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Definition of the Best Prediction Criteria of the Time Domain Signal-Averaged Electrocardiogram for Serious Arrhythmic Events in the Postinfarction Period

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Objectives. **The goal of this study was to establish guidelines for the prognostic use of the time domain signal-averaged electrocardiogram (ECG) after myocardial infarction.**

Background. **Previous studies of the prognostic use of the signal-averaged ECG in postinfarction patients had one or more of the following limitations: a small study group, empiric definition of an abnormal recording and possible bias in the selection of high risk groups or classification of arrhythmic events, or both. To correct for these limitations, a substudy was conducted in conjunction with the Cardiac Arrhythmia Suppression Trial (CAST).**

Methods. **Ten centers recruited 1,211 patients with acute myocardial infarction without application of the ejection fraction or Holter criteria restrictions of the main CAST protocol. Several clinical variables, ventricular arrhythmias on the Holter recording, ejection fraction and six signal-averaged ECG variables were analyzed. Patients with bundle branch block were excluded from the analysis, and the remaining 1,158 were followed for up to 1 year after infarction. The classification of arrhythmic events was reviewed independently by the CAST Events Committee.**

Results. **During an average (±SD) follow-up of 10.3 ± 3.2 months, 45 patients had a serious arrhythmic event (nonfatal ventricular tachycardia or sudden cardiac arrhythmic death). A Cox regression analysis with only the six signal-averaged ECG variables indicated that the filtered QRS duration at 40 Hz ≥120 ms (QRSD-40 Hz) at a cutpoint ≥120 ms was the most predictive criterion of arrhythmic events. In a regression analysis that included all clinical, Holter and ejection fraction variables, a QRSD-40 Hz ≥120 ms was the most significant predictor ($p < 0.0001$). The positive, negative and total predictive accuracy and odds ratio for QRSD-40 Hz ≥120 ms were 17%, 98%, 88% and 8.4, respectively, and improved to 32%, 97%, 94% and 16.7, respectively, after combination with ejection fraction ≤40% and complex ventricular arrhythmias on the Holter recording.**

Conclusions. **The signal-averaged ECG predicts serious arrhythmic events in the first year after infarction better than do clinical, ejection fraction and ventricular arrhythmia variables, and QRSD-40 Hz ≥120 ms provides the best predictive criterion in this clinical setting.**

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In the past few years a number of studies have shown that the signal-averaged electrocardiogram (ECG) can stratify patients recovering from acute myocardial infarction into high and low risk groups for late serious arrhythmic events (defined as nonfatal ventricular tachycardia or sudden cardiac arrhythmic death) (1–4). However, these studies had a number of limitations: 1) The definition of abnormal signal-averaged ECG results was either determined empirically or was derived from relatively small study groups. 2) The investigators classified unwitnessed death as due to cardiac arrhythmia without an independent review process. This difficulty with the classification of unwitnessed death (5) may have subjected those studies to a certain degree of bias. 3) The incidence of serious arrhythmic events in the first year after infarction in some of the studies (as high as 14% [2]) is significantly higher than the current incidence. Thus, previous study groups may not represent the current postinfarction population. To correct for these limitations and to establish guidelines for the prognostic use of the time domain signal-averaged ECG after myocardial infarc-

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tion, a substudy was conducted prospectively in conjunction with the Cardiac Arrhythmia Suppression Trial (CAST) (6). A large study group was recruited from 10 of the 27 CAST centers, and the classification of arrhythmic death was reviewed independently by the CAST Events Committee. To obtain a study group representative of the general population with acute myocardial infarction, patients were recruited without application of the ejection fraction and arrhythmia restrictions of the main CAST protocol.

Methods

Patients. When the study was designed as a CAST substudy, it was agreed that participating CAST centers would attempt to recruit all available patients who were screened and found to have a CAST-qualifying acute myocardial infarction (6). This was done before those patients were screened further to ascertain whether they would qualify for CAST according to specific Holter and ejection fraction criteria. Patients who later qualified for CAST were randomized according to CAST protocol and were followed up in the present study. Those patients represented 15% of the study sample. They also represented a majority but not necessarily all of the patients who received antiarrhythmic drugs. It was thought that this design would provide a study group representative of the general postinfarction population.

