Late potentials detected after myocardial infarction: natural history and prognostic significance


ABSTRACT The risk of developing spontaneous ventricular tachycardia (VT) and/or sudden death ("arrhythmic events") was prospectively assessed in 165 patients who survived acute myocardial infarction. Signal-averaged electrocardiograms (ECGs) were performed before hospital discharge and then serially at regular intervals over the following year. In addition, 24 hr Holter monitoring was performed and left ventricular ejection fraction was determined. Sixty-five patients (group 1) had abnormal signal-averaged ECGs (voltage in the last 40 msec of the filtered QRS < 20 μV or filtered QRS duration > 120 msec), 92 had normal signal-averaged ECGs (group 2), and eight had bundle branch block (excluded from analysis). In group 1, spontaneous normalization of the voltage in the last 40 msec of the QRS complex occurred in 30% of patients after 12 months, although total filtered QRS duration did not change overall. During follow-up of up to 20 months (median 11), seven patients died suddenly and six presented again with spontaneous, symptomatic VT. Eleven of 65 (17%) group 1 patients had an arrhythmic event compared with one of 92 patients (1%) in group 2 (p < .001). The sensitivity of the signal-averaged ECG as a predictor of arrhythmic events was 92% with a specificity of 62%. Patients with subsequent arrhythmic events had considerably lower voltage in the last 40 msec of the QRS (11.0 ± 8.3 vs 32.0 ± 21.9 μV; p < .001) than those without such events, and longer filtered QRS complexes (121 ± 14 vs 105 ± 12 msec; p < .001). Multivariate logistic regression determined that the signal-averaged ECG provided independent prognostic information from the presence of complex ventricular ectopy and the degree of left ventricular dysfunction assessed at the time of hospital discharge. Signal-averaged ECGs provide important prognostic information in identifying patients at risk of arrhythmic events after myocardial infarction. Dynamic changes in the terminal QRS voltage are observed during the first year after myocardial infarction. Circulation 74, No. 6, 1280–1289, 1986

AFTER RECOVERY from acute myocardial infarction, a significant number of patients remain at risk of sudden death, which is generally attributable to ventricular tachyarrhythmias.1,2 Previous studies have attempted to identify a high-risk group by Holter Monitoring, left ventriculography, exercise testing, and various clinical indexes.3–5 Recently, several investigators reported that the induction of ventricular tachycardia (VT) by programmed stimulation in patients recovering from acute infarction identifies those patients prone to serious spontaneous ventricular arrhythmias and sudden death.6–8 By means of high-resolution electrocardiograms recorded from the body surface, low-amplitude high-frequency signals can be identified at the end of the QRS complex in a large proportion of patients with VT and ventricular fibrillation (VF).9–12 These "late potentials" are thought to identify regions of delayed conduction in the border zone of an acute infarction and correspond in timing with fractionated electrograms recorded directly from the heart in both experimental and clinical studies.12,13 Although late potentials are frequently recorded in patients with VT occurring in the setting of chronic healed myocardial infarction, the significance of these signals in predicting future arrhythmic events in patients recovering from recent myocardial infarction is not known. Furthermore, the natural history of these signals has not been explored by regular serial assessment.

The purpose of this prospective study was to (1) determine the prognostic significance of the presence...
of a late potential at the time of discharge from hospital after recovery from acute myocardial infarction, (2) observe and document temporal changes in the characteristics of these signals over a period of 12 months, and (3) determine the relationship between late potentials, findings on Holter monitoring, and the presence of left ventricular dysfunction.

**Materials and methods**

One hundred sixty-five consecutive patients with acute myocardial infarction were studied prospectively. Patients were primary admissions to the coronary care unit who survived the hospital phase of recovery. Age greater than 72 years and dwelling outside the metropolitan area were the only criteria for exclusion. The diagnosis of acute myocardial infarction was based on the documentation of characteristic chest pain, serial elevation of serum cardiac enzyme (creatine kinase-MB), and evolving electrocardiographic changes with or without the development of pathologic Q waves.

