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The Signal-Averaged Electrocardiogram As a Screening Test for Inducibility of Sustained Ventricular Tachycardia in High Risk Patients: A Prospective Study

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The role of the signal-averaged electrocardiogram in predicting the induction of sustained monomorphic ventricular tachycardia in high risk patients was assessed prospectively in 100 consecutive patients. Presenting diagnoses were syncope (38 patients), nonsustained ventricular tachycardia (24 patients), sustained ventricular tachycardia (25 patients) and sudden cardiac arrest (13 patients). Using programmed ventricular stimulation, 71 patients (group I) did not have and 29 patients (group II) did have inducible sustained monomorphic ventricular tachycardia. Using the signal-averaged electrocardiogram with filtering (6 dB/octave) at high pass corner frequencies of 67 and 100 Hz, the two groups were compared.

The signal-averaged electrocardiogram was considered abnormal if *all* of the following criteria were satisfied: 1) the total filtered QRS complex duration was >120 ms, 2) the duration of the terminal QRS complex of ≤20 μV was ≥30 ms, and 3) at least one deflection (late potential) was present in this region. Differences between groups I and II in these three measures were highly significant ($p \leq 0.001$). The sensitivity and specificity of signal averaging for predicting the induction of sustained ventricular tachycardia were 93 and 94%, respectively. Stepwise logistic regression analysis identified the signal-averaged electrocardiogram as the best predictor of induction of sustained monomorphic ventricular tachycardia, independent of left ventricular ejection fraction, presence of ventricular aneurysm, myocardial infarction and other clinical variables (chi-square = 93.2, $p < 0.0001$). The signal-averaged electrocardiogram is a sensitive and specific test for the induction of sustained monomorphic ventricular tachycardia, having independent predictive value.

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In recent years, signal averaging of the surface electrocardiogram has been shown to be a useful technique in identifying patients at risk for ventricular tachycardia and sudden death (1–10). Advanced methods of signal processing using both time and frequency domain analysis of the terminal portion of the QRS complex have contributed to our understanding of abnormal late potentials in these high risk patients (11–13). These noninvasive techniques may improve patient selection for programmed ventricular stimulation (2,6,9,13). However, small sample sizes, patient selection bias, differences in stimulation protocols, heterogeneity of end points of programmed ventricular stimulation and signal processing methodologies have blunted the value of these studies and their clinical application (2,4,6,7,10,11–14).

The purpose of our study was to prospectively assess the clinical utility of the signal-averaged electrocardiogram in a large group of consecutive high risk patients referred for programmed ventricular stimulation, using a standardized stimulation protocol. Specifically, our aims were 1) to define criteria indicating abnormality in the signal-averaged electrocardiogram using a unidirectional filtering technique; 2) to determine the sensitivity and specificity of the signal-averaged electrocardiogram in predicting the inducibility of sustained monomorphic ventricular tachycardia; 3) to examine whether the clinical mode of presentation (syncope, nonsustained or sustained ventricular tachycardia or sudden cardiac arrest) affected the utility of the signal-averaged

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electrocardiogram; and 4) to apply sophisticated statistical techniques to evaluate whether an abnormal signal-averaged electrocardiogram in a given patient correlated with the induction of sustained monomorphic ventricular tachycardia, independent of other variables such as age, sex, clinical presentation, prior myocardial infarction, left ventricular ejection fraction and ventricular aneurysm, thereby containing information not present in these other clinical variables.

Methods

Patient selection. One hundred thirteen consecutive patients referred for programmed ventricular stimulation between July 1985 and April 1986 were evaluated prospectively using the signal-averaged electrocardiogram. Informed consent was obtained in all patients for the electrophysiologic study. Patients were excluded if 1) there was no indication for the complete programmed ventricular stimulation protocol (a primary diagnosis of Wolff-Parkinson-White syndrome or other supraventricular tachyarrhythmias, sinus node dysfunction or conduction disturbances); 2) an adequate signal-averaged electrocardiogram could not be obtained (pacemaker-dependent patients); 3) the patient refused the evaluation; 4) noise levels >1.5 μV were present in the composite lead of the signal-averaged electrocardiogram; or 5) the patient was taking any antiarrhythmic agent that could affect the results of either signal averaging or programmed ventricular stimulation. Patients with intraventricular conduction delay or left or right bundle branch block were included in the study. Patients were excluded if they had a history of an acute myocardial infarction within 3 weeks.

Electrophysiologic study. Patients were studied after antiarrhythmic agents had been discontinued for at least five half-lives, and sedation was provided with a benzodiazepine preparation. A quadripolar electrode catheter was introduced percutaneously from the femoral vein after local anesthesia and advanced to the apex of the right ventricle for stimulation and recording. Frequently other electrode catheters were introduced to the high right atrium and the His bundle region. Recordings were made using a multichannel recorder (Electronics for Medicine, VR-12) and included three surface leads and at least one intracardiac lead (right ventricular electrogram) at paper speeds of 25, 50 and 100 mm/s. Stimulation was performed using a programmable stimulator (Bloom Associates, Ltd.). The stimulation protocol consisted of burst pacing at cycle lengths from 600 to 300 ms (in 50 ms increments) and progressive introduction of up to three extrastimuli at two pacing rates (initially at 550 or 500 ms, followed by 400 ms). Pacing was performed at twice diastolic threshold with a pulse width of 2 ms from the right ventricular apex. This stimulation protocol was chosen because it has about a 90% yield for induction of ventricular tachycardia in patients with recurrent sustained ventricular tachycardia (15,16). Additionally, studies at our institution (17) and by other investigators (15,16) have shown only a 2 to 3% increase in yield with stimulation of additional sites from the right ventricle or from the left ventricle. The study was terminated with the induction of sustained monomorphic ventricular tachycardia, ventricular fibrillation or the completion of the preceding protocol, when ventricular refractoriness was reached.

