Improved Diagnostic Value of Combined Time and Frequency Domain Analysis of the Signal-Averaged Electrocardiogram After Myocardial Infarction

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BACKGROUND Time domain analysis (TD) of the signal-averaged electrocardiogram (SAECG) presents a higher incidence of false positives in inferior myocardial infarction (MI), whereas spectral turbulence analysis (STA) suffers from a higher incidence of false positives in anterior MI. We investigated the hypothesis that a combined TD and STA (TD+STA) analysis of the SAECG could improve its predictive accuracy for major arrhythmic events (MAE) after MI.

METHODS Signal-averaged electrocardiograms were prospectively recorded 10.1 ± 2.6 days after acute MI in 602 patients. Time domain analysis and STA were performed using standard parameters and criteria for abnormality. For the combined TD+STA model, stepwise discriminant analysis was utilized to optimize prediction of MAE. Receiver operating characteristic curves were utilized to optimize cutoff values for each SAECG parameter separately, and also for the combined TD+STA model.

RESULTS During a one-year follow-up period, 38 patients had MAE: 14 sustained ventricular tachycardia, 2 resuscitated ventricular fibrillation and 22 sudden cardiac deaths. The total predictive accuracy of combined TD+STA (89.9%) was significantly higher than TD (75.1%) or STA (77.6%). The negative predictive accuracy of all three analyses was high (98%). The positive predictive accuracy of TD (19.6%) or STA (18.3%) was quite low, and significantly improved to 35.8% by combined TD+STA analysis. The positive predictive accuracy of TD+STA improved to 51.2% in patients with left ventricular ejection fraction ≤40%.

CONCLUSIONS Combined TD+STA analysis of the SAECG significantly improves its prognostic ability for MAE in post-MI patients compared with TD or STA analyzed separately. (J Am Coll Cardiol 1999;33:385–94) © 1999 by the American College of Cardiology

It is widely accepted that late potentials detected on the signal-averaged electrocardiogram (SAECG) are noninvasive markers for major arrhythmic events (MAE: ventricular tachycardia, ventricular fibrillation and sudden cardiac death) after acute myocardial infarction (MI) (1–4). Late potentials have been reported to correspond to delayed and fragmented signals, which have been observed in epicardial and endocardial electrograms registered in postinfarction animal models (5–8), and in patients with ventricular tachycardia (9). Initial studies used the time domain analysis (TD) technique exclusively (10–11). This is still the most often used technique, and has proven highly reproducible (12–14), but it has significant limitations; high-pass filters are required, discrimination between noise and late potentials may be difficult, and patients with bundle branch block have generally been excluded from analysis (15–17). To overcome these limitations, several frequency-based analysis techniques were developed in recent years (18–24). The two frequency domain techniques most used are spectral temporal mapping and spectral turbulence analysis (STA); the lack of reproducibility of the former limits its clinical application (25–27). For that reason, STA and TD are the most useful SAECG techniques for arrhythmic risk stratification post-MI.

The predictive accuracy of TD in post-MI patients is limited by the high incidence of false positives in inferior infarction, while STA presents a higher incidence of false positives in anterior infarction. The aim of this prospective study was to investigate the hypothesis that combined TD and STA (TD+STA) analysis of the SAECG could improve its predictive accuracy for MAE in the post-MI period.
METHODS

Subject population. This prospective study comprised 712 subjects, consisting of 602 consecutive patients with acute MI (473 men, 129 women, mean age 61.3 ± 10.9 years) admitted to the Coronary Care Unit, and who survived the 1st week after admission, and 110 healthy volunteers (60 men and 50 women, mean age 46.0 ± 18.7 years, Table 1). The patients were recruited between January 1992 and December 1993. Exclusion criteria were: 1) the presence of atrial fibrillation; 2) the presence of a noise level >0.3 mV in the SAECG; 3) pacemaker patients; 4) preexcitation syndromes, and 5) refusal or inability to participate in the protocol. One patient who developed sustained polymorphic ventricular tachycardia (VT) on day 3 after MI and before the recording of the SAECG was included in the analysis. For purposes of comparing analysis techniques, patients with conduction defects with QRS duration >120 ms were not excluded. Conduction defects were subgrouped into three types: 1) right bundle branch block (RBBB); 2) left bundle branch block (LBBB), and 3) nonspecific intraventricular conduction defects with QRS prolongation >120 ms (“other IVCD”). The rate of thrombolysis in our series was 37.7%, and no antiarrhythmic drugs (except beta-adrenergic blocking agents that were given to 50.5% of the patients) were used.