**Signal-averaged ECG.** All patients underwent signal averaging before hospital discharge. Ten 10.5 ± 6.1 days (range 7 to 40) after initial presentation. Signal averaging was performed with the Arrhythmia Research Technology high-resolution ECG based on methods previously described by Simson and Denes et al.18 The ECG was recorded in sinus rhythm with standard bipolar orthogonal leads X, Y, and Z in an unshielded room. Signals from 200 to 300 beats were amplified, digitized, averaged, and then filtered with a bidirectional filter with a high bandpass frequency of 40 Hz. The use of this filter eliminates the artifact of filter ringing seen with commonly used filters.16 The filtered leads were combined into a vector magnitude, \( V_x^2 + V_y^2 + V_z^2 \), a measure that combines the high frequency content from all three leads, termed the “filtered QRS complex.”

In previous studies,16, 18, 19 a low-amplitude, high-frequency signal in the last 40 msec of the filtered QRS and a prolonged filtered QRS duration have been shown to identify patients with VT. We therefore used these variables to quantify the signal-averaged ECG. A late potential was defined as a low-amplitude signal (<20 \( \mu \)V) in the last 40 msec of the filtered QRS complex; a long filtered QRS complex was defined as total filtered QRS duration greater than 120 msec. These variables were defined by a computer algorithm. An abnormal signal-averaged ECG was defined as the presence of a late potential and/or a long filtered QRS (figure 1). Patients with evidence of bundle branch block on the standard ECG were excluded from this analysis.

![FIGURE 1. Examples of signal-averaged ECGs in two patients with prior myocardial infarction. The vector magnitude tracings of the filtered QRS complex are shown. The left-hand tracing (control) is taken from a patient without evidence of VT. The tracing on the right is taken from a patient with sustained VT after infarction. The arrow denotes the late potential.](http://circ.ahajournals.org/)

The filtered leads were combined into a vector magnitude, \( V_x^2 + V_y^2 + V_z^2 \), a measure that combines the high frequency content from all three leads, termed the “filtered QRS complex.” A late potential was defined as a low-amplitude signal (<20 \( \mu \)V) in the last 40 msec of the filtered QRS complex; a long filtered QRS complex was defined as total filtered QRS duration greater than 120 msec. These variables were defined by a computer algorithm. An abnormal signal-averaged ECG was defined as the presence of a late potential and/or a long filtered QRS (figure 1). Patients with evidence of bundle branch block on the standard ECG were excluded from this analysis.

Four-hour ambulatory Holter recordings were obtained within 48 hr of signal-averaged ECGs. Ventricular arrhythmias were classified according to the Lown grading system2: grade I, uniform ventricular premature complexes (VPCs) \(< 30/ hr\); grade II, uniform VPCs \(\geq 30/ hr\); grade III, multiform VPCs; grade IV, repetitive VPCs; grade V, R on T VPCs. Repetitive ventricular activity was defined as two or more consecutive VPCs with a rate of 120/min or higher.

Left ventricular ejection fraction (LVEF) was assessed by radionuclide ventriculography before hospital discharge in 143 patients and by single plane cineangiography in 22 who underwent coronary angiography. Left ventricular aneurysm was defined as the presence of regional paradoxical systolic wall motion.

**Follow-up studies.** Patients were recalled for assessment of clinical status and repeat electrocardiography 6 weeks after discharge from hospital and then at 3, 6, and 12 months. All patients were followed-up for at least 6 months (median 11). Comparison was made between the voltage in the last 40 msec of the filtered QRS and the filtered QRS duration. Our previous experience in 38 subjects, without recent myocardial infarction, showed that the mean coefficients of variation for these variables was 6.6% and 1.0%, respectively, with 95% confidence intervals of \( \pm 3.8 \mu \)V and \( \pm 2 \) msec, respectively (unpublished observations). When a patient died, an eyewitness account was sought. Autopsy was performed when possible. An “arrhythmic event” was defined as sudden death or occurrence of symptomatic or sustained ventricular arrhythmia. Sustained ventricular arrhythmia was defined as spontaneous VF or VT lasting more than 30 sec or necessitating cardioversion because of hemodynamic collapse. This definition was also used to include patients who subsequently presented with witnessed syncope and were found to have inducible sustained VT at electrophysiologic study, in the absence of other identifiable causes for syncope.

