PATHOPHYSIOLOGY AND NATURAL HISTORY

MYOCARDIAL INFARCTION

Prognostic significance of ventricular tachycardia and fibrillation induced at programmed stimulation and delayed potentials detected on the signal-averaged electrocardiograms of survivors of acute myocardial infarction


ABSTRACT The relative prognostic significance of ventricular tachycardia and ventricular fibrillation inducible at programmed stimulation within 1 month of acute myocardial infarction was compared in a prospective study of 403 clinically well survivors of transmural infarction who were 65 years old or younger. The prognostic significance of delayed potentials on the signal-averaged electrocardiogram was also examined in a subset of 306 patients without bundle branch block. Among the study patients, 20% had inducible ventricular tachycardia, 14% had inducible ventricular fibrillation, and 66% had no inducible arrhythmias. The 2 year probability of remaining free from cardiac death or nonfatal ventricular tachycardia or fibrillation was 0.73 for those with inducible ventricular tachycardia, 0.93 for those with inducible ventricular fibrillation, and 0.92 for those with no inducible arrhythmias. The cycle length of inducible ventricular tachycardia was 230 msec or more in 70% of the patients with inducible tachycardia who died. Of the patients studied by signal-averaged electrocardiography, 26% had delayed potentials. At 2 years, the probability of remaining free from cardiac death or nonfatal ventricular tachycardia or fibrillation was 0.73 for patients with delayed potentials and 0.95 for patients with no delayed potentials. There was a significant correlation (p < .001) between the presence of delayed potentials and the ability to induce ventricular tachycardia. In conclusion, in survivors of recent infarction who have not had spontaneous ventricular tachycardia or fibrillation, inducible tachycardia (but not inducible fibrillation) at programmed stimulation predicts a significant risk of death or spontaneous tachycardia or fibrillation. A similar risk is found for patients with delayed potentials on the signal-averaged electrocardiogram.


A MAJORITY of patients with spontaneous ventricular tachycardia or fibrillation late after myocardial infarction have inducible sustained ventricular tachyarrhythmias on programmed stimulation1-8 or delayed potentials detectable in the ST segment of the signal-averaged electrocardiogram.9-13 However, it is only recently that the prognostic implications of inducible sustained ventricular tachyarrhythmias14-16 and delayed potentials17, 18 have been noted in survivors of recent myocardial infarction who have not had spontaneous late ventricular tachycardia or fibrillation. To date, there have been no studies on the relationship of the morphology of the induced arrhythmia to prognosis, and the relative prognostic significance of inducible ventricular tachyarrhythmias and delayed potentials has not been examined.

The present study was designed to assess the relative significance of inducible ventricular tachycardia vs inducible ventricular fibrillation with respect to prediction of mortality and spontaneous ventricular tachycardia and fibrillation in survivors of recent myocardial
infarction. In addition, the predictive value of the presence of delayed potentials for these events was compared with that of inducible ventricular tachycardia in a subgroup of patients without bundle branch block.

Methods

Patients. All patients 65 years old or younger admitted to Westmead Hospital between July 1, 1981, and June 30, 1984 with transmural myocardial infarction (development of new Q waves) were registered. At the end of 1 week of hospitalization, survivors were reviewed, and some were excluded from the study. Reasons for exclusion were (1) early recurrence of angina requiring treatment with β-blockers or coronary artery bypass grafting, (2) spontaneous ventricular tachycardia or fibrillation occurring more than 48 hr after infarction (ventricular tachycardia or fibrillation within the first 48 hr was considered to be related to the acute ischemic or infarction process and was not a reason for exclusion), (3) clinical heart failure not controlled by 40 mg/day furosemide, and (4) significant noncardiac disease.

The study group thus comprised patients who were clinically well at the time of programmed stimulation. No study patient had received β-blockers, digoxin, or other antiarrhythmic therapy for at least 7 days before programmed stimulation. The patients in this study were a new cohort and there was no overlap with the patients reported in previous studies. Mean age of the study group was 52 years (range 28 to 65), and the site of infarction was anterior in 170 (42%).

Programmed stimulation. Programmed stimulation was performed 7 to 28 days after infarction. The stimulation protocol was uniform from patient to patient, and was commenced after measurement of the QRS duration and HV and QT intervals during sinus rhythm. Extrastimuli were applied during paced rhythm, which comprised drive trains of eight stimuli set as long as possible (usually 600 msec). Only one paced cycle length was tested in each patient. Each drive train was followed by single then paired extrastimuli applied first at the right ventricular apex and then at the right ventricular outflow tract. This sequence was first applied at twice diastolic threshold (1 to 4 mA) and was then repeated at 20 mA. Stimuli were 2 msec rectangular pulses and were delivered from a Medtronic 5325 programmable stimulator. There was a 3 sec delay between each pacing sequence.

The stimulation protocol was terminated at the conclusion of the protocol or if ventricular tachycardia or fibrillation lasting more than 10 sec was induced. Patients were considered to have no inducible arrhythmias if nonstimulated ventricular beating terminated within 10 sec. The body surface Frank vectorcardiogram and intracardiac electrograms were recorded simultaneously on paper at 250 mm/sec. The morphology of an induced arrhythmia was classified as ventricular tachycardia or fibrillation depending on the initial QRS morphology. Ventricular tachycardia was said to be present if there was a well-organized rhythm with a constant or nearly constant (±5%) cycle length and a stable surface vectorcardiogram with stable configuration of the QRS complexes in all three leads and a constant relation of inscription of the QRS complexes in the three leads. A regular tachycardia with sawtooth QRS morphology and no isoelectric segments was classified as ventricular tachycardia. The classification of an arrhythmia as ventricular tachycardia was not altered if ventricular fibrillation subsequently supervened. Ventricular tachycardia was arbitrarily subclassified as fast ventricular tachycardia (“flutter”) with a cycle length of less than 230 msec or slow ventricular tachycardia (cycle length ≥230 msec). Ventricular fibrillation was said to be present if from the outset there was a disorganized rhythm with irregularly timed endocardial electrograms, and either no clearly defined QRS complexes on the surface vectorcardiogram or QRS complexes of continuously varying configuration. Fast polymorphic arrhythmias (with cycle length <230 msec) were classified as ventricular fibrillation in this study. All episodes of inducible ventricular tachycardia or fibrillation reverted to sinus rhythm spontaneously or were terminated by pacing or direct-current cardioversion without neurologic or other significant sequelae.

Signal averaging. Signal averaging of the electrocardiogram was performed on the same day as programmed stimulation in 306 of 328 consecutive patients without bundle branch block. X, Y, and Z leads of the Frank vectorcardiogram were recorded for 5 min, filtered (0.05 to 500 Hz), and digitized simultaneously at 1000 samples/sec. Signal averaging was performed with a DEC 11/34 computer (Fortran averaging program) after an iterative cross-correlation procedure was used to optimize QRS alignment. QRS onset and offset in the averaged recordings were determined manually by displaying segments of each trace at high amplification. For each patient, an encoded recording was presented to the analyst, who then measured ventricular activation time in milliseconds as the total time from earliest QRS onset in any lead to latest QRS offset in any lead. QRS offset was measured to the end of any low-amplitude, high-frequency components extending into the ST segment, provided they had an amplitude more than twice that of the simultaneously displayed noise level, which was usually 0.5 to 1.0 μV. These low-amplitude signals were defined as delayed potentials if they extended more than 140 msec after QRS onset. Determination of ventricular activation time by this method is free from significant interobserver variability.