Signal-averaged electrocardiogram. The signal-averaged electrocardiogram (Fidelity Medical, Inc.) was obtained within 48 hours of the invasive electrophysiologic study, in the absence of antiarrhythmic agents. Standard bipolar X, Y and Z leads were used. Signal averaging of 128 electrocardiographic cycles was performed and a template recognition algorithm for rejection of abnormal or noisy complexes was employed. High pass filtering of the electrocardiographic signal was performed at 67 and 100 Hz and a low pass frequency of 400 Hz. The filter used for this purpose was a single pole (6 dB/octave) analog filter. Results of signal processing were recorded on a Marquette electrocardiographic cart at an effective time-base resolution of 200 mm/s. Individual X, Y and Z leads were simultaneously displayed in both the filtered and unfiltered modes, as was a composite QRS complex, which represented the summing of the absolute values of the X, Y and Z leads and was displayed at gain selections of 0.33 and 1.33 μV/mm. All measured values from signal-averaged electrograms were obtained by two individuals (one blinded). Mean intra- and interobserver variability in the filtered QRS duration was ± 5 ms and for late potential amplitude was ± 1 μV.

The following measurements were then made at both high pass corner frequencies: A) Individual X, Y and Z lead filtered QRS duration (ms), terminal QRS duration ≤ 20 μV (ms) and amplitude (μV) and number of high frequency deflections in this terminal QRS portion. B) Filtered *composite* QRS duration (ms), terminal QRS duration ≤ 20 μV (ms) and amplitude (μV) and number of high frequency deflections in this terminal composite QRS portion. C) Measurement of the longest unfiltered QRS complex (QRSu) in the X, Y or Z leads or in the composite lead, which was displayed on a scale of 20 μV/mm. D) The *difference* between the filtered *composite* QRS duration and the longest unfiltered QRS duration. E) The *ratio* between the filtered composite QRS duration and the longest unfiltered QRS duration.

Patients with an intraventricular conduction delay or left bundle branch block were analyzed in the same fashion as were patients with normal surface QRS duration. In patients with right bundle branch block, the filtered QRS complex tended to have a prolonged low amplitude (≤ 20 μV) terminal R′ portion. In order not to label this entire terminal QRS region a late potential, the *difference* between the

Table 1. Characteristics of Patients Without (Group I) and With (Group II) Inducible Sustained Ventricular Tachycardia

	Group I	Group II
No. of patients	71	29
Age (mean ± SD)	64 ± 14	62 ± 8*
Male	39 (55%)	23 (79%)†
Principal diagnosis		
Coronary artery disease	31 (44%)	26 (90%)‡
Mitral valve prolapse	13 (18%)	0
Rheumatic heart disease	5 (7%)	0
Hypertension	5 (7%)	0
Idiopathic dilated cardiomyopathy	2 (3%)	3 (10%)
No structural heart disease	15 (21%)	0
Presentation		
Syncope	35 (49%)	3 (10%)‡
Nonsustained VT	17 (24%)	7 (24%)*
Sustained VT	9 (13%)	16 (56%)‡
Sudden cardiac arrest	10 (14%)	3 (10%)*
Myocardial infarction	28 (39%)	26 (90%)‡
Anterior	16	14
Inferior	12	12
Left ventricular aneurysm	13 (18%)	13 (45%)§
LV ejection fraction (mean ± SD)	0.56 ± 0.20	0.27 ± 0.10‡
Surface QRS duration (mean ± SD)	106 ± 23	127 ± 29‡
Conduction disturbance	15 (21%)	16 (55%)‡
IVCD (QRS ≥120 ms)	3	10
LBBB	7	5
RBBB	5	1

*p = NS; †p < 0.05; ‡p < 0.001; §p < 0.01. IVCD = intraventricular conduction delay; LBBB = left bundle branch block; LV = left ventricle; RBBB = right bundle branch block; VT = ventricular tachycardia.

filtered and unfiltered QRS complexes was measured and used as the "terminal QRS duration ≤20 μV."

Definition of terms. A) Nonsustained ventricular tachycardia was defined as three or more beats of repetitive ventricular activity lasting <30 seconds, at rates >120 beats/min, which was self-terminating (15). B) Sustained monomorphic ventricular tachycardia was defined as ventricular tachycardia lasting >30 seconds or requiring an intervention before this because of hemodynamic collapse. The cycle length had to be constant and ≥200 ms and the configuration unchanging from beat to beat (18). C) Late potentials were defined as discrete low amplitude (≤20 μV) high frequency deflections in the terminal portion of the filtered QRS complex having an amplitude greater than twice the level of background noise. These were required at *both* corner frequencies of 67 and 100 Hz in *both* the composite and at least one individual X, Y or Z lead. D) An intraventricular conduction delay was defined in this study as a QRS complex ≥120 ms without definitive features of right or left bundle branch block (19).

