Identification of patients with ventricular tachycardia after myocardial infarction: signal-averaged electrocardiogram, Holter monitoring, and cardiac catheterization

MARTIN S. KANOVSKY, M.D., RITA A. FALCONE, M.S., CAROL A. DRESDEN, M.S., MARK E. JOSEPHSON, M.D., AND MICHAEL B. SIMSON, M.D.

ABSTRACT  Electrocardiographic signal averaging techniques have demonstrated a low-amplitude late potential and a long filtered QRS complex in patients with ventricular tachycardia (VT) after myocardial infarction. Complex ventricular ectopy and left ventricular aneurysms have also been associated with VT. The purposes of this study were (1) to determine whether the findings from the signal-averaged electrocardiogram (ECG) were independent of those from Holter monitoring and cardiac catheterization and (2) to determine the combination of findings from the signal-averaged ECG, cardiac catheterization, and Holter monitoring that best characterize patients with VT after myocardial infarction. We studied 174 patients after myocardial infarction, 98 of whom had recurrent sustained VT. By multivariate logistic regression only three parameters were found to be independently significant, listed in order of power: positive signal-averaged ECG (presence of a late potential or a long filtered QRS duration), peak premature ventricular contraction greater than 100/hr, and presence of a left ventricular aneurysm (p < .001). The signal-averaged ECG provides independent information in identifying patients with VT after myocardial infarction.


SUDDEN DEATH in patients after myocardial infarction is generally caused by ventricular tachyarrhythmias.1-4 Accurate identification of patients prone to ventricular arrhythmias by noninvasive methods is highly desirable to rationally treat the group of patients at high risk. At the present time there is no such test or combination of tests to reliably predict which patients are at risk for ventricular arrhythmias after a myocardial infarction. Holter monitoring, cardiac catheterization, exercise testing, and clinical findings have been used separately and in combination to identify patients with ventricular tachycardia (VT).5-10 Recently, invasive electrophysiologic stimulation studies have been suggested as a means to identify these patients.3, 11-14 However, because of the invasive nature of the electrophysiologic test, it is not desirable as a screening test for large numbers of patients.

Within the last few years, several investigators have used a noninvasive signal-averaged electrocardiogram (ECG) to detect low-amplitude, high-frequency potentials at the end of the QRS complex in patients with VT.15-22 These signals, termed “late potentials,” appear to correspond to the delayed and fragmented ventricular activation that has been observed with direct electrogram recordings in patients and animals with VT.15, 23-25 Several studies have demonstrated that the signal-averaged ECG can distinguish patients with and without VT after myocardial infarction.17-22

The purposes of this study were (1) to determine whether the signal-averaged ECG provides information useful in identifying patients with VT that is independent from that which can be obtained from Holter monitoring and catheterization and (2) to determine the combination of findings from the signal-averaged ECGs, cardiac catheterization, and Holter monitoring that best characterize patients with VT after myocardial infarction.

---

From the Clinical Electrophysiology Laboratory, Hospital of the University of Pennsylvania, Cardiovascular Section, Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia.

Supported in part by grants HL24278, HL27925, and HL22315 from the NHLBI; grants from the American Heart Association, Southeastern Pennsylvania Chapter, Philadelphia; and Arrhythmia Research Technology, Inc.

Address for correspondence: Michael B. Simson, M.D., 945 Gates Bldg., Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia, PA 19104.

Received June 22, 1983; revision accepted May 10, 1984.

Dr. Simson is the Samuel Bellet Associate Professor of Medicine in Cardiology.
al infarction. A study population with a high incidence of VT was used on the assumption that if a test cannot identify patients with VT in such a group, it would be unlikely to distinguish patients with VT in a study group with a lower incidence of the arrhythmia.

**Methods**

**Patients.** Patients were chosen from those scheduled for a cardiac catheterization and/or an electrophysiologic study. The control group comprised 76 patients referred for study between January 1982 and February 1983. They had no clinical history of sustained VT. The VT group consisted of 98 patients referred for electrophysiologic study between January 1980 and February 1983 because of repeated episodes of documented sustained VT. All 174 patients had a myocardial infarction more than 2 weeks old as documented by chest pain compatible with acute myocardial infarction, elevation of serum cardiac enzyme levels, and an ECG consistent with acute myocardial infarction. The median age of infarction for all patients was 16 weeks. Patients with left ventricular hypertrophy, valvular heart disease, nonischemic cardiomyopathy, or bundle branch block were excluded.