Other investigations

Ambulatory electrocardiographic monitoring. Twenty-four-hour ambulatory electrocardiographic recordings were analyzed manually. The total numbers of ventricular premature contractions (VPCs) each hour and every 24 hr were noted, as was the maximum Lown grade.

Exercise testing. Treadmill exercise tests were performed 2 and 8 weeks after infarction by a modified Naughton protocol, as described by Sarni et al. Patients were separated into two groups, those having a 2 mm or more change in the ST segment (depression or elevation) for 80 msec after the J point at either test, and those with a less than 2 mm change in the ST segment. Cardiac catheterization. Significant coronary artery disease at coronary arteriography was defined as a greater than 50% reduction in luminal diameter of the left main coronary artery or a greater than 75% reduction in luminal diameter in any other major coronary artery. A left ventricular aneurysm was defined as dyskinetic wall motion on a right anterior oblique ventriculogram.

Radionuclide ventriculography. Resting left ventricular ejection fraction (LVEF) was quantified during sinus rhythm with 99mTc radionuclide ventriculography and computer-generated time-activity curves. This method has been found to be reliable for identification of left ventricular aneurysms and for quantification of LVEF in the presence of an aneurysm. The normal range of LVEF was 0.50 to 0.65. A left ventricular aneurysm was said to be present if there was dyskinetic wall motion.

Follow-up. During follow-up, patients were not placed on β-blockers unless angina developed or therapy was required for hypertension. Patients were placed on antiarrhythmic drugs (quinidine, mexiletine, or disopyramide given to achieve therapeutic serum levels) if they developed frequent symptomatic VPCs documented on the electrocardiogram or if they were randomly assigned to antiarrhythmic therapy as part of a prospective trial of antiarrhythmic drugs in patients with inducible ventricular tachyarrhythmias.
All patients with inducible ventricular tachycardia or fibrillation were approached to join the trial, and those who agreed to do so were randomly assigned either to no treatment (control) or to treatment with antiarrhythmic drugs. In patients assigned to treatment, oral therapy was commenced with a class I drug. A β-blocker was not selected as one of the trial drugs since the intention was to test the effects of antiarrhythmic drugs that do not have an anti-ischemic action. The aim was to commence quinidine therapy, but if there were unacceptable side effects or problems with attaining an acceptable serum level, disopyramide or mexiletine was substituted.

Once an oral drug with no side effects had been found, the dose was adjusted to achieve a serum level within the "therapeutic" range for the assay laboratory. The methods for assaying serum drug levels were as follows: (1) quinidine, immunofluorescence polarization (Abbott), therapeutic level = 6 to 15 μmol/liter, (2) disopyramide, emit enzyme immunoassay (Syva), therapeutic level = 6 to 12 μmol/liter, (3) mexiletine, gas-liquid chromatography, therapeutic level = 3.5 to 9 μmol/liter. Patients were discharged from the hospital once therapeutic serum levels of the drugs had been attained. Ambulatory electrocardiographic monitoring and serial programmed stimulation studies were not used to arrive at appropriate drug therapy.

The study patients were followed for up to 24 months (mean 12). The study end points were death or spontaneous, documented sustained ventricular tachycardia or fibrillation detected as a clinical event.

Categorization of deaths. Deaths were categorized according to the same criteria detailed in a previous study.16 Deaths were attributed to reinfarction or fresh ischemia if they were associated with chest pain and either electrocardiographic evidence of ischemia or fresh infarction or postmortem evidence of infarction or fresh antemortem intracoronary thrombus.

Ventricular tachyarrhythmias were presumed to be the cause of death if ventricular tachycardia or fibrillation was documented and had not been associated with antecedent chest pain or ischemic electrocardiographic changes, or if the death was witnessed to be instant and the patient had been well and free from chest pain immediately before death. It was appreciated that myocardial rupture and pulmonary embolism could also have caused instantaneous death, and when possible, postmortem examination was performed to exclude the presence of these conditions. Unwitnessed deaths were classified as cardiac deaths if there was no clinical or postmortem evidence for a noncardiac cause.

Statistics. For continuous variables, the two-tailed t test was used for comparison of two groups, with the Bonferroni procedure24 being applied when three groups were compared. For discrete variables, Fisher's exact test or Yates' corrected chi-square test was used. The actuarial survival data were calculated by the method of Cutler and Edeler25 and the log-rank test was applied to the data with use of the method of Peto et al.26

To identify variables of independent prognostic value, multiple logistic regression using the computer package GLIM27 was performed on data from the 306 patients who underwent both programmed stimulation and signal averaging of the electrocardiogram. In addition to the findings at programmed stimulation (inducible ventricular tachycardia, inducible ventricular fibrillation, no inducible arrhythmias) and at signal averaging (delayed potentials, no delayed potentials), the following variables were included in the analysis: age, sex, site of infarction, previous infarction, presence or absence of acute ventricular tachycardia or fibrillation, maximum creatine kinase, pulmonary congestion on chest x-ray in the coronary care unit, QRS duration on unaveraged electrocardiogram, QT interval, corrected QT, and presence or absence of ST segment change at exercise testing. Data on coronary anatomy and LVEF were not included in the analysis because they were obtained routinely only in patients with inducible ventricular tachycardia or fibrillation. When the variables of independent prognostic value were identified, the effect of treatment when allowing for these variables was also assessed. The treatment modalities assessed were β-blockers, antiarrhythmic medications, and coronary artery revascularization.

Statistical significance was defined as a p value less than .05. The odds ratio28 was used as an index of relative risk.

Results

Patients studied. Of 528 patients from 28 to 65 years old admitted with transmural myocardial infarction, 33 (6%) died within 1 week of infarction. Of the 495 survivors, 403 (81%) entered the study group. The reasons for exclusion were recurrent angina requiring treatment (n = 36), heart failure requiring digoxin (n = 26), patient refusal (n = 17), spontaneous late ventricular tachycardia or fibrillation (n = 7), and significant noncardiac disease (n = 6).

Results of programmed stimulation. No ventricular tachycardia or fibrillation was inducible in 267 of the 403 patients (66%). The maximum numbers of nonstimulated ventricular beats were 0 to 18 at the right ventricular apex and 0 to 36 at the right ventricular outflow tract. The mean number of nonstimulated ventricular beats was 4.3, with 95% of patients having 0 to 13 beats as the maximum throughout the whole protocol.

Ventricular fibrillation was inducible in 56 patients (14%) and ventricular tachycardia was inducible in 80 patients (20%). An arrhythmia was inducible with two extrastimuli at 20 mA stimulation, but not at twice diastolic threshold, in 32 patients (57%) with ventricular fibrillation and in 37 patients (46%) with ventricular tachycardia, these proportions not being statistically different. There was no difference between the cycle length of ventricular tachycardia induced by high-current stimulation (210 ± 6 msec, mean ± SEM) and that induced by low-current stimulation (221 ± 8 msec). High-current stimulation enabled introduction of earlier extrastimuli. Minimum coupling interval for the first extrastimulus was 233 ± 2 msec for low current and 216 ± 3 msec for high current (p < .001). Minimum coupling interval for the second extrastimulus was 214 ± 4 msec for low current and 197 ± 5 msec for high current (p < .02).

