Abnormal signal-averaged electrocardiograms in patients with nonischemic congestive cardiomyopathy: relationship to sustained ventricular tachyarrhythmias

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ABSTRACT We assessed whether signal-averaged electrocardiography could identify patients with sustained ventricular arrhythmias in 41 patients with non-ischemic cardiomyopathy. Twelve of these patients presented with sustained ventricular arrhythmia and 29 patients had no history of sustained ventricular arrhythmias. The mean ejection fractions in the groups were 30 ± 9% and 24 ± 9%, respectively. Results were compared with signal-averaged electrocardiograms in 55 normal individuals. The filtered QRS duration was longest in patients with sustained ventricular arrhythmias (130.2 ± 19.5 vs 105.0 ± 13.1 msec in the group without sustained ventricular arrhythmia, p < .001 and 95.9 ± 9.1 in the normal group, p < .001). The voltage in the last 40 msec of the filtered QRS was lower in the sustained ventricular arrhythmia group (11.3 ± 9.3 μV) than the group without sustained ventricular arrhythmia (53.5 ± 28.3 μV; p < .001) or the normal group (53.7 ± 25.2 μV; p < .001). Eighty-three percent of patients in the sustained ventricular arrhythmia group had an abnormal signal-averaged electrocardiogram characterized by both a long filtered QRS duration and a late potential of low voltage level; only 2% of normal subjects and 14% of patients without sustained ventricular arrhythmias had an abnormal signal-averaged electrocardiogram. The signal-averaged electrocardiogram can identify patients with nonischemic congestive cardiomyopathy and sustained ventricular arrhythmias.

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PATIENTS with congestive cardiomyopathy have a high incidence of life-threatening ventricular arrhythmias and sudden cardiac death. To date, however, no clinical predictors of sudden cardiac death have been identified.1 In recent years, signal-averaged electrocardiography has developed as a technique for the noninvasive evaluation of intracardiac conduction. In patients with coronary artery disease, the presence of abnormalities of the signal-averaged electrocardiogram such as low voltage, high-frequency potentials late in the QRS complex and prolonged QRS duration has successfully identified patients with sustained ventricular tachycardia.2-8 Thus, this technique may be useful in the noninvasive identification of patients with nonischemic disease who are prone to ventricular arrhythmias.

In this study, we characterize the signal-averaged electrocardiogram in 41 patients with nonischemic congestive cardiomyopathy with and without sustained ventricular arrhythmias and compare them with the signal averaged electrocardiograms of 55 normal individuals.

Methods

Patients. The study population consisted of 26 men and 15 women with nonischemic congestive cardiomyopathy. The mean age was 50 ± 14 years (mean ± SD). All patients met the following criteria for nonischemic congestive cardiomyopathy: (1) left ventricular ejection fraction of 45% or less by angiographic left ventriculography (14 patients), radionuclide angiography (25 patients), or two-dimensional echocardiography.
(two patients), \(^9\) (2) exclusion of coronary artery disease by (a) absence of significant coronary stenosis by angiography (25 patients) or (b) absence of history of angina or myocardial infarction (16 patients). In addition, no patient had left ventricular dyskinesis. The cause of congestive cardiomyopathy was idiopathic in 35 patients, related to alcohol abuse in five patients, and doxorubicin toxicity in 1 patient. Patients with bundle branch block were not included because of possible masking of low voltages late in the filtered QRS complex. \(^{10}\)

The study group was divided according to clinical arrhythmia presentation. Twelve patients presented with sustained, uniform ventricular tachycardia (eight patients), defined as a tachycardia lasting longer than 30 sec, or cardiac arrest and ventricular fibrillation (four patients). These patients made up the sustained VT/VF group. Twenty-nine patients had no history of sustained ventricular arrhythmias and made up the no sustained VT/VF group.

The normal group consisted of 55 individuals without clinical evidence of organic heart disease by history, physical examination, and routine electrocardiography. The mean age for the control group was 36 ± 11 years.

**Signal averaging.** Bipolar X, Y, and Z leads were each recorded for 133 sec and amplified by a high-gain, low-noise amplifier. Each signal was then converted to digital information at 1000 samples/sec with a resolution of 1 to 2.5 \(\mu\)V. A bandpass filtered Z lead served as a reference signal to set a reference time for signal averaging. Signal averaging was performed after each new beat was tested with a template-recognition program to reject ectopic and grossly noisy beats. Acceptable beats were signal averaged over a 512 msec segment beginning 100 msec before the QRS complex. Each averaged lead was then filtered (>25 Hz) in a bidirectional fashion to eliminate impulse ringing of the filter at the end of the QRS complex. \(^6\) The three filtered signals were then combined into a vector magnitude, \(V(X^2 + Y^2 + Z^2)^{1/2}\), which allowed the detection of high-frequency voltage in any lead. This filtered vector magnitude is referred to as the "filtered QRS complex." The QRS onset and end were determined by a computer algorithm that found the points at which the mean filtered voltage, measured over a 5 msec interval, exceeded the mean plus 3 SDs of the noise sample. \(^6\) The noise sample (20 to 80 msec) was located in the PR segment for the filtered QRS onset and in the ST segment for the end of the QRS. All voltages reported were measured by the root-mean-square method. Total filtered QRS voltage refers to the amplitude measured over the entire filtered QRS duration. The voltage for the last 40 msec of the filtered QRS complex was calculated separately. These techniques were derived from a study of patients with coronary artery disease. \(^6\)