There was no significant difference in age, sex, or location of infarct between the control and VT groups (table 1). Patients with VT, however, did have a higher median age of infarction than the control patients.

Ninety-six of the VT patients were studied in the clinical electrophysiology laboratory with previously described techniques. Ninety-three of these patients had sustained VT (>30 sec or requiring cardioversion to alleviate hemodynamic compromise) inducible by one to three ventricular premature depolarizations. Torres de Pointes was induced in one patient and nonsustained VT was induced in another. One patient had no inducible ventricular arrhythmias, although he did have recurrent sustained VT clinically. Fifteen control patients underwent programmed ventricular stimulation as part of another research study that they voluntarily entered. None of these patients had inducible VT. The incidence of inducible VT in the other 62 control patients is unknown.

**Signal-averaged ECGs.** A signal-averaged ECG was recorded during sinus rhythm from bipolar X, Y, Z leads by previously described techniques. Ectopic and grossly noisy beats were rejected by a template algorithm. A mean of 142 ± 12 beats were averaged. Each lead was filtered with a bidirectional, high-pass digital filter designed to eliminate filter ringing. The bandpass was 25 to 250 Hz and the rate of high-pass attenuation was 24 dB/octave. The filtered X, Y, Z leads were combined into a vector magnitude, \( \sqrt{(X^2 + Y^2 + Z^2)} \), a measure that sums the high-frequency information from all three leads, termed the "filtered QRS complex." The end points of the filtered QRS complex were determined by a computer algorithm.

Figure 1 shows a normal and an abnormal signal-averaged ECG. The abnormal signal-averaged ECG is longer in duration and has low-amplitude, high-frequency voltage in its terminal portion. In previous studies, a prolonged filtered QRS duration and low voltage in the last 40 msec of the filtered QRS complex were found to identify patients with VT; those parameters were used in this study to quantify the filtered QRS complex. The findings on the signal-averaged ECGs of 29 patients of the VT group, but none of the control group, have been previously reported.

In this article, a "late potential" is defined as a low-amplitude signal (<25 \( \mu V \)) in the last 40 msec of the filtered QRS complex (figure 1, arrow). A long filtered QRS duration is defined as a filtered QRS duration longer than 120 msec.

**Cardiac catheterization.** Cardiac catheterization was performed in 83 VT patients and 58 control patients. All patients underwent ventriculographic studies (right anterior oblique position) and coronary angiographic examination. Ejection fraction was calculated by the area-length method. An aneurysm was defined as a dyskinetic segment, regardless of size. A coronary artery was considered obstructed if a stenosis causing a reduction in luminal diameter of 70% or more was present. Catheterization data were interpreted by independent observers who had knowledge of the patients’ histories.

**Holter monitoring.** Holter monitoring was performed in 64 VT and 57 control patients who were on no antiarrhythmic drugs other than \( \beta \)-blockers. The Holter analysis was done commercially (CardioData, Inc.). The reported error rate for determination of premature ventricular contractions (PVCs) is less than 7%. The presence of multifocal PVCs, couplets, and nonsustained VT, as well as mean hourly and peak hourly PVC rate, was recorded.

**Statistics.** A 2 × 2 chi-square analysis was used to compare the presence of individual parameters between the control and VT groups. Stepwise logistic regression was used to determine the significance of several parameters simultaneously. In each case, the dependent (y) variable was the presence of clinical sustained VT. The independent (x) variables were dichotomous (0,1) results from Holter monitoring, catheterization, and/or the signal-averaged ECG. For each test, all significant parameters from univariate analysis were used in the logistic regression. Logistic regression determines which variables are independently significant and it ranks these variables by assigning coefficients (\( \beta_i \)) to them. The process generates an equation that can be used to determine the probability of VT [P(VT)] in a given patient:

\[
P(VT) = \frac{e^{\text{logit} y}}{1 + e^{\text{logit} y}}
\]

where logit (y) = \( \beta_0 + \beta_1X_1 + \beta_2X_2 + \ldots + \beta_nX_n \). For a given variable, the larger the \( \beta_i \) the more it influences the predicted probability of VT.

The threshold for inclusion of a specific variable into the model is \( p < .05 \). The accuracy of classification is determined by entering the patients’ values back into the logistic equation. An average logit (L_avg) is determined for each group, control or VT. The threshold for predicting VT is determined by the mean between the logit for the VT and control groups.