Patients were enrolled between days 5 and 30 after infarction. Patients were excluded from the study if they were >79 years old, had cardiogenic shock, advanced cancer or renal disease or were unable to participate in the protocol. The following clinical profile was collected for each patient: age, gender, site of myocardial infarction, peak creatine kinase-MB (CK-MB) isoenzyme concentrations, use of antiarrhythmic or beta-adrenergic blocking agents, history of congestive heart failure, history of diabetes, previous myocardial infarction and previous coronary artery revascularization procedures (coronary artery bypass grafting or coronary artery angioplasty). An attempt was made to obtain left ventricular ejection fraction measurements for all patients, as defined by CAST protocol (6).

Signal-averaged ECG and Holter recordings. A signal-averaged ECG was obtained 5 to 30 days after the qualifying myocardial infarction while the patient was not receiving antiarrhythmic drugs. The signal-averaged ECG was recorded with either the Arrhythmia Research Technology model 1200 EPX or Corazonix Predictor Unit. These two units were chosen because they use similar algorithms for defining the end of the QRS complex, and previous studies have shown that they provide comparable results (7). The signal-averaged ECG was recorded with standard bipolar orthogonal X, Y and Z leads. Signal averaging of ≥300 beats was performed to achieve a diastolic noise level <1 μV. A noise level <0.5 μV was desirable but not required. Six signal-averaged ECG time domain variables were obtained: the filtered QRS duration, root-mean-square voltage in the last 40 ms and duration of late potentials of ≤40-μV amplitude recorded at both 25 to 250 and 40 Hz bandpass filter settings. A 24-h Holter recording was obtained in accordance with CAST protocol (6), within 48 h of the baseline signal-averaged ECG. The signal-averaged ECG records and Holter tapes were retained by the local center. Subsequent review and analysis of a random sample of these records were conducted by the CAST Quality Assurance Committee.

Follow-up and study end points. All patients were followed for up to 1 year after the qualifying myocardial infarction. Follow-up information with regard to clinical events, antiarrhythmic agents or beta-blockers and coronary artery revascularization procedures was obtained at 4 and 12 months after baseline either by telephone or during a clinic visit. The primary end point events were sustained ventricular tachycardia (≥120 beats/min lasting ≥30 s), arrhythmic cardiac arrest with resuscitation or arrhythmic death as defined in CAST (8). The classification of primary end points was reviewed independently by the CAST Events Committee. In addition to the primary end points of serious arrhythmic events, secondary end points of nonarrhythmic cardiac death and total mortality were also considered.

Statistical analysis. The aim of the analysis was to determine time domain signal-averaged ECG criteria that predict serious arrhythmic events during the first year after infarction. All exposure times were censored at ≤365 days. Because of the unreliability of time domain signal-averaged ECG criteria in the presence of bundle branch block (9), patients with either right or left bundle branch block as defined by CAST ECG criteria (6) were excluded from analysis. Survival analyses were conducted using a Cox proportional hazards regression model (10). Separate analyses were conducted for arrhythmic and nonarrhythmic death. The following variables were entered into the model: age, gender, site of myocardial infarction, peak CK-MB isoenzyme concentration, QRS duration in the 12-lead ECG, history of congestive heart failure, history of diabetes, previous myocardial infarction, previous antiarrhythmic or beta-blocker therapy, left ventricular ejection fraction, frequency of ventricular premature depolarizations and presence or absence of ventricular tachycardia runs (defined as ≥3 consecutive ventricular beats at a rate of ≥120 beats/min) on the baseline Holter recording. The six signal-averaged ECG variables, as continuous variables, were then allowed to enter stepwise.

After determining that signal-averaged ECG variables were predictive of arrhythmic events, the most predictive continuous signal-averaged ECG variable was determined using Cox regression without controlling for baseline characteristics. Dichotomous variables were then created from the most predictive measure to find the "best" cutoff. "Best" was determined by the highest chi-square value to enter the model. One-year survival was estimated by Kaplan-Meier survival on the basis of the two groups created by discriminating signal-averaged ECG criteria (11).

Baseline characteristics of patients with arrhythmic events were compared with those of patients without arrhythmic events. Baseline characteristics of patients with abnormal

signal-averaged ECG results, as determined by the Cox regressions, were compared with those with normal signal-averaged ECG results.

