Significance of Discordant ST Alternans in Ventricular Fibrillation

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With the use of epicardial mapping, we investigated the electrical alternans of the ST segment during acute myocardial ischemia and studied the difference in ST alternans between dogs with resultant ventricular fibrillation and those without it. During the 7-minute occlusion of the left anterior descending coronary artery below its first diagonal branch, 60 epicardial unipolar electrograms were recorded simultaneously at 1-minute intervals by a computerized mapping system. ST alternans was found in the eight dogs we observed. The amplitude of ST alternans (difference in the ST segment elevation of two consecutive electrograms) was greater in dogs with ventricular fibrillation ($n=4$) than in those without it ($n=4$) ($3.92 \pm 1.24$ versus $0.58 \pm 0.49$ mV, $p<0.05$). Three of the four dogs with ventricular fibrillation demonstrated discordant ST alternans (i.e., adjacent leads were out of phase). Results from the present study indicate that an increased amplitude and discordance of ST alternans during acute myocardial ischemia are related to ventricular fibrillation and act as indicators of time and spatial unevenness of ventricular repolarization. (Circulation 1990;82:2185–2189)

Electrical alternans refers to the occurrence of different configurations of electrocardiographic waveform morphology on an every-other-beat basis. The occurrence of ST alternans has been observed frequently in experimental animals and in patients with either prolonged QT syndrome or Prinzmetal’s angina. Many studies have demonstrated that ST alternans is frequently followed by ventricular arrhythmias. However, few reports have considered the phase and distribution of the alternans from the viewpoint of their relation to malignant ventricular arrhythmias. The purpose of the present study was to determine whether there is a correlation between the property of electrical alternans and susceptibility to ventricular fibrillation.

Methods

Eight mongrel dogs (weight, 11–20 kg) were anesthetized by intravenous administration of sodium pentobarbital (25 mg/kg body wt). Additional pentobarbital was given as needed to maintain deep anesthesia.

Respiration with room air and oxygen was maintained by an air-cuffed endotracheal tube connected to a constant-volume respirator. Body temperature was maintained by a heating pad. Aortic pressure was monitored via an intra-arterial catheter. Another catheter was placed into a femoral vein for infusion of additional pentobarbital and fluid. A recorder was used to monitor a lead II surface electrocardiogram and systemic arterial pressure. Surgical preparation for each of the experiments was begun with a fifth intercostal space thoracotomy. The pericardium of each dog was incised, and the heart was cradled in the opened pericardium. In these experiments, the sinus node was crushed and the right atrial appendage was paced by bipolar epicardial electrodes at a fixed cycle length of 440 msec. To produce myocardial ischemia, the left anterior descending coronary artery at the level just distal of its first diagonal branch was prepared for occlusion by passing a ligature around the artery. We attached 60 silver electrodes through a sock to the epicardium and to the area covering the region of the entire left and right ventricles. The electrodes were placed in six rows and 10 columns and spaced at 10-mm intervals. During the 7-minute occlusion, we recorded 60 epicardial unipolar electrograms (in reference to Wilson’s central terminal) simultaneously at 1-minute intervals using a 64-channel multiplexer recording and data processing system.

Our system consisted of the following components: 1) an input box with a total of 64 buffer preamplifiers;
2) a main unit with multiplexing modules, an analog-to-digital (A-D) and a digital-to-analog (D-A) converter, a 16-Mbyte random access memory (RAM), and a central processing unit; and 3) an NEC PC9801 personal computer (NEC, Tokyo, Japan). Each input signal with respect to the Wilson's central terminal was channeled through its own amplifier. The following data acquisition steps were then executed within the sampling interval of 0.5, 1, 2, or 4 msec. First, the 64 potentials were scanned by multiplexing modules. Second, these data were digitized into 10 bits (3 \(\mu\)sec/channel; a sign bit plus 9 bits). Third, the 4,000 sampled digitized data of each of the 64 leads were stored in the data area of RAM, using a direct memory access (0.6 \(\mu\)sec/channel). Finally, all of the digitized data were transmitted to the personal computer and displayed on the computer terminal. From baseline corrected data, isopotential maps were displayed on the computer terminal after designating the suitable equipotential interval. Shown on the maps are the epicardial distribution of ST elevation and the amplitude of ST alternans. The amplitude of alternans was represented in terms of the differences in the voltage of ST elevation of two consecutive potentials in epicardial electrograms. ST segment elevation was measured 40 msec after the end of the QRS complex. The voltage of the ST segment at each of 60 electrode sites was then subtracted from that of the next heart beat. In electrograms recorded from adjacent leads, when ST alternans was in phase, we considered the ST alternans as concordant; when it was out of phase, we considered the ST alternans as discordant. The array of the map is shown in Figure 1. The ST alternans was evaluated only in the leads showing ST elevation.

Statistics

Mann-Whitney's \(U\) test was used to compare differences. Probability values of less than 0.05 were considered statistically significant.

Results

Figure 2 shows the isopotential maps of the amplitude of ST alternans from one of the dogs with ventricular fibrillation. The progressive change of the amplitude of ST alternans can be seen. The map for control is located in the upper left portion, and the map after 6 minutes of ligation is shown in the lower right portion. The dotted area represents the area of ST elevation. Isopotential contour lines that indicate the amplitude of ST alternans are drawn for increments of 0.5 mV. Numbers on the maps show maximum amplitude of ST alternans. The area of ST elevation increased with time, and the maximum amplitude of ST alternans also increased. In the lower right corner of Figure 2 on the 6-minute map, we show the positions of two consecutive electrograms that were recorded from adjacent leads. This displays discordant ST alternans because when the lower ST segment appeared in one lead, the higher ST segment appeared in the adjacent lead. When the zero line runs inside of the area of ST elevation with a dense contour line, the region surrounding the zero line shows the location of the discordant ST alternans.

