Critical Analysis of the Signal-Averaged Electrocardiogram
Improved Identification of Late Potentials

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Background. This study performed a critical analysis of signal-averaging methods. The objective was to optimize detection of late potentials.

Methods and Results. We studied two patient populations: a low-arrhythmia-risk group with no evidence of heart disease and a group with clinically documented ventricular tachycardia (VT). Filtered QRS duration (QRSd) and terminal QRS amplitude (RMS40) were measured from the vector magnitude. A QRSd duration based on the latest detectable ventricular activity in any of the three individual XYZ leads was also measured. Because of improved signal-to-noise ratio, both individual lead analysis and extended (600- versus 200-beat) averaging yielded significant changes in signal-averaged ECG parameters. Both approaches gave an increased sensitivity for VT identification. Sensitivity, specificity, and accuracy were evaluated as functions of critical values of QRSd and RMS40. RMS measurements in the terminal QRS, ranging from 20 to 100 msec and including RMS40, did not contribute to maximizing sensitivity and were highly correlated with QRSd. Our results from the low-arrhythmia-risk group suggest that age and sex should be considered in the definition of late potentials.

Conclusions. We propose a VT risk stratification scheme using signal-averaged ECG parameters obtained from both individual lead and vector magnitude analysis. This allows definition of four categories of VT risk derived statistically from the study data. This definition is based on combined measures of sensitivity, specificity, and negative and positive predictive value. (Circulation 1993;87:105-117)

KEY WORDS • signal averaging • tachycardia, ventricular • risk factors • electrocardiography

Ventricular late potentials originate from regions within and surrounding a ventricular infarct and are the result of slow or delayed conduction. They occur at the end of or after the normal QRS complex and are at the microvolt level when recorded on the body surface. Several studies have linked late potentials measured in the body surface signal-averaged electrocardiogram (SAECG) to late activation measured directly from the myocardium.1-5 Subsequently, many reports have appeared in the clinical literature linking late potentials to the presence of a reentrant substrate for ventricular tachycardia (VT).6-16

A survey of 10 representative studies of late potentials in postinfarction patients illustrates the wide range of signal-averaging methods used and results obtained.6-18 The definition of late potentials in the 10 studies above are based on filtered QRS duration (QRSd), amplitude of the terminal QRS (RMS40), and the duration of the low-amplitude signal. Values of QRSd ranging from >110-120 msec are considered significant, whereas values of RMS40 <20-25 μV have been used. These measures have been combined in different ways by different authors. The sensitivities and specificities in these studies ranged from 60% to 90% and 50% to 80%, respectively. Accuracy was not always reported, so the overall efficacy of methods could not be directly compared.

The duration of averaging has been set either by averaging a fixed number of beats or by averaging until a preset noise value is reached.19 Unfortunately, many studies do not report final averaged noise levels. In those that do, a useful comparison is impossible because of the different technical approaches taken to measuring noise. A similar problem occurs with measuring QRS limits. The operations on SAECG data of the various (unpublished) algorithms available in different signal-averaging systems are not directly comparable.

Although moves toward standardizing SAECG methods have been proposed,20 present signal-averaging techniques do not optimally detect late potentials. Evidence of the limitation of current methods is found in the reports that have compared measurements of epicardial and body surface late potentials.1-5 Discrepancies of ≥20 msec between the latest body surface activity and epicardial signals are commonly noted.4

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Our objective in the present study is to perform a critical analysis of SAECG methods with the aim of improving clinical performance. Clinical performance was quantified for a new definition of late potentials combining vector magnitude and individual lead SAECG parameters. The influence of noise on each SAECG parameter was considered and related to late potential detection rates.

We studied two patient groups from opposite ends of the arrhythmia risk spectrum. Continuing from previous theoretical work, we evaluated the advantages of analyzing individual leads as opposed to their vector magnitude. These results were compared with increasing the number of averaged beats (from 200 to 600). The effects of postaveraging noise levels can cause a significant underestimation of the QRS offset. This in turn affects QRS and RMS40. The relative usefulness of these late potential parameters and their performance with regular and extended averaging and with individual lead analysis were evaluated in terms of sensitivity, specificity, and accuracy of VT identification.

Finally, from our results and observations, we propose a new SAECG interpretation scheme. This classifies SAECG results into one of four arrhythmia risk categories defined statistically using the data of this study.

Methods

Patient Selection

We selected two groups of patients for study. Group 1 consists of 73 patients who initially presented with syncope. All subjects subsequently underwent thorough arrhythmia risk evaluation and were considered to have no evidence of significant heart disease. The specific criteria for inclusion into this low-arrhythmia-risk control group are a normal electrophysiological study result (no induction of any form of arrhythmia), a normal left ventricular ejection fraction (>50%), and the absence of any sign of myocardial infarction. Group 2 consists of 63 patients with clinical (spontaneous) VT, the induction of sustained monomorphic VT during electrophysiological study, and a prior myocardial infarction. These two patient groups permit a direct comparison of SAECG recordings between a low-arrhythmia-risk group similar demographically to the VT population and a VT group with a high probability of arrhythmogenic reentry substrate. Patients with bundle branch block were excluded from both groups.

Electrophysiological Testing

Ventricular stimulation was performed during normal sinus rhythm and with pacing at 600-, 500-, and 400-msec cycle lengths. Single, double, triple, and quadruple extrastimuli were applied at both the apex and the outflow tract. S1 was applied with progressively decreasing coupling interval to S1 until VT was induced or until effective refractoriness was encountered. In the latter case, S1 coupling was increased by 40 msec, and the procedure was repeated with S1 and S2.

