>
<td>VF</td>
<td>aMI</td>
<td>Quinidine</td>
<td>1</td>
</tr>
<tr>
<td>B3</td>
<td>56, M</td>
<td>VT</td>
<td>aMI</td>
<td>Procainamide</td>
<td>1</td>
</tr>
<tr>
<td>B4</td>
<td>58, M</td>
<td>VF</td>
<td>aMI, LVA</td>
<td>Quinidine</td>
<td>-120</td>
</tr>
<tr>
<td>B5</td>
<td>69, M</td>
<td>VF</td>
<td>IHD, LVA</td>
<td>Disopyramide</td>
<td>180</td>
</tr>
<tr>
<td>B6</td>
<td>62, M</td>
<td>VF</td>
<td>IHD, LVA</td>
<td>Procainamide</td>
<td>21</td>
</tr>
<tr>
<td>B7</td>
<td>54, M</td>
<td>VF</td>
<td>IHD</td>
<td>Brettyllium</td>
<td>6</td>
</tr>
<tr>
<td>B8</td>
<td>60, M</td>
<td>VT</td>
<td>IHD</td>
<td>Procainamide</td>
<td>—</td>
</tr>
<tr>
<td>B9</td>
<td>30, M</td>
<td>VF</td>
<td>IHD</td>
<td>Disopyramide</td>
<td>—</td>
</tr>
<tr>
<td>B10</td>
<td>47, F</td>
<td>VT</td>
<td>LQT</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>B11</td>
<td>52, M</td>
<td>VT</td>
<td>IHD</td>
<td>—</td>
<td>14</td>
</tr>
<tr>
<td>B12</td>
<td>8, M</td>
<td>VT</td>
<td>LQT</td>
<td>Diphenylhydantoin</td>
<td>60</td>
</tr>
<tr>
<td>B13</td>
<td>68, M</td>
<td>VT</td>
<td>LQT, IHD</td>
<td>—</td>
<td>6</td>
</tr>
<tr>
<td>B14</td>
<td>63, F</td>
<td>VT, TdP</td>
<td>LQT</td>
<td>—</td>
<td>15</td>
</tr>
<tr>
<td>B15</td>
<td>75, M</td>
<td>VT</td>
<td>aMI</td>
<td>—</td>
<td>3</td>
</tr>
<tr>
<td>B16</td>
<td>47, M</td>
<td>VF</td>
<td>aMI</td>
<td>—</td>
<td>2</td>
</tr>
</tbody>
</table>

VT = ventricular tachycardia; VF = ventricular fibrillation; aMI = acute myocardial infarction; IHD = chronic ischemic heart disease; LQT = long QT interval; LVA = left ventricular aneurysm; TdP = torsades de pointes.

*This column lists the time in days from the initial arrhythmia to the body surface potential mapping (BSPM), with negative numbers referring to BSPM recorded before the arrhythmia.

of the QRS and ST-T time integrals (figure 1). The physical units of time integral values are microvolt seconds.

The display format for individual QRST isointegral maps appearing in figure 2 is as follows. The rectangular area of each map represents the torso with both left and right margins corresponding to the right mid-axillary line. The left half of the map, therefore, represents the anterior torso and the right half the back. Each contour line within the rectangle connects points of equal time integral value. The contour lines progress logarithmically from the zone of near-zero integral value. The solid lines represent positive values and the interrupted lines, negative values.

Previous study of normal adults has shown that the normal QRST time integral pattern has a dipolar character with two extrema: one positive (maximum) and one negative (minimum). A QRST extremity was defined as a circumscribed peak or trough in the otherwise smooth and graduated potential distribution. We also recognized a feature in the QRST integral distribution sometimes termed a pseudopod. This was defined as a narrow extension of positive or negative potentials into a zone of potentials of opposite polarity. This feature was included in the BSPM evaluated. It was valued as one-half of a scoring point, while an extreme counted one full point. Maps with negativity on the right shoulder that occasionally split into an anterior and a posterior minimum were an exception; these maps were treated as if the anterior and posterior minimum were only one extreme. For the purposes of this study, a QRST isointegral map that scored 3 or more points was considered abnormal and designated as "multipolar." The number of extrema per map, the multipolarity score per map, the mean number of extrema and mean score per group, and the percentage of "multipolar" maps in each group were then calculated. Differences between groups were compared by one-way analysis of variance.

