Improved selection of patients for programmed ventricular stimulation by frequency analysis of signal-averaged electrocardiograms*

BRUCE D. LINDSAY, M.D., H. DIETER AMBOS, KENNETH B. SCHECHTMAN, PH.D., AND MICHAEL E. CAIN, M.D.

ABSTRACT Improved selection of patients with suspected sustained ventricular tachycardia (VT) for programmed ventricular stimulation is needed. To determine if frequency analysis detects patients in whom sustained VT might be induced, we first obtained fast-Fourier transforms (FFT) of signal-averaged electrocardiograms (ECGs) from 20 patients with spontaneous sustained VT (group I) and compared them with the results of programmed ventricular stimulation with single and double extra-stimuli during two cycle lengths and burst pacing from two right ventricular sites. The FFT data were expressed as an area ratio that quantified the relative contributions of 20 to 50 Hz frequencies in the terminal QRS and ST segment. A logistic regression with inducibility as the dependent variable was used to help define area ratio values greater than 20 as abnormal. Sustained monomorphic VT was induced in 18 patients, each with an area ratio value greater than 20. Sustained VT was not induced in two patients, each with an area ratio value less than 20. FFT data were then compared prospectively with the results of programmed stimulation in 38 patients (group II) with nonsustained VT (12 patients) or syncope (26 patients) referred for electrophysiologic study. In none of the 26 patients in group II with normal FFT values was VT inducible. Sustained monomorphic VT was induced in five of 12 patients with abnormal FFT values. Thus, the results of FFT analysis correctly predicted the results of programmed ventricular stimulation in 88% of patients studied and in 82% of patients in group II with syncope or nonsustained VT. Moreover, all five patients in group II in whom sustained VT was induced were identified correctly. Results of multivariate analysis demonstrated that area ratio values were independent of other determinants of inducibility, including left ventricular ejection fraction and prior myocardial infarction. The approach developed offers promise for improving identification of patients in whom sustained VT will be induced during programmed ventricular stimulation.

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PATIENTS at risk for sustained ventricular tachycardia (VT) are frequently referred for electrophysiologic study.1-3 Improved selection of patients requiring programmed ventricular stimulation would facilitate patient management. Distinguishing features in signal-averaged electrocardiograms (ECGs) have been reported that differentiate patients with documented sustained VT from those without sustained VT.3-10 Recently, we have shown that frequency analysis detects low-amplitude, oscillatory potentials in signal-averaged ECGs.13,15 The results of quantitative analysis of the terminal QRS and ST segments from patients with sustained VT have demonstrated a 10- to 100-fold greater proportion of components in the 20 to 50 Hz range compared with the proportion in corresponding electrocardiographic segments of patients without sustained VT.16 The clinical value of advanced signal-processing techniques depends ultimately on whether or not they prospectively detect vulnerability to the development of life-threatening ventricular arrhythmias. Accordingly, to determine if frequency analysis facilitates identification of patients who will have sustained VT induced during programmed ventricular stimulation, fast-Fourier transforms (FFTs) of signal-averaged ECGs were obtained and compared prospectively with
the results of programmed ventricular stimulation in patients with sustained VT, nonsustained VT, or syncope who were referred for electrophysiologic study.

Methods

Patients studied. Electrophysiologic studies and FFT analysis of signal-averaged ECGs were performed in 58 patients. Group I comprised 20 patients with documented sustained VT or cardiac arrest not associated with new myocardial necrosis, electrolyte imbalance, or drug toxicity. Nineteen patients in group I had remote myocardial infarction and one had a cardiomyopathy. Nine of these patients have been reported previously. Group II comprised 38 patients with nonsustained VT (12 patients) or one or more episodes of syncope (26 patients) without documented sustained ventricular arrhythmias who were referred to Barnes Hospital for electrophysiologic study because of suspected arrhythmias or for diagnostic purposes. Sixteen patients in group II had remote myocardial infarction, four had coronary artery disease without evidence of infarction, six had cardiomyopathies of diverse types, five had mitral valve prolapse, and seven had no evidence of heart disease. Pertinent clinical features of patients in group I and II are summarized in Table 1. Left ventricular function was assessed with radionuclide angiography or cardiac catheterization in the 20 patients in group I and in 28 patients in group II, and by echocardiography in the remaining 10 group II patients. No other neurologic abnormalities were evident in any patient with syncope. All patients were monitored on the Barnes Hospital telemetry unit for a minimum of 72 hr before the electrophysiologic study.