The predictive value of abnormal signal-averaged ECG results was compared with two other commonly utilized predictive criteria: low left ventricular ejection fraction (dichotomized at ≥40%, ≥35% and ≥30%) and complex ventricular arrhythmia on Holter recording (defined as ≥10 ventricular premature depolarizations/h or any ventricular tachycardia run, or both). For various combinations of these criteria, the sensitivity, specificity, predictive accuracy (percent correctly predicted), positive predictive accuracy (percent of "abnormal" results associated with events), negative predictive accuracy (percent of "normal" results not associated with events) and odds ratio were determined (12).

Results

Arrhythmic events. During the enrollment period for the study, the 10 CAST participating centers had a total of 1,839 patients with a CAST-qualifying infarction, 1,211 of whom were recruited into the study. Of these 1,211 patients, 52 had either right or left bundle branch block and were excluded from further analysis. One patient had no follow-up and was also excluded. The remaining 1,158 patients were followed up for an average (±SD) of 10.3 ± 3.2 months (range 0 to 12, median 11.7). Fifteen patients died of noncardiac-related causes, and 29 died of cardiac-related causes judged not to be due to cardiac arrhythmia. Forty-five patients had a serious arrhythmic event (an incidence of 4.3% for the first year after infarction). Three patients had symptomatic nonfatal sustained ventricular tachycardia. In 42 patients death was judged to be due to arrhythmia. Eleven of the 42 arrhythmic deaths occurred in-hospital or in the emergency room, and 28 occurred out-of-hospital. A record of the final cardiac rhythm was available for 21 of the 42 patients. Ventricular tachycardia/ventricular fibrillation was documented in 15 patients and asystole in 5. One patient had an "unknown" rhythm. Four of the patients with asystole as a final cardiac rhythm had experienced out-of-hospital cardiac arrest. Thirty-six percent of the arrhythmic events occurred in the first 2 months and 67% in the first 6 months after myocardial infarction.

Clinical profile and signal-averaged ECG in patients with and without an arrhythmic event. Table 1 summarizes the clinical profile and signal-averaged ECG characteristics of patients with and without an arrhythmic event. There was no difference in age, gender, peak CK-MB isoenzyme concentrations or revascularization procedures between patients with and without an arrhythmic event. The incidence of combined anterior and inferior wall myocardial infarction and non-Q infarction, congestive heart failure, diabetes and previous infarction were significantly higher in patients with an arrhythmic event. Less than 4% of all patients received antiarrhythmic therapy. Although patients with an arrhythmic event received statistically more antiarrhythmic therapy than patients without a serious arrhythmic event, only 5 of the 45 patients with a serious arrhythmic event received antiarrhythmic therapy. The incidence of complex ventricular arrhythmia on the baseline Holter recording was higher, left ventricular ejection fraction significantly lower and QRS duration on the 12-lead ECG significantly longer in patients with an arrhythmic event. The filtered QRS duration of the signal-averaged ECG and duration of late potentials were significantly longer in patients with an arrhythmic event at both 25 and 40 Hz. However, although the root-mean-square voltage of the signals in the last 40 ms was lower in patients with an arrhythmic event, this difference reached statistical significance only at 25 Hz. Using the Cox proportional hazards regression model to control for clinical variables that showed a significant difference between patients with and without an arrhythmic event, the signal-averaged ECG variables were found to be independently predictive of an arrhythmic event ($p < 0.011$). However, the signal-averaged ECG variables did not predict nonarrhythmic death after controlling for other baseline variables.

Table 1. Clinical Profile and Signal-Averaged Electrocardiographic Results in Patients With and Without an Arrhythmic Event

	With Arrhythmic Event (n = 45)	Without Arrhythmic Event (n = 1,113)	p Value
Mean age (yr)	63.1	60.1	0.068
% Male	75.6	72.3	0.760
Ant MI (%)	25.0	22.2	0.797
Inf MI (%)	36.4	31.1	0.569
Ant+Inf MI (%)	22.7	8.6	0.003
Non-Q wave MI (%)	15.6	37.2	0.005
Peak CK-MB (IU/liter)	10.5	12.1	0.116
Antiarrhythmic agents (%)	11.1	3.0	0.010
Beta-blockers (%)	17.8	38.5	0.008
Revascularization procedure since baseline	13.3	19.4	0.411
History of			
CHF (%)	25.0	6.8	0.0000
Diabetes (%)	42.2	20.0	0.001
MI (%)	48.9	21.7	0.0000
Ejection fraction (%)	33.6	47.4	0.0000
VA on Holter (%)	60.0	28.9	0.0000
QRSD/ECG (ms)	98.7	91.1	0.0004
QRSD/25 Hz (ms)	119.0	104.2	0.0001
RMS-40/25 Hz (μV)	42.7	60.6	0.030
LPD/25 Hz (ms)	38.8	28.4	0.006
QRSD/40 Hz (ms)	115.2	101.4	0.0000
RMS-40/40 Hz (μV)	29.4	38.7	0.060
LPD/40 Hz (ms)	40.1	32.9	0.017