Assessment of left ventricular function. Left ventricular ejection fraction was determined in MI patients by two-dimensional echocardiography in 439 patients (72.9%), by contrast left ventricular angiography in 122 patients (20.3%) and by radionuclide ventriculography (using technetium-99m pertechnate) in the remaining 41 patients (6.8%). As in most studies of risk stratification post-MI, an ejection fraction <40% was considered as an indicator of significant left ventricular dysfunction.

Signal-averaged electrocardiogram recording technique. In MI patients, SAECGs were recorded during the 2nd week (10.1 ± 2.6 days) after MI, using the 1200 EPX unit (Arrhythmia Research Technology, Austin, TX). The procedure used for SAECG recording was conventional (10). At least 200 sinus beats (395 ± 88 beats) were averaged.
during each recording. In all included cases the noise levels were \( \leq 0.3 \) mV (mean noise level = 0.2 ± 0.1 mV).

**Time domain analysis of SAECG.** The three conventional TD parameters were determined according to the methods of Simson (10), with a high-pass filter setting of 40 Hz: “total filtered QRS duration” (QRSD); “duration of terminal low amplitude signals \( < 40 \) mV” (LAS40), and the “root mean square voltage of the last 40 ms of the filtered QRS” (RMS40). Time domain analysis was considered positive for late potentials when at least two parameters reached the standard criteria of abnormality (28): QRSD > 114 ms; LAS40 > 38 ms; RMS40 > 20 μV. Patients with conduction defects with QRS duration > 120 ms were considered “not analyzable” by the TD technique.

**Spectral turbulence analysis of SAECG.** This frequency domain analysis was performed according to the methods of Kelen et al (24). Beginning 25 ms before the QRS onset, overlapping signal segments of 24 ms were analyzed, in steps of 2 ms, terminating 125 ms after the QRS offset. After differentiation, mean subtraction, windowing (Blackman-Harris), Fourier transformation and normalization, the following four parameters were derived from the sum of the three leads (X+Y+Z), with the definitions described by Kelen et al (24): 1) low slice correlation ratio (LSCR), the percentage of adjacent slice pairs with a correlation coefficient < 0.985; 2) interslice correlation mean (ISCM), the mean correlation coefficient of all adjacent time slices; 3) interslice correlation standard deviation (ISCSD), the standard deviation of all correlations of adjacent slices, multiplied by 100, and 4) spectral entropy (SE), the average discordance of each slice with an “average slice,” multiplied by 100. An abnormal parameter was defined as described by Kelen et al. (24): LSCR > 73.5; ISCM > 92.3, ISCSD > 104.8 and SE > 14.4. Each recording was scored for “spectral abnormality,” from 0 (no abnormal parameters) to 4 (all abnormal parameters), and was considered abnormal when the score was 3 or 4 (24).

**Combined TD and STA analysis of SAECG.** Receiver operating characteristic (ROC) curves were plotted for each SAECG parameter (Fig. 1) to optimize their cutoff values for the prediction of MAE in the group of 602 MI patients. The three TD and four STA parameters were dichotomized using those optimal cutoff values. Then, stepwise discriminant analysis was utilized for the combination of the seven SAECG parameters and three more variables indicating the presence of RBBB, LBBB or “other IVCD.” Receiver operating characteristic curves were again plotted using the model selected by stepwise discriminant analysis (Fig. 2), and its optimal cutoff value was used to classify the results of the combined TD+STA method as “normal” or “abnormal.” The same procedure was also performed for TD and STA techniques separately (Fig. 3), using two different sets of cutoff values: 1) standard criteria for abnormality (28) for TD parameters, and the abnormal limits described by Kelen et al. for STA parameters (24); and 2) the same
optimal cutoffs used in the combined TD+STA model. Using both sets of cutoff values, ROC curves for isolated TD (left panel) or STA (right panel) were plotted along with the corresponding ROC curves of the combined TD+STA model.

Follow-up. All patients were followed up for 1 year after acute MI. In those patients who died during the follow-up period, the details of the circumstances of death were painstakingly obtained from several sources, including hospital case records, direct inquiries to the general practitioner or hospital physician who certified the death, and interviews with the patient’s relatives.