As noted in table 2, nine of 16 group B subjects were being treated with type I antiarrhythmic medications at the time of body surface mapping. The effect of such medication on the standard electrocardiogram is well known, with recognized increases in QRS and QT interval duration. To determine whether such medications could independently cause multipolarity in QRST isointegral maps, 15 group A subjects underwent repeat potential mapping after infusion of 500 mg procainamide. QRST isointegral maps before and after drug infusion were compared with respect to the presence or absence of multipolarity.

Results

Figure 2, a, depicts QRST isointegral maps from 15 normal subjects randomly selected from group A (see table 1), and column b shows maps after the infusion of quinidine. Figure 3 displays the maps for patients in group B (see tables 1 and 2), i.e., patients with repetitive ventricular arrhythmias; and figure 4 depicts the maps of group C (see table 1), i.e., patients with previous uncomplicated myocardial infarction. Note that in comparison with the normal patterns in figure 2 many of the maps of the patients with ventricular tachycardia/fibrillation in figure 3 have multiple extrema and pseudopods. Table 3 outlines the results of the
quantitative analysis. Ten of 16 (62.5%) patients with ventricular arrhythmias (group B) had multipolar maps by our criteria. This was different (p << .01) from results in group A, in which only one of 97 normal subjects had a multipolar map. Patients in group C had an intermediate result, with eight of 27 (29.6%) having "multipolar" maps; this was less than in group B (p < .01), and more than in group A (p < .05). Thus, patients with malignant ventricular arrhythmias tended to have a multipolar distribution of QRST time integrals compared with normal subjects and even compared with patients with previous myocardial infarction. Table 3 also reveals that the span of amplitudes measured between the main maximum and the main minimum of the QRST integral distribution is larger in normal subjects than in patients with ventricular tachycardia/fibrillation (p << .01). This probably reflects the more organized (nonfragmented) distribution of repolarization properties through the ventricular myocardium in normal individuals.

The incidence or degree of multipolarity of the QRST isointegral maps in group B subjects did not seem to be dependent on their underlying heart disease, type of ventricular arrhythmias (tachycardia or fibrillation), or whether or not they were being treated with antiarrhythmic medication. A more rigorous comparison between the various subsets of patients was not possible because of the limited sample size.

Figure 2 further shows the 15 QRST isointegral maps from group A subjects before and after infusion of procainamide. No significant differences are noted in the distribution patterns. The medication tended, however, to alter the amplitude of the extrema.

**Discussion**

The results of this investigation reveal that patients with malignant ventricular arrhythmias have a very high prevalence of multipolarity in the body surface distribution of the QRST integral. We believe that this abnormality represents a measure of the heterogeneity of underlying repolarization properties in these patients. Such heterogeneity of repolarization is an important substrate for the development of ventricular arrhythmias. Han and Moe26 have demonstrated previously that the vulnerability to ventricular fibrillation was increased by factors that created a disparity in the recovery properties of ventricular muscle. Such disparity, or nonuniform repolarization, may be a consequence of myocardial ischemia or infarction, metabolic abnormalities, or adrenergic imbalances. Not only the presence but also the degree of nonuniform repolarization is important, because increasing disparity in local recovery times resulted in lower ventricular fibrillation thresholds.

Wilson et al.33 first theorized that the QRST integral reflected primary ventricular repolarization properties. If repolarization was uniform throughout the ventricle, that is if action potentials were identical for all myocardial cells, one would expect the T wave to be of opposite polarity and of the same area as the QRS waveform. The fact that it is not so indicates that the recovery process is not uniform. Wilson et al. carried this argument further by stating that the adding of the area under the ST-T wave to the QRS area would cancel out those repolarization properties predetermined by the ventricular activation process ("secondary repolarization properties"), and the result would reflect primary repolarization properties. More recently, Abildskov et al.34 have demonstrated that changes in QRST area measured on the epicardial surface correlate very closely with changes in local refractory periods at the same site when these properties are altered by various maneuvers such as altering the surface temperature at that site. Urie et al.38 have further dem-
GARDNER et al. demonstrated in dogs that QRST isointegral (or isoarea) maps on the body surface are multipolar before the onset of ventricular arrhythmias associated with digitalis toxicity. Our results further support the concept that QRST isointegral mapping represents an index of the repolarization properties present in ventricular myocardium.

In this study, a multipolar map (with three extrema) was seen in only one normal subject. However, this report and others have demonstrated that a significant number of patients with previous myocardial infarction but no ventricular arrhythmias have multipolar maps. Whether or not this reflects increased vulnerability to malignant ventricular arrhythmia will require long-term follow-up in a large group of patients and/or correlation with other predictors of arrhythmogenic substrate, such as programmed ventricular stimulation.