Sudden death was defined as witnessed death within 1 hr of the onset of symptoms, or unexpected death occurring during sleep. Patients in whom electrocardiographic monitoring performed during sudden death revealed a primary arrhythmia other than VT or VF were not classified as having arrhythmic events.

Treatment was not standardized in this study and was left to the discretion of attending physicians. The results of signal averaging were not disclosed.

**Statistical analysis.** Data analysis was performed with Student’s t test, Fisher’s exact test, and chi-square analysis where appropriate. Data were expressed as means ± 1 SD unless otherwise specified. Actuarial life-table analysis22 was used to generate hazard curves for patients with normal and abnormal signal-averaged ECGs. Stepwise logistic regression9 was used to determine whether signal-averaged ECGs contributed independent prognostic information to the prediction of arrhythmic
Results

Clinical features of patients. Of the 165 patients in this study, 60 had anterior, 59 had inferior, and the remaining 38 had subendocardial (non-Q wave) myocardial infarction; eight additional patients had bundle branch block on the standard ECG and were not included in the analysis. During the period of follow-up there were 16 deaths; seven of these patients died suddenly. Three patients were monitored during this episode: two had VF (one in hospital, one out of hospital), and one patient had documented sinus bradycardia associated with electromechanical dissociation. This patient was not classified as having an arrhythmic event. In addition, six patients died from cardiac failure and three died from noncardiac causes (one each from cerebral embolus, cerebral tumor, and suicide).

Seven patients presented again with spontaneous symptomatic VT. The mean cycle length of VT was 368 ± 33 msec (rate 164 ± 14 beats/min). In three patients the arrhythmia was associated with syncope, in one patient it was incessant and led to progressive cardiogenic shock over a 72 hr period, and in three patients it was well tolerated. Only one of these seven patients with organized VT was taking an antiarrhythmic medication (oral quinidine) for complex ventricular ectopy. Two patients who died suddenly were also taking a type I agent; one of these had a normal signal-averaged ECG, the other had bundle branch block. In addition, nine patients had recurrent myocardial infarction, and coronary revascularization was performed in 18 patients.

One hundred fifty-seven patients were divided into two groups based on the findings on signal-averaged ECGs obtained before hospital discharge: group 1 consisted of 65 patients with either a late potential (n = 63) and/or a long filtered QRS (n = 22), and group 2 comprised 92 patients with normal signal-averaged ECGs. The clinical profiles of these patients are summarized in Table 1. Patients in group 1 tended to have higher peak CK-MB values, lower LVEF, and more often had inferior transmural myocardial infarction. There were no significant differences in the distribution of age, sex, or clinical status on admission. The incidence of left ventricular aneurysm (31% overall) was similar in both groups.

Relationship of abnormal signal-averaged ECG to ambulatory monitoring and left ventricular function. The prevalence of high-grade ventricular ectopy (Lown grade III to V) was similar in groups 1 (35%) and 2 (36%). Although the prevalence of repetitive VPCs was similar in both groups, nonsustained VT was more common in group 2 (7% vs 2%). Mean LVEF in group 1 was 43 ± 13% compared with 49 ± 13% in group 2 (p < .001); 40% of group 1 patients had significant depression of left ventricular function (LVEF < 40%) compared with 23% of group 2 patients (p < .05).

Natural history of signal-averaged ECG tracings. Signal-averaged ECG variables were assessed serially in all patients. The following data were obtained in those patients who survived at least 6 months and who did not have recurrent myocardial infarction or undergo coronary revascularization or change in antiarrhythmic therapy. In group 1 patients, the mean duration of the filtered QRS complex did not change significantly during follow-up. Mean voltage in the last 40 msec of the filtered QRS complex increased significantly from the initial study to the second study performed 6 weeks after hospital discharge (from 12.8 ± 7.5 to 20.0 ± 12.6 μV; p < .001) (figure 2). This increase was outside the 95% confidence limits of reproducibility. No further significant change in voltage occurred in the group overall at the remaining studies at 3, 6, and 12