Data analysis. Patients were placed into two groups depending on the induction of sustained monomorphic ventricular tachycardia at programmed ventricular stimulation. Values obtained by the signal-averaged electrocardiogram from the two groups were analyzed using the unpaired *t* test. When comparing filtered and unfiltered data from the same patient the paired *t* test was used. Discriminant analysis using a statistical software package (BMDP) was performed using a DEK VAC-750 computer. Multiple linear regression analysis (20) was used to determine the individual correlation coefficients for signal-averaging data with the dependent variable being the induction of sustained monomorphic ventricular tachycardia. Stepwise logistic regression analysis (21) was used to evaluate relative information content of individual clinical variables and signal-averaging results in predicting the induction of sustained ventricular tachycardia (dependent variable). Results are expressed as an improvement in chi-square value to enter a specific variable into the model (see Table 4). Data are presented as mean ± SD and statistical significance was set at the 0.05 level.

Results

Patient characteristics (Table 1). One hundred consecutive patients underwent programmed ventricular stimulation and met the entry criteria for the study. All patients evaluated presented with either unexplained syncope (without documented arrhythmias or primary neurologic origin), nonsustained ventricular tachycardia (mean number of beats was 9 ± 7), prior sustained ventricular tachycardia or sud-

den cardiac arrest. Patients were classified into two groups depending on the results of programmed ventricular stimulation. Group I comprised 71 patients, in whom the prospectively identified end point of sustained monomorphic ventricular tachycardia was not obtained. Nonsustained ventricular tachycardia (21 patients) or ventricular fibrillation (8 patients) was induced in 29 of these 71 patients. Group II comprised 29 patients with inducible sustained monomorphic ventricular tachycardia. The mean cycle length of ventricular tachycardia was 281 ± 51 ms (range 200 to 400). Coronary artery disease was defined as documented prior myocardial infarction (54 patients) or the presence of >75% stenosis of two or more coronary arteries at angiography (three patients). A left ventricular aneurysm was defined as a dyskinetic systolic segmental wall motion abnormality on nuclear gated blood pool analysis, echocardiography or left ventriculography at cardiac catheterization. Left ventricular ejection fraction was measured by nuclear gated blood pool analysis (53 patients), echocardiography (25 patients) or left ventriculography (22 patients) (22–24).

Signal-averaged electrocardiography (Table 2). During preclinical testing of the equipment, no visible ringing artifact was seen from any of the individual X, Y or Z leads or the composite lead at either 67 or 100 Hz, using a single pole analog filter. Mean noise levels were less than 1.0 μV in amplitude. Figures 1 and 2 show representative signal-averaged electrocardiograms from patients in group I and II with either a normal unfiltered QRS duration or left bundle branch block. In Table 2, the signal averaging results are shown for patients in groups I and II with a normal or prolonged (≥120 ms) unfiltered QRS duration. In Figure 3, the filtered composite QRS durations are shown separately for patients with normal and prolonged unfiltered QRS durations. A filtered QRS composite duration >120 ms significantly separates the patients in groups I and II ($p < 0.001$), if the unfiltered QRS complex is not prolonged (69 patients). However, in the presence of bundle branch block or intraventricular conduction delay (31 patients), the filtered QRS composite durations were not significantly different between groups I and II ($p = 0.07$).

In Figure 4, the duration of the terminal filtered composite QRS duration ≤20 μV is shown separately for patients with normal and prolonged unfiltered QRS durations. This figure shows that regardless of unfiltered QRS duration, a terminal filtered QRS duration ≥30 ms significantly separates group I and II patients ($p < 0.001$). In patients with both normal and prolonged (≥120 ms) unfiltered QRS duration, the ratio and the difference between filtered and unfiltered QRS duration, as well as the late potential duration (≤20 μV) and the number of terminal QRS deflections, *all* separated group I from II patients (Table 2). This relation was consistent regardless of the presence of an intraventricular conduction delay or left or right bundle branch block.

Results at different corner frequencies. The amplitude of late potentials was greater at a corner frequency of 67 Hz than at 100 Hz (10 ± 6 versus 13 ± 7 μV, $p < 0.001$). The filtered QRS duration was minimally shorter (about 3 ms) at the 100 Hz corner frequency compared with 67 Hz. The number of late potentials and ratio and difference between filtered and unfiltered QRS duration were not significantly different comparing the two corner frequencies (p = NS).