Definition of major arrhythmic events. Three types of arrhythmic events were defined prospectively as study end points: 1) sudden cardiac death, defined as in the Cardiac Arrhythmia Pilot Study (29), as death within 1 h of the onset of new symptoms. The definition also included instantaneous death and death during sleep, as well as unexpected death that occurred within 1 h of the time the patient was last seen alive; 2) sustained ventricular tachycardia, defined as an electrocardiogram-documented ventricular tachycardia, with a rate $\geq 120$ min$^{-1}$ and lasting $\geq 30$ s, and 3) documented ventricular fibrillation, requiring defibrillation, not associated with acute MI. Only spontaneous episodes of these arrhythmias were considered as end points.

Statistical analysis. Continuous variables are expressed as mean value $\pm$ SD. Comparisons between groups were performed using Student $t$ test for normally distributed continuous variables, the Mann–Whitney $U$ test for non-parametric continuous variables and chi-square analysis for categoric variables. The type I error (significance level) was fixed at 0.05. Receiver operating characteristic curves were created and compared using the ROCKIT software (developed by Metz (30), University of Chicago). In brief, this software computes the specificity at any sensitivity level, for each value of the independent variable(s) (isolated or combined in a multivariable model), for the prediction of the dependent variable (presence or absence of MAE in this study). Receiver operating characteristic curves were plotted to optimize the cutoff values of each SAECG parameter (Fig. 1) and of the combined model TD+STA (Fig. 2). These curves were also plotted to compare the combined model TD+STA with the isolated TD and STA techniques, using standard as well as optimized cutoffs (Fig. 3).

![Figure 2](image2.png)

**Figure 2.** Receiver operating characteristic curve with the combined model of time domain and spectral turbulence analysis (TD+STA). The arrow points to the best sensitivity–specificity balance, obtained when the mathematical model reaches the value of 1.4. RBBB = right bundle branch block. Other abbreviations as in Figure 1.

![Figure 3](image3.png)

**Figure 3.** Receiver operating characteristic (ROC) curves of the combined time domain and spectral turbulence analysis (TD+STA) model, compared with isolated time domain (TD, left panel) or spectral turbulence analysis (STA, right panel) techniques. In each panel the thick solid line represents the curve obtained with the combined TD+STA model. For each isolated technique, the thin solid line represents the curves obtained with its conventional cutoffs, and the dotted line represents the corresponding curve, using its “optimal” cutoffs (shown in Fig. 1). Both lines are quite close, but the optimized curves have a slightly higher specificity up to sensitivity levels of 90%; however, the differences between those ROC curves were not statistically significant. Note that in each panel, the best sensitivity–specificity balance is obtained with the combined TD+STA model, with a significantly greater area than any other ROC curve.
For these comparisons, the ROCKIT software estimates the area under each curve ($A_Z$) with their corresponding standard errors, 95% confidence intervals and the p value for the difference between each pair of areas.

The predictive characteristics of the three types of analysis of the SAECG (TD, STA and TD+STA) were estimated by computing their sensitivity, specificity, positive, negative and total predictive accuracy. These calculations were made for the 602 MI patients, and for the following subgroups (Table 2): patients with anterior (n = 225), inferior (n = 276) or “non-q” (n = 101) MI, patients with left ventricular ejection fraction $\leq 40\%$ (n = 165), and patients with (n = 32) or without (n = 570) conduction defects. The three analyses of the SAECG were also performed in control subjects to investigate the false positive rates of each technique in normal individuals. Comparisons among positive and total predictive accuracy of different tests were conducted using chi-square analysis. Stepwise discriminant function analysis was performed with the Statistical Package for the Social Sciences (31), utilizing the default settings. We entered 10 candidate variables (QRSD, LAS40, RMS40, LSCR, ISCM, ISCS, SE, RBBB, LBBB and “other IVCD”), and minimizing the Wilks’ lambda, the model included only those parameters that could significantly improve its statistical ability to discriminate between groups (with or without MAE), in stepwise fashion, from most significant parameter to least. In that way, we obtained the multivariate model (Fig. 2) that was used for the combined TD+STA analysis. To reduce the bias caused by deriving and testing the combined TD+STA model in the same patient population, we performed a “Jackknife” evaluation, with the “Crossvalidation” method, included in the “DISCRIM” procedure of the SAS software (SAS Institute Inc, Cary, NC). This method treats n − 1 out of n observations as a training set. It determines the discriminant functions based on these n − 1 observations and then applies them to classify the one left out. This is performed for each of the n training observations, to test the misclassification rate.