### Table 1

<table>
<thead>
<tr>
<th>Characteristics of patients</th>
<th>Group I (sustained VT/VF)</th>
<th>Group II (Nonsustained VT or Syncope)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>57 ± 9</td>
<td>48 ± 11</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac pathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>Anterior</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Inferior</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>CAD without infarction</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>MVP</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>None</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Mean LVEF (%)</td>
<td>33 ± 13</td>
<td>47 ± 19</td>
</tr>
<tr>
<td>Highest grade ventricular</td>
<td></td>
<td>52 ± 17</td>
</tr>
<tr>
<td>arrhythmia documented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained VT</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Sustained VF</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Nonsustained VT</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>VPDs</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD.

MVP = mitral valve prolapse; LVEF = left ventricular ejection fraction; VF = ventricular fibrillation; VPDs = ventricular premature depolarizations.

Electrophysiologic studies. Electrophysiologic studies were performed in patients in the postabsorptive, nonsedated state after informed written consent was obtained. All antiarrhythmic drugs were discontinued at least 48 hr before the study. No patient had been treated with amiodarone. Under fluoroscopic guidance, multielectrode catheters were positioned in the high right atrium, atrioventricular junction, and right ventricular apex. Three surface ECGs were recorded simultaneously with intracardiac electrograms (Electronics for Medicine VR-16). The data were stored on analog magnetic tape (Honeywell 5600C) and printed simultaneously on a 16-channel inkjet recorder (Siemens Mingograph). Programmed ventricular stimulation was performed with a programmable stimulus and optically isolated constant current source (Bloom Associates). The stimuli were rectangular pulses 1 msec in duration and were delivered at twice diastolic threshold (<2 mA). The stimulation protocol included the introduction of single and double ventricular extrastimuli during ventricular pacing at cycle lengths (S1-S2 interval) of 600 and 400 msec. A single ventricular extrastimulus (S2) was introduced in late diastole and the S2-S3 coupling interval was decreased in 10 msec decrements until the S3 failed to capture. Double ventricular extrastimuli were introduced at a S1-S2 coupling interval 50 msec longer than the ventricular effective refractory period and a second extrastimulus (S3) was introduced at a S2-S3 coupling interval equal to the S1-S2 coupling interval. The S2-S3 interval was then decreased in 10 msec decrements until S3 failed to capture. The S1-S3 interval was then decreased by 10 msec and the process was repeated until S3 failed to capture. Ventricular burst pacing was performed at cycle lengths of 350 to 250 msec. The pacing protocol was performed at the right ventricular apex and right ventricular outflow tract. The end point was completion of the protocol or the reproducible initiation of sustained monomorphic VT (>30 sec in duration or associated with hemodynamic collapse).

Surface electrocardiographic recording. Signal averaging was performed on ECGs obtained during sinus rhythm immediately before the electrophysiologic study. The results of frequency analysis were not made available until the programmed ventricular stimulation protocol had been completed. A description of the signal-average processing system has been published in detail previously. Standard Frank X, Y, and Z lead signals were amplified approximately 1000-fold (Hewlett-Packard 1057A) with a bandwidth of 0.05 to 470 Hz. The amplitudes of the analog electrocardiographic signals were optimized to encompass the maximum ±2.5 V input range of the analog-to-digital converter. Normalized signals were digitized at 1 kHz (12-bit accuracy). The digitized data were processed with a portable cart designed for this purpose with a DEC VT 103 LSI 11/23 microcomputer system with 64 kbytes of memory, two serial communication ports, a dual floppy disk system, and a Selanar raster graphics board with joystick control.