There was no significant difference between the groups with respect to the mean time interval after infarction at which programmed stimulation was performed (no ventricular tachycardia/fibrillation, 11 days; ventricular fibrillation, 13 days; ventricular tachycardia, 12 days).
The index infarction was anterior in a higher proportion of patients in the group with no inducible arrhythmias than in patient groups in which either ventricular tachycardia or fibrillation was inducible (table 1). Mean maximum creatine kinase was highest in the group with inducible ventricular tachycardia, as was the mean Norris coronary prognostic index, although in both instances there was considerable overlap between the groups. The incidence of delayed potentials on the signal-averaged electrocardiogram was highest (53%) in patients with inducible ventricular tachycardia and lowest (16%) in patients in whom no ventricular tachycardia or fibrillation was inducible (table 2).

At 24 hr ambulatory electrocardiographic monitoring (performed in 88 consecutive patients), VPC count/hour tended to be highest in patients with inducible ventricular tachycardia and lowest in patients with inducible ventricular fibrillation, but this trend did not reach statistical significance (table 2). There was considerable overlap between groups with respect to the VPC count/hour — the ranges were 0 to 537 for those with no inducible ventricular tachycardia or ventricular fibrillation, 0 to 114 for those with inducible ventricular fibrillation, and 0 to 614 for those with inducible ventricular tachycardia. In patients with inducible ventricular tachycardia, the mean cycle length of tachycardia was longer at 254 ± 16 msec in the eight patients with complex ectopy, compared with 205 ± 6 msec for the 11 patients with simple ectopy (p < .01).

In the 335 patients (83%) who underwent exercise testing, there was no relationship between an exercise-induced change in ST segment of 2 mm or more and the results of programmed stimulation (table 2).

As part of the protocol for this study, radionuclide ventriculography and coronary arteriography with left ventriculography were performed in as many of the 136 patients with inducible ventricular tachycardia or fibrillation as was possible. LVEF was assessed by radionuclide ventriculography in 128 patients (94%), coronary anatomy was assessed in 120 patients (88%), and the presence or absence of a left ventricular aneurysm was assessed in 131 patients (96%) who underwent ventriculographic examinations performed by either radionuclide techniques or left heart catheterization. As shown in table 3, there was no difference in coronary anatomy between groups with inducible ventricular tachycardia and those with inducible ventricu-

### TABLE 1
Clinical and electrophysiologic profiles of patients studied by programmed stimulation

<table>
<thead>
<tr>
<th></th>
<th>No VT/VF inducible (n = 267)</th>
<th>VF inducible (n = 56)</th>
<th>VT inducible (n = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarction (%)</td>
<td>48</td>
<td>25</td>
<td>35</td>
</tr>
<tr>
<td>Previous infarction (%)</td>
<td>12</td>
<td>14</td>
<td>19</td>
</tr>
<tr>
<td>Acute VT or VF (%)</td>
<td>15</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Maximum CK (IU/L)</td>
<td>1719 ± 73</td>
<td>1919 ± 184</td>
<td>2137 ± 132</td>
</tr>
<tr>
<td>Norris CPI</td>
<td>2.8 ± 0.1</td>
<td>2.4 ± 0.2</td>
<td>3.5 ± 0.3</td>
</tr>
<tr>
<td>QRS duration (msec)</td>
<td>91 ± 1</td>
<td>93 ± 2</td>
<td>95 ± 2</td>
</tr>
<tr>
<td>QT interval (msec)</td>
<td>378 ± 3</td>
<td>390 ± 5</td>
<td>379 ± 4</td>
</tr>
<tr>
<td>Corrected QT interval</td>
<td>438 ± 3</td>
<td>437 ± 6</td>
<td>448 ± 4</td>
</tr>
<tr>
<td>HV interval (msec)</td>
<td>47 ± 0.5</td>
<td>48 ± 0.9</td>
<td>48 ± 0.9</td>
</tr>
</tbody>
</table>

"Plus or minus" values are mean ± SEM.

Unless stated otherwise, statistical comparisons were not significant (NS).

CK = creatine kinase; CPI = coronary prognostic index; VT = ventricular tachycardia; VF = ventricular fibrillation.

### TABLE 2
Results of signal-averaged electrocardiography, ambulatory electrocardiographic monitoring, and exercise testing in patients studied by programmed stimulation

<table>
<thead>
<tr>
<th></th>
<th>No VT/VF inducible (n = 267)</th>
<th>VF inducible (n = 56)</th>
<th>VT inducible (n = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal-averaged electrocardiogram</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessed (n)</td>
<td>201 (75%)</td>
<td>43 (77%)</td>
<td>62 (78%)</td>
</tr>
<tr>
<td>DP (%)</td>
<td>16</td>
<td>35</td>
<td>53</td>
</tr>
<tr>
<td>p &lt; .01</td>
<td></td>
<td>NS</td>
<td>p &lt; .001</td>
</tr>
</tbody>
</table>

| VAT (msec)     | 127 ± 2                     | 138 ± 4             | 151 ± 4             |
|               | p < .005                    | p < .05             |

Ambulatory electrocardiogram

| Assessed (n)   | 57 (21%)                    | 12 (21%)            | 19 (24%)            |
| Mean VPCs/hour | 25 ± 82                     | 12 ± 31             | 48 ± 136            |
| ≥30 VPCs in any hour (%) | 23                  | 25                  | 32                  |
| Lown grade 4 or 5 arrhythmias (%) | 33                  | 42                  | 42                  |

Exercise testing

| Assessed (n)   | 222 (83%)                   | 50 (89%)            | 63 (79%)            |
| ST change ≥2 mm (%) | 19                   | 24                  | 24                  |

"Plus or minus" values are mean ± SEM.

Unless stated otherwise, statistical comparisons were not significant (NS).

DP = delayed potentials; VAT = ventricular activation time; other abbreviations as in table 1.
TABLE 3
Coronary anatomy and ventricular function in patients with inducible ventricular tachycardia or fibrillation (VT or VF)

<table>
<thead>
<tr>
<th>Coronary anatomy</th>
<th>VF inducible (n=56)</th>
<th>VT inducible (n=80)</th>
<th>p</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessed (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease vessels (%)</td>
<td>52 (93%)</td>
<td>68 (85%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean LVEF (% of patients)</td>
<td>0.39±0.01</td>
<td>0.32±0.01</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>LV contractility</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessed (n)</td>
<td>52 (93%)</td>
<td>76 (95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean LVEF (≤ 0.30) (%)</td>
<td>8</td>
<td>41</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>LV wall motion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessed (n)</td>
<td>55 (98%)</td>
<td>76 (95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV aneurysm (%)</td>
<td>18</td>
<td>20</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

"Plus or minus" values are mean ± SEM.
LV = left ventricular.

lar fibrillation. However, mean LVEF was higher in patients with inducible ventricular fibrillation than in patients with inducible ventricular tachycardia, with an LVEF of 0.30 or less occurring in 41% of patients with inducible ventricular tachycardia and in only 8% of patients with inducible ventricular fibrillation. Comparisons were not made with the group with no inducible arrhythmias, since only a biased sample of patients in this group was studied (those who developed angina or symptoms suggestive of heart failure during follow-up).