Criteria for defining an abnormal signal-averaged electrocardiogram (Table 3). The signal-averaged electrocardiographic variables were scrutinized for specific criteria indicating an increased likelihood of having inducible sustained ventricular tachycardia. Positive criteria included *all* of the following: 1) total filtered composite QRS duration

Table 2. Signal-Averaging Results (corner frequency of 100 Hz)

Measurement	Group I	Group II	p Value
Filtered QRS duration (ms)			
No IVCD	107 ± 9	141 ± 17	<0.001
IVCD	154 ± 22	172 ± 31	NS
QRS duration <20 μV (ms)			
No IVCD	24 ± 8	47 ± 16	<0.001
IVCD	23 ± 12	49 ± 16	<0.001
No. of terminal deflections			
No IVCD	0.8 ± 0.9	3.2 ± 2.2	<0.001
IVCD	0.9 ± 1.3	3.0 ± 1.5	<0.001
Ratio (filtered/unfiltered)			
No IVCD	1.13 ± 0.06	1.33 ± 0.15	<0.001
IVCD	1.07 ± 0.06	1.19 ± 0.10	<0.001
Difference (filtered − unfiltered) (ms)			
No IVCD	11.6 ± 6	35.0 ± 16	<0.001
IVCD	10.6 ± 9	27.3 ± 15	<0.001

Results not significantly different at a corner frequency of 67 Hz. IVCD = intraventricular conduction delay (unfiltered QRS ≥ 120 ms).

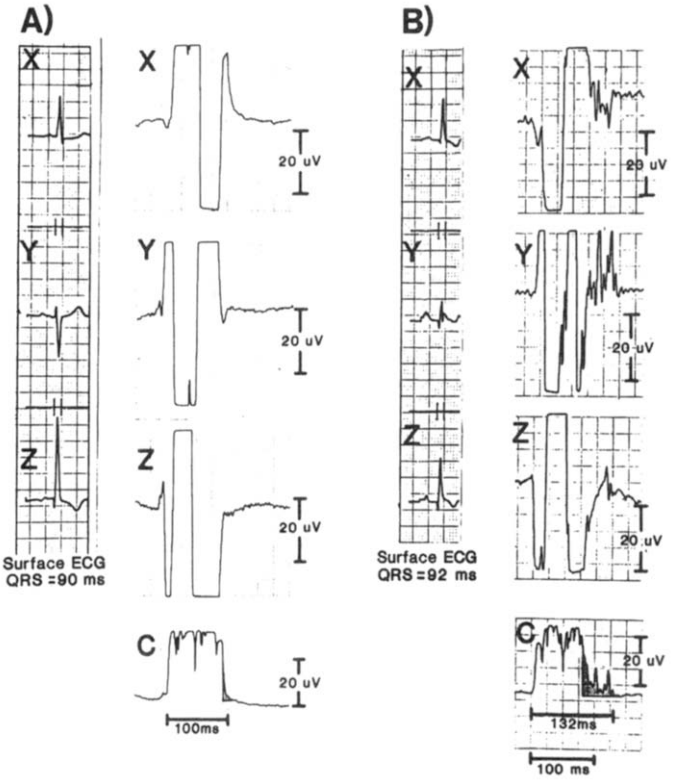


Figure 1. Signal-averaged electrocardiograms. **A,** Patient with a normal unfiltered QRS duration, without inducible ventricular tachycardia. The surface electrocardiographic (ECG) X, Y and Z leads (**left**) are shown with the filtered X, Y and Z leads and a composite (C) QRS complex (**right**). The **shaded region** corresponds to the terminal QRS duration of ≤20 μV. Note the absence of late potentials and the short duration (15 ms) below 20 μV in the composite lead. **B,** Patient with a normal unfiltered QRS duration and inducible sustained monomorphic ventricular tachycardia. Note the presence of late potentials in the filtered X, Y and Z leads and in the composite (C) QRS complex with a filtered QRS duration of 132 ms. The **shaded area** in the composite lead corresponds to the terminal QRS duration ≤20 μV with two major late potential deflections. The time scale (**horizontal axis**) and voltage amplitude scale (**vertical axis**) are as shown.

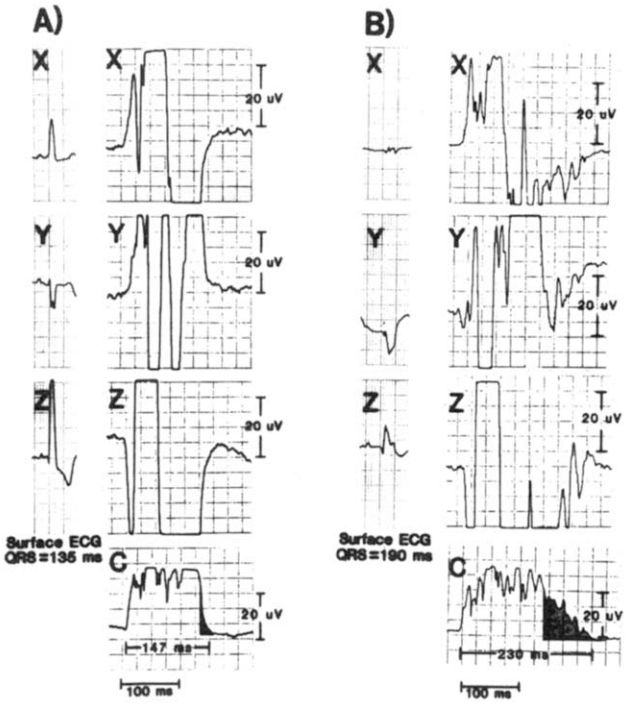


Figure 2. Signal-averaged electrocardiograms. **A,** Patient with left bundle branch block, without inducible ventricular tachycardia. The surface X, Y and Z leads (**left**) are shown with the filtered X, Y and Z leads and the composite (C) QRS complex (**right**). Note the absence of late potentials and short duration (20 ms) below 20 μV in the composite lead. **B,** Patient with left bundle branch block with inducible sustained monomorphic ventricular tachycardia. Note the presence of late potentials in the filtered X, Y and Z leads and in the composite (C) QRS complex with a filtered duration of 230 ms. The late potential duration (≤20 μV) is 90 ms, with multiple deflections.