Signal-averaged electrocardiographic (ECG) variables were recorded at 25 and 40 Hz high bandpass filter settings, respectively. Ant = anterior; CHF = congestive heart failure; CK-MB = creatine kinase-MB isoenzyme; Inf = inferior; LPD = late potential duration ≤40 μV; MI = myocardial infarction; QRSD = duration of filtered QRS complex; QRS/ECG = QRS duration on the 12-lead ECG; RMS-40 = root-mean-square voltage of signals in the last 40 ms; VA = complex ventricular arrhythmias.

Definition of the best prediction criteria of the signal-averaged ECG. Having determined that the signal-averaged ECG variables were independently predictive of arrhythmic events, we found that the most predictive continuous variable

Table 2. Predictive Values of Continuous Signal-Averaged Electrocardiographic Variables and Best Cutoff for QRSD/40 Hz (ms)

	Chi-Square Value	p Value
Variable		
QRSD/25 Hz	30.08	0.0000
RMS-40/25 Hz	4.68	0.0305
LPD/25 Hz	21.91	0.0000
QRSD/40 Hz*	34.46	0.0000
RMS-40/40 Hz	3.63	0.0568
LPD/40 Hz	12.95	0.0003
Cutpoint		
100	13.49	0.0002
110	31.19	0.0000
112	33.41	0.0000
114	39.27	0.0000
116	41.26	0.0000
118	44.80	0.0000
120*	54.89	0.0000
122	54.56	0.0000
124	40.86	0.0000
126	32.38	0.0000
128	20.71	0.0000
130	18.91	0.0000
140	3.31	0.0687

*Variable with highest chi-square value. Abbreviations as in Table 1.

Table 3. Clinical Profile of Patients With Normal and Abnormal Signal-Averaged Electrocardiographic Results

	Abnormal SAECG Results (n = 138)	Normal SAECG Results (n = 1,024)	p Value
Mean age (yr)	61.4	60.1	0.195
% Male	71.4	80.6	0.032
Ant MI (%)	16.8	23.0	0.134
Inf MI (%)	38.2	30.4	0.089
Ant+Inf MI (%)	11.5	8.8	0.412
Non-Q wave MI (%)	32.8	36.8	0.422
Peak CK-MB (IU/liter)	12.0	12.1	0.928
Antiarrhythmic agents (%)	8.2	2.6	0.002
Beta-blockers (%)	29.9	38.8	0.056
Revascularization procedure since baseline (%)	15.7	19.6	0.328
History of			
CHF (%)	21.1	5.8	0.0000
Diabetes (%)	30.6	19.6	0.005
MI (%)	42.5	20.2	0.0000
Ejection fraction (%)	38.1	48.1	0.0000
VA on Holter (%)	50.7	27.4	0.0000
QRSD/ECG (ms)	105.4	89.4	0.0000
QRSD/25 Hz (ms)	135.1	100.8	0.0000
RMS-40/25 Hz (μV)	24.8	64.4	0.0000
LPD/25 Hz (ms)	42.9	26.9	0.0000
QRSD/40 Hz (ms)	133.9	97.7	NA
RMS-40/40 Hz (μV)	15.0	41.4	0.0000
LPD/40 Hz (ms)	51.0	30.8	0.0000

Abnormal SAECG Results = duration of filtered QRS complex (QRSD) at 40 Hz ≥120 ms on the signal-averaged electrocardiogram (SAECG); other abbreviations as in Table 1.