A late potential is defined as a waveform with voltage not exceeding 25 \(\mu\)V in the last 40 msec of the filtered QRS complex. An abnormal signal-averaged electrocardiogram is defined as that having both a filtered QRS duration of 110 msec or more and a late potential. \(^6\)

Five patients in the sustained VT/VF group and two patients in the no sustained VT/VF group were studied while taking antiarrhythmic drugs. Antiarrhythmic agents have been shown to prolong the filtered QRS complex by 5 to 15 msec, but have no influence on the incidence of late potentials. \(^11\)

**Data analysis.** Results were analyzed with the unpaired \(t\) test, Fischer's exact test, chi square with or without Yate's correction, and \(R\) by \(C\) contingency analysis. Continuous data are expressed as mean ± SD.

**Results**

**Patient characteristics.** The ejection fraction in the study group was 26 ± 10%. The ejection fraction in the sustained VT/VF group was 30 ± 9%, and that in the no sustained VT/VF group was 24 ± 9% (\(p = NS\)).

**FIGURE 1.** Examples of signal-averaged electrocardiograms obtained from each of the three patient groups. On top are the signal-averaged bipolar \(x\), \(y\), and \(z\) leads shown at high gain. The filtered QRS complex appears on the bottom. The dashed lines indicate the end points of the filtered QRS complex as determined by a computer algorithm. The example from a normal individual shows a symmetric filtered QRS complex lasting less than 100 msec and containing no persistent low-amplitude activity in the last 40 msec. The example from a patient with congestive cardiomyopathy and no sustained ventricular arrhythmia shows a normal filtered QRS complex and no late potential. The example from a patient with congestive cardiomyopathy and sustained ventricular arrhythmia shows a prolonged filtered QRS duration with low-level late potential at the end of the filtered QRS complex.
Eleven of 16 patients (69%) in the no sustained VT/VF group who underwent 24 hr ambulatory electrocardiographic monitoring had nonsustained ventricular tachycardia lasting up to 10 beats.

**Signal averaging.** Examples of signal processing from individuals in the normal, cardiomyopathy and no sustained VT/VF, and cardiomyopathy and sustained VT/VF groups are illustrated in figure 1. Patients with cardiomyopathy and no sustained arrhythmias usually had a filtered QRS duration similar to that of normal subjects and no late potentials. Patients with sustained arrhythmias usually had a prolonged filtered QRS duration with a late potential. Ten of 29 (34%) patients with no sustained VT/VF had mildly prolonged filtered QRS duration (figure 2).

The filtered QRS duration was longest in patients in the sustained VT/VF group (130.2 ± 19.5 vs 105.0 ± 13.1 msec in the no sustained arrhythmia group, p < .001) and vs 95.9 ± 9.1 in the normal group, p < .001) (figure 3). Of note, 11 patients (92%) in the sustained VT/VF group had a QRS duration of 110 msec or more, in contrast to 10 patients (34%) in the no sustained VT/VF group (p < .001) and three patients (5%) in the normal group.

The voltage in the last 40 msec of the filtered QRS (figure 4) was 53.7 ± 25.2 μV in the normal and 53.5 ± 28.3 μV in the no sustained VT/VF group. The mean voltage in the sustained VT/VF group was significantly lower at 11.3 ± 9.3 μV (p < .001). Eighty-three percent of patients in the sustained VT/VF group had a late potential compared with 17% of those in the no sustained VT/VF group (p < .001) and 7% of those in the normal group.

The total QRS voltage was similar in the normal and the cardiomyopathy no VT/VF groups (figure 5), with values of 109.0 ± 29.1 and 102.7 ± 35.1 μV, respectively. The sustained arrhythmia group had lower total voltage (71.4 ± 17.0 μV, p < .005), but there was considerable overlap between groups.

Eighty-three percent of patients with sustained VT/VF entered sustained VT/VF within 10 beats of the first sampled beat. No patient with nonsustained VT/VF progressed to sustained VT/VF. The mean time from initial to sustained VT/VF was 39 ± 19 beats.

**Figure 2.** Further examples of signal-averaged electrocardiograms from the three patient groups. The example from a patient with cardiomyopathy and no sustained ventricular arrhythmia shows a prolonged filtered QRS complex and no late potential.