>120 ms, 2) duration of the filtered terminal QRS complex ≤20 μV of ≥30 ms, and 3) one or more late potentials in this terminal QRS region. Using this definition of abnormality, the signal-averaged electrocardiogram was very sensitive and specific for predicting the induction of sustained ventricular tachycardia at programmed ventricular stimulation, regardless of the mode of clinical presentation.

Patients with a history of sustained ventricular tachycardia or sudden cardiac arrest. The signal-averaged electrocardiogram correctly identified 17 of 19 patients with a history of sustained ventricular tachycardia or sudden cardiac arrest in whom sustained ventricular tachycardia was *not* inducible. Of these 19 patients, ventricular fibrillation was induced in 3 and nonsustained ventricular tachycardia in an additional 3. Conversely, in 17 of 19 patients who presented with sudden cardiac arrest or prior sustained ventricular tachycardia in whom ventricular tachycardia *was* inducible at programmed ventricular stimulation, this response was again concordant with the results of signal averaging. One of two patients with a "false negative" signal-averaged electrocardiogram had left bundle branch block, which may have masked late potentials.

Coronary artery disease and the signal-averaged electrocardiogram. Coronary artery disease was present in 21 of 25 patients (84%) presenting *with* a history of sustained ventricular tachycardia. Sixteen (76%) of these 21 patients had inducible sustained ventricular tachycardia and 14 (88%) of these 16 patients were correctly identified with an abnormal signal-averaged electrocardiogram. All five patients without inducible ventricular tachycardia were correctly identified with the signal-averaged electrocardiogram. None of the remaining four patients without coronary artery disease in this group had either inducible ventricular tachycardia or an abnormal signal-averaged electrocardiogram.

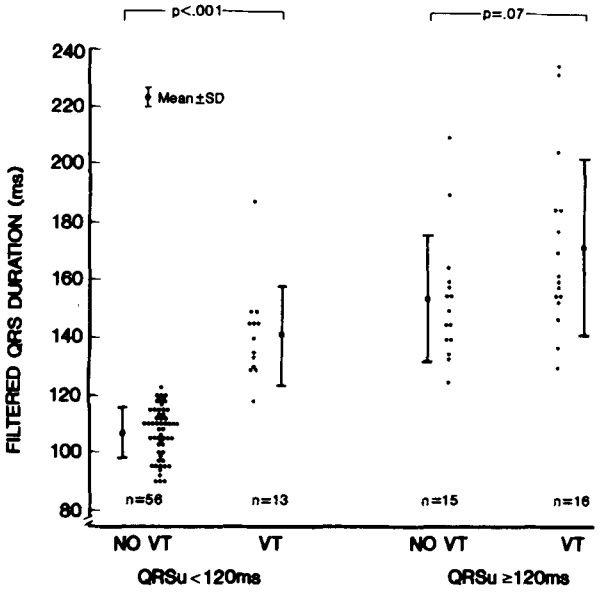


Figure 3. Individual data points for filtered QRS duration in patients with a normal or prolonged (≥120 ms) unfiltered QRS duration (QRSu), according to whether sustained ventricular tachycardia (VT) was inducible. Note that a filtered QRS duration >120 ms significantly separates the 69 patients with and without inducible ventricular tachycardia, if the unfiltered duration QRS is not prolonged ($p < 0.001$) (**left**). Among the 31 patients with a prolonged unfiltered QRS duration (≥120 ms) (**right**), the patients with inducible ventricular tachycardia have a slightly longer filtered QRS duration than that of patients without inducible tachycardia, but this difference does not reach statistical significance ($p = 0.07$).

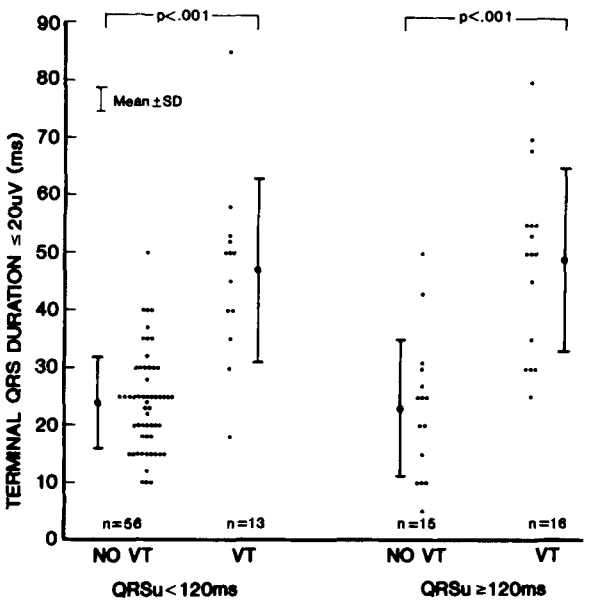


Figure 4. Individual data points for filtered terminal QRS duration ≤20 μV in patients with a normal and prolonged (≥120 ms) unfiltered QRS duration (QRSu), according to whether sustained ventricular tachycardia (VT) was inducible. Note that regardless of unfiltered QRS duration, a terminal QRS duration ≥30 ms significantly separates patients with and without inducible sustained ventricular tachycardia.