Signal Averaging

Recording. All patients had SAECG recording performed either just before or shortly after electrophysiological study, typically in patients’ rooms. After careful skin preparation, three orthogonal bipolar XYZ leads were acquired (Predictor SAECG, Corazonix Corp.). Signal averaging was performed in real time using lead placement, equipment, and algorithms described previously. For each patient, three consecutive signal averages were computed, each average consisting of 200 beats. Signal averages were accepted for analysis if the peak-to-peak noise in the ST segment of the vector magnitude was <2.5 μV. This corresponds to 0.4 μV RMS of noise in an individual lead. With this conservative noise quality control, only high-fidelity recordings were accepted into the study.

Filtering. All SAECG recordings were analyzed after bandpass (a combination of high pass and low pass) digital filtering. A fourth order 40–250-Hz bandpass Butterworth filter was used in a bidirectional mode. The filtered XYZ leads are combined into a vector magnitude function, VM=(X²+Y²+Z²)½.

Combining averages. Before filtering and before the vector magnitude was calculated, three consecutive 200-beat signal averages were added together to produce a 600-beat average. This was possible because each signal average maintained the same fiducial point for QRS alignment and average formation. In four VT subjects, only one SAECG was available for analysis. These patients were included in all analyses except those involving 600-beat averages. The selection of 200- and 600-beat ensemble sizes was designed to give a normal and a very low noise average for each subject. The amount of noise reduction between 200- and 600-beat averages varies between subjects. This variation permits us to correlate averaged noise levels with other variables.

QRS measurements. Derivation of both QRS and RMS40 depends on identifying the onset and, most importantly, the offset of the QRS. The QRS limits are identified with a computer algorithm. Identification of the QRS onset is usually straightforward, although filtering of the P wave into the QRS complex can sometimes obscure the exact point of onset. Identification of the QRS offset, i.e., the latest moment of ventricular activation, is more complicated. Late potentials generally decrease in amplitude as they become later until the smallest signals merge with and become indistinguishable from the noise of the filtered ST segment. The computer algorithm must therefore define a nominal QRS offset with respect to the noise. This point was defined as the latest moment that the SAECG terminal QRS waveform exceeds three times the RMS noise level in the filtered ST segment. Variants of this algorithm are commonly used in commercial SAECG systems. The algorithm was used in this study to identify QRS offset both in the vector magnitude and in all three of the filtered leads, using the absolute value of the latter waveforms. With individual lead analysis, the QRS duration was measured from the vector magnitude onset to the latest QRS offset of the three leads. The RMS40 value was found from the vector magnitude, using the 40-msec period preceding the latest individual lead QRS offset.

Measuring noise. Measurements of noise were made in a 70-msec interval in the filtered ST segment of the vector magnitude, ending at the start of the filtered T wave. In the few cases in which the filtered ST interval was <70 msec, a period of 40 msec was used. All intervals were checked visually to ensure no overlap
with the QRS. Noise measurements were made in all original signal averages and the 600-beat SAECG for each patient.

Time-varying RMS measurements. For each patient, an RMS-time (RMSxx) function was computed starting at the vector magnitude-derived QRS offset and moving in reverse time for a period of 100 msec. This function is defined as

$$\text{RMSxx}(T) = \sqrt{\frac{\sum_{t=\text{QRS offset}}^{\text{QRS offset} - T} VM(t)/T}{M0}}$$

for T equal to QRS offset minus 20 msec to QRS offset minus 100 msec, where VM(t) is the vector magnitude waveform. The RMS40 parameter is a single value of this function, which allows us to compare terminal RMS measurements over a range of 20–100 msec (e.g., RMS20, RMS60, etc.). The mean and SD of the RMSxx function were obtained for each of the two patient groups by averaging the RMSxx functions from all patients in each group. By use of these group-mean RMSxx functions, the relative separation of terminal QRS amplitudes between the two patient groups could be examined over any terminal QRS interval.

Defining late potentials. Late potentials were defined in terms of the SAECG parameters QRSd and RMS40. Representative critical values of QRSd of 120, 114, and 110 msec were used primarily to define late potentials. An RMS40 value of <20 µV was also used, where indicated, to define late potentials. Part of the experimental objective was to investigate the effect on sensitivity of varying the QRSd/RMS40 definitions of late potentials continuously throughout a range of QRSd and RMS40 critical values. The exact definitions of late potentials used in each experiment are stated in the “Results.”

Data processing and quality control. A total of 132 patients were studied. Approximately 1,000 waveforms, three individual leads, and a vector magnitude for each original signal average and the summed averages were analyzed. The operations of filtering, vector magnitude calculation, QRS onset and offset determination, noise measurements, and summing of averages were performed automatically in a “batch processing” mode. The processed SAECG waveform, with QRS limits and SAECG parameters (QRSd and RMS40) indicated, were available as hard-copy output. These results were overread by two of the investigators independently to correct for obvious algorithmic errors.

Statistical Analysis

All statistical analysis was done with the SAS software package (SAS Institute Inc.). The methods used consisted of multivariate regression to test for correlation between variables, Student's t test for comparing means of two independent variables, and ANOVA for comparing means and seeking significant differences among more than two independent variables. When ANOVA was used, comparison of means was performed with the Tukey-Kramer test to minimize type 1 errors, i.e., to minimize the number of untrue significant differences between variables. Consequently, the ANOVA results should be considered conservative tests for significant differences.