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Clinical characteristics of 157 patients according to findings on signal-averaged ECG</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Group 1 (n = 65)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>59 ± 9</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>54/11</td>
</tr>
<tr>
<td>Prior MI</td>
<td>10</td>
</tr>
<tr>
<td>Peak CK-MB (I/liter)</td>
<td>134 ± 88</td>
</tr>
<tr>
<td>1° VF (1st 48 hr)</td>
<td>9</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>43 ± 13</td>
</tr>
<tr>
<td>Killip class III-IV</td>
<td>8</td>
</tr>
<tr>
<td>Myocardial infarct location</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>21</td>
</tr>
<tr>
<td>Inferior</td>
<td>33</td>
</tr>
<tr>
<td>Non-Q wave</td>
<td>11</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>20</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>18</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>5</td>
</tr>
</tbody>
</table>

CK-MB = creatine kinase, MB fraction; 1° VF = primary ventricular fibrillation.
months (figure 3). A representative tracing is shown in figure 4.

In group 2, mean filtered QRS duration was 100 ± 9 msec at initial study and did not change significantly during follow-up. Mean voltage in the last 40 msec of the filtered QRS complex also did not change significantly during the follow-up period.

Although 65 patients (41%) had an abnormal signal-averaged ECG at hospital discharge, by 6 weeks 11 (18%) had undergone spontaneous normalization of the terminal portion of the QRS complex (figures 5 and 6). By 12 months, only 70% of the patients originating from group 1 still had an abnormal signal-averaged ECG tracing. At each of the follow-up assessments, between 2% and 4% of patients in group 2 were noted to have abnormal signal-averaged ECGs. In two patients these abnormalities followed a recurrent myocardial infarction (figure 7); however, in the remainder there was no obvious precipitant or change in therapy to explain the change in terminal QRS voltage.

**Relationship of abnormal signal-averaged ECG to late arrhythmic events.** Eleven patients in group 1 (17%) had an arrhythmic event during follow-up; four had sudden death (VF documented in two) and five had spontaneous sustained VT not obviously associated with acute ischemia. Two more patients developed syncope and were considered to have VT on the basis of electrophysiologic testing and ambulatory ECG monitoring during investigation for syncope. Two patients with documented spontaneous VT died later from progressive cardiac failure after intensive pharmacologic therapy for arrhythmia control.

**FIGURE 2.** Serial changes in the terminal QRS voltage and filtered QRS duration of patients with abnormal signal-averaged ECGs at hospital discharge (group 1). The circle with the horizontal line represents the group mean. The horizontal dashed line indicates the criteria for identifying patients with VT (voltage in the last 40 msec of the filtered QRS < 20 μV and filtered QRS duration > 120 msec).

**FIGURE 3.** Serial assessment of signal-averaged ECG variables. Mean values for the voltage in the last 40 msec of the filtered QRS and filtered QRS duration are shown at each recording: 10 days after hospital discharge, and then 6 weeks, 3, 6, and 12 months later. These are presented separately for patients in groups 1 and 2. Data are expressed as mean ± SEM.
There were five cardiac and two noncardiac deaths in group 2 patients. One death occurred instantaneously without an ischemic prodrome. No patients in this group developed sustained ventricular tachyarrhythmias during follow-up. Hence, 92% of patients with an arrhythmic event were correctly classified; the specificity of an abnormal predischarge signal-averaged ECG was 62%.

One sudden death and one noncardiac death occurred among patients with bundle branch block on the 12 lead ECG.

Hazard curves comparing the outcome of patients in groups 1 and 2 are shown in figure 8. All events were noted to occur within the first 6 months. The probability of remaining free of arrhythmic events at 12 months was 83% in group 1 compared with 99% in group 2 (p < .001).

Relationship of ambulatory monitoring and LVEF to ar-

**FIGURE 4.** Temporal changes in terminal voltage and filtered QRS duration in a patient with anterior myocardial infarction. At 10 days, voltage in the last 40 msec of the QRS was 0.8 µV and increased to 13.3 µV at 12 months. Filtered QRS duration became progressively shorter during this period. Vertical dashed line indicates the end of the QRS complex.