Coronary artery disease was present in 36 (48%) of the 75 patients *without* a history of sustained ventricular tachycardia. Ten (28%) of these 36 patients had inducible sustained ventricular tachycardia and all 10 were correctly identified with an abnormal signal-averaged electrocardiogram. In the remaining 26 patients without inducible ventricular tachycardia, the signal-averaged electrocardiogram was normal in 22 patients (85%). Of the 39 patients (52%) *without* a history of sustained ventricular tachycardia *or* coronary artery disease, 3 had an abnormal signal-averaged electrocardiogram. All three of these patients had inducible sustained ventricular tachycardia and dilated cardiomyopathy. None of the remaining 36 patients had an abnormal signal-averaged electrocardiogram or inducible sustained ventricular tachycardia.

Electrocardiographic correlates of ventricular tachycardia induction. Multiple linear regression analysis was performed to correlate signal-averaging variables with the induction of sustained monomorphic ventricular tachycardia. Individual signal-averaging correlation coefficients were as follows: 1) terminal filtered QRS duration ≤20 μV ($r = 0.69$), 2) difference between filtered and unfiltered QRS composite ($r = 0.66$), 3) number of late potentials in this terminal QRS region ($r = 0.62$), and 4) total filtered composite QRS duration ($r = 0.60$). All of these values correlated better than, or as well as, any of the clinical variables with the induction of sustained ventricular tachycardia. When signal-averaging measurements were combined into a *single* normal or abnormal result based on the previously described criteria, the individual correlation with the induction of sustained monomorphic ventricular tachycardia rose to $r = 0.86$. The correlation coefficient between ejection fraction and an abnormal signal-averaged electrocardiogram was $r = -0.60$. We found no relation between site of infarction and late potentials or the inducibility of sustained ventricular tachycardia.

Table 3. Sensitivity and Specificity of an Abnormal Signal-Averaged Electrocardiogram for Induction of Sustained Ventricular Tachycardia According to Diagnosis at Presentation

Presentation	No. With VT Induced/Total	Sensitivity (%)	Specificity (%)
Syncope	3/38	100	100
Nonsustained VT	7/24	100	88
Sustained VT	16/25	88	100
Sudden cardiac arrest	3/13	100	80
Total	100	93	94

VT = ventricular tachycardia.

End point of programmed ventricular stimulation. The preceding results apply *only* to the induction of sustained monomorphic ventricular tachycardia. The induction of ventricular fibrillation or nonsustained ventricular tachycardia was more poorly correlated with the results of the signal-averaged electrocardiogram. Specifically, if ventricular fibrillation was included as a positive response to programmed ventricular stimulation (eight patients), there was a drop in the individual correlation coefficient of an abnormal signal-averaged electrocardiogram from r = 0.86 to 0.72. If the induction of nonsustained ventricular tachycardia was also considered as a positive response to programmed ventricular stimulation (21 patients; mean number of ventricular tachycardia beats 14 ± 11), then there was a further drop in the individual correlation coefficient of an abnormal signal-averaged electrocardiogram from r = 0.75 to 0.45.

Stepwise logistic regression analysis. In Table 4, the individual chi-square coefficients to enter the stepwise logistic regression analysis are shown (for clinical variables and the results of signal averaging), with the dependent variable being the induction of sustained monomorphic ventricular tachycardia. If all of the variables are *removed* in step 0, the entry of the signal-averaged electrocardiogram in step 1 results in the greatest improvement in the chi-square value chi-square = 93.2, $p < 0.0001$). In step 2 of the analysis, only the history of sustained ventricular tachycardia results in a further significant increase in the chi-square value (chi-square = 16.3, $p < 0.001$) and the analysis terminates. The remainder of the variables yielded no further significant increment in predictive information content after these two variables had entered the model. Although the individual chi-square values to enter were initially high for ejection fraction, age, aneurysm, a history of myocardial infarction and unfiltered QRS duration, their predictive information content was already present in the signal-averaged electrocardiogram and history of sustained ventricular tachycardia.

If the same analysis is repeated with *all* of the variables required to enter the equation in step 0, except the signal-averaged electrocardiogram, the entry of this latter variable still results in a significant improvement in the chi-square value (chi-square = 36.3, $p < 0.0001$). Therefore, additional predictive information is present in the signal-averaged electrocardiogram above that found in common variables available to the clinician. On the basis of the preceding results of stepwise logistic regression analysis, a probability estimate for the induction of sustained ventricular tachycardia was calculated (Fig. 5) that depends *only* on the signal-averaged electrocardiogram and a history of sustained ventricular tachycardia. For example, if there were both a history of ventricular tachycardia *and* an abnormal signal-averaged electrocardiogram then ventricular tachycardia was induced in 14 of 14 patients (100%).