**RESULTS**

**Patient characteristics.** The clinical characteristics of subjects are summarized in Table 1. MI was inferior and/or posterior in 276 (45.8%), anterior in 225 (37.4%) and “non-q” in the remaining 101 patients (16.8%). There was evidence of previous MI in 106 patients (17.6%). Conduction defects were present in 32 (5.3%) MI patients: 17

### Table 2. Diagnostic Value of the Signal-Averaged Electrocardiogram in Post-MI Patients

<table>
<thead>
<tr>
<th>Group of MI Patients</th>
<th>Method of SAECG</th>
<th>n</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Accuracy (%)</th>
<th>Negative Predictive Accuracy (%)</th>
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<td>84.8*</td>
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*A statistically significant difference (p < 0.05) was found between the positive or total predictive accuracy of the TD+STA method and those of TD or STA.

CD = conduction defects; EF = ejection fraction; MI = myocardial infarction; Not A. = not analyzable; SAECG = signal-averaged electrocardiogram; STA = spectral turbulence analysis; TD = time domain analysis; TD+STA = combined time domain and spectral turbulence analysis.
RBBB, 10 LBBB and 5 "other IVCD." Left ventricular ejection fraction was <40% in 165 (27.4%) MI patients. During follow-up, 38 MI patients presented with MAE: 14 sustained ventricular tachycardia, 2 resuscitated ventricular fibrillation and 22 sudden cardiac death (3 of them with previous documented ventricular fibrillation). The clinical characteristics of the subgroups of patients with and without MAE are also displayed in Table 1; the proportion of patients with left ventricular dysfunction and with previous MI were significantly higher (p < 0.05) among patients with MAE. There was no significant difference between MI patients with and without MAE in terms of age, gender, site of MI or presence of conduction defects (Table 1).

**Optimal cutoffs for the combined TD+STA model.** The optimal cutoffs found for TD variables were identical to the limits of abnormality described by Caref et al. (32,33): QRSD >111 ms, LAS40 >39 ms, RMS40 <16 μV (Fig. 1). The optimal cutoffs found for STA parameters were: LSCR >73.5, ISCM <92.2, ISCD >105.2 and SE >14.8; these limits of abnormality were very similar to those published by Kelen et al. (24) (exactly the same for LSCR). The model selected by stepwise discriminant analysis included two TD parameters (RMS40 and LAS40), three STA variables (SE, ISCM and LSCR) and the presence/absence of RBBB (Fig. 2). The QRSD, ISCD and the presence of LBBB or "other IVCD" did not give any additional information, and were not included in this combined TD+STA model, mathematically described as:

\[
(2.55 \text{ RMS40}) + (0.77 \text{ SE}) - (1.25 \text{ RBBB}) + (0.29 \text{ ISCM}) + (0.28 \text{ LSCR}) - (0.44 \text{ LAS40}) - 0.762.\]

The best predictions with this combined TD+STA analysis were obtained classifying the SAECG as “+” when the result of the model was ≥1.4.

**Results in MI Patients**

The number of positive SAECGs by the three analysis techniques was significantly higher (p < 0.05) among patients with MAE (Table 1). Thrombolytic therapy was used in 227 patients (37.7%). These patients presented a significantly (p < 0.05) lower proportion of positive SAECGs by any of the three analysis methods, compared with the patients who did not receive fibrinolytics: 11.9% versus 29.6% by TD, 12.8% versus 33.1% by STA and 9.3% versus 16.0% by the combined TD+STA method, respectively. The results of each SAECG analysis technique, in terms of sensitivity, specificity and predictive values, are described in the following sections.

**Time domain analysis results.** The SAECG was considered “positive” for late potentials in 138 patients, “negative” in 432 subjects and “not analyzable” by TD technique in the remaining 32 patients with conduction defects; 27 patients with positive TD results had MAE (sensitivity = 71.1%), and 425 patients with negative TD analysis were free of MAE (specificity = 75.4%). The positive, negative and total predictive accuracy were: 19.6%, 98.4% and 75.1%, respectively (Table 2). The site of infarction influenced the results; in the subgroup with inferior MI, the sensitivity of TD was the highest (93.8%), but the specificity was the lowest (71.2%), compared with the patient subgroups having anterior or non-q MI (Table 2). In the subgroup of patients without conduction defects the sensitivity, specificity and total predictive accuracy were very close to 80%; however, the positive predictive accuracy was still low (19.6%), and only improved to 35.2% in the subgroup of patients with left ventricular ejection fraction <40% (Table 2).