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**FIGURE 5.** Example of filtered QRS complex 10 days and 8 weeks after myocardial infarction. The vertical dashed lines indicates the end of the filtered QRS complex. In the left-hand panel, the voltage in the last 40 msec of the QRS is 12.5 µV and increased to 34.9 µV at 8 weeks. By definition, a late potential is present in the first tracing but not on the later tracing. The filtered QRS duration is also reduced on the second tracing.
arrhythmic events among patients with significant left ventricular dysfunction (LVEF < 40%) was 23% (11/47) compared with 1% (1/110) in patients with an LVEF of 40% or higher (p < .001). Only two of 48 patients with left ventricular aneurysm had an arrhythmic event at follow-up. The sensitivity of depressed left ventricular function was thus 92%, with a specificity of 75%.

Relative importance of signal-averaged ECG, ambulatory monitoring, and LVEF. A comparison of the prognostic value of signal-averaged ECG, ambulatory monitoring, and LVEF is illustrated in table 2. Multivariate logistic regression was used to construct a model for predicting the likelihood of arrhythmic events, based on the results of these investigations. Both an abnormal signal-averaged ECG (b = 2.8, p = .01) and LVEF under 40% (b = 3.0, p = .006) were independently significant; however, evidence of complex ventricular ectopy during Holter monitoring was not found to be significant (b = 1.0, p = .18) in the multivariate model.

Characteristics of patients with arrhythmic events. The clinical features of patients with and without arrhythmic events during the follow-up period are shown in table 3. Patients with arrhythmic events more often had anterior transmural infarction, with higher peak CK-MB values and lower LVEFs. Signal-averaged ECGs revealed considerably lower voltage in the last 40 msec of the filtered QRS complex in patients with arrhythmic events (11.0 ± 8.3 vs 32.0 ± 21.9 μV; p < .001) and significantly longer filtered QRS duration (121 ± 14 vs 105 ± 12 msec; p < .001) when assessed at the time of discharge. All group 1 patients with arrhythmic
events had abnormal signal-averaged ECGs at the last recording performed before presentation with that event.

Discussion

The important findings of this study include: (1) a relatively high prevalence of late potentials after acute myocardial infarction, (2) the dynamic nature of the terminal QRS, especially during the first 2 months after myocardial infarction, (3) the important late prognostic information derived from their identification at the time of hospital discharge, and (4) the apparently independent nature of their prognostic import compared with other well-described indexes of risk.

Previous studies have demonstrated the high prevalence of late potentials in patients with chronic reentrant ventricular arrhythmias, especially those with prior myocardial infarction and wall motion abnormalities. Most of these, however, have been retrospective studies that were biased toward patients with known sustained ventricular arrhythmias who had been referred to tertiary care centers for electrophysiologic evaluation. The limited prospective information available has usually included a “mixed bag” of patients with coronary artery disease identified at cardiac catheterization and not necessarily associated with recent myocardial infarction. Two recent prospective postinfarction studies assessed the risk of early (in-hospital) ventricular arrhythmias after recording signal-averaged ECGs within the first 5 days of infarction. Such studies provide limited information about late risk after the patient has been released from the “protected” environment of the coronary care unit, where resuscitative measures are available should sudden arrhythmic events occur. Furthermore, the anatomic and electrophysiologic milieu within acutely ischemic myocardium would be expected to be changing dramatically at least within the first 48 hr after the myocardial infarction, and therefore the identification of an electrical substrate at this time may not offer accurate long-term assessment of risk. In addition, nonsustained VT was used as an arrhythmic end point. We therefore decided to obtain signal-averaged ECGs just before hospital discharge when the patient was stable and well, at which time intervention could be considered should the patient fall into a high-risk group.