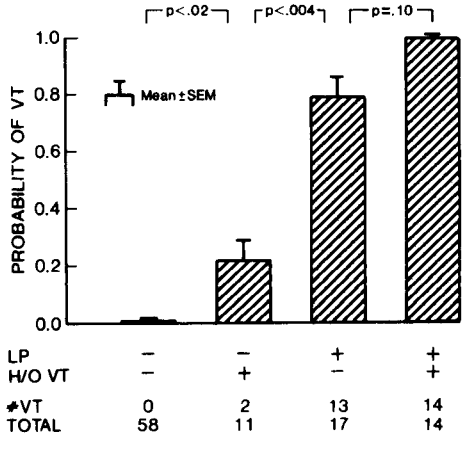
Follow-up results. During a mean follow-up period of 11 months, there were a total of 4 patients with sudden cardiac arrest and 3 additional patients with recurrences of sustained ventricular tachycardia among the 31 patients with an abnormal signal-averaged electrocardiogram. Six of these seven patients also had inducible sustained ventricular tachycardia with the programmed ventricular stimulation protocol described. Two of the patients with a normal signal-averaged electrocardiogram (patient with a probable automatic ventricular tachycardia and a false negative patient with left bundle branch block) had a recurrence of sustained ventricular tachycardia. There were no sudden deaths in the group with a normal signal-averaged electrocardiogram de-

Table 4. Stepwise Logistic Regression Analysis: Chi-Square Values to Enter the Analytic Model

Variable	Chi-Square Value	p Value
1. Abnormal signal-averaged ECG	93.2	<0.0001
2. Ejection fraction	42.1	<0.0001
3. Dx = sustained VT	33.3	<0.0001
4. Age	18.8	<0.0001
5. LV aneurysm	18.2	<0.0001
6. Myocardial infarction	14.8	<0.0002
7. Unfiltered QRS duration	11.3	<0.0009
8. Dx = sudden cardiac arrest	8.0	<0.005
9. Dx = syncope	4.9	<0.03
10. Dx = nonsustained VT	4.9	<0.03
11. Sex	1.0	NS

Ejection fraction, unfiltered QRS duration and age are expressed as continuous variables, with the remainder being categorical variables. Dx = diagnosis on presentation; ECG = electrocardiogram (normal versus abnormal); LV = left ventricle; VT = ventricular tachycardia.

Figure 5. Probability of inducing sustained ventricular tachycardia (VT) according to the presence of late potentials (LP) (see text for definition) and a history of sustained ventricular tachycardia (H/O VT), using stepwise logistic regression analysis. The lower values represent the number of patients with inducible ventricular tachycardia (#VT) over the total number of patients in each subgroup.



spite a previous history of sudden cardiac arrest or sustained ventricular tachycardia in 19 of these patients.

Discussion

Improved selection of patients for programmed ventricular stimulation. In this study, the signal-averaged electrocardiogram had an excellent sensitivity and specificity for identifying patients who had sustained monomorphic ventricular tachycardia with programmed ventricular stimulation. We have established criteria indicating abnormality in the signal-averaged electrocardiogram using analog filtering methods in a large group of consecutive patients with a high risk clinical presentation, who underwent an identical programmed ventricular stimulation protocol. The clinical presentation did not appear to affect the utility of this test. The end point of programmed ventricular stimulation, however, had a significant effect on the usefulness of the signal-averaged electrocardiogram (10). The signal-averaged electrocardiogram appears to be much more useful in predicting which patients will have inducible sustained monomorphic ventricular tachycardia than in predicting the induction of nonsustained ventricular tachycardia or ventricular fibrillation, both of which are considered by some investigators to be nonspecific results (25–27). Using stepwise logistic regression analysis it can be seen that the signal-averaged electrocardiogram is the most accurate single predictor of inducible sustained ventricular tachycardia when compared with historical data and assessment of left ventricular function. It also provides significant incremental information with regard to inducibility of ventricular tachycardia over and above the information content of left ventricular function and clinical variables.

Prior studies. Our study differs from prior studies that evaluated the utility of the signal-averaged electrocardiogram for predicting the induction of ventricular tachycardia during programmed ventricular stimulation. Using stepwise logistic regression analysis, Kanovsky et al. (6) also found the signal-averaged electrocardiogram to have the greatest predictive value for the induction of ventricular tachycardia. However, we agree with their comments that their results were limited by the patient selection bias that existed in their study. Specifically, half the patients had known recurrent ventricular tachycardia and the other half were referred for cardiac catheterization (more than 80% of whom did not undergo programmed ventricular stimulation). Also, these two patient groups were collected over two different time periods in a nonprospective fashion.