During follow-up, the proportion of patients placed on β-blockers was similar in each group (no ventricular tachycardia/fibrillation, 33%; ventricular fibrillation, 32%; ventricular tachycardia, 25%), as was the incidence of coronary artery revascularization either by grafting or by angioplasty (no ventricular tachycardia/fibrillation, 16%; ventricular fibrillation, 20%; ventricular tachycardia, 15%). The incidence of antiarrhythmic therapy was 3% in the group with no inducible ventricular tachycardia/fibrillation, but was higher for patients with inducible ventricular fibrillation (36%) or inducible ventricular tachycardia (44%). The higher incidence in these groups was due to participation by 96 of the 136 patients with inducible arrhythmias in the randomized controlled trial of antiarrhythmic therapy, in which 49 patients were randomly assigned to therapy and 47 received no treatment.

Results of signal averaging. For the patients without bundle branch block, ventricular activation time averaged 133 ± 2 msec, with a range of 89 to 267 msec. Mean ventricular activation time was longer in patients with inferior infarcts (137 ± 2 msec) than in those with anterior infarcts (127 ± 3 msec, p < .005). Delayed potentials were detectable in 80 patients (26%). The mean time after infarction at which signal averaging was performed was similar in patients with and without delayed potentials (12 and 11 days, respectively).

Mean maximum creatine kinase and the mean Norris coronary prognostic index were both higher in the group with delayed potentials (table 4). Mean QRS durations measured from the unaveraged electrocardiogram and mean HV intervals were each only slightly (3 msec) longer in the group with delayed potentials.

There was a much higher incidence of inducible ventricular tachycardia (41%) in the patient group with delayed potentials than in the group with no delayed potentials (13%, p < .001). There was a significant correlation between the presence or absence of inducible ventricular tachycardia and the presence or absence of delayed potentials (p < .001), but overlap was not complete (table 5). The presence of delayed potentials predicted the presence of inducible ventricular tachycardia with a sensitivity of 53% and a specificity of 81%.

Exercise testing was performed in 61 patients (76%) with delayed potentials and in 195 patients (86%) without delayed potentials. The incidence of a change in ST segment of 2 mm or more was similar in patients with and without delayed potentials (21% vs 23%).

Coronary arteriography and radionuclide ventriculography were performed in the absence of clinical indications for investigation in 87% and 97%, respectively, of patients with inducible arrhythmias. In these patients, there was no difference between subgroups with and without delayed potentials with respect to mean number of diseased vessels (1.9 ± 0.1 vs 1.8 ±

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TABLE 4
Profiles of patients studied by signal-averaged electrocardiography

<table>
<thead>
<tr>
<th></th>
<th>Delayed potentials (n=80)</th>
<th>No delayed potentials (n=226)</th>
<th>p</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarction (%)</td>
<td>34</td>
<td>44</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Previous infarction (%)</td>
<td>19</td>
<td>13</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Acute VT or VF (%)</td>
<td>16</td>
<td>13</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Maximum CK (IU/l)</td>
<td>2080±158</td>
<td>1762±76</td>
<td>&lt;.01</td>
<td></td>
</tr>
<tr>
<td>Norris CPI</td>
<td>3.4±0.3</td>
<td>2.7±0.1</td>
<td>&lt;.01</td>
<td></td>
</tr>
<tr>
<td>QRS duration (msec)</td>
<td>94±1</td>
<td>91±1</td>
<td>&lt;.05</td>
<td></td>
</tr>
<tr>
<td>QT interval (msec)</td>
<td>386±4</td>
<td>379±3</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Corrected QT</td>
<td>448±4</td>
<td>438±3</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>HV interval (msec)</td>
<td>49±1.0</td>
<td>46±0.5</td>
<td>&lt;.02</td>
<td></td>
</tr>
</tbody>
</table>

"Plus or minus" values are mean ± SEM.
Abbreviations are as in table 1.
TABLE 5
Correlation between delayed potentials on signal-averaged electrocardiogram and inducible ventricular tachycardia (VT) at programmed stimulation

<table>
<thead>
<tr>
<th></th>
<th>DPs</th>
<th>No DPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inducible VT (n)</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>No VT inducible (n)</td>
<td>47</td>
<td>197</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>226</td>
</tr>
</tbody>
</table>

DPs = delayed potentials.

0.1) or incidence of left ventricular aneurysm (19% vs 22%). There was, however, a lower mean LVEF of 0.33 ± 0.02 in patients with delayed potentials, compared with a mean LVEF of 0.38 ± 0.01 in patients without delayed potentials (p < .02). Ventricular activation times were similar in patients with and without left ventricular aneurysms (145 ± 7 vs 145 ± 3 msec) and also in patients with and without triple-vessel disease (152 ± 9 vs 144 ± 3 msec).

The percentage of patients on β-blocker therapy during follow-up was similar in groups of those with and without delayed potentials (31% vs 33%), as was the incidence of coronary revascularization (12% vs 17%). The percentage on antiarrhythmic drug therapy was higher (28%) in the group of patients with delayed potentials than in those without delayed potentials (11%, p < .005) due to participation of the subgroup with inducible arrhythmias in the randomized trial of antiarrhythmic therapy.

Prediction of cardiac events by programmed stimulation

All cardiac events. During follow-up, 37 patients (9%) suffered either a cardiac death or nonfatal sustained ventricular tachycardia or fibrillation. To enable comparison of the results obtained in this study with those obtained in our previous study,14 actuarial analysis of cardiac events was performed with the patient cohort divided into a group with inducible arrhythmias (ventricular tachycardia or fibrillation) and a group with no inducible arrhythmias (table 6). In addition, analysis was performed with the patients divided into three groups according to whether they had inducible ventricular tachycardia, inducible ventricular fibrillation, or no inducible arrhythmias (figures 1 to 3). As shown in table 6, patients with inducible arrhythmias fared significantly worse than did patients with no inducible arrhythmias.

As shown in figure 1 for all cardiac events, the morphology of the induced arrhythmia was found to be of great importance prognostically. For patients with no inducible ventricular tachycardia or fibrillation, the probability of remaining incident free was 0.95 at 1 year and 0.92 at 2 years, not significantly different from the figures of 0.96 and 0.93 for patients with inducible ventricular fibrillation (figure 1). For patients with inducible ventricular tachycardia, the probability of remaining incident free was much lower — 0.79 at 1 year (p < .001 vs no ventricular tachycardia/ fibrillation, p < .002 vs ventricular fibrillation) and 0.73 at 2 years (p < .001 vs no ventricular tachycardia/ fibrillation, p < .002 vs ventricular fibrillation).

The data for cardiac mortality and primarily tachyarrhythmic events (instantaneous death + nonfatal ventricular tachycardia or fibrillation) are analyzed in detail below.

Cardiac mortality. During follow-up, there were 22 deaths due to cardiac causes (mortality 5.5%). Twelve deaths (55%) were attributable to ventricular tachyarrhythmias, either documented or presumed because of instantaneous death without prodrome. Five deaths (23%) were directly attributable to recurrent myocardial ischemia, four were unwitnessed, and one was due to bradyarrhythmias associated with digoxin toxicity.

For patients with no inducible ventricular tachycardia or fibrillation, the probability of survival was 0.97 at 1 year and 0.96 at 2 years (figure 2). Of the nine deaths in these patients, four were of primarily tachyarrhythmic causes and three were of primarily ischemic causes.