Results

Use of Individual Lead Analysis and Extended Averaging

Figure 1 illustrates how reproducible late potentials in the SAECG can be lost in the vector magnitude transformation because of the effects of residual noise. This patient is taken from the VT group. The three XYZ leads have differing signal-to-noise ratios, with the low-level late potentials prominent only in the Y lead. Panel A shows the 600-beat signal-averaged Y lead and the three constituent 200-beat waveforms. Late potentials are not obviously present in any of the 200-beat SAECGs and are not detected by the computer algorithm. In the 600-beat SAECG, the improved signal-to-noise ratio allows the computer algorithm to recognize the latest ventricular activity in the Y lead, which has a peak-to-peak amplitude of about 1 µV. In retrospect, this late signal activity can be seen to be reproduced in
each of the 200-beat Y lead waveforms but at a poorer signal-to-noise ratio, which accounts for its nondetection by the computer algorithm. Panel B shows the 600-beat SAECG vector magnitude. The late signals present in the Y lead are not visible in the vector magnitude. Since the X and Z leads have a worse signal-to-noise ratio than the Y lead, the combination of the three leads into their vector magnitude degrades the overall signal-to-noise ratio. The computer algorithm misses the latest activity, and the vector magnitude underestimates the latest moment of ventricular activity by 52 msec. The vector magnitude QRS duration is thus 113 msec as opposed to 165 msec when measured in the Y lead.

Table 1 shows the mean QRS and RMS40 values in the low-arrhythmia-risk and VT patient groups. These data are evaluated for four cases: using 200-beat and 600-beat signal averages and using the computer-derived QRS offset from the vector magnitude waveform and from the longest individual XYZ lead. (Note that individual lead QRSd is measured from the vector magnitude QRS onset to the latest individual lead QRS offset.) Referring to Table 1, in the low-arrhythmia-risk group, only the differences in QRS duration between the 600-beat vector magnitude and 200-beat individual lead cases are not significantly different. For the VT group, only the differences in QRS duration between the 200-beat vector magnitude and 600-beat individual lead cases are significantly different (ANOVA; criterion, p<0.05).

Figures 2 and 3 illustrate results for subjects from the VT and low-arrhythmia-risk groups, respectively. Note that all traces are shown with the same scaling (0–20 μV) so that noise levels and algorithm-selected QRS offsets can be compared. In Figure 2, panel A shows the absolute value of the filtered XYZ lead waveforms of a 200-beat signal average. Panel B shows the vector magnitude. The QRS offsets for both the XYZ and vector magnitude waveforms are chosen with the same computer algorithm. Panels C and D are in the same

Table 1. Mean QRS and RMS40 Values in Two Patient Groups

<table>
<thead>
<tr>
<th>SAECG</th>
<th>Patient group</th>
<th>QRSd (msec) (mean±SD)</th>
<th>RMS40 (μV) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200-Beat VM</td>
<td>Low-risk</td>
<td>100.0±9.7</td>
<td>34.4±22.3</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>142.2±31.3</td>
<td>17.6±17.2</td>
</tr>
<tr>
<td>600-Beat VM</td>
<td>Low-risk</td>
<td>102.9±9.6</td>
<td>29.2±20.0</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>148.1±30.0</td>
<td>13.6±12.0</td>
</tr>
<tr>
<td>200-Beat IL</td>
<td>Low-risk</td>
<td>102.0±10.1</td>
<td>30.5±21.6</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>145.5±30.6</td>
<td>14.7±15.2</td>
</tr>
<tr>
<td>600-Beat IL</td>
<td>Low-risk</td>
<td>106.0±10.0</td>
<td>23.4±16.7</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>153.2±28.2</td>
<td>9.8±9.7</td>
</tr>
</tbody>
</table>

QRSd, QRS duration; RMS40, amplitude of the terminal 40 msec of QRS; SAECG, signal-averaged ECG; VM, vector magnitude; IL, individual lead; VT, ventricular tachycardia.

Figures 2. Signal-averaged ECG. Comparison of 200-beat, 600-beat, and individual lead versus vector magnitude analysis in a ventricular tachycardia subject. Panel a: 200-beat individual X, Y, and Z leads (top to bottom), filtered and displayed as an absolute value; panel b: the corresponding 200-beat vector magnitude; panel c: 600-beat individual XYZ leads; panel d: 600-beat vector magnitude. QRSd, QRS duration; RMS40, amplitude of the terminal 40 msec of QRS.
format and show the results of the 600-beat signal average. Using a late potential definition of QRSD >120 msec, the 200-beat vector magnitude is a negative result. However, a late signal in the 200-beat Z lead (panel A) is reproduced in the Z lead of the 600-beat average (panel C). The 600-beat vector magnitude has a lower noise level, the QRS offset is subsequently detected later, and the study becomes positive. The latest signals detected in the 600-beat vector magnitude can be seen in the 200-beat vector magnitude but with a poorer signal-to-noise ratio and are not detected by the computer algorithm. Using a QRS duration derived from individual lead analysis, both the 200- and 600-beat averages are positive studies. Figure 3 shows the results from a low-arrhythmia-risk subject in the same format. Using a late potential definition of QRSD >120 msec, both the 200- and 600-beat averages are negative studies with analysis of the vector magnitude and individual leads.

Relation Between SAECG Parameters and Sensitivity, Specificity, and Accuracy

Figure 4 is a graphical representation of sensitivity, specificity, and accuracy as functions of critical values of QRSD and RMS40. Data from the 600-beat vector magnitude case were used. Late potentials or an abnormal SAECG were defined as QRSD >80–160 msec in steps of 5 msec or RMS40 <1–50 μV in steps of 5 μV. Sensitivity, specificity, and accuracy values are shown for each combination of QRSD and RMS40 critical values. This figure gives a global perspective of the interaction between sensitivity, specificity, and accuracy and SAECG parameters. Notice that the maximum values of sensitivity, specificity, and accuracy occur at the extreme ends of the RMS40 range. The maximum accuracy is obtained with a QRSD criterion alone of 120 msec (RMS40=0 μV).