could be determined by the Cox regression without correcting for baseline characteristics. The filtered QRS duration at 40 Hz was the most predictive, with the highest chi-square value of 34.46 (Table 2). To determine the best cutoff value for the filtered QRS duration at 40 Hz, dichotomous variables were created. A filtered QRS duration ≥120 ms had the highest chi-square value and thus provided the best predictive criterion (Table 2). The combination of filtered QRS duration at 40 Hz ≥120 ms with other dichotomized signal-averaged ECG variables did not improve the predictive value of the test. Thus, abnormal signal-averaged ECG results were defined as a filtered QRS duration at 40 Hz ≥120 ms. The incidence of abnormal signal-averaged ECG results in this group of postinfarction patients was 12%. In a regression analysis including all clinical, Holter and left ventricular ejection fraction variables, the filtered QRS duration at 40 Hz ≥120 ms was the most significant predictor of an arrhythmic event ($p < 0.0001$). Table 3 compares the clinical profile of patients with normal and abnormal signal-averaged ECG results. Figure 1 shows that the probability of remaining free of a serious arrhythmic event during the first year after infarction was significantly higher in patients with normal (98%) than abnormal (81%) signal-averaged ECG results ($p < 0.0001$).

Prognostic significance of signal-averaged ECG, left ventricular ejection fraction and complex ventricular arrhythmias for an arrhythmic event. Table 4 shows the sensitivity, specificity, total predictive accuracy, positive and negative predictive accuracy, chi-square value and odds ratio for the signal-averaged ECG, left ventricular ejection fraction, complex ventricular arrhythmia on the baseline Holter recording and various combinations of the three tests for prediction of an arrhythmic event in the first year after infarction. Left ventricular ejection fraction is shown dichotomized at ≤40%. We compared the predictive accuracy of left ventricular ejection fraction dichotomized at ≤40%, ≤35% and ≤30%. The best values were obtained at ≤40%. This could possibly be related to the relatively small number of patients in the lower ejection fraction group. Mean left ventricular ejection fraction in patients without an arrhythmic event, who comprised >95% of the study group, was 47.4%. Table 4 shows that the negative predictive accuracy of all three tests was high (98%). However, both positive (17%) and total (88%) predictive accuracy of the signal-averaged ECG were significantly higher than those of ejection fraction alone and complex ventricular arrhythmias alone and remained slightly higher than the combination of both tests. Combining either ejection fraction ≤40% or complex ventricular arrhythmias with abnormal signal-averaged ECG results improved positive and total predictive accuracy significantly. The best positive predictive accuracy of 32% was obtained by a combination of a filtered QRS ≥120 ms, left ventricular ejection fraction ≤40% and complex ventricular arrhythmias on the baseline Holter recording. However, only a small fraction of all patients with acute myocardial infarction

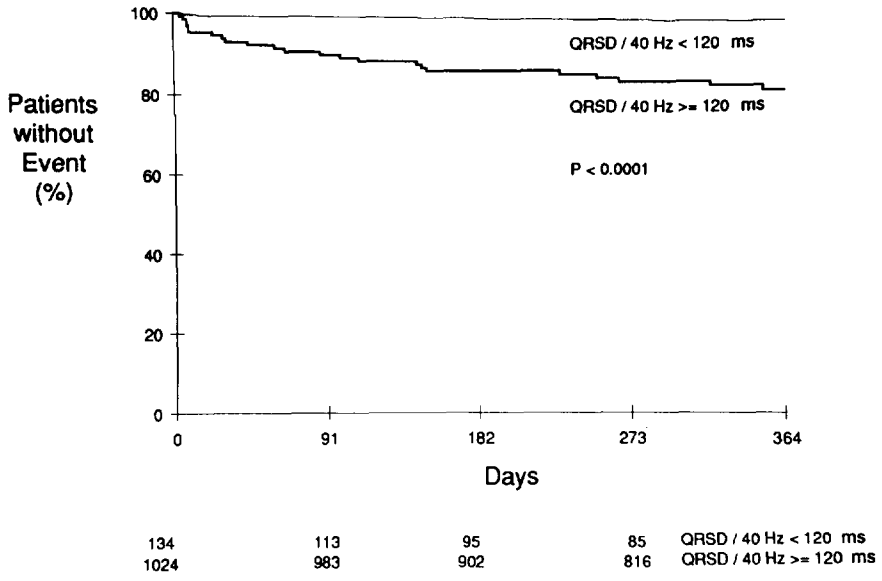

Figure 1. Probability of remaining free of arrhythmic events in patients with filtered QRS duration at 40 Hz (QRSD/40 Hz) <120 ms (normal signal-averaged electrocardiographic [ECG] results) and ≥120 ms (abnormal signal-averaged ECG results).

had abnormal results on all three tests (34 [4.1%] of 826). However, in addition to abnormal results on these tests, a number of clinical high risk variables (e.g., incidence of congestive heart failure and history of previous infarction) were also higher among patients with an arrhythmic event.