For patients with inducible ventricular fibrillation, the probability of survival was 0.96 at 1 year and 0.93 at 2 years, not significantly different from the findings in patients with no inducible ventricular tachycardia or fibrillation (figure 2). Of the three deaths in the group of patients with inducible ventricular fibrillation, two were of primarily tachyarrhythmic causes and one was due to reinfarction.

TABLE 6
Actuarial data for patients studied by programmed stimulation: probability of remaining incident free

<table>
<thead>
<tr>
<th></th>
<th>VT/VF inducible</th>
<th>No VT/VF inducible</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death + nonfatal VT/VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>0.86</td>
<td>0.95</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>2 years</td>
<td>0.81</td>
<td>0.92</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>Cardiac death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>0.90</td>
<td>0.97</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>2 years</td>
<td>0.87</td>
<td>0.96</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Instantaneous death + nonfatal VT/VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>0.90</td>
<td>0.96</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>2 years</td>
<td>0.84</td>
<td>0.95</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

VT/VF = ventricular tachycardia or fibrillation.
For patients with inducible ventricular tachycardia, the probability of survival was 0.88 at 1 year and 0.85 at 2 years (figure 2). Both the 1 and 2 year probabilities of survival were significantly lower (at p < .005) than the respective probabilities for patients without inducible arrhythmias. Of the 10 deaths in patients with inducible ventricular tachycardia, six (60%) were of primarily tachyarrhythmic cause and only one (10%) was due to recurrent ischemia.

Table 7 shows that within the group with inducible ventricular tachycardia, the subgroup of patients who died had a higher incidence of anterior infarction, a significantly longer mean cycle length of inducible ventricular tachycardia, and a lower mean LVEF than did the subgroup who survived, with all deaths occurring in patients with LVEFs of 0.30 or less.

**Instantaneous death plus nonfatal ventricular tachycardia or fibrillation.** During follow-up, 12 patients suffered primarily tachyarrhythmic deaths and another 15 patients were resuscitated from sustained ventricular tachycardia or fibrillation.

For patients with no inducible ventricular tachycardia or fibrillation, the probability of remaining incident free was 0.97 at 1 year and 0.95 at 2 years. There were similar figures of 0.98 at 1 year and 0.95 at 2 years for patients with inducible ventricular fibrillation (figure 3).

For patients with inducible ventricular tachycardia, the probability of remaining incident free was lower, at 0.84 for 1 year (p < .001 vs no ventricular tachycardia/fibrillation, p < .005 vs ventricular fibrillation),

### TABLE 7
Profiles of patients with inducible ventricular tachycardia who died

<table>
<thead>
<tr>
<th>Profile</th>
<th>Dead (n=10)</th>
<th>Alive (n=70)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarction</td>
<td>7/10 (70%)</td>
<td>21/70 (30%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CL of inducible VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM (msec)</td>
<td>264±10</td>
<td>210±4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥230 msec</td>
<td>7/10 (70%)</td>
<td>17/70 (24%)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Ventricular activation time (msec) on averaged electrocardiogram (mean ± SEM)</td>
<td>161±18</td>
<td>150±4</td>
<td>NS</td>
</tr>
<tr>
<td>Delayed potentials</td>
<td>5/8 (63%)</td>
<td>28/54 (52%)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>0.20±0.02</td>
<td>0.33±0.01</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≤0.30</td>
<td>8/8 (100%)</td>
<td>23/68 (34%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≤0.40</td>
<td>8/8 (100%)</td>
<td>56/68 (82%)</td>
<td>NS</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>3/8 (38%)</td>
<td>12/68 (18%)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of diseased coronary vessels (mean ± SEM)</td>
<td>2.3±0.3</td>
<td>1.8±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Therapy during follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>3/10 (30%)</td>
<td>17/70 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td>Other antiarrhythmic drugs</td>
<td>4/10 (40%)</td>
<td>31/70 (44%)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>1/10 (10%)</td>
<td>11/70 (16%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CL = cycle length; LV = left ventricular.
and 0.78 for 2 years (p < .001 vs no ventricular tachycardia/fibrillation, p < .002 vs ventricular fibrillation). Compared with the group with no inducible arrhythmias, patients with inducible ventricular tachycardia had an excess of instantaneous deaths and nonfatal ventricular tachycardia or fibrillation in both the first (p < .001) and the second year (p < .002).

Table 8 shows that within the group with inducible ventricular tachycardia, the subgroup of patients suffering either instantaneous death or nonfatal ventricular tachycardia or fibrillation had a higher incidence of anterior infarction, a longer mean cycle length of inducible ventricular tachycardia, a lower mean LVEF, and a much higher incidence of left ventricular aneurysms than did patients without these events.

Sensitivity and specificity of inducible ventricular tachycardia as a predictor of cardiac events. For prediction of primarily tachyarrhythmic events, inducible ventricular tachycardia had a sensitivity of 52% and a specificity of 82%, while predictive accuracy of a positive test was 18% and that of a negative test was 96% (table 9). The sensitivity of inducible ventricular tachycardia as a predictor of cardiac events was lower when either cardiac deaths or cardiac deaths plus nonfatal arrhythmias were examined. When only the results of stimulation at twice diastolic threshold were considered (table 9), inducible ventricular tachycardia had only very low sensitivity for prediction of cardiac events.

Follow-up of patients with a maximum of 14 to 36 nonstimulated ventricular beats during programmed stimulation. This group of 13 patients comprised the 5% upper tail of the patients in whom no sustained ventricular tachycardia or fibrillation was inducible. There was only one cardiac event in this group, a death due to cardiac rupture 3 weeks after infarction in a patient with a maximum of 36 nonstimulated beats. Of the 13 patients in this group, 10 underwent signal-averaged electrocardiography and ventricular activation time averaged 135 ± 12 msec, with only one patient (the patient who died) having delayed potentials.

### Table 8
Profiles of patients with inducible ventricular tachycardia who developed instantaneous death or nonfatal ventricular tachycardia or fibrillation

<table>
<thead>
<tr>
<th>Instantaneous death or nonfatal VT/VF</th>
<th>Yes (n = 14)</th>
<th>No (n = 66)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CL of inducible VT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM (msec)</td>
<td>248 ± 14</td>
<td>209 ± 4</td>
<td>&lt;.002</td>
</tr>
<tr>
<td>≥230 msec</td>
<td>8/14 (57%)</td>
<td>16/66 (24%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Ventricular activation time (msec) on averaged electrocardiogram (mean ± SEM)</td>
<td>175 ± 14</td>
<td>146 ± 4</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Delayed potentials</td>
<td>9/12 (75%)</td>
<td>24/50 (48%)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>0.20 ± 0.02</td>
<td>0.33 ± 0.01</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>≤0.30</td>
<td>7/11 (64%)</td>
<td>24/65 (37%)</td>
<td>NS</td>
</tr>
<tr>
<td>≤0.40</td>
<td>10/11 (91%)</td>
<td>54/65 (83%)</td>
<td>NS</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>8/11 (73%)</td>
<td>7/65 (11%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of diseased coronary vessels (mean ± SEM)</td>
<td>1.9 ± 0.1</td>
<td>1.8 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Therapy during follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers</td>
<td>3/14 (21%)</td>
<td>17/66 (26%)</td>
<td>NS</td>
</tr>
<tr>
<td>Other antiarrhythmic drugs</td>
<td>6/14 (43%)</td>
<td>29/66 (44%)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>2/14 (14%)</td>
<td>10/66 (15%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CL = cycle length; other abbreviations as in previous tables.
Repeat programmed stimulation. Seven patients with inducible ventricular tachycardia who were subsequently resuscitated from spontaneous ventricular tachycardia or fibrillation underwent repeat programmed stimulation on no medications at a mean of 8 months after infarction. Ventricular tachycardia was still inducible in six (86%) at repeat study after spontaneous ventricular tachycardia or fibrillation.