The data in Table 2 are abstracted from these graphs. Sensitivity, specificity, and accuracy are shown for late potential definitions of QRSD >110, 114, and 120 msec and RMS40 <20 μV using both 200- and 600-beat individual leads and vector magnitudes. QRSD and RMS40 are not combined in any way. Referring to Table 2, with a late potential definition of QRSD >120 msec, sensitivity increases from 74.6% to 86.4% between the 200-beat vector magnitude and 600-beat individual lead cases. With a late potential definition of QRSD >110 msec, the sensitivity for the 600-beat individual lead case increases to 96.6%. Specificity decreases as sensitivity increases. This decrease is caused by the presence of very-low-level late QRS signals observed in many of the low-arrhythmia-risk subjects. Accuracy (which reflects the balance between the two) is more or less constant for late potential definitions of QRSD >120 and 114 msec but drops off for QRSD >110 msec. Table 2 also shows the clinical performance of the SAECG based on RMS40 alone. This was inferior to the use of the QRSD criterion, particularly in accuracy. Combining the two parameters failed to improve clinical performance (compare with Figure 4), as will be discussed below.

Relation Between QRSD and RMS40 Parameters

Figure 5 shows a scatterplot of the two variables, QRSD and RMS40, computed from the 600-beat SAECG vector magnitude for both the low-arrhythmia-risk and VT groups. Statistically, both QRSD and RMS40 significantly differentiate the two groups (Table 1). The scatterplot format for displaying SAECG parameters allows a number of observations to be made.
First, although most VT subjects have an abnormal RMS40 value, i.e., <20 $\mu$V, in the low-arrhythmia-risk group the RMS40 parameter appears uniformly spread over the range of 4–90 $\mu$V. This suggests that RMS40 is a nonspecific parameter. Very-low-level late QRS signals (RMS40 <4 $\mu$V) uniquely identify 19% (11 of 59) of the VT subjects. However, if late potential definitions of QRS >120 msec and 114 msec are used (typical in the literature), the RMS40 parameter does not independently identify any VT subject. This can be seen from Figure 5. No VT subject has an RMS40 value <4 $\mu$V (i.e., outside the range of the low-arrhythmia-risk group) who does not also have a QRS duration >120 msec. Hence, in this data set, RMS40 is not useful for VT prediction independently of QRS.

A computer was used to test combined criteria for QRS and RMS40 in the ranges shown in Figure 4. Both logical “or” and logical “and” rules were applied. No critical value for RMS40 could be found that improved both the sensitivity and accuracy compared with using QRS alone. The maximum sensitivity of 96.6% was obtained in the 600-beat individual lead analysis using only a criterion of QRS >110 msec. Accuracy in this case was 77.3%.

Figure 5 also shows a computer-calculated trend line for the QRS and RMS40 parameters in the low-arrhythmia-risk group. QRS and RMS40 values are highly correlated (regression line: QRS = -0.32x RMS40+112.4, correlation coefficient = 0.68, p=0.001). A similar trend was found for the VT group (regression line: QRS = -1.07xRMS40+160.0, correlation coefficient = 0.45, p=0.0001). The p values result from a t test to determine whether or not the correlations differ significantly from zero. In both patient groups, QRS and RMS40 are very significantly correlated.

Use of Terminal QRS Measurements

We investigated whether an interval for computing a terminal QRS RMS amplitude existed that could optimally separate the two patient groups. An RMSxx function, where xx is 20–100 msec, was computed for each subject in the low-arrhythmia-risk group. The RMSxx functions for each patient were then averaged. This procedure was repeated for the VT group. The results are shown in Figure 6A. The two curves depicted are the two average RMSxx curves for the two patient groups, using the 600-beat vector magnitude data. Because of their wide variance, it is difficult to assess the degree of separation of these two curves statistically. A reasonable approach is to compute their ratio at each value. This ratio curve, shown in Figure 6B, suggests that short-duration RMSxx parameters (e.g., RMS20) and long-duration RMSxx parameters (e.g., RMS80) will not be useful for distinguishing VT and non-VT patients.

The maximum separation, as suggested by this ratio curve, would be at the peak value, i.e., at RMS55, rather than RMS40. The RMS55 parameter for the 600-beat vector magnitude SAECGs was subsequently computed. Using a computer-derived optimum criterion of RMS55 <50 $\mu$V, the RMS55 values resulted in a greater separation between the two patient groups than RMS40 (Table 3). However, RMS55 values still did not independently identify a single VT subject with a QRS duration <120 msec. QRS was also highly correlated with RMS55. (Low-arrhythmia-risk group regression line, QRS = -0.15xRMS55+112.7; correlation coefficient = 0.63; p=0.0001. VT group regression line, QRS = -0.90xRMS55+165.6; correlation coefficient = 0.59; p=0.0001.)

Influence of Noise

Table 4 shows the correlations (r) between noise and QRS and RMS40 in the 600-beat vector magnitude SAECG and the probability (p) that each correlation coefficient is insignificant (i.e., does not differ from zero). In this case a low p value reflects a significant correlation. In both the VT and low-arrhythmia-risk
TABLE 2. Sensitivity, Specificity, and Accuracy as Functions of Critical Values of QRSD and RMS40

<table>
<thead>
<tr>
<th>SAECG</th>
<th>Late potential definition</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
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<tbody>
<tr>
<td>200-Beat VM</td>
<td>QRSD&gt;120 msec</td>
<td>74.6</td>
<td>98.6</td>
<td>87.5</td>
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<td>QRSD&gt;114 msec</td>
<td>79.4</td>
<td>93.2</td>
<td>86.8</td>
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<tr>
<td></td>
<td>QRSD&gt;110 msec</td>
<td>82.5</td>
<td>83.6</td>
<td>83.1</td>
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<td>RMS40&lt;20 μV</td>
<td>68.3</td>
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<td>90.4</td>
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<td>81.0</td>
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<td>75.3</td>
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<td>RMS40&lt;20 μV</td>
<td>77.8</td>
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<td>600-Beat IL</td>
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<td>RMS40&lt;20 μV</td>
<td>93.2</td>
<td>52.1</td>
<td>70.0</td>
</tr>
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</table>

QRSD, QRS duration; RMS40, amplitude of the terminal 40 msec of QRS; SAECG, signal-averaged ECG; VM, vector magnitude; IL, individual lead.

groups, QRSD is not correlated with noise. RMS40 values for the low-arrhythmia-risk group are also uncorrelated with noise. This suggests that RMS40 values in patients without late potentials are not particularly sensitive to noise-induced variability in the QRS offset. In contrast, for the VT group, a correlation exists between RMS40 and noise. In patients with late potentials, RMS40 values appear to be significantly influenced by noise.