**Spectral turbulence analysis results.** Spectral turbulence analysis was considered abnormal in 153 patients and normal in the remaining 449 subjects. There were 28 patients with abnormal STA who had MAE (sensitivity = 73.7%), and 439 patients with normal STA were free of MAE (specificity = 77.8%). The positive, negative and total predictive accuracy were: 18.3%, 97.8% and 77.6%, respectively (Table 2). The site of infarction also influenced the results of STA. In the subgroup with anterior MI, the sensitivity of STA was the highest (83.3%), but the specificity was the lowest (71.5%), compared with the subgroups of patients with inferior or non-q MI (Table 2). The results of STA in the subgroup of MI patients without conduction defects were very similar to those of the whole MI group. In the small subgroup of patients with conduction defects (n = 32), there were four with MAE, all of them with an abnormal STA (sensitivity = 100%); however, the STA was only normal in 12 out of the 28 patients without MAE (specificity = 42.9%). The positive predictive accuracy of STA was low (27.8%), even in the subgroup of patients with left ventricular dysfunction (Table 2).

**Combined TD+STA results.** The combined TD+STA method gave abnormal results in 81 patients and normal results in the remaining 521 subjects. Twenty-nine patients with abnormal TD+STA had MAE (sensitivity = 76.3%), and 512 patients with normal TD+STA were free of MAE (specificity = 90.8%). The positive, negative and total predictive accuracy were: 35.8%, 98.3% and 89.9%, respectively (Table 2). These results were confirmed utilizing the Jackknife procedure, which offered nearly identical predictive statistics: sensitivity 73.7%, specificity 90.8% and positive, negative and total predictive accuracy 35.0%, 98.1% and 89.7%, respectively. The site of infarction influenced very little the results of TD+STA. The sensitivity of the combined model was slightly higher in the subgroup with inferior MI (81.3%), but the specificity and the positive, negative and total predictive accuracies were very similar in the three sites of MI (Table 2). The results of TD+STA in the subgroup of patients without conduction defects were almost identical to those of the whole MI group. In the subgroup of patients with conduction defects, the four patients with MAE also had an abnormal TD+STA (sensitivity = 100%); the TD+STA was normal in 23 out of the 28 patients without MAE (specificity = 82.1%). The positive predictive accuracy of TD+STA was higher than
either TD or STA in all groups of patients, and improved to 51.2% in the subgroup of patients with left ventricular ejection fraction <40% (Table 2). On the other hand, ROC curves with the combined TD+STA model showed a better sensitivity–specificity balance than isolated TD or STA, with either standard or optimized cutoff values (Fig. 3).

Statistical comparison of the positive and total predictive accuracies between TD, STA and TD+STA techniques. The total predictive accuracy of the combined model TD+STA was significantly (p < 0.05) higher than either TD or STA in MI patients (89.9% vs. 75.1% or 77.6%, respectively), as well as in the subgroups of MI patients with ventricular dysfunction (84.8% vs. 66.1% or 64.8%), or without conduction defects (90.2% vs. 79.3% or 79.1%) (Table 2). The positive predictive accuracy of the combined TD+STA was significantly higher than TD or STA alone in the whole MI group (35.8% vs. 19.6% or 18.3%, respectively), as well as in all the subgroups described in Table 2. No statistically significant differences were found between TD and STA in terms of positive or total predictive accuracies in any group of patients (Table 2).