Another nine patients with no inducible arrhythmias at initial study subsequently underwent repeat programmed stimulation at a mean of 6 months after infarction after successful resuscitation from spontaneous ventricular tachycardia or fibrillation. Ventricular tachycardia was inducible in six (67%), ventricular fibrillation was inducible in two, and only one patient still had no inducible arrhythmias.

Thirteen patients with inducible ventricular tachycardia at the initial study within 1 month of infarction who had remained well during follow-up underwent programmed stimulation on no medications 12 months after infarction. Ventricular tachycardia at that time was inducible in only six (46%) and ventricular fibrillation was inducible in another two patients.

Prediction of cardiac events by signal-averaged electrocardiography

All cardiac events. For patients with delayed potentials, the probability of remaining free from death or nonfatal ventricular tachycardia or fibrillation was 0.79 at 1 year and 0.73 at 2 years, significantly lower than that for patients without delayed potentials (0.98 at 1 year, \( p < .005 \); 0.96 at 2 years, \( p < .01 \)). The differences between the two groups were due to a higher mortality in patients with delayed potentials in the first year. Table 10 shows that within the group with delayed potentials, patients who died had a longer mean ventricular activation time and a lower mean LVEF. The incidence of antiarrhythmic therapy was 44% in the patients who died, compared with 25% in the patients who were alive at follow-up. This difference was not statistically significant.

Instantaneous death plus nonfatal ventricular tachycardia or fibrillation. As shown in figure 6, for patients with delayed potentials, the probability of remaining free from instantaneous death or nonfatal ventricular tachycardia or fibrillation was 0.85 at 1 year and 0.79 at 2 years, much lower than the corresponding figures of 0.98 (\( p < .001 \)) and 0.96 (\( p < .001 \)) for patients without delayed potentials.

Table 11 shows that within the group with delayed potentials, the patients who either died instantly or had nonfatal ventricular tachycardia or fibrillation had a longer mean ventricular activation time, a lower mean LVEF, and a higher incidence of left ventricular aneu-

### Table 9

<table>
<thead>
<tr>
<th></th>
<th>Cardiac death + nonfatal VT/VF</th>
<th>Cardiac death + nonfatal VT/VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>49% (24%)</td>
<td>45% (14%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>83% (91%)</td>
<td>82% (90%)</td>
</tr>
<tr>
<td>Predictive accuracy</td>
<td>23% (21%)</td>
<td>13% (7%)</td>
</tr>
<tr>
<td>Positive test</td>
<td>94% (92%)</td>
<td>96% (95%)</td>
</tr>
<tr>
<td>Negative test</td>
<td>4.6 (3.2)</td>
<td>3.7 (1.4)</td>
</tr>
</tbody>
</table>

**FIGURE 4.** Prediction of death and nonfatal ventricular tachycardia or fibrillation (VT or VF) by signal-averaged electrocardiography.

**FIGURE 5.** Prediction of mortality by signal-averaged electrocardiography.

at 1 year and 0.87 at 2 years, significantly lower than that for patients without delayed potentials (0.98 at 1 year, \( p < .005 \); 0.96 at 2 years, \( p < .01 \)). The differences between the two groups were due to a higher mortality in patients with delayed potentials in the first year. Table 10 shows that within the group with delayed potentials, patients who died had a longer mean ventricular activation time and a lower mean LVEF. The incidence of antiarrhythmic therapy was 44% in the patients who died, compared with 25% in the patients who were alive at follow-up. This difference was not statistically significant.

**Instantaneous death plus nonfatal ventricular tachycardia or fibrillation.** As shown in figure 6, for patients with delayed potentials, the probability of remaining free from instantaneous death or nonfatal ventricular tachycardia or fibrillation was 0.85 at 1 year and 0.79 at 2 years, much lower than the corresponding figures of 0.98 (\( p < .001 \)) and 0.96 (\( p < .001 \)) for patients without delayed potentials.

Table 11 shows that within the group with delayed potentials, the patients who either died instantly or had nonfatal ventricular tachycardia or fibrillation had a longer mean ventricular activation time, a lower mean LVEF, and a higher incidence of left ventricular aneu-

### Table 9

<table>
<thead>
<tr>
<th></th>
<th>Cardiac death + nonfatal VT/VF</th>
<th>Cardiac death + nonfatal VT/VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>49% (24%)</td>
<td>45% (14%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>83% (91%)</td>
<td>82% (90%)</td>
</tr>
<tr>
<td>Predictive accuracy</td>
<td>23% (21%)</td>
<td>13% (7%)</td>
</tr>
<tr>
<td>Positive test</td>
<td>94% (92%)</td>
<td>96% (95%)</td>
</tr>
<tr>
<td>Negative test</td>
<td>4.6 (3.2)</td>
<td>3.7 (1.4)</td>
</tr>
</tbody>
</table>

**FIGURE 4.** Prediction of death and nonfatal ventricular tachycardia or fibrillation (VT or VF) by signal-averaged electrocardiography.

**FIGURE 5.** Prediction of mortality by signal-averaged electrocardiography.
TABLE 10
Profiles of patients with delayed potentials who died within 2 years

<table>
<thead>
<tr>
<th>Ventricular activation time (mean ± SEM, msec) (^a)</th>
<th>Dead (n = 9)</th>
<th>Alive (n = 71)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF Mean ± SEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤0.30</td>
<td>0.21 ± 0.03</td>
<td>0.34 ± 0.01</td>
<td>&lt;.002</td>
</tr>
<tr>
<td>≤0.40</td>
<td>6/7 (86%)</td>
<td>12/51 (24%)</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>7/7 (100%)</td>
<td>42/51 (82%)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of diseased coronary vessels (mean ± SEM)</td>
<td>2.4 ± 0.4</td>
<td>1.9 ± 0.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

\( LV = \) left ventricular.
\( ^a \)On signal-averaged electrocardiogram.

dysms than did patients who were event free. The incidence of antiarrhythmic therapy was similar in the group with primarily tachyarrhythmic events (33%) and the group without such events (26%).

Comparison of prognostic significance of delayed potentials and inducible ventricular tachycardia. Table 12 shows the distribution of cardiac events in patients without bundle branch block studied by both programmed stimulation and signal averaging. There was incomplete correspondence between the two tests with respect to correct identification of patients who suffered cardiac events during follow-up, but each test taken individually had a similar sensitivity, specificity, predictive accuracy, and odds ratio (table 13). Specificity was very high if both delayed potentials and inducible ventricular tachycardia were present, but sensitivity was low. On the other hand, the presence of either delayed potentials or inducible ventricular tachycardia predicted events with high sensitivity but low specificity (table 13). Of the 33 patients with both delayed potentials and inducible ventricular tachycardia, 11 (33%) developed a cardiac event, whereas an event occurred in only six of 197 patients (3%) with neither delayed potentials nor inducible ventricular tachycardia (p < .001).