The "bootstrap" method was used to determine the variability of the logistic regression model. A computer formed

---

**TABLE 1**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Control</th>
<th>VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)A</td>
<td>56.8 ± 10.2</td>
<td>56.9 ± 9.4</td>
</tr>
<tr>
<td>Sex (F/M)B</td>
<td>22/54</td>
<td>17/81</td>
</tr>
<tr>
<td>MI locationC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>25 (33%)</td>
<td>48 (49%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>33 (43%)</td>
<td>40 (40%)</td>
</tr>
<tr>
<td>Anterior and inferior</td>
<td>14 (18%)</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Subendocardial</td>
<td>4 (5%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>MI age (median)D</td>
<td>8 wk</td>
<td>46 wk</td>
</tr>
</tbody>
</table>

Statistical comparisons: \( Ap = NS, \) Student’s t test (unpaired); \( Bp = NS, \) 2 × 2 chi square; \( Cp = NS, \) 2 × 4 chi square; \( Dp < .001, \) Mann-Whitney U test.

---

**DIAGNOSTIC METHODS—ELECTROPHYSIOLOGY**
KANOFSKY et al.

1000 “bootstrap” samples of the original population. Each patient in the “bootstrap” sample was an independent random selection from the original population; some patients were selected zero times, some once, some twice, and so forth. The model was applied to the sample, and the means and standard deviations were calculated for the sensitivity, specificity, and the percentage of patients correctly classified. “Sensitivity” is percentage of patients with VT correctly classified; “specificity” is the percentage of patients without VT correctly classified. Results are reported as the mean ± SD.

Results

Signal-averaged ECG. All 174 patients had a signal-averaged ECG while in sinus rhythm and on no antiarrhythmic drugs (table 2). Patients in the VT group more commonly had a late potential and/or a long filtered QRS duration. Ninety percent of the VT group had either a late potential or a long filtered QRS duration compared with 30% in the control group. Logistic regression was used to determine how to best score the results from the signal-averaged ECG to distinguish the VT patients from the control patients. The presence of a late potential or a long filtered QRS duration were independently significant and of equal weight (β = 1.8 for each; p < .001). By designating a positive signal-averaged ECG as the presence of either a late potential or a long filtered QRS duration the β value increases (β = 2.1; p < .001). The signal-averaged ECG alone identified VT patients with a sensitivity of 89% and specificity of 69%; 81% of patients were correctly classified.

Holter monitoring. A 24 hr Holter monitor was performed on 121 patients (57 control, 64 VT). Eight parameters from the Holter monitor were examined (table 3). There was a higher incidence of each of these parameters in the VT group. However, they were also commonly present in the control group. For example, complex ventricular ectopy was present in 79% of the VT patients but also in 56% of the control patients. Logistic regression identified the peak PVC rate greater than 100/hr as the only parameter from the Holter monitor to independently distinguish the VT patients from the control patients (β = 2.1; p < .001). No other parameter used in combination with peak PVC

FIGURE 1. Normal and abnormal signal-averaged ECGs (top). Signal-averaged leads from the body surface (bottom). Filtered QRS complex. The abnormal signal-averaged ECG has a low-amplitude signal (arrow) at the end of the filtered QRS complex that is not present in the filtered QRS complex from the control patient. The filtered QRS complex is longer in the abnormal averaged ECG.

266

TABLE 2

<table>
<thead>
<tr>
<th>Signal-averaged ECG</th>
<th>Late potentialA</th>
<th>Long filtered QRS A</th>
<th>Late potential, long filtered QRS, or bothA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 76)</td>
<td>21 (28%)</td>
<td>11 (14%)</td>
<td>23 (30%)</td>
</tr>
<tr>
<td>VT (n = 98)</td>
<td>81 (83%)</td>
<td>67 (68%)</td>
<td>88 (90%)</td>
</tr>
</tbody>
</table>