Figure 7 shows a comparison of noise in the 200-beat and 600-beat SAECGs for each VT subject. Note that the (relatively high) noise values shown are for the vector magnitude. Both individual lead and vector magnitude mean noise levels are given in Table 5. For the VT group, the noise values from individual leads are 0.50 and 0.29 μV for the 200- and 600-beat averages, respectively. The expectation is a reduction in amplitude of noise by a factor of 1.732 (≈ \sqrt{3} ≈ \sqrt{600/200}) when going from 200 to 600 beats. As Figure 7 shows, the actual improvement varies greatly because of the unpredictable and statistical nature of noise. The mean noise reduction factor between the 200- and 600-beat SAECGs is 1.70 (0.39/0.23) for the low-arrhythmia-risk group and 1.72 (0.50/0.29) for the VT group. These figures are very close to the predicted value of 1.732, verifying that, considering each group, mean noise values are equivalent to those that would have been obtained by averaging to a fixed noise end point. Individual subjects deviate significantly from this expected noise reduction.

Noise is significantly less in the low-arrhythmia-risk group than in the VT group. This finding reflects the presence of late signal components present in individual leads but masked in the vector magnitude. These signals may extend into the noise measurement period in some VT subjects, artificially biasing the measured noise value. Note that in all subjects, the noise interval was visually checked to ensure no evident overlap with the QRS interval.

Variations in SAECG Parameters Due to Demographics and Site of Myocardial Infarction

Table 6 shows the breakdown of age and sex with signal-averaging parameters taken from the 600-beat SAECG for the two patient groups. The two groups are very closely age matched, with a higher proportion of men in the VT group. The signal-averaging parameters are significantly different between the men and women in the low-arrhythmia-risk group. Their ages are closely matched (probability of no difference, p=0.71). Both QRSD and RMS40 values are significantly different (p=0.0001 and p=0.02, respectively). In the VT group, the women both are older and have more abnormal SAECG parameters. However, the number of women is too small to test the significance of this observation statistically.

![Figure 5](http://circ.ahajournals.org/). Scatterplot of QRS duration and RMS40 values for each subject, measured from the 600-beat vector magnitude (VM). A computed trend line for the low-arrhythmia-risk (LAR) subjects illustrates the strong correlation between QRS duration and RMS40. VT, ventricular tachycardia.
Table 3. Separation Between Two Patient Groups at RMS40 and RMS55

<table>
<thead>
<tr>
<th>Patient group</th>
<th>QRSD (msec)</th>
<th>RMS40 (μV) (mean±SD)</th>
<th>RMS55 (μV) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>102.9±9.6</td>
<td>29.2±20.0</td>
<td>63.1±39.2</td>
</tr>
<tr>
<td>VT</td>
<td>148.1±30.0</td>
<td>13.6±12.0</td>
<td>23.0±19.4</td>
</tr>
</tbody>
</table>

RMS40, amplitude of terminal QRS; RMS55, peak QRS value; QRSD, QRS duration; VT, ventricular tachycardia.

Table 4. Correlations Between Noise and QRSD and RMS40 in 600-Beat Vector Magnitude Signal-Averaged ECG

<table>
<thead>
<tr>
<th>Group</th>
<th>QRSD vs. noise</th>
<th>RMS40 vs. noise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>r=0.66</td>
<td>R=0.07</td>
</tr>
<tr>
<td></td>
<td>p=0.65</td>
<td>P=0.44</td>
</tr>
<tr>
<td>VT</td>
<td>r=0.43</td>
<td>R=0.23</td>
</tr>
<tr>
<td></td>
<td>p=0.61</td>
<td>P=0.04</td>
</tr>
</tbody>
</table>

QRSD, QRS duration; RMS40, amplitude of terminal 40 msec of QRS; VT, ventricular tachycardia; r, correlation; p, probability that each correlation coefficient is insignificant.

definition of late potentials of QRSD >120 msec, the sensitivity of the SAECG is higher for patients with inferior as opposed to anterior infarctions. Sensitivity improves as noise is decreased both by extended averaging and individual lead analysis and is similar for both types of infarction in the 600-beat individual lead case.

Interpretive SAECG Chart

Using only the study data, an interpretive SAECG chart was developed that is based on VT risk stratification. The SAECG chart is shown in Figure 8. The SAECG parameters used are RMS40, individual lead QRSD (ILD), and vector magnitude QRSD (VMD). If RMS40 is <4 μV, the study is immediately considered abnormal (compare with Figure 5). The chart is divided into four VT risk regions: normal, borderline normal, borderline abnormal, and abnormal. SAECG values of ILD and VMD are read from the chart to locate the VT risk region. The increased sensitivity given by ILD is combined with the more specific VMD parameter. Regions of probable algorithm error for detection of QRS limits are also defined. The statistical techniques used to develop the region boundaries are developed in the "Appendix."

Discussion

Use of Individual Lead Analysis and Extended Averaging

In an earlier theoretical study,21 we analyzed the relative performances of the vector magnitude function and individual lead analysis for detecting late potentials using a computer simulation. Results of this simulation indicated that the performance of the vector magnitude was limited because its signal-to-noise ratio is degraded compared with that of the individual XYZ leads. This causes the QRS offset to be chosen at a consistently earlier point than it would be if taken as the latest QRS offset of the three leads analyzed individually. The data presented in Table 1 confirm the previous theoretical findings. Both extended averaging and individual lead analysis enhance the detection of late potentials.