Signal averaging. The X, Y, and Z electrocardiographic signals were averaged after passage through a template recognition program generated from a 3 sec display of normal sinus rhythm. The lead having the largest R wave amplitude was selected, the RR interval and fiducial point (peak of the R wave) were set with an adjustable cursor, and the QRS amplitudes were calculated for all three leads. All subsequent beats were tested against the template with a cross-correlating technique and accepted for averaging only if (1) the RR interval was within 20% of the previously set RR interval, (2) the QRS amplitude was within 5%, and (3) the fiducial point ±20 sample values on either side of the fiducial point had a correlation coefficient of 98% or more in comparison with the template beat. The beat immediately after a rejected beat was rejected also. Data from 100 beats were averaged and stored on a floppy disk for further processing. The X, Y, and Z leads were moni-
tored continuously in real time during averaging to allow detection of grossly noisy signals. We have demonstrated previously that a 100 beat average reduces the inherent noise level from 15 to 1.5 μV and allows detection of a 2 μV signal.14 Reference jitter did not exceed 1 msec.

**FFT analysis.** FFT analysis was performed on the terminal 40 msec of the QRS complex and ST segment of each signal-averaged X, Y, and Z lead. This region of interest was identified with the use of the computer graphics cursor and standard electrocardiographic criteria. The region of interest was multiplied by a four-term Blackman-Harris window to reduce spectral leakage.17 To enhance frequency resolution, FFT analysis was performed on the terminal QRS and ST segment as a single unit. The averaged signal was scaled before computation of the FFT to reduce variations in magnitude of the transformed data. The maximum magnitude was identified and scaled to unity. A 512-point FFT was calculated. The magnitude of the FFT was then squared to obtain the energy spectrum of the input signal.18 Data were plotted on a scale defined by the maximum of the data curve. By this method, the magnitude of the energy spectrum is determined by phase and by the voltage amplitude at the point of intersection of the computer graphics cursor that defines the terminal 40 msec of the QRS with the descending limb of the QRS complex. Thus, voltage amplitude varies among patients and with QRS configuration. As a result, scaling on the vertical axis of each spectral plot is relative and absolute values on this scale from one patient should not be compared with those from another patient. To detect smaller peaks that might be obscured by the dominant amplitudes of low-frequency components, a second plot was generated by dividing the initial scale by 500. Values exceeding those on the reduced scale were not plotted.

After FFT analysis, the data were plotted on a high-resolution plotter (Versatec, Inc.) and transferred to disk for further storage.

**Data analysis.** For each spectral plot, the data were analyzed for peaks between 20 and 50 Hz. A frequency range of 20 to 50 Hz was chosen after analysis over the bandwidth had demonstrated previously that frequencies above 70 Hz did not contribute substantially to the terminal QRS and ST segments in any group.16 In addition, because of potential 60 Hz interference, frequencies between 50 to 70 Hz were not analyzed. The area under the magnified curve between 20 to 50 Hz was divided by the area under the initial curve between 0 to 20 Hz (area ratio). This ratio defined the relative contribution of frequencies between 20 to 50 Hz to the entire signal. For patient-to-patient comparisons, individual X, Y, and Z values for the area ratios were averaged after log transformation and mean values were expressed as antilogs multiplied by a constant \(1 \times 10^3\) to facilitate graphic display. The reproducibility of the results of this method was evaluated in five normal subjects in whom data were recorded serially over an interval of 3 months. All subjects had area ratio values less than 20. Mean values of individual area ratios varied by only 1.3 units.

To determine if frequency analysis detects patients in whom sustained VT can be induced, area ratios were first obtained in patients with sustained VT clinically (group I) and compared with the results of programmed ventricular stimulation. A logistic regression was used to help define normal and abnormal area ratio values based on the response to programmed ventricular stimulation. The predictive value of FFT results in identifying patients in whom sustained monomorphic VT can be induced during programmed ventricular stimulation was then assessed prospectively in patients in group II.