Discussion

Incidence of serious arrhythmic events in the first year after infarction. In the present study the calculated total mortality rate for the first year after infarction was 8.0% (1.3% for noncardiac death, 2.7% for cardiac nonarrhythmic death and 4.0% for cardiac arrhythmic death). The incidence of sudden cardiac "arrhythmic" death in the present study of 4.0% is remarkably similar to that for sudden death of 3.6% at 12 months reported previously by Surawicz (13). However, the incidence of nonfatal sustained ventricular tachycardia in the present study was very low (0.3% in the first year after infarction). The incidence of sustained ventricular tachycardia (defined by CAST as ≥15 beats/min) in both CAST I (6) and CAST II (14) placebo groups was also low (0.9% and 1%, respectively), even though the CAST population represented a higher risk group for arrhythmic events (15). Several studies that evaluated the prognostic significance of the signal-averaged ECG in the first year after infarction reported an incidence of nonfatal sustained ventricular tachycardia of 1.6% (16) to 7% (2). The reasons for the difference between these studies and the results of CAST and the present study are not evident. This could possibly be related to differences in patient selection and the bias introduced by the relatively small sample size in the signal-averaged studies, or it may reflect changes in the contemporary natural history of postinfarction patients.

Table 4. Relation of Signal-Averaged Electrocardiogram, Left Ventricular Ejection Fraction and Complex Ventricular Arrhythmias on Holter Recording to Arrhythmic Events

Risk	Sens (%)	Spec (%)	TPA (%)	PPA (%)	NPA (%)	Chi	OR
SAECG	48	90	88	17	98	42	8.4
VA	61	69	69	8	98	12	3.5
EF	70	69	69	9	98	20	5.1
VA+EF	58	86	85	15	98	43	8.4
SAECG+VA+EF	33	97	94	32	97	67	16.7
SAECG+VA	36	95	93	24	97	49	11.0
SAECG+EF	39	95	93	25	97	57	12.2

Chi = chi-square value; EF = left ventricular ejection fraction; NPA (PPA) = negative (positive) predictive accuracy; OR = odds ratio; SAECG = signal-averaged electrocardiogram; Sens = sensitivity; Spec = specificity; TPA = total predictive accuracy; VA = complex ventricular arrhythmias on Holter recording.

Definition of the best predictive criteria of the signal-averaged ECG in the postinfarction period. Two general approaches have been utilized to derive time domain criteria for abnormal time domain signal-averaged ECG results. The first approach investigated "normal" study groups to obtain "upper limits" for normal signal-averaged ECG results (17,18). This approach has been criticized because "normal" study groups are not representative of the population with coronary artery disease. The second approach evaluated the predictive value of signal-averaged ECG criteria in patients with spontaneous or inducible sustained ventricular tachycardia, or both (19,20). In these patients, time domain signal-averaged ECG criteria reflecting the presence of late potentials (i.e., the root-mean-square voltage in the last 40 ms or the duration of the late potentials of ≤40 μV, or both) were usually the most predictive. The electrophysiologic rationale for the predictive value of these criteria was that late potentials represent slowed and disorganized conduction of localized myocardial zones that could provide the anatomic–electrophysiologic substrate for reentrant ventricular tachycardia (21). It does not necessarily follow that these criteria would be also predictive in the

post–myocardial infarction period, where the majority of serious arrhythmic events are fatal ventricular tachyarrhythmias rather than nonfatal sustained ventricular tachycardia. In the present study, time domain signal-averaged ECG indexes of late potentials did not provide the best prediction criteria for a serious arrhythmic event. The signal-averaged QRS duration at 40 Hz high bandpass filter was found to be the single best predictive criterion. It should be emphasized that the signal-averaged QRS duration includes the low amplitude late potential signal. That is why the signal-averaged QRS duration is usually longer than the QRS duration measured from the surface 12-lead ECG (Tables 1 and 3). In the present study the surface ECG QRS duration lacked independent predictive significance. The electrophysiologic rationale as to why an abnormally long signal-averaged QRS duration best predicts fatal arrhythmic events in the first year after infarction is not clear. However, it is possible to speculate that a long signal-averaged QRS duration may reflect slowed and nonhomogeneous conduction of a larger mass of ventricular myocardium. Such hearts may be more vulnerable to fast ventricular tachycardia/fibrillation.