Extended averaging increases the duration of the SAECG test significantly: noise levels are reduced by a factor of √2, with each doubling of the number of beats averaged. The duration of the test increases rapidly, with diminishing improvements in noise reduction. Hence, analysis of individual leads advantageously detects low-level late potentials in some patients.

Relation Between SAECG Parameters and Sensitivity, Specificity, and Accuracy

The study results suggest that both individual lead analysis and extended averaging can each increase
sensitivity by between 5% and 10%. This is achieved by raising the signal-to-noise ratio of the SAECG. However, the gain in sensitivity is at the expense of an almost equal cost in specificity. This is caused by the appearance of very-low-level terminal QRS signals, 0.25–0.5 μV peak, in low-arrhythmia-risk subjects. These signals are not apparently related to arrhythmia risk. The significance of these signals, which may be influenced by the presence of coronary artery disease or other clinical factors, is unknown and remains to be investigated. 

The trade-off between sensitivity and specificity can be set by adjusting the definition of late potentials based on QRS duration. Accuracy was optimized for critical values of QRSD between 114 and 120 msc. Hence, despite the choice of patient groups, the optimal definition of late potentials derived from these data agrees very well with other reports. 6–15 Sensitivity was effectively maximized for a critical QRSD value of 110 msc, although accuracy was compromised compared with values of 114 and 120 msc.

For any particular definition of late potentials, sensitivity increases and specificity decreases as the signal-to-noise ratio of the SAECG improves. The three-dimensional displays of sensitivity, specificity, and accuracy versus QRSD and RMS40 (Figure 4) show how these clinical measures can be established using different definitions of late potentials. A definition of late potentials may be selected to give either a high positive or high negative predictive value for the SAECG result. Using the study data, we have used this approach to produce an interpretive SAECG chart, discussed in the “Appendix.” The chart combines sensitivity, specificity, and positive and negative predictive value to classify SAECG results into one of four categories. These categories are normal, borderline normal, borderline abnormal, and abnormal. The categories are defined by use of a single critical value of RMS40 and stratified values of QRSD measured from both the vector magnitude and individual leads.

Relation Between QRSD and RMS40 Parameters

The very significant correlation (p<0.001) found between QRSD and RMS40 indicates that these parameters are not independent. They are not contributing unique information for identifying the presence of late potentials. Many recent studies have found QRSD to be the most useful parameter for identifying late potentials but have also found RMS40 to be useful. The scatter-plot showing the distribution of QRSD and RMS40 values (Figure 5) suggests that RMS40 is of limited use as an independent parameter. The uniform spread of RMS40 values in the low-arrhythmia-risk group (4–90 μV) suggests that this parameter is nonspecific and that a low value is not necessarily associated with risk of VT. In particular, no VT subject with a normal QRSD was identified by an RMS40 value that did not fall within the range of values from low-arrhythmia-risk subjects.

Why have other studies found RMS40 to be independently useful? Since QRS offset is determined by the signal-to-noise ratio, it must be strongly correlated with noise. The lack of correlation between QRSD and noise (Table 5) in both patient groups implies that a wide range of QRSD values occurs naturally. An abnormal QRSD value falling in the normal range may have an associated abnormal RMS40 value.

The data of Table 5 also show that RMS40 is correlated with noise level in the VT group but not in the low-arrhythmia-risk group. This suggests that the value of RMS40 is heavily dependent on the exact QRS offset chosen when late potentials are present. A small change in QRS offset (1–5 msec) induces a small change in QRSD, typically <5% but can cause a large change in RMS40, e.g., ≥50%. At higher noise levels, the QRS offset is underestimated and RMS40 values will be greater. Hence, the RMS40 parameter will show a bias toward specificity with SAECG studies on the order of >0.5 μV RMS noise in an individual lead. In the low-arrhythmia-risk group, there is no correlation between RMS40 and noise, which suggests that RMS40 values also have a wide natural variability unrelated to noise or to VT risk. Hence, RMS40 is an unreliable parameter for VT identification, becoming less specific as noise is reduced and the quality of the SAECG study is improved.

Use of Terminal QRS Measurements

RMS55, the amplitude of the terminal 55 msec of the QRS, showed the best separation of the VT and low-arrhythmia-risk groups. However, the mean RMSxx functions computed for the two patient groups were otherwise unremarkable. Measurements of filtered QRS amplitude were therefore of marginal use in defining late potentials in this study.

### Table 5. Individual Lead and Vector Magnitude Mean Noise Levels

<table>
<thead>
<tr>
<th>SAECG</th>
<th>Patient group</th>
<th>VM noise (μV RMS)</th>
<th>IL noise (μV RMS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200-Beat</td>
<td>Low-risk</td>
<td>0.68±0.21</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>0.86±0.41</td>
<td>0.50</td>
</tr>
<tr>
<td>600-Beat</td>
<td>Low-risk</td>
<td>0.40±0.17</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>0.51±0.31</td>
<td>0.29</td>
</tr>
</tbody>
</table>

SAECG, signal-averaged ECG; VM, vector magnitude; IL, individual lead; RMS, QRS amplitude; VT, ventricular tachycardia.
Influence of Noise

Residual noise present after averaging is a major factor influencing SAECG results. Different noise estimation procedures in use in commercial devices can produce a wide range of values for the same intrinsic noise level. This is because of the random nature of noise. The most accurate method of measuring noise is to compute the signal variance over the ensemble during averaging.25 Otherwise, an RMS measurement of noise can be made retrospectively from the filtered ST segment. This approach has the advantage of recording noise levels as they are perceived by the algorithm for QRS offset detection. Its major disadvantage is that low-level signals hidden in the noise contribute to the measured noise level. These signals are distinguished from noise when the signal variance method is used. Hence, this latter method is superior for monitoring the noise estimate during averaging.