The equipment used in this study is similar to that used by several other groups in patients with and with-

| TABLE 2 |
| Predictive value of prognostic indexes (%) |

<table>
<thead>
<tr>
<th>Prognostic index</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal signal-averaged ECG&lt;sup&gt;a&lt;/sup&gt;</td>
<td>92</td>
<td>62</td>
<td>17</td>
</tr>
<tr>
<td>Left ventricular dysfunction (LVEF &lt; 40%)</td>
<td>92</td>
<td>75</td>
<td>23</td>
</tr>
<tr>
<td>Holter monitor (Lown III-V)</td>
<td>73</td>
<td>67</td>
<td>15</td>
</tr>
</tbody>
</table>

<sup>a</sup>Voltage in the last 40 msec of the filtered QRS < 20 μV and/or filtered QRS duration > 120 msec.

| TABLE 3 |
| Relationship of clinical variables to arrhythmic events |

<table>
<thead>
<tr>
<th></th>
<th>AE (n = 12)</th>
<th>No AE (n = 145)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>64 ± 5</td>
<td>58 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/3</td>
<td>111/34</td>
<td>NS</td>
</tr>
<tr>
<td>Peak CK-MB (IU/liter)</td>
<td>158 ± 75</td>
<td>104 ± 88</td>
<td>&lt;.001</td>
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<tr>
<td>LVEF (%)</td>
<td>31 ± 12</td>
<td>48 ± 13</td>
<td>&lt;.001</td>
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<td>Holter</td>
<td></td>
<td></td>
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<tr>
<td>Lown III-V</td>
<td>8</td>
<td>46</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Rep. VPCs</td>
<td>1</td>
<td>22</td>
<td>NS</td>
</tr>
<tr>
<td>VT (&gt; 3 VPCs)</td>
<td>1</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Signal-averaged ECG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V last 40 msec (μV)</td>
<td>11 ± 8</td>
<td>32 ± 22</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Filtered QRS (msec)</td>
<td>121 ± 14</td>
<td>105 ± 12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Abnormal tracing</td>
<td>11</td>
<td>54</td>
<td>&lt;.001</td>
</tr>
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<td>Myocardial infarct location</td>
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<td>Anterior</td>
<td>8</td>
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<td>NS</td>
</tr>
<tr>
<td>Inferior</td>
<td>3</td>
<td>56</td>
<td>NS</td>
</tr>
<tr>
<td>Non-Q wave</td>
<td>0</td>
<td>38</td>
<td>&lt;.05</td>
</tr>
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</table>

AE = arrhythmic events; Rep. VPC’s = repetitive (≥ 2) ventricular premature complexes; V = voltage.
out VT. Specifically, Simson showed that 92% of patients with recurrent VT had a low-amplitude high-frequency signal (<25 μV) in the last 40 msec of the QRS complex, and in 72% of the patients the filtered QRS duration was greater than 120 msec. We have been able to reproduce these findings in similar patients and to apply this technique in predicting occurrence of spontaneous and inducible VT in patients presenting with syncope. The use of a 40 Hz filter was selected because of its improved sensitivity and reproducibility over the 25 Hz filter originally described by Simson. Although the definition of abnormality is still controversial, we used the criteria of terminal QRS voltage (<20 μV) and filtered QRS duration (>120 msec) previously described in patients with VT. The lower cut-off for V₄₀ in defining a late potential (20 μV) is due to the narrower bandwidth of the 40 Hz filter. One other advantage of this technique is that it provides a totally objective, quantitative assessment derived from a computer algorithm, thereby minimizing observer bias.

An abnormal signal-averaged ECG was present in 41% of patients at the initial recording. However, during the first 6 months after infarction, there was an overall increase in terminal QRS voltage, without a significant change in the filtered QRS duration. Only two-thirds of the patients originally in group 1 still had an abnormal signal-averaged ECG at the 6 month follow-up. This change may be due to amelioration of ischemia from development of collateral circulation or recovery of “stunned myocardium” occurring in the peri-infarct border zone. The disappearance of late potentials may also be caused by fibrosis leading to electrical isolation of portions of the abnormal myocardium that were responsible for fractionated electrical activity. The possible influence of antiarrhythmic drugs on the temporal changes in the terminal QRS complex cannot be ignored; however, previous studies have reported a nonspecific prolongation of low-amplitude signals and a decrease in terminal QRS voltage, irrespective of the effect on inducibility of VT. In the absence of reinfarction, the subsequent appearance of late potentials de novo was rare. This suggests that the optimal time for recording the signal-averaged ECG to detect these abnormalities is at the time of hospital discharge.