**Statistical analysis.** Data are presented as mean ± SD. Statistical analysis was performed with the Statistical Analysis System (SAS).19, 20 Statistical comparisons of group means were performed with t tests. Computation of the sensitivity and specificity of the simultaneous prediction of inducibility by several independent variables was performed with a stepwise logistic regression with the use of PROC LOGIST, a user-contributed SAS procedure. Logistic regression also provided an assessment of the relative importance of left ventricular ejection fraction and FFT results, and the presence or absence of prior myocardial infarction and FFT results, in predicting inducibility of VT in each group of patients. Sensitivity was calculated as the percent of patients in whom sustained VT was induced who were correctly identified by FFT analysis and specificity was calculated as the percent of patients in whom sustained VT was not induced who were correctly identified by FFT analysis. Because of the highly skewed nature of FFT data, statistical comparisons were made after data transformation to normality. FFT data were first ranked and the ranks were then transferred to normality by the method of Blom.21 Significance refers to a p value < .05.

**Results**

Analysis of energy spectra of signal-averaged X, Y, and Z electrocardiographic recordings showed significant differences (p < .0001) in area ratio values of the terminal 40 msec of the QRS and ST segments of patients in whom sustained VT was induced during programmed ventricular stimulation and those in whom VT was not induced. These differences reflect a relative increase in the contribution of frequency components between 20 to 50 Hz. As expected, comparison of values for the area under the curve between 0 to 20 Hz did not distinguish patients in whom sustained VT was induced (19,917 ± 4999) from patients in whom it was not induced (23,187 ± 4123) or from normal subjects (20,800 ± 2490).

**Studies in patients in group I.** Representative plots of squared FFT data from the terminal 40 msec of the QRS complex and ST segments of group I patients (those with known spontaneous sustained VT) are shown in figure 1. Each panel depicts magnitude vs frequency plots of the terminal 40 msec of the QRS complex and ST segments of signal-averaged electrocardiographic complexes recorded from orthogonal leads along with values for the area ratios. In each lead the terminal QRS and ST segment from the patient in whom sustained VT was induced contains relatively more high-frequency components than the complex from the patient in whom sustained VT was not induced. Twenty patients presented with documented sustained VT. Eighteen patients had sustained monomorphic VT induced during programmed ventricular stimulation. Twelve-lead ECGs obtained during sustained VT occurring clinically and that induced during programmed ventricular stimulation were identical in the 12 patients in whom the spontaneous morphology was documented. In the remaining six patients, 12-lead ECGs of the clinical VT were not available for comparison. In two patients in group I VT was not
inducible. One patient had monomorphic sustained VT during an exercise stress test and the other had a witnessed cardiac arrest.

Comparisons between values for the area ratios and the results of programmed ventricular stimulation for patients in group I are shown in figure 2. A logistic regression with inducibility as the dependent variable was used to determine a range of area ratio values that would define normal and abnormal FFT results. All 18 patients in group I in whom sustained VT was induced had area ratio values greater than 20. The two patients in whom VT was not induced had area ratio values less than 20. To test whether or not the results of FFT analysis were a sensitive predictor of inducibility, area ratio values greater than 20 were defined as abnormal. The predictive value of area ratio values greater than 20 in identifying patients in whom sustained VT would be induced during programmed ventricular stimulation was tested prospectively in patients in group II.

Studies in patients in group II. Representative plots of energy spectra of the terminal QRS and ST segments of group II patients who had nonsustained VT clinically are shown in figure 3. In each lead, the terminal QRS and ST segment from the patient in whom sustained monomorphic VT was induced during programmed ventricular stimulation contains relatively more high-frequency components, as reflected by large area ratio values, than the complex from the patient in whom sustained VT was not induced. Representative plots of FFT results in group II patients with syncope and the results of programmed ventricular stimulation are illustrated in figure 4. Analysis of the terminal QRS and ST segments demonstrated a marked increase of frequency components between 20 and 50 Hz in the patient in whom sustained VT was induced compared with the frequency components in this range in the patient in whom VT was not induced.