A p < .001.
TABLE 3
Holter monitoring

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 57)</th>
<th>VT (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multifocal</td>
<td>26 (46%)</td>
<td>45 (70%)</td>
</tr>
<tr>
<td>Couplets</td>
<td>21 (37%)</td>
<td>40 (62%)</td>
</tr>
<tr>
<td>Nonsustained VT</td>
<td>14 (25%)</td>
<td>24 (38%)</td>
</tr>
<tr>
<td>Complex ventricular ectopy</td>
<td>32 (56%)</td>
<td>51 (79%)</td>
</tr>
<tr>
<td>M PVC &gt;5</td>
<td>20 (35%)</td>
<td>42 (66%)</td>
</tr>
<tr>
<td>M PVC &gt;10</td>
<td>13 (23%)</td>
<td>41 (64%)</td>
</tr>
<tr>
<td>P PVC &gt;10</td>
<td>23 (40%)</td>
<td>49 (77%)</td>
</tr>
<tr>
<td>P PVC &gt;100</td>
<td>8 (14%)</td>
<td>36 (56%)</td>
</tr>
</tbody>
</table>

M PVC = mean hourly PVC rate; P PVC = peak hourly PVC rate.
Statistical comparisons: \(^{A}p < .01; \)\(^{B}p = .13\).

rate was statistically significant in differentiating the VT patients from the control patients.

**Cardiac catheterization.** Cardiac catheterization was performed in 141 patients (58 control, 83 VT) (table 4). Aneurysms were present in 71% of the VT patients and in 26% of the control patients. A low ejection fraction was found more commonly in the VT group than the control group. The mean ejection fraction for the VT group was 33 ± 13% compared with 49 ± 16% for the control group. Seventy-one percent of the VT group had an ejection fraction less than 40% as compared with 32% of the control group. Wall motion abnormalities were found commonly in both groups.

There was no significant difference between the two groups in the number of obstructed coronary arteries or the incidence of obstructions in each of the main coronary arteries. The independent variables found by logistic regression were the presence of an aneurysm (\(\beta = 1.7; p = .002\)) and an ejection fraction less than 40% (\(\beta = 1.03; p = .02\)). No other independent variable was significant.

**Signal-averaged ECG and Holter monitoring.** A total of 141 patients had both a signal-averaged ECG and Holter monitoring (figure 2). Logistic regression was applied to all the findings from both of these tests. Only two of the nine parameters were found to be statistically significant: a positive signal-averaged ECG (the presence of a late potential or a long filtered QRS duration) and a peak PVC rate greater than 100/hr (\(p < .001\)). Patients with both of these parameters had a 91% probability of developing VT, whereas patients with neither of these had only a 13% probability of developing VT. Those with only a peak PVC rate greater than 100/hr or only a positive signal-averaged ECG had a 50% to 59% probability of having VT. In this model, the sensitivity was 94% and the specificity 61%; 78% of the patients were correctly classified.

**Signal-averaged ECG and cardiac catheterization.** When the signal-averaged ECG and cardiac catheterization were examined, the significant parameters were a positive signal-averaged ECG (\(\beta = 3.3; p < .001\)) and the presence of an aneurysm (\(\beta = 2.0; p = .001\)) (figure 3). The presence of wall motion abnormalities and decreased ejection fraction did not increase the predictive accuracy of this model. Eighty-three percent of patients were correctly classified by this model (sensitivity 90%, specificity 72%).

**Signal-averaged ECG, Holter monitoring, and cardiac catheterization.** The final model used all 14 parameters from the signal-averaged ECG, Holter monitoring, and catheterization. Eighty-eight patients (39 control, 49 VT) had all three of these tests. The following three parameters were independently significant: positive signal-averaged ECG (\(\beta = 2.8; p < .001\)), peak PVC rate greater than 100/hr (\(\beta = 2.5; p < .001\)), and presence of an aneurysm (\(\beta = 2.2; p < .001\)). Patients with all three of these parameters had a 99% probability of developing VT, whereas patients with none of these parameters had only a 4% probability of having VT. Patients with only one of these parameters had a probability of developing VT of about 30%. Patients

![Graph](image_url)

**FIGURE 2.** Results of signal-averaged ECG studies and Holter monitoring. LP = late potential; LF-QRS = long (>120 msec) filtered QRS duration; P PVC >100 = peak PVC rate >100/hr on Holter monitor. The number of patients for each category are listed below the bars.
FIGURE 3. Results of signal-averaged ECG studies and cardiac catheterization. LP = late potential; LF QRS = long (>120 msec) filtered QRS duration.

with any two of these parameters had an 82% to 88% probability of having VT. With this model, 85% of the patients were correctly classified (sensitivity 81%, specificity 90%). When the “bootstrap” technique was used to estimate the variability of the model with different populations, the sensitivity was 81 ± 6%, the specificity was 90 ± 5%, and 85 ± 4% of patients were classified correctly.