Multiple logistic regression analysis showed that inducible ventricular tachycardia and delayed potentials were not independent predictors of either mortality or primarily tachyarrhythmic events. Anterior infarction was an independent predictor of mortality (p < .01), while pulmonary congestion on the chest x-ray was the only variable tested that was an independent predictor of spontaneous ventricular tachyarrhythmias (p < .02). Multiple logistic regression analysis also showed that treatment with \( \beta \)-blockers, antiarrhythmic medications, or coronary revascularization did not affect occurrence of cardiac events.

Discussion

Prognostic significance of inducible ventricular tachycardia vs inducible ventricular fibrillation. We have shown previously that the presence of inducible ventricular tachycardia or fibrillation predicts sudden death after acute myocardial infarction. This finding has been corroborated by studies in survivors of acute myocardial infarction who have had heart failure, conduction defects, early ventricular tachycardia or fibrillation, or high-grade ventricular ectopy after infarction. However, two smaller studies have failed to find an association between inducibility of arrhythmias and prognosis when only survivors of uncomplicated infarctions were studied. The present study, using a new, much larger cohort of patients, not only confirms that programmed stimulation can be used to arrive at a prognosis after acute myocardial infarction, but also demonstrates that inducible ventricular tachycardia rather than inducible ventricular fibrillation is the important variable in prognosis.
Induction of ventricular fibrillation proved to be of no prognostic significance in this study. However, it may have more sinister implications in patients with a history of spontaneous ventricular tachycardia or fibrillation. Nevertheless, the idea that ventricular tachycardia is the only significant arrhythmia is in accord with recent reports of findings of ambulatory monitoring at the time of sudden death. These reports showed that the initiating arrhythmia at the time of cardiac arrest was not ventricular fibrillation, as commonly thought, but ventricular tachycardia that degenerated into ventricular fibrillation. Computer modeling of induction of ventricular tachyarrhythmias has suggested that ventricular fibrillation is associated with fewer electrophysiologic abnormalities than is ventricular tachycardia. In particular, ventricular fibrillation was found to be associated with less marked conduction delay in sinus rhythm. This finding is supported by the present study in which patients with inducible ventricular tachycardia had longer ventricular activation times on the signal-averaged electrocardiogram than did patients with inducible ventricular fibrillation.

In the present study, patients with nonsustained ventricular beats were not a high-risk group, and did not develop clinical ventricular tachycardia or fibrillation. This finding is in agreement with that of other groups maintaining that nonsustained ventricular beats are too nonspecific to be of use prognostically. Such patients with nonsustained ventricular beats might not have marked conduction delay in sinus rhythm or a stable reentrant circuit, and so may be “protected” from clinically significant sustained ventricular tachyarrhythmias.

### Table 11
Profiles of patients with delayed potentials who developed instantaneous death or nonfatal ventricular tachycardia or fibrillation

<table>
<thead>
<tr>
<th>Instantaneous death + nonfatal VT/VF</th>
<th>Yes (n = 15)</th>
<th>No (n = 65)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular activation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>time (mean ± SEM, msec)</td>
<td>184 ± 10</td>
<td>165 ± 3</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.30</td>
<td>0.26 ± 0.02</td>
<td>0.34 ± 0.02</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>≤0.40</td>
<td>8/14 (57%)</td>
<td>10/44 (23%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of diseased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>coronary vessels (mean ± SEM)</td>
<td>1.9 ± 0.3</td>
<td>1.8 ± 0.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

*On signal-averaged electrocardiogram.

### Table 12
Cardiac events after myocardial infarction: relationship to presence of delayed potentials and inducible ventricular tachycardia

<table>
<thead>
<tr>
<th></th>
<th>Delayed potentials (n = 80)</th>
<th>No delayed potentials (n = 226)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death + nonfatal VT/VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT inducible (n = 62)</td>
<td>11</td>
<td>4</td>
<td>15 (24%)</td>
</tr>
<tr>
<td>No VT inducible (n = 244)</td>
<td>8</td>
<td>6</td>
<td>14 (6%)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (24%)</td>
<td>10 (4%)</td>
<td>29</td>
</tr>
<tr>
<td>Cardiac death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT inducible (n = 62)</td>
<td>5</td>
<td>3</td>
<td>8 (13%)</td>
</tr>
<tr>
<td>No VT inducible (n = 244)</td>
<td>4</td>
<td>4</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (11%)</td>
<td>7 (3%)</td>
<td>16</td>
</tr>
<tr>
<td>Instantaneous death + nonfatal VT/VF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT inducible (n = 62)</td>
<td>9</td>
<td>4</td>
<td>13 (21%)</td>
</tr>
<tr>
<td>No VT inducible (n = 244)</td>
<td>6</td>
<td>4</td>
<td>10 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (19%)</td>
<td>8 (4%)</td>
<td>23</td>
</tr>
</tbody>
</table>

VT = ventricular tachycardia; VF = ventricular fibrillation.
TABLE 13
Prediction of cardiac events after myocardial infarction: comparison of predictive value of delayed potentials and inducible ventricular tachycardia in patients without bundle branch block

<table>
<thead>
<tr>
<th></th>
<th>DPs only</th>
<th>Inducible VT only</th>
<th>DPs + inducible VT</th>
<th>DPs or inducible VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death + nonfatal VT/VF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>66</td>
<td>52</td>
<td>38</td>
<td>79</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>78</td>
<td>83</td>
<td>92</td>
<td>69</td>
</tr>
<tr>
<td>Predictive accuracy (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive test</td>
<td>24</td>
<td>24</td>
<td>33</td>
<td>21</td>
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<tr>
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<tr>
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<td>4.3</td>
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<tr>
<td>Specificity (%)</td>
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DPS = delayed potentials; VT/VF = ventricular tachycardia/fibrillation.

Characteristics of patients with inducible ventricular tachycardia. When compared with either of the two low-risk groups (inducible ventricular fibrillation, no ventricular tachycardia/fibrillation inducible), patients with inducible ventricular tachycardia had evidence of more extensive infarction, as reflected in higher maximum creatine kinase levels and higher values on the Norris coronary prognostic index. In a previous study,
we noted that the patients with inducible arrhythmias had poorer left ventricular function than did patients with no inducible arrhythmias. In the present study, patients with inducible ventricular tachycardia had poorer left ventricular function than did patients with inducible ventricular fibrillation. However, quantification of the degree of left ventricular dysfunction by radionuclide ventriculography was performed in a biased selection of patients (those with inducible arrhythmias), and so multiple logistic regression analysis could not be performed to determine whether inducible ventricular tachycardia and left ventricular dysfunction were independent risk factors. Determination of whether they are independent predictors is clearly a high priority for any future study.

In the patients with inducible ventricular tachycardia, an event during follow-up (death or ventricular tachycardia/fibrillation) was more likely if the index infarction was anterior, if cycle length of ventricular tachycardia was 230 msec or more, if LVEF was low, or if there was an aneurysm. However, there was no cutoff value for either cycle length of ventricular tachycardia or ejection fraction that could reliably identify the patients who had an event. Patients with poor ventricular function are probably prone to death because they cannot tolerate arrhythmias hemodynamically. The reason that patients with inducible slow ventricular tachycardia are at high risk is less obvious, but may be related to an increased probability of developing ventricular tachycardia in the context of long ventricular activation times in sinus rhythm.