Using this approach, Steinberg and Bigger19 showed that detection rates for late potentials improved significantly when averaging was terminated at a residual noise level of 0.3 μV RMS as opposed to 1.0 μV RMS. These noise levels are typical individual lead values measured by the signal variance method. Referring to Table 5, individual lead noise values in this study are typically 0.39–0.50 μV for the 200-beat averages and 0.23–0.29 μV for the 600-beat averages. These are group-mean values and are approximately comparable to Steinberg’s figures. However, for any individual SAECG, the values of noise given by the signal variance method and the RMS measurement of the filtered ST segment will diverge significantly.

Our results confirm that noise reduction during averaging varies greatly between subjects for a fixed number of beats averaged (Figure 7). Our data also suggest that SAECGs with a residual noise level of 0.2–0.3 μV RMS will give results superior to those with noise levels on the order of 0.5 μV RMS. Hence, averaging to a fixed noise end point of 0.2–0.3 μV seems advisable. Adoption of a standard noise measurement technique is necessary to ensure an objective measure of the quality of SAECGs.

When the automatically selected QRS limits were overread by the investigators, it was observed that the interaction between algorithm operation and residual noise could be important in determining whether a particular SAECG result was positive or negative. Paradoxically, this is less of a problem with higher noise levels, where the lowest level, latest cardiac activity, is masked by the noise. At very low noise levels, particularly in some very quiet individual leads, false detection of the QRS offset was possible because of variations in noise level. The QRS offset detection algorithm suffers from the same problems as other noise measurements. Overreading of automatically detected QRS offsets on a suitably scaled display seems advisable.

Variations in SAECG Parameters Due to Demographics and Site of Myocardial Infarction

In the low-arrhythmia-risk group, the ages of the men and women were well matched (59.7 versus 60.8 years). Their SAECG parameters were significantly different, with the men having a longer QRS duration on average by 8.7 msec. This difference may be great enough to warrant adjusting the definition of late potentials according to sex. A possible explanation for the longer QRS duration in men is that their hearts are typically larger, and therefore, ventricular depolarization takes longer.

In the VT group, the women had a longer QRS duration by an average of 8.0 msec. However, the women were also significantly older (8.0 years). There is an insufficient number of women in the VT group to test reliably by ANOVA hypotheses that age and sex influence Sudden Cardiac Death (SCD), which is the leading cause of death among middle-aged and older people.

Table 6. Breakdown by Age and Sex for Two Patient Groups

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Sex/No.</th>
<th>Age (years) (mean±SD)</th>
<th>QRSD (msec) (mean±SD)</th>
<th>RMS40 (msec) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>M/40</td>
<td>59.7±15.9</td>
<td>106.9±8.3</td>
<td>24.3±14.5</td>
</tr>
<tr>
<td></td>
<td>F/33</td>
<td>60.8±14.6</td>
<td>98.2±9.0</td>
<td>35.0±23.8</td>
</tr>
<tr>
<td>VT</td>
<td>M/52</td>
<td>59.6±12.8</td>
<td>147.1±29.4</td>
<td>13.6±10.7</td>
</tr>
<tr>
<td></td>
<td>F/7</td>
<td>67.6±13.6</td>
<td>155.1±33.6</td>
<td>14.0±18.8</td>
</tr>
</tbody>
</table>

QRSD, QRS duration; RMS40, amplitude of the terminal 40 msec of QRS; VT, ventricular tachycardia.

Table 7. Breakdown of Results by Myocardial Infarction Location in Ventricular Tachycardia Group

<table>
<thead>
<tr>
<th>SAECG</th>
<th>MI location</th>
<th>No. of subjects</th>
<th>QRSD (msec) (mean±SD)</th>
<th>RMS40 (μV) (mean±SD)</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200-Beat VM</td>
<td>Inferior</td>
<td>23</td>
<td>148.7±26.2</td>
<td>12.3±9.2</td>
<td>82.6</td>
</tr>
<tr>
<td></td>
<td>Anterior</td>
<td>15</td>
<td>145.5±30.0</td>
<td>16.6±22.0</td>
<td>73.3</td>
</tr>
<tr>
<td>200-Beat IL</td>
<td>Inferior</td>
<td>23</td>
<td>151.2±24.8</td>
<td>9.9±7.1</td>
<td>91.3</td>
</tr>
<tr>
<td></td>
<td>Anterior</td>
<td>15</td>
<td>148.5±29.5</td>
<td>14.9±21.1</td>
<td>80.0</td>
</tr>
<tr>
<td>600-Beat VM</td>
<td>Inferior</td>
<td>23</td>
<td>153.3±25.8</td>
<td>9.9±7.3</td>
<td>91.3</td>
</tr>
<tr>
<td></td>
<td>Anterior</td>
<td>15</td>
<td>148.0±28.7</td>
<td>14.7±13.6</td>
<td>86.7</td>
</tr>
<tr>
<td>600-Beat IL</td>
<td>Inferior</td>
<td>23</td>
<td>156.3±24.3</td>
<td>8.4±6.2</td>
<td>95.7</td>
</tr>
<tr>
<td></td>
<td>Anterior</td>
<td>15</td>
<td>153.5±25.4</td>
<td>7.8±5.6</td>
<td>93.3</td>
</tr>
</tbody>
</table>

SAECG, signal-averaged ECG; MI, myocardial infarction; QRSD, QRS duration; RMS40, amplitude of the terminal 40 msec of QRS; VM, vector magnitude; IL, individual lead.
ence SAECG parameters irrespective of VT risk. In summary, the age and sex of subjects undergoing an SAECG study might be factored advantageously into the definition of late potentials. The relation between age, sex, and SAECG parameters requires further study before any firm conclusions can be drawn.