The sensitivity of signal-averaged ECGs for predicting late arrhythmic events was 92%. This corresponds with the findings of Simson and others, who studied signal-averaged ECGs in patients with prior myocardial infarction known to have VT. The low specificity of the signal-averaged ECG, however, differs markedly in this prospective assessment. There are several possible explanations for this: (1) The close correlation between late potentials and inducibility of VT suggests that abnormalities on the signal-averaged ECG reflect the presence of an anatomic substrate that will support a reentrant tachycardia if appropriately timed extrastimuli are provided. Hence patients with arrhythmic events presumably require a trigger to initiate their tachycardia. This is supported by the findings of Kanovsky et al., who found that the occurrence of frequent VPCs (>100/hr) on Holter monitoring in addition to abnormal signal-averaged ECG differentiated those patients with and without clinical VT. In addition, programmed stimulation after myocardial infarction has been shown to have similar sensitivity, specificity, and predictive accuracy for late arrhythmic events. (2) There is a change in the electrophysiologic properties of healing myocardial infarction that leads to the normalization of the terminal QRS complex in a proportion of patients; these patients may no longer be at risk of developing arrhythmic events. (3) Although late potentials have been shown to correlate in timing with fractionated endocardial electrical activity within the myocardium, such activity may be quite diffusely located; a critical mass of tissue leading to conduction delay may be necessary for the development of tachycardia. This is further supported by the observation that clinical VT is more often seen in patients with significant left ventricular dysfunction, especially in those with a well-defined aneurysm. We were not able to show a correlation between the presence of left ventricular aneurysm and occurrence of arrhythmic events; this is probably because the finding of dyskinesias within 2 weeks of an acute myocardial infarction is not necessarily predictive of later development of a “surgical” fibromuscular aneurysm.

One difficulty in interpreting the results of this study lies in the assumption that sudden death was caused by a pathophysiologic mechanism similar to that operative in patients with sustained VT. Several studies strongly suggest that sudden death is generally caused by ventricular tachyarrhythmias; in most cases of sudden death, where electrocardiographic monitoring had recorded the event, an organized VT immediately preceded the occurrence of VF. Also, in survivors of out-of-hospital cardiac arrest, VT is commonly induced at electrophysiologic study. However, sudden death can also result from acute ischemia, from electrolyte disorders, and from mechanical disturbances of the heart. The prognostic value of the signal-averaged ECG may apply only to those patients whose arrhyth-
mria is related to reentry within a chronic electrophysiologic substrate, associated with regional slow conduction. In this study, all patients with a documented sustained ventricular arrhythmia were identified by an abnormal signal-averaged ECG; one patient who died suddenly, with a normal signal-averaged ECG, was not monitored during this episode.

The major importance of an abnormal finding on the signal-averaged ECG in a patient who has survived myocardial infarction lies in the possible therapeutic implications. Whereas LVEF has been repeatedly shown to be a strong predictor of major cardiac events after myocardial infarction,7,8 left ventricular dysfunction is usually irreversible. Similarly, although several studies stress the predictive value of pre-discharge Holter monitoring,7-8 no studies have shown that the incidence of cardiac events is reduced with any intervention.36 Since left potentials presumably represent an anatomic substrate for VT, therapy specifically directed at ablating or modifying the electrical properties of such tissue may prove to be effective.37 In patients with clinical VT, disappearance of late potentials after map-guided surgery has been shown to correlate well with abolition of VT.38

The predictive value of an abnormal signal-averaged ECG recorded before hospital discharge was 17%; this compared with only a 1% likelihood of arrhythmic event if the signal-averaged ECG was normal at this time (p < .001). By logistic regression, the prognostic value of the signal-averaged ECG was found to be independent of the presence of left ventricular dysfunction. Holter monitoring did not provide significant independent information after consideration of these two variables.

This study describes the value of signal averaging of the surface ECG in predicting future risk of developing spontaneous ventricular arrhythmias during the first year after myocardial infarction. Presence or absence of abnormalities on the signal-averaged ECG at the time of hospital discharge differentiates two distinct subgroups with markedly diverse risk. Intervention studies, based on the findings of signal averaging, may be beneficial and have far-reaching effects.

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