Thirty-eight patients with nonsustained VT or syncope (group II) were referred for programmed ventricular stimulation because of suspected ventricular arrhythmias. Comparisons between values for the area ratios and the results of programmed ventricular stimulation for patients in group II are shown in figure 2. Frequency analysis of signal-averaged ECGs obtained in patients in sinus rhythm was performed immediately before programmed ventricular stimulation and the area ratio criteria defined in group I patients was applied to classify the FFT data as normal or abnormal. Twelve patients in group II had area ratio values greater than 20. Five of these patients had sustained monomorphic VT induced during programmed ventricular stimulation. The mean rate of sustained VT induced in

FIGURE 1. Energy spectra of the terminal QRS and ST segments from a patient in group I in whom sustained VT was induced during programmed ventricular stimulation (right) and from a patient in group I in whom it was not induced (left). Shown in each panel are the initial (left scale, solid curve) and magnified (right scale, broken curve) energy vs frequency plots of the terminal 40 msec of the QRS complex and ST segment of signal-averaged X, Y, and Z leads and values for the area ratio. To facilitate graphic display, values for the area ratio of each lead have been multiplied by a constant (1 × 10²). In each lead, the combined terminal QRS and ST segment from the patient in whom sustained VT was induced contains a substantially greater proportion of components in the 20 to 50 Hz range compared with corresponding ECG segments from the patient in whom sustained VT was not induced.
patients in group II was not significantly different from that of VT induced in group I (254 ± 35 vs 294 ± 70 msec). All five patients had organic heart disease (a prior myocardial infarction, coronary artery disease without infarction, mitral valve prolapse, or cardiomyopathy). Seven patients had area ratio values greater than 20, but sustained VT was not induced. Asymptomatic nonsustained VT was induced in four of these patients, nonsustained VT with symptoms of lightheadedness was induced in one patient, and no arrhythmias were induced in two patients. None of the remaining 26 patients in group II with area ratio values less than 20 had sustained VT induced during programmed ventricular stimulation. Electrophysiologic studies demonstrated atrioventricular conduction abnormalities in three patients and a vasovagal reaction in one patient. Asymptomatic nonsustained VT was induced in six patients, and one patient had enhanced atrioventricular nodal conduction with a rapid ventricular rate during atrial fibrillation. No abnormalities were found in the remaining 15 patients. Ventricular fibrillation was not induced in any patient. Thus, the results of frequency analysis correctly predicted the response to programmed stimulation in 31 of 38 patients (82%) with nonsustained VT or syncope. Each of the five patients in whom sustained VT was induced and 26 of the 33 patients in whom it was not induced were identified correctly. The sensitivity of the prediction of inducibility was 100%, and specificity was 77%.

Comparison with other determinants of inducibility. To assess the relative importance of left ventricular ejection fraction, FFT results, and clinical presentation (group I or II) with regard to the results of programmed ventricular stimulation, a stepwise logistic regression analysis was performed with the use of these three variables as the potential predictors of inducibility. These independent variables were entered in a stepwise manner, with the most significant variable selected first. All variables with a p value < .2 after adjusting for the effect of previously included variables were added to the model. Only clinical presentation (p < .003) and results of FFT analysis (p < .005) satisfied the .2 criterion. When the logistic regression was repeated with a model requiring left ventricular ejection fraction to be entered first, both clinical presentation (p < .003) and FFT results (p < .01) were highly significant after adjusting for the effect of the other two variables. The adjusted significance level of ejection fraction was .425. Because both FFT results and clinical presentation were significant after adjustment for ejection fraction while the converse was not the case, left ventricular ejection fraction is the least powerful descriptor of inducibility among the three variables considered. Comparisons of values of left ventricular ejection fraction with area ratio values and the results of programmed ventricular stimulation are shown in figures 5 and 6, respectively. Abnormal FFT values and the initiation of sustained VT were observed in patients with a wide range of left ventricular ejection fractions.