In the VT group, site of infarction appeared to exert an influence on QRS duration. These differences in QRS duration at lower noise levels and were not statistically significant by ANOVA. However, the number of patients studied was small. One possible interpretation of these results is that late potentials have lower amplitudes in patients with anterior as opposed to inferior infarcts. Consequently, they are more likely to remain undetected at higher noise levels.

**Interpretive SAECG Chart**

The SAECG chart of Figure 8 offers two advantages compared with using a single threshold value of QRSD/RMS40 to assess VT risk. First, it uses the increased sensitivity of ILD in combination with the higher specificity of VMD. Second, a strict binary decision on VT risk is avoided. Although the chart was developed solely by use of the present study data, its risk boundaries for VMD agree well with the consensus in the literature (113 and 120 msec define the borderline normal/borderline abnormal and borderline abnormal/abnormal decision lines, respectively).

The clinical usefulness of the chart for the general arrhythmia risk population needs to be verified by further studies. The concept of risk stratification by defining decision boundaries based on clinical performance measures can be adapted to specific populations. Evaluation of subjects who fall in the borderline regions is problematic. For this reason, the borderline abnormal region is qualified by a statement suggesting that other arrhythmia risk factors should be considered in these cases. In the absence of bundle branch block and other nonspecific conduction defects, the normal and abnormal regions of the chart can identify subjects from this study with a high predictive value (95%).

**Conclusions**

1) Individual lead analysis can significantly enhance the sensitivity of the SAECG by up to 10%. Signals that are detectable in one or more leads can be lost in the
vector magnitude transformation. The increase in sensitivity obtained by individual lead as opposed to vector magnitude analysis approaches that gained by averaging three times as many beats.

2) The filtered QRS duration (QRSD) and amplitude of the terminal 40 msec of the QRS (RMS40) are highly correlated and thus are not independent measurements. In the VT and low-arrhythmia-risk patient populations studied, RMS40 was of limited use in defining late potentials. In particular, when late potentials were present, RMS40 is actually significantly correlated with residual noise level. This is because of the dependence of RMS40 on selected QRS offset, which in turn is affected by noise. Examination of other terminal QRS measurements showed RMS55 to be the best separator of low-arrhythmia-risk and VT subjects. However, no measurement of the terminal QRS (RMS40 or RMS55) was useful in independently identifying VT subjects. Optimum sensitivity and accuracy were achieved using QRSD alone.

3) Our results show that noise reduction is unpredictable during averaging, supporting previous arguments that averaging is best terminated at a preset noise level. A residual noise level of 0.2–0.3 μV RMS effectively maximized sensitivity for VT in the study.

4) Based on combined use of individual lead and vector magnitude measurements, an interpretive SAECG chart was developed as a means of VT risk stratification. We defined four categories of risk: normal, borderline normal, borderline abnormal, and abnormal.

5) The study results suggest that age and sex could be advantageously factored into SAECG criteria for VT risk assessment.

Appendix

Our study used two patient groups from opposite ends of the spectrum of arrhythmia risk. The distributions of SAECG parameters from the normal and abnormal patient groups still show significant overlap. On the basis of our results, we have drawn up a chart (Figure 8) for the interpretation of the SAECG using three parameters. These are the vector magnitude QRS duration (VMD), the longest individual XYZ lead QRS duration (ILD), and the RMS40 value taken from the vector magnitude.

Four VT risk categories are defined: abnormal, borderline abnormal, borderline normal, and normal. Each category is also described by a qualifying statement (Figure 8). The boundaries of these categories are defined statistically in terms of sensitivity, specificity, accuracy, and positive and negative predictive value. These five clinical perspectives are combined into the SAECG interpretive chart of Figure 8. The positive and negative predictive values are possibly the most useful clinical measures for the SAECG. They denote the likelihood of a test positive being a true positive and a test negative being a true negative, respectively.

The chart contains check boxes to verify that the automatically defined QRS limits have been read and to note whether any manual adjustments to QRS onset or offset were made. The RMS40 value is then examined. If RMS40 is <4 μV, the SAECG is considered abnormal without further analysis. The vector magnitude and individual lead QRS durations are read off to locate a point on the SAECG chart. This point will fall into one of six regions. The triangular regions in the top left and bottom right corners are highly unlikely combinations of VMD and ILD values. These areas represent probable measurement error.

Proceeding from the origin (bottom left corner), the first shaded area represents an unqualified normal SAECG. This area is the union of 95% sensitivity and 95% negative predictive value obtained from the results of the present study. The second shaded area represents a borderline normal SAECG. This area is the union of 90% sensitivity and 90% negative predictive value. The third shaded area represents a borderline abnormal. This area is the union of 85% specificity and 85% positive predictive value. The last category is that of unqualified abnormal. This represents the union of 95% specificity and 95% positive predictive value.

These criteria are designed to be unbiased, in the sense of the above region definitions. The criteria do, however, categorize a borderline positive result a little more liberally than a borderline negative result (85% versus 90%). This was done to reflect the current tendency to use the SAECG as a screening device for identifying those not at risk of VT. Table 8 gives the values of VMD and ILD that define the four categories of SAECG results. The vector magnitude QRS durations that define the boundary between a borderline normal and a borderline abnormal result and define an unqualified abnormal result (113 and 120 msec, respectively) agree well with the consensus in the clinical literature.

Use of the chart is simply illustrated by considering the SAECG results of Figures 3 and 4. Figure 3, showing a VT subject, has VMD=117 msec, ILD=125 msec, and RMS40=12 μV for the 200-beat average. From the standards adopted in the literature, neither VMD nor RMS40 is a clear-cut result. From the chart, the location of ILD=125 msec, VMD=117 msec identifies this subject as abnormal. Figure 4, showing a low-arrhythmia-risk subject, is identified as an unqualified normal for the 200-beat average (VMD=103 msec, ILD=103 msec, RMS40=17 μV).

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