At least one previous study (22) also found that the duration of the signal-averaged QRS complex at 40-Hz high filter setting had the most significant relation to an arrhythmic event in the postinfarction period. However, this study (22) did not evaluate the best dichotomized value for the use of the signal-averaged QRS complex. Furthermore, the incidence of both sustained ventricular tachycardia (7%) and overall serious arrhythmic events (14%) was much higher than most other studies, possibly reflecting the selection of a higher risk group.

In the present study the incidence of abnormal signal-averaged ECG results of 12% in the postinfarction population was lower than previously reported rates of 31% (4) to 52% (23) using various different criteria. Also, the positive predictive accuracy of the signal-averaged ECG in the present study of 17% is lower than most of the previously reported values of 17% (1) to 29% (2). However, the incidence of serious arrhythmic events in the present study of 4.3% is also lower than that of 7% (4) to 14% (2) reported in other studies.

Conclusions. The signal-averaged QRS duration at 40-Hz high bandpass filter ≥120 ms is a better predictor of serious arrhythmic events in the first year after infarction than a battery of clinical variables, complex ventricular ectopic activity on the Holter ECG or left ventricular ejection fraction. Because the positive predictive accuracy of the test is still relatively low (17%), the most appropriate strategy for management of postinfarction patients with abnormal signal-averaged ECG findings is not yet established. However, the combination of abnormal signal-averaged ECG results, low ejection fraction and complex ventricular ectopic activity on the Holter ECG can provide a higher positive predictive accuracy for a serious arrhythmic event (32%) in postinfarction patients.

Appendix

Cardiac Arrhythmia Suppression Trial-II Investigators Participating in the Signal-Averaged Electrocardiogram Substudy