Statistical comparison of the ROC curves obtained with TD, STA and TD+STA models. Receiver operating characteristic curves comparing the performance of each technique are shown in Figure 3. The area indices (A_Z) for the combined TD+STA method were: A_Z = 0.88 ± 0.04, with a 95% confidence interval (CI) for A_Z = 0.80, 0.94. The corresponding indices for TD were 0.80 ± 0.04 (CI = 0.69, 0.88) with standard cutoffs, and 0.82 ± 0.04 (CI = 0.73, 0.89) with optimal cutoffs. The same indices for STA were 0.77 ± 0.07 (CI = 0.63, 0.88) with the cutoffs of Kelen, and 0.79 ± 0.07 (CI = 0.64, 0.90) with optimal cutoffs. The area indices (A_Z) for the combined TD+STA method (0.88 ± 0.04), were significantly higher than the corresponding indices of isolated TD technique, using either standard (p = 0.03) or optimized cutoffs (p = 0.04) (Fig. 3, left panel). The area under the combined TD+STA ROC curve was also significantly greater than those obtained with the STA method using either Kelen cutoffs (p = 0.02) or optimized cutoffs (p = 0.04) (Fig. 3, right panel). On the other hand, areas under ROC curves of each isolated technique were greater with the optimized cutoffs than with standard cutoffs, but the difference was not statistically significant.

Results in Control Subjects

The number of false positive results with TD, STA and TD+STA was 4 (3.6%), 1 (0.9%) and 0 (0.0%), respectively, and the corresponding specificity of each technique among control subjects was 96.4%, 99.1% and 100%, respectively (Table 1).

DISCUSSION

Comparison with previous studies. Most prospective studies investigating the prognostic value of the SAECG for the prediction of MAE after MI used only the TD technique, and excluded patients with conduction defects (1,4,34–37). In those studies, the negative predictive value was uniformly high (96% to 99%), but the positive predictive value was low (10% to 27%); the sensitivity ranged from 63% to 93% and the specificity from 51% to 81% (1,4,34–37). Our TD results in the subgroup of patients without conduction defects (sensitivity = 79%, specificity = 79%, positive predictive value = 20% and negative predictive value = 98%) are fully comparable to those of the previous studies mentioned, despite a two- to fivefold increase in the sample population.

The main advantage of STA over TD is that the former was found more useful than the latter in identifying patients with spontaneous or induced ventricular tachycardia in studies that included patients with conduction defects (24,38,39); for that reason, we did not exclude those patients from our study. Another reason for including patients with conduction defects is that they constitute a significant percentage of the post-MI population, and they present a higher risk of MAE. Other previous studies in smaller groups of patients have shown that a combination of TD and frequency domain variables can improve the overall predictive value of the SAECG (40,41).

Findings of the study. The main finding of this study is that a combined model of TD+STA significantly improves the positive and total predictive accuracies of the SAECG in the whole group of MI patients, as well as in the subgroups of patients without conduction defects or with left ventricular dysfunction. Not surprisingly, the differences previously found between the sensitivity and specificity of TD and STA, showing a dependency of the predictive characteristics of each technique on the site of MI, are now smoothed by the combined model, as it integrates parameters from both types of analysis of the SAECG. On the other hand, the TD+STA model gave no false positive results in the control group, whereas there was 1 false positive with STA and 4 with TD analysis. Therefore, this combined model TD+STA appears to discriminate better than conventional TD or STA in all the groups and subgroups of patients studied.

Noteworthy is the fact that the mathematical model did not include QRSD or ISCSD. It is not surprising based on the ROC curves of these two parameters (Fig. 1), which showed a lower specificity than the other SAECG parameters with most levels of sensitivity. This is in contrast to the CAST/SAECG Substudy (42), which found the QRSD to be the best TD predictor of MAE. Three differences between this study and the CAST/SAECG Substudy that could account for this are: 1) the CAST/SAECG Substudy excluded patients with bundle branch block; 2) the propor-
tion of presenting tachyarrhythmias defined as MAE was different; and 3) the noise level for inclusion into the present study was <0.3 $\mu$V, which is three times lower than the noise level cutoff for inclusion into the CAST/SAECG Substudy. The ISCSD, besides its limited prognostic value, also has poor reproducibility (25,27), and the scoring of the conventional STA may improve if this parameter is ignored. Another modification of the STA method that may improve its low positive predictive accuracy for MAE after MI would be to slightly readjust the cutoff values for abnormality described by Kelen et al. (24), shifting them to more specific values. This is reasonable, as those abnormality limits were developed to predict inducibility at electrophysiologic study, rather than spontaneous arrhythmic events. In that sense, the optimal cutoff values of STA parameters found in this study, although very similar to those of Kelen et al. (24), are somewhat more specific. Figure 3 shows that the specificity of STA is slightly but uniformly higher with these optimal cutoffs, than with those described by Kelen et al. (24), at almost any level of sensitivity. Therefore, if the STA method is used for the arrhythmic risk stratification after MI, we propose a simpler score with only three variables and with more specific limits for abnormality, as proposed in the present study. Not surprisingly, the sensitivity–specificity balance of either TD or STA improved slightly using the optimal cutoffs, instead of the conventional ones, although these differences were not statistically significant (Fig. 3). However, combining TD and STA (TD+STA model) resulted in a statistically significant improvement of the sensitivity–specificity balance, compared with either isolated technique, using the same optimal cutoff values (Fig. 3). Therefore, the results with this model TD+STA were better, not only because it used optimal cutoffs, but also because combining TD and STA parameters further improved the predictive accuracy of the SAECG.