As noted in table 1, the median age of infarction was higher in the VT patients. To control for age of infarct, subsets of patients from each group who had had an infarction from 4 to 52 weeks before testing were studied. There were 26 patients in the VT group with a median age of infarction of 14 weeks and 23 patients in the control group with a median age of infarction of 15 weeks (p = .45). Reapplying the final logistic regression model to this population, 80% of the patients were correctly identified (sensitivity 75%, specificity 87%). These results were similar to those obtained when all the patients were included.

Recent studies have found that the radionuclide ejection fraction and PVC rate are risk factors for mortality and sudden death after myocardial infarction. To evaluate the ejection fraction without knowledge of the presence of an aneurysm, we excluded aneurysm as a variable in a logistic regression model. An abnormal signal-averaged ECG (β = 2.4), a peak PVC rate greater than 100/hr (β = 2.0), and an ejection fraction less than 40% (β = 1.2) were found to be the only independently significant variables (each p < .05). The sensitivity was 84%, the specificity was 79%, and 81% of patients were correctly classified.

**Discussion**

The presence of a left ventricular aneurysm and ventricular ectopy have been associated with an increased incidence of VT in patients after myocardial infarction. However, only a minority of patients with aneurysms have sustained VT. Results of Holter monitoring have been used in an attempt to identify patients with VT. In individual patients there is a marked variability in PVC frequency and complexity and the specificity of the test is limited. In this study, complex ventricular ectopy was found in 79% of VT patients but also in 56% of control patients. The frequency of PVCs alone or complex ventricular ectopy cannot reliably identify patients with VT.

Recently the presence of a late potential and/or a long filtered QRS duration on the signal-averaged ECG has also been associated with VT. This study confirms that an abnormal signal-averaged ECG, i.e., the presence of a late potential or a long filtered QRS duration, does distinguish patients with VT from those without VT after myocardial infarction. It is also important, however, to determine whether the signal-averaged ECG provides independent information from that which can be readily obtained from Holter monitoring and cardiac catheterization. Multivariate testing was used to demonstrate that not only is the presence of an abnormal signal-averaged ECG an independent descriptor, but it also has more predictive value for VT when compared with Holter monitor and catheterization data.

VT has been conceptualized as having two requirements: a substrate of slow conduction and a trigger of a premature beat to initiate the reentrant tachycardia.

---

**FIGURE 4.** Results of signal-averaged ECG studies, Holter monitoring, and cardiac catheterization. LP = late potential; LF QRS = long (>120 msec) filtered QRS duration; PVC >100 = peak PVC rate >100/hr on Holter monitoring.
Our results support this concept. Fractionated electrograms of long duration recorded from intracardiac electrodes have been recognized as a potential marker of the electrical substrate for VT.\textsuperscript{24, 41} We have demonstrated that the late potential corresponds to delayed and fragmented electrograms.\textsuperscript{24} A peak PVC rate greater than 100/\textperthousand designates those patients with triggers for initiating VT. Premature beats may prolong the duration of slow conduction in damaged tissue and decrease refractoriness in normal ventricular myocardium, thus initiating reentrant arrhythmias.\textsuperscript{41-45} The presence of an aneurysm represents the anatomic substrate of reentrant pathways for VT. As expected from this concept, patients with all three of these parameters should have a high probability of VT.

The patient population used for this study is not representative of all patients after myocardial infarction because of the high incidence of VT and the biases introduced by selecting the control population predominantly from patients undergoing cardiac catheterization. The predictive value of the regression model applies only to our group of patients and cannot be reliably applied prospectively to a randomly selected group of patients after myocardial infarction. However, we were able to differentiate the VT and control patients with high accuracy. It is important to validate the results further by applying them to patients prospectively after an acute infarction and observing which patients do indeed go on to develop VT.

References

45. Cain ME, Martin TC, Marchlinski FE, Josephson ME: Changes in ventricular refractoriness after an extrastimulus: effects of prematurity, cycle length and procainamide. Am J Cardiol 52: 996, 1983
Identification of patients with ventricular tachycardia after myocardial infarction: signal-averaged electrocardiogram, Holter monitoring, and cardiac catheterization.
M S Kanovsky, R A Falcone, C A Dresden, M E Josephson and M B Simson

Circulation. 1984;70:264-270
doi: 10.1161/01.CIR.70.2.264
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1984 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/70/2/264

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

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

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