Contrary to another study in which a smaller number of patients was included, we did not find an increased incidence of inducible ventricular tachycardia in patients with acute tachycardia or fibrillation within 48 hr of infarction.

The time course of inducible ventricular tachycardia was not studied formally. However, it was apparent that inducibility of ventricular tachycardia decreased some months after myocardial infarction in patients who had not had a spontaneous arrhythmia. Changes in the inducibility of ventricular tachycardia after infarc-
tion are consistent with late tissue changes in the infarct or peri-infarct region, such as reestablishment of intercellular connections ("tight junctions") or scar contracture and remodeling.41,44

The optimum time at which to perform programmed stimulation was not determined in this study. Since a high proportion of patients who died or developed ventricular tachycardia did so within 1 month of infarction, it would seem best to perform programmed stimulation within the first month. Investigation within the first week after infarction may be too soon to yield useful prognostic information, since the tissue changes are not stable.43

**Prognostic significance of delayed potentials.** Our results also show that delayed ventricular activation in patients in sinus rhythm, as detected by the signal-averaged electrocardiogram, identifies patients at high risk of death and ventricular tachycardia or fibrillation. The prognostic implications of delayed ventricular activation are similar to those of ventricular tachycardia that is inducible at programmed stimulation. Earlier smaller studies17,18 have indicated that delayed potentials in patients with coronary artery disease may predict sudden death and spontaneous ventricular tachycardia, but not all patients in these previous studies had sustained a myocardial infarction.

It appears that delayed potentials represent localized conduction delay through small areas of myocardium and that initiation of reentrant ventricular arrhythmias is facilitated if there are areas of particularly marked conduction delay adjacent to areas of early recovery during sinus rhythm.45

Delayed potentials detected from the body surface appear to be able to identify patients with the substrate for reentrant ventricular tachyarrhythmias. However, spontaneous appearance of ventricular tachycardia or fibrillation probably depends not only on the presence of suitable anatomic and electrophysiologic substrate, but also the chance occurrence of appropriately timed VPCs. The optimum time at which to obtain the signal-averaged electrocardiogram was not determined in this study, but since a high proportion of cardiac events occurred within 1 month of infarction, it would seem best to obtain the electrocardiogram before discharge of the patient from the hospital.

**Characteristics of patients with delayed potentials.** Patients with and without delayed potentials were not significantly different with respect to clinical profiles, although mean maximum creatine kinase levels and values on the Norris coronary prognostic index were higher in the group with delayed potentials. There were only small differences of 3 msec between the two groups with respect to mean QRS duration (on the unaveraged electrocardiogram) and mean HV interval, these differences being insufficient to account for the differences in ventricular activation time detected on the signal-averaged electrocardiogram. There was no difference between groups with and without delayed potentials in terms of QT interval or corrected QT, implying that late repolarization is not accompanied by late repolarization.46

Several other groups have correlated the presence of delayed potentials with findings at cardiac catheterization, programmed stimulation, and ambulatory electrocardiographic monitoring.47-50 The common theme of these studies was that there was a high incidence of delayed potentials in patients who had already exhibited spontaneous ventricular tachycardia late after myocardial infarction (many of whom also had inducible ventricular tachycardia), with the signal-averaged electrocardiogram providing information independent of the results of electrocardiographic monitoring. The presence of delayed potentials was also unrelated to the extent of coronary artery disease. Two studies that included patients without previous myocardial infarction47,49 concluded that delayed potentials were associated with low LVEF, but when only patients with infarction were studied,49,50 delayed potentials were not found to relate specifically to low LVEF, but were found to be independent of global or regional left ventricular dysfunction. In another study,51 delayed potentials and nonstimulated ventricular beats induced at programmed stimulation were found not to be closely correlated.

In the patients with delayed potentials in the present study, an event at follow-up was more likely if ventricular activation time was particularly prolonged, if LVEF was 0.30 or less, or if there was an aneurysm. However, a policy of obtaining a signal-averaged electrocardiogram only in patients with a poor LVEF (≤0.30) would have missed 43% of the patients with delayed potentials who either died instantly or had nonfatal ventricular tachycardia/fibrillation during follow-up. A cutoff of LVEF of 0.40 or less would be more appropriate for a screening test, since only 7% of patients with delayed potentials who developed a ventricular tachyarrhythmia had an LVEF greater than 0.40.

**Comparison of prognostic powers of delayed potentials and inducible ventricular tachycardia.** As shown in table 12, delayed potentials and inducible ventricular tachycardia have similar predictive accuracy for cardiac events. The predictive accuracy is much better than that generally obtained with use of complex or frequent
VPCs at ambulatory monitoring as the predictor, and is very similar to that obtained when low LVEF is used. The presence of delayed potentials or inducible ventricular tachycardia as a predictor of cardiac death or ventricular tachycardia or fibrillation is potentially very useful since either implies that there is potential for ventricular tachyarrhythmias, whereas the presence of low LVEF does not indicate whether the most likely cardiac event is a ventricular tachyarrhythmia or death due to loss of contractile power.

The similar prognostic implications of delayed potentials and inducible ventricular tachycardia are not surprising since there was a significant correlation between the presence of each. However, there was not complete overlap, and delayed potentials and inducible ventricular tachycardia appeared to identify slightly different patient groups. The observation that ventricular tachycardia could be induced in the absence of delayed potentials and vice versa may reflect imperfections in the techniques for their demonstration. For example, the programmed stimulation protocol might not be sufficiently aggressive for induction of ventricular tachycardia in susceptible patients, and the signal-averaged electrocardiogram might miss delayed potentials if they vary from beat to beat or arise from areas of the heart not covered adequately by the electrocardiographic leads used. Holley and Uther, using a computer model of induction of ventricular tachyarrhythmias, have noted that induction and maintenance of reentrant arrhythmias is critically dependent on the relationship between conduction times and refractory periods at short coupling intervals in infarcted and adjacent normal tissue. The relative contribution of conduction delay and prematurity of extrastimuli may vary from patient to patient, and may contribute to incomplete correspondence between the ability to induce ventricular tachycardia and the presence of delayed potentials.

**Clinical implications.** Programmed stimulation and signal averaging of the surface electrocardiogram can each identify a high-risk group of patients who comprise one-quarter of clinically well survivors of recent myocardial infarction. These patients with either inducible ventricular tachycardia or delayed potentials have a 27% chance of death or nonfatal ventricular tachycardia or fibrillation within 2 years of infarction, with the peak incidence in the first 6 months. Because most events in these patients are attributable to primarily tachyarrhythmic events, therapeutic interventions should be directed at the tendency to spontaneous reentrant ventricular tachycardia.

However, had the signal-averaged electrocardiogram been used as the sole screening test for identifying high-risk patients in the present study, 10 of 29 patients (34%) who developed a cardiac event would have been missed. For identification of a high-risk group of patients with greater accuracy, it may be best to use a combination of investigations, including the signal-averaged electrocardiogram analyzed in the time domain and possibly also in the frequency domain, programmed stimulation, ambulatory electrocardiographic monitoring, and radionuclide ventriculography. This would give greater predictive accuracy than is possible when any of these techniques is used alone. The best order in which to perform these tests has yet to be determined.

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Prognostic significance of ventricular tachycardia and fibrillation induced at programmed stimulation and delayed potentials detected on the signal-averaged electrocardiograms of survivors of acute myocardial infarction.
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