More recently Lindsay et al. (13) prospectively evaluated 38 patients using fast Fourier transform analysis of the signal-averaged electrocardiogram and found a sensitivity of 100% and a specificity of 77% for predicting ventricular tachycardia induction with a stimulation protocol using two different ventricular sites and two extrastimuli. Using stepwise logistic regression analysis, they found that clinical presentation and results of the signal-averaged electrocardiogram had incremental information over and above that provided by left ventricular ejection fraction data. Unlike our study group, the patients prospectively evaluated included only those presenting with syncope and nonsustained ventricular tachycardia and did not include those with sudden cardiac arrest or documented ventricular tachycardia.

Signal-processing methodology. The signal-filtering methodology described in this report is very similar to that previously reported by us (28) and Breithardt et al. (14), who used a single pole (6 dB/octave) analog filter with bandpass filter settings from 100 to 300 Hz. Their analysis lacked a composite XYZ recording, the use of a filtered QRS duration and the use of a specific cutoff amplitude ($\leq 20\ \mu V$) for the terminal portion of the QRS complex, all of which correlated highly with the induction of sustained ventricular tachycardia in our study. Breithardt et al. (14) also found that the duration of late potentials was associated more highly with the induction of ventricular arrhythmias. However, the end point of their stimulation protocol was the induction of four repetitive ventricular beats and they evaluated patients referred for cardiac catheterization, without a history of ventricular arrhythmias. Other investigators (2,4,5–9) have obtained similar results in sensitivity and specificity for ventricular tachycardia induction, with different signal-processing analytic techniques. These include more powerful four pole, bidirectional filters (24 dB/octave) and high pass corner frequencies ranging from 25 to 80 Hz. Results with these methods have confirmed the predictive value of a cutoff value >120 ms for the filtered QRS composite duration and some measure of amplitude of the terminal QRS portion (root-mean-squared voltage) and duration of late potentials for the induction of sustained ventricular tachycardia.

Implications for clinical management. Several conclusions that can be drawn from our results can be applied to the clinical management of patients referred for programmed ventricular stimulation. In patients with *both* a history of sustained ventricular tachycardia and the presence of late QRS potentials, programmed ventricular stimulation may not contribute significantly to *diagnostic* information, but may be of great value in the selection of appropriate therapy for ventricular tachycardia, which is nearly always inducible in this group. In patients who present with sustained ventricular tachycardia or sudden cardiac arrest, *without* late potentials on signal averaging, sustained monomorphic ventricular tachycardia is rarely inducible. In this situation, the clinical circumstances that precipitated the arrhythmic event should be carefully examined and other studies (treadmill testing, coronary angiography, and so on) should be performed first. If the results obtained by these tests are nondiagnostic, programmed ventricular stimulation should then be performed. Programmed ventricular stimu-

lation in this patient subset can be justified by the catastrophic presentation, the potential for a false negative signal-averaging result and the possible significance of inducible ventricular fibrillation. Prior studies (10) have shown that signal averaging does not predict the induction of ventricular fibrillation during programmed ventricular stimulation.

Patients who present with syncope (28) or nonsustained ventricular tachycardia and have no late QRS potentials on signal averaging rarely have inducible sustained ventricular tachycardia during programmed ventricular stimulation. An argument can be made for not subjecting this group to invasive electrophysiologic testing unless there is suspicion for supraventricular arrhythmias, sinus node dysfunction or conduction disorders. The benign course during follow-up in this patient subgroup also supports this recommendation.

Limitations of the study. Studies involving the use of invasive electrophysiologic testing inherently suffer from some degree of referral bias in patient selection, especially when performed in a tertiary referral center. Recognizing this limitation, we purposely chose to perform this study prospectively on consecutive patients with a high risk clinical presentation. It is possible that several patients may have been misclassified into the noninducible group because of the stimulation protocol used in this study and would have had induction of sustained ventricular tachycardia if two ventricular sites or higher stimulation currents had been used. The corollary of this, however, is that with more aggressive protocols there is an increased incidence of induction of nonclinical arrhythmias resulting in an increased sensitivity of the signal-averaged electrocardiogram, but with a reduction in specificity (15,16).

We prospectively chose the end point of the electrophysiologic study to be the induction of sustained monomorphic ventricular tachycardia and to evaluate its relation with the signal-averaged electrocardiogram. We realize that the induction of ventricular fibrillation or nonsustained ventricular tachycardia in patients with these as their clinical arrhythmias may have significance. However, we restricted our study to this particular end point to best determine the relation of late potentials with regular sustained monomorphic ventricular tachycardia, based most clearly on a reentrant mechanism.

Conclusion. The described method for recording the signal-averaged electrocardiogram is highly accurate in detecting late QRS potentials and in predicting responses to programmed ventricular stimulation, using a standard stimulation protocol. The signal-averaged electrocardiogram is specific for the induction of sustained monomorphic ventricular tachycardia, regardless of the mode of clinical presentation and provides incremental predictive information not provided by clinical variables or assessment of left ventricular function. Significant clinical implications exist in patients with discordance between signal averaging and mode of clinical presentation, regarding the timing and role of programmed ventricular stimulation. Further work needs to be done in investigating the value of the signal-averaged electrocardiogram in patients with distal conduction system disease. Also, studies are needed to investigate the long-term outcome of patients in whom the signal-averaged electrocardiogram is used in patient selection for programmed ventricular stimulation.

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