Brown University Affiliated Hospitals Center, Providence, Rhode Island: Robert J. Capone, MD* (1986–1991), Eric E. Berger, MD* (1991–), Chester Chmielewski, MD, Lawrence Gorkin, PhD, Abdul Hakim Khan, MD, Kenneth Korr, MD, Kathy Handshaw, RN, BS, Emily Connolly, RN, Donna Fitzpatrick, RN, BS, Tina Cameron, RN. **University of Calgary and Cooperating Hospitals, Calgary, Alberta, Canada:** D. George Wyse, MD, PhD,* Henry J. Duff, MD, L. Brent Mitchell, MD, Anne M. Gillis, MD, J. Wayne Warnica, MD, Robert S. Sheldon, MD, PhD, N. Robert Lesoway, MD, Joyce Kellen, RN, BN, Charlotte Hale, RN, Mary Inkster, RN, BSCN. **Case Western Reserve University, Cleveland, Ohio:** Albert L. Waldo, MD,* Mark D. Carlson, MD, Dale S. Adler, MD, Joel B. Holland, MD, Carol M. Buchter, MD, Robert C. Bahler, MD, Frank X. Pamelia, MD, Richard A. Josephson, MD, Richard W. Henthorn, MD, Jorge Gonzalez Zuelgaray, Kathy Wood, RN, MSN, Pamela Redmon, RN, BS, Melinda A. Vargas, RN, BSN, Laura Vargo, RN, Susan E. Schaller, RN, Christopher E. Kobus, RN, BSN, Nancy L. Choban, RN, BSN. **George Washington University Medical Center, Washington, D.C.:** Richard J. Katz, MD,* George A. Besch, MD, David Brill, MD, Robert DiBianco, MD, Dennis Donohue, MD, Gregory Fisher, MD, Cleveland Francis, MD, Dennis Friedman, MD, Daniel Goldberg, MD, Samuel Goldberg, MD, Gregorio Koss, MD, Louis Larca, MD, Roger Leonard, MD, Keith Lindgren, MD, James Ronan, MD, Arnold Rosenblatt, MD, Douglas Rosing, MD, Allan Ross, MD, Alberto Rotsztain, MD, Fayez Shawl, MD, Thomas Sinderson, MD, Roger Stevenson, MD, Bruce Tinker, MD, Jacob Varghese, MD, John Yackee, MD, Harry Bigham, MD, William Franklin, MD, Robert Gold, MD, Gordon Graham, MD, David Grossberg, MD, Raymond Hoare, MD, Warren Levy, MD, Tariq Mahmood, MD, Eric Tannenbaum, MD, William Tullner, MD, Ellen Eisenhower, RN, Therese Geraci, RN. **University of Kentucky, Lexington, Kentucky:** Anthony N. DeMaria, MD,* Chien-Suu Kuo, MD, James M. Kammerling, MD, Jody Corum, RN, Marilyn Thiemann, RN, Rita Schrodt, RN. **University of Minnesota, Minneapolis, Minnesota:** M. Hodges, MD,* D. Salerno, MD, B. Anderson, MD, R. Collins, MD, P. Denes, MD, D. Dunbar, MD, G. Granrud, MD, J. Haugland, MD, W. Hession, MD, J. McBride, MD, C. Gornick, MD, J. Simonson, MD, M. Tolins, MD, A. Ettinger, RN, S. Peterson, RN, R. Slivken, RN, L. Grimaldi. **Rush-Presbyterian–St. Luke's Medical Center, Chicago, Illinois:** Pablo Denes, MD* (1986–1988), James A. Schoenberger, MD* (1989–), Philip R. Liebson, MD, Nicholas J. Stamato, MD, A. Tom Petropulos, MD, Thomas A. Buckingham, MD, Tracy Remijas, MPH, Joanne Kocourek, RN, Kimberly Janko, RN. **Salt Lake Clinic Research Foundation, Salt Lake City, Utah:** Allan H. Barker, MD,* Jeffrey L. Anderson, MD, Robert E. Fowles, MD, Thomas B. Keith, MD, C. Basil Williams, MD, Fidela L. Moreno, MD, Ellen N. Doran, Barbara Fowler, Kaye Summers, RN, Carla White, LPN. **Saint Louis University Medical Center, Saint Louis, Missouri:** Jerome D. Cohen, MD,* Preban Bjerregaard, MD, PhD, William P. Hamilton, MD, Mary Garner, RN, BSN, Sally Anderson, RN, BSN. **State University of New York Health Science Center at Brooklyn, Brooklyn, New York:** Nabil El-Sherif, MD,* Shantha N. Ursell, MD,

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George E. Gabor, MD, Bassiema Ibrahim, MD, Mashid Assadi, MD, Mary Lynn Brezsnyak, RN, MS, Ann V. Porter, RN, BSN, Anne Staniorski, RN. **Coordinating Center, University of Washington, Seattle, Washington:** Alfred P. Hallstrom, PhD,* Ruth McBride, H. Leon Greene, MD, Maria Mori Brooks, PhD, Robert Ledingham, MS, Robin Reynolds-Haertle, MS, Melissa Huther, Margit Scholz, Mary Morris. **Program Office, Clinical Trials Branch, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland:** Lawrence M. Friedman, MD, Eleanor Schron, RN, MS, Joel Verter, PhD, Cheryl Jennings, Michael Proschan, PhD. **Events Review Subcommittee:** David W. Richardson, MD, Chairman *(Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia)*; Robert Capone, MD, Co-Chairman *(Brown University Affiliated Hospitals Center, Providence, Rhode Island)*; John McAnulty, MD *(Oregon Health Sciences University, Portland, Oregon)*; Allan Barker, MD *(Salt Lake Clinic Research Foundation, Salt Lake City, Utah)*; Toshio Akiyama, MD *(University of Rochester, Rochester, New York)*; Lars Wilhelmsen, MD *(University of Goteborg, Goteborg, Sweden)*; Dan Roden, MD *(Vanderbilt University, Nashville, Tennessee)*; Gunnel Hedelin, RN *(University of Goteborg, Goteborg, Sweden)*; Mary Lynn Brezsnyak, RN *(State University of New York Health Science Center at Brooklyn, Brooklyn, New York)*; Joel Verter, PhD *(Program Office, Clinical Trials Branch, Divison of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, Bethesda, Maryland)*; Leon Greene, MD *(Coordinating Center, University of Washington, Seattle, Washington)*.

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