It might be argued that continuous models, containing the actual data of each parameter, should be more helpful than dichotomized models. Although not presented in this study, we also tested the corresponding continuous models including the actual TD and STA data. However, the proportion of correctly classified cases by each continuous model was always slightly lower than that of the corresponding dichotomized models (using either the “standard” or “optimized” cutoff values). One of the reasons that could explain why the continuous models “classified worse” than the dichotomized models might be that there is more dispersion of the data in the former than in the latter. On the other hand, it has been a common practice in most classical risk stratification studies to dichotomize many parameters, such as: age (>65 years), Killip class (≥2), ejection fraction (<40%), Holter findings (ventricular ectopic beats >10/h, or presence/absence of complex ventricular arrhythmias), heart rate variability index (<20 ms), baroreflex sensitivity slope (<3) and so forth.

Left ventricular ejection fraction did not add additional predictive value to the model. The reason may be due to the very low pretest risk of the study group. When the pretest risk is very low, the maximum positive predictive accuracy (PPA) achievable by an ideal discriminating parameter in the whole group is also low. Furthermore, the combined TD+STA model included the existence of RBBB, but did not take into account the presence of LBBB or “other IVCD.” This agrees with previous studies (16,43) concluding that RBBB is the conduction defect that most limits the diagnostic value of the TD technique, whereas LBBB needs only an appropriate adjustment in criteria for abnormality. In the study by Fontaine et al. (43), a reduction of the abnormality limit of the RMS40 (with the 25-Hz high-pass filter) from the standard value of 25 $\mu$V to 17 $\mu$V, and a prolongation of the LAS40 cutoff from 38 to 55 ms, provided good predictive accuracy for the inducibility of ventricular tachycardia in patients with LBBB. In our mathematical model, the cutoff value for the RMS40 was already lowered to 16 $\mu$V, compared with the standard value of 20 $\mu$V with the 40-Hz high-pass filter. The STA variables included in this model also help to identify those patients with conduction defects who had MAE; however, this discrimination is more difficult if RBBB exists, and explains the presence of this variable in the model.

**Value and limitations of the study.** This study is based on the largest series of prospectively recorded SAECG in acute MI patients, analyzed by both TD and STA techniques, without excluding patients with conduction defects. However, the subgroup of patients with conduction defects is too small ($n = 32$) to allow statistical comparisons of the three methods of SAECG analysis among these patients. Nevertheless, according to our results (Table 2), the combined model TD+STA seems to discriminate patients with conduction defects who presented with MAE from those who did not. Further studies including a substantially larger number of such patients are warranted to confirm these results. Another limitation of this study is that the combined model TD+STA was tested in the same group of patients used to derive the model. However, this theoretical limitation minimally affected our results; the predictive statistics of the combined TD+STA method were almost identical after a Jackknife validation, which is known to achieve a nearly unbiased estimate of the correct classification rate (44). Nevertheless, further studies are needed to test the proposed model in other groups of post-MI patients.

**Clinical implications.** The main limitation of the SAECG in predicting MAE after MI is its very low positive predictive accuracy. With the combined TD+STA model, the positive predictive accuracy nearly doubled compared to conventional TD or STA (35.8% vs. 19.6% or 18.3%, respectively). This improvement was obtained without any loss in sensitivity; indeed, in the whole group of MI patients, the sensitivity, specificity and total predictive accuracy were also better with the combined TD+STA model than with TD or STA alone (Table 2). Although
efforts to improve the overall predictive value of the SAECG have been successful, future directions for risk stratification for major arrhythmic events dictate that the test be utilized as a part of an algorithm in conjunction with several other risk stratifiers. These may include ambulatory arrhythmias, heart rate variability, QT dispersion and T-wave alternans.

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