A similar analysis was performed to assess the relative importance of the presence of myocardial infarction and FFT results in patients in group II. This analysis was performed within group II because 19 of 20 group I patients had a history of myocardial infarction. A logistic model was used for the prediction of inducibility of VT. The potential predictors, FFT results and the presence of a prior myocardial infarction, were entered only if they had a significance level less than .2. The result was that FFT results were entered into the model (p = .0153), while myocardial infarction did not meet the .2 criterion. When the model required
that myocardial infarction be entered first, the p value for FFT results after adjusting for the presence of infarction was .019, whereas the significance level of infarction after adjusting for FFT was .391. Thus, within group II, FFT results were clearly more important in predicting the response to programmed ventricular stimulation than was the presence of a prior myocardial infarction.

Discussion

Several investigators have reported the results of electrophysiologic testing in patients with syncope or nonsustained VT.\textsuperscript{1-2} The incidence of induction of ventricular arrhythmias during programmed ventricular stimulation in patients without documented sustained VT depends on patient selection, the definition of inducibility, and the stimulation protocol. Structural heart disease has been reported in approximately half of patients with syncope or nonsustained VT, induction of nonsustained VT in 6% to 32%, and induction of sustained VT in 0 to 21%. In view of the expense, low incidence of induction of sustained VT, and potential morbidity of electrophysiologic testing, improved noninvasive methods for selection of patients with suspected sustained ventricular arrhythmias for programmed ventricular stimulation would facilitate their management. Recently, Breithardt et al.\textsuperscript{22} correlated the presence of late potentials detected with signal-processing techniques in the time domain with the results of programmed ventricular stimulation in patients without documented sustained VT. Late potentials were found to be a sensitive predictor of the initiation of four or more repetitive ventricular responses; however, the study did not address whether the presence of late potentials differentiated patients in whom sustained VT was induced from those in whom it was not induced.

Quantitative differences in the frequency content of signal-averaged ECGs from patients with and without sustained VT have been reported.\textsuperscript{14-16} The quantitative approach developed offers promise as a means of noninvasively identifying patients at risk for developing sustained ventricular arrhythmias. In this study, we tested the hypothesis that the results of FFT analysis of signal-averaged ECGs would improve selection of patients for programmed ventricular stimulation. The relationship between the results of FFT analysis and the response to programmed ventricular stimulation was defined first in patients with known sustained VT (group I) since results of studies by others have demonstrated that sustained VT comparable to that occurring clinically can be induced in up to 90% of patients.\textsuperscript{23, 24}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3}
\caption{Energy spectra of the terminal QRS and ST segments from a patient in group II having nonsustained VT clinically in whom sustained VT was induced during programmed ventricular stimulation (right) and from a patient having nonsustained VT clinically in whom sustained VT was not induced (left). Data are displayed in a format similar to that used in figure 1. In each lead, the terminal QRS and ST segments from the patient in whom sustained VT was induced contain a substantially larger fraction of components in the 20 to 50 Hz range compared with corresponding ECG segments from the patient in whom sustained VT was not induced.}
\end{figure}
FIGURE 4. Energy spectra of the terminal QRS and ST segments from a patient in group II with syncope in whom sustained VT was induced during programmed ventricular stimulation (right) and from a patient with syncope in whom it was not induced (left). Data are displayed in a format similar to that used in figure 1. In each lead, the terminal QRS and ST segments from the patient in whom sustained VT was induced contain a substantially larger fraction of components in the 20 to 50 Hz range compared with corresponding ECG segments from the patient in whom sustained VT was not induced.

FIGURE 5. Comparison of left ventricular ejection fractions and normal (closed circles) and abnormal (open circles) FFT results in patients with sustained VT clinically (group I) and those with nonsustained VT (NSVT) or syncope (group II). Abnormal FFT results were observed in patients in groups I and II with a wide range of ejection fractions.