**Figure 3.** Values for filtered QRS duration in the three study groups. The dashed lines represent the mean value for all patients in each group. The dotted line represents a threshold of 110 msec.
FIGURE 4. Values for filtered QRS voltage in the last 40 msec. The dotted line represents mean values for patients in each group. The dashed line represents a voltage threshold of 25 μV demonstrating low-level late potentials below it.

VT/VF had abnormal signal-averaged electrocardiograms, i.e., both long filtered QRS duration and a late potential. Only 2% of normal subjects and 14% of patients with no sustained VT/VF had abnormal signal-averaged electrocardiograms. This difference between the cardiomyopathy groups was highly significant ($\chi^2 = 15.3; p < .001$). The combined criteria of a QRS duration of 110 msec or more and presence of a late potential identified patients with cardiomyopathy and sustained ventricular arrhythmias with a sensitivity of 83% and a specificity of 86% in this study.

Exclusion of the seven patients who were taking antiarrhythmic medications did not alter the results. Five of six patients (83%) with sustained VT/VF had an abnormal signal-averaged electrocardiogram in contrast to four of 27 (15%) patients without sustained VT/VF ($p < .003$).

Of the 11 patients with nonsustained ventricular tachycardia, two patients had abnormal signal-averaged electrocardiograms (18%). Additionally, one patient had a late potential only and two patients had a QRS duration of 110 msec or more.

The QRS duration determined by the routine surface electrocardiogram did not distinguish between the cardiomyopathy groups. Fifty-five percent of patients in the no sustained VT/VF group had a routine surface QRS duration of 100 msec or more compared with 67% of patients in the sustained VT/VF group ($p = NS$). Patients with low-level late potentials on the signal-averaged electrocardiogram had ejection fractions similar to those of patients without late potentials (27.7 ± 9.4% vs 24.5 ± 9.6%, $p = NS$).

Discussion

Signal-averaged electrocardiography appears to be a useful test for identifying patients with coronary artery disease and ventricular tachycardia.2-8 This study extends the application of this technique to patients with nonischemic cardiomyopathy and demonstrates that abnormalities of the signal-averaged electrocardiogram can identify patients with sustained ventricular arrhythmias. Patients with cardiomyopathy have longer filtered QRS durations than normal individuals, and the presence of a long filtered QRS duration together with a late potential differentiated the cardiomyopathy population with sustained ventricular arrhythmias from those with no sustained ventricular arrhythmias. This distinction is not discernible on the routine electrocardiogram and most likely relates to the ability to detect microvolt-level high-frequency potentials by the signal-averaging technique.

Signal-averaged electrocardiography has developed as a noninvasive measure of late and slow activation, which has been associated with reentrant arrhythmias.12-15 Low-level late potentials detected by signal-averaging techniques have been correlated with localized areas of delayed ventricular activation in animal and human preparations.10, 16, 17 Additionally, fractionated electrograms have been recorded by endocardial and epicardial mapping techniques in patients with...
ventricular tachycardia and coronary artery disease\textsuperscript{18, 19} as well as in those with right ventricular dysplasia, a diffuse myocardial process.\textsuperscript{10, 20-22} These fractionated electrograms have been correlated with the surface late potential and the duration of these fragmented electrograms has correlated with the surface filtered QRS duration.\textsuperscript{10, 16} The precise role of these abnormal areas of myocardium in arrhythmogenesis has not been established, but it appears that among patients with coronary disease and prior myocardial infarction, the extent and severity of fragmentation is greatest in patients with recurrent sustained ventricular tachycardia.\textsuperscript{23, 24}

The substrate for ventricular arrhythmias in patients with nonischemic congestive cardiomyopathy has not been characterized. We recently reported data that supported reentry as a mechanism for uniform ventricular tachycardia in patients with idiopathic cardiomyopathy based on initiation and termination of tachycardias and the resetting phenomenon in response to programmed stimulation.\textsuperscript{25} Fontaine et al.\textsuperscript{20} have reported delayed and abnormal electrograms both endocardially and epicardially in patients with right ventricular dysplasia, suggesting that slow conduction is an element of arrhythmogenesis in that patient population. We present evidence here that patients with nonischemic congestive cardiomyopathy and sustained ventricular arrhythmias have a detectable electrophysiologic substrate. Detection of low-level late potentials and a prolonged filtered QRS duration implies that these patients have delayed ventricular activation. Whether this slow conduction participates in arrhythmogenesis or merely reflects the severity and extent of diseased myocardium remains to be determined. Describing the anatomic and electrophysiologic characteristics of this slow conduction requires further investigation.

The abnormalities of the signal-averaged electrocardiogram we describe appear to be markers of electrical instability in patients with non-ischemic congestive cardiomyopathy. The utility of this test as a noninvasive predictor of risk in this patient population awaits prospective evaluation.

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References


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