Encouraged by our preliminary results, we have also applied the technique of QRST integral mapping in the investigation of sudden infant death syndrome. We found that the QRST isointegral maps in the population of infants at risk for sudden death were all "normal," i.e., smooth and bipolar, lending support to the

![FIGURE 2. QRST isointegral contour maps of 15 randomly selected normal subjects (group A) before (a) and after (b) infusion of procainamide. Rectangularly shaped maps depict in a cylindrical projection the torso-surface distribution of QRST integral values (in microvolt-seconds); the right and left borders correspond to the right midaxillary line and the upper/lower border to the neck/waist. Positive/negative values are indicated by solid/interrupted contour lines. The global extrema are identified by a sign symbol with the numerical value (in microvolt-seconds) and the local extrema are marked by a sign symbol (+ or −) only. Pseudopods are marked by an asterisk.](image-url)
FIGURE 3. QRST isointegral contour maps from 16 subjects (group B) who experienced episodes of ventricular tachycardia or fibrillation. The format is the same as in figure 2, with local extrema marked by a symbol sign ( + or - ) and pseudopods indicated by an asterisk.
concept that the cause of death in this syndrome is not primarily ventricular arrhythmia.

The interpretation of the results of this study must be done cautiously. While there is theoretical basis for correlating the QRST area with primary repolarization properties, there may be other factors that influence the

QRST area. One such factor may be the influence of antiarrhythmic medications. The use of such medications was not controlled in this study and it is possible that the results were influenced by the use of these drugs. We have demonstrated that QRST maps do not become multipolar simply as a result of such drug use.

**FIGURE 4.** QRST isointegral contour maps from 27 subjects (group C) with uncomplicated myocardial infarction. The format is as in figure 3.
TABLE 3
Statistical results

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean No. of extrema (± SD)</th>
<th>Mean point score (± SD)</th>
<th>No. with multipolar maps</th>
<th>Mean p-p amplitude (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.01±0.10</td>
<td>2.11±0.22</td>
<td>97/100 (97%)</td>
<td>180.6±75.0</td>
</tr>
<tr>
<td>B</td>
<td>2.94±0.93</td>
<td>3.16±1.08</td>
<td>10/16 (63%)</td>
<td>87.3±51.4</td>
</tr>
<tr>
<td>C</td>
<td>2.30±0.67</td>
<td>2.46±0.83</td>
<td>8/27 (27%)</td>
<td>117.9±51.1</td>
</tr>
</tbody>
</table>

Significance levels:

For No. of extrema and score

A vs B: p < .01
A vs C: p < .05
B vs C: p < .01

For p-p amplitude

A vs B: p < .01
A vs C: p < .01
B vs C: NS

Not all patients with sustained ventricular arrhythmias had abnormalities of repolarization as detected by this technique. It is also known that abnormalities of ventricular activation or depolarization are important in patients with recurrent sustained ventricular tachycardia and previous infarction. Such abnormalities are not assessed by QRST isointegral mapping.

In conclusion, the results of this study indicate that patients with ventricular fibrillation or recurrent ventricular tachycardia tend to have multipolar QRST body surface maps, a finding that is consistent with the presence of heterogeneity of ventricular recovery properties. Since this is frequently the substrate for the development of ventricular arrhythmia, this approach as well as other surface recording techniques warrant further investigation. Only with the development of sensitive and specific noninvasive means to detect and quantitate the risk of malignant ventricular arrhythmias will it be possible to determine whether the incidence of sudden cardiac death is importantly modified.

References

12. Wellens HJJ, Lie KI, Durrer D: Further observations on ventricular tachycardia as studied by electrical stimulation of the heart: chronic recurrent ventricular tachycardia and ventricular tachycardia during acute myocardial infarction. Circulation 49: 647, 1974
32. Abildskov JA, Evans AK, Lux RL, Burgess MJ: Direct evidence
relating QRS deflection area and ventricular recovery properties. Circulation 60(suppl II): II–110, 1979
33. Wilson FN, MacLeod AG, Barker PS, Johnston FD: The determination and significance of the areas of the ventricular deflections of the electrocardiogram. Am Heart J 10: 46, 1934
Vulnerability to ventricular arrhythmia: assessment by mapping of body surface potential.

M J Gardner, T J Montague, C S Armstrong, B M Horacek and E R Smith

Circulation. 1986;73:684-692
doi: 10.1161/01.CIR.73.4.684

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1986 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/73/4/684

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/