FIGURE 6. Comparison of left ventricular ejection fractions and the response to programmed ventricular stimulation (PVS) in patients with sustained VT clinically (group I) and those with nonsustained VT (NSVT) or syncope (group II). Open circles represent patients in whom sustained VT was induced and closed circles represent patients in whom it was not induced.
The predictive value of the results of FFT analysis in identifying patients in whom sustained VT would be induced during programmed ventricular stimulation was then determined prospectively in patients without documented sustained VT (group II). Patients with documented or suspected sustained ventricular arrhythmias within 2 weeks of acute myocardial infarction were excluded. The stimulation protocol included single and double ventricular extrastimuli from two ventricular sites with the expectation that sustained VT would be induced with a high degree of specificity.\textsuperscript{23, 24} Triple ventricular extrastimuli were not used to avoid induction of nonclinical arrhythmias in patients without documented sustained VT.\textsuperscript{25–28} Reproducible initiation of sustained monomorphic VT was chosen as an end point because it is generally accepted as evidence that an arrhythmia substrate is present, and is highly specific in patients with a clinical history of sustained VT.\textsuperscript{23–25} Induction of nonsustained VT was excluded as an end point since its clinical significance remains unknown.\textsuperscript{26–29}

Concordance between the results of FFT analysis and the response to programmed ventricular stimulation was consistent. Analysis of energy spectra of signal-averaged ECGs showed significant differences (p < .0001) between area ratio values of the terminal QRS and ST segments of patients in whom sustained VT was induced and those in patients in whom VT was not induced. Overall, FFT results correctly predicted the response to programmed ventricular stimulation in 51 of 58 patients (88%). When definitions of normal and abnormal FFT results determined in group I (training set) were prospectively tested in group II (test set), FFT results correctly predicted the response to programmed ventricular stimulation in 31 of 38 patients (82%). Moreover, in no group II patient with an area ratio value less than 20 was VT inducible, while all five patients in whom sustained VT was induced had area ratio values greater than 20. In seven patients in group II area ratio values were abnormal but VT was not inducible. These patients may have a substrate for sustained VT that has not yet been manifested clinically, but the prognostic significance of this finding has yet to be determined.

Results of FFT analysis were independent of other determinants of inducibility of VT, including left ventricular ejection fraction and prior myocardial infarction. Most patients with spontaneous sustained VT have a history of prior myocardial infarction and, as a group, patients with spontaneous sustained VT have lower ejection fractions than a group of patients with prior myocardial infarction without sustained VT.\textsuperscript{11, 12, 14, 16} In this study, the mean left ventricular ejection fraction in group I was, as expected, lower than the mean value in group II. However, within each group the values of left ventricular ejection fraction ranged widely. Abnormal FFT results (figure 5) and initiation of sustained VT (figure 6) were observed in patients in both groups with a wide range of ejection fractions. Moreover, in patients in group II, the results of FFT and concordance with the response to programmed ventricular stimulation were independent of a history of prior myocardial infarction. Thus, FFT results did not simply identify patients with a history of prior myocardial infarction and low left ventricular ejection fractions, but also provided improved prediction of an individual response to programmed ventricular stimulation when compared with more traditional predictors used for groups of patients.

In addition to FFT results, the mode of clinical presentation was identified as an independent predictor of the response to programmed ventricular stimulation. This finding confirms the results of studies by others that 85% to 90% of patients with documented sustained VT clinically have sustained VT induced during programmed ventricular stimulation\textsuperscript{22–29} and that 0 to 20% of patients without sustained VT documented clinically referred for electrophysiologic study have sustained VT induced.\textsuperscript{17} In this study, 18 of 20 patients (90%) in group I had sustained VT induced compared with five of 38 patients (13%) in group II. Prospective application of FFT criteria derived from patients in group I correctly identified all five patients in group II in whom sustained VT was induced. Moreover, in no patient in group II with normal FFT results was sustained VT induced. Thus, 38 patients presenting clinically with nonsustained VT or syncope underwent invasive electrophysiologic study to identify five patients in whom sustained VT was induced. Based on FFT results and the observed concordance with the results of programmed ventricular stimulation, only 12 patients in group II would have required invasive electrophysiologic study to exclude the possibility of initiation of sustained VT.

Judging from the results of this study, frequency analysis of signal-averaged ECGs is a sensitive, noninvasive method for identifying patients who may have sustained VT induced during programmed ventricular stimulation. The approach developed offers promise for improving selection of patients at risk for sustained VT who require programmed ventricular stimulation.

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