In the present study, ventricular fibrillation occurred in four of the eight dogs. The electrical alternans of ST segments was found in all eight dogs. Figure 3 shows isopotential maps of the amplitude of ST alternans that we recorded either just before the occurrence of ventricular fibrillation or, in dogs without ventricular fibrillation, 7 minutes after ligation. The dotted areas show the area of ST elevation, and the isopotential contour lines indicate the amplitude of ST alternans. The maps from contour lines are drawn in increments of 0.5 mV. The four dogs with ventricular fibrillation are shown on the right side. There is no statistical difference in the size of the area and magnitude of ST elevation between the dogs with ventricular fibrillation and those without (maximum magnitudes of ST elevation in the dogs with ventricular fibrillation were 22.75, 10.8, 7.6, and 14.44 mV; those in the group without were 12.22, 7.36, 12.6, and 4.98 mV). The amplitude of ST alternans (differences in the ST segment elevation of two consecutive electrograms) were greater in dogs with ventricular fibrillation than in those without (maximum amplitudes of ST alternans among the 60 leads in the group with ventricular fibrillation were 3.73, 5.65, 2.73, and 3.55; these in the group without were 0.68, 0.15, 1.23, and 0.25 mV). All dogs without
ventricular fibrillation demonstrated concordant ST alternans, whereas three of the four dogs with ventricular fibrillation (dogs 5, 6, and 8) demonstrated discordant ST alternans. The number of leads showing discordant ST alternans in dogs with ventricular fibrillation were six in dog 5, four in dog 6, zero in dog 7, and four in dog 8.

Discussion

Many reports have shown that the alternans of ST segments frequently occurs in experimental ischemic myocardium.\textsuperscript{1,3,4–6,9,11} Many studies have demonstrated that ST alternans is frequently followed by ventricular arrhythmias.\textsuperscript{1–6} Although ST alternans has been reported repeatedly, few articles have considered the phase and distribution of ST alternans that are related to the development of malignant ventricular arrhythmias. We used a computerized epicardial mapping system to demonstrate the properties of the ST alternans in relation to malignant ventricular arrhythmias.

Our experiments demonstrated that increased amplitude and discordance of ST alternans during early acute myocardial ischemia were related to development of ventricular fibrillation. There was no significant difference of the mean level of the ST segment between the dogs with ventricular fibrillation and those without it. The discordant ST alternans was most frequently found in the peripheral region of the ischemic area.

The electrical alternans of surface electrograms during ischemia was accompanied by an alternans in action potential amplitude and duration.\textsuperscript{9} Hashimoto et al also reported that the discordant ST alternans was accompanied by discordant alternation of the repolarization phase of monophasic action potentials. The border zone can be explained by the presence of a heterogeneous mixture of areas of severely ischemic myocardium and nonischemic myocardium. Alternation in action potential duration and amplitude, especially in the case of discordant alternation, could cause a chaotic distribution of repolarization gradient. The large dispersion of repolarization creates an environment that facilitates the development of a conduction delay that is required to induce dangerous ventricular arrhythmias.\textsuperscript{12} Discordant alternans of action potential duration might be expected to generate an excitory current of a sufficient magnitude to initiate a spontaneous activity. There might be some differences in the frequency of ventricular premature beats between the dogs with and those without ventricular fibrillation. In the present study, the electrocardiographic map recording was not contin-

\textbf{FIGURE 2. Isopotential maps demonstrating progressive change of amplitude of ST alternans after coronary occlusion.} Isopotential maps constructed from epicardial electrograms in a dog heart. Isopotential lines show differences in voltage of ST elevation of two consecutive potentials. Isopotential contour lines are drawn in increments of 0.5 mV. Dotted area represents area of ST elevation. Area of ST elevation increased with time, and the maximum amplitude of ST alternans also increased. At bottom right corner, simultaneously recorded epicardial electrograms from adjacent leads are shown. Note that ST alternans is out of phase (discordant ST alternans). Vf, ventricular fibrillation.
uous. Therefore, we did not have sufficient data regarding this aspect. In two dogs in which we could record the beginning of ventricular fibrillation, the earliest epicardial activation during ventricular premature contractions was close to the border zone between the two areas having different types of ST alternans. Further research must be conducted to resolve this problem. Dilly and Lab1 reported that all preparations with ventricular fibrillation showed electrical alternans in the border area. Large dispersions of action potential duration and amplitude could cause discordant alternans of ST segments in epicardial electrograms.

Electrical alternans in the surface electrogram can be accounted for by alternation of the action potential configuration.4 Carson et al3 showed that electrical alternans of unipolar waveforms observed in the ischemic zone was related to changes in the action potential configuration rather than to changes in the activation process. Regarding possible mechanisms of electrical alternans during ischemia, many investigators have reported that transmembrane or intracellular calcium movement may play a major role in the mechanism of electrical alternans.1,11 Hirata et al13 reported that electrical alternans was suppressed by verapamil.

Our system permitted us to simultaneously record 60 epicardial electrograms consisting of eight beats each. Therefore, we could analyze the electrical alternans that varies on an every-other-beat basis.

In clinical study, alteration of ST segments has been observed frequently in patients with either prolonged QT syndrome or Prinzmetal's angina and during percutaneous transluminal coronary angioplasty.7,8,10,14 Smith et al8 reported that statistical analysis of subtle beat-to-beat variability in electrocardiographic morphology might provide a noninvasive measure of cardiac electrical stability (susceptibility to ventricular fibrillation).5 A body surface electrocardiographic mapping technique that has been recently developed could detect a discordant ST alternans. Discordant ST alternans in electrocardiograms may provide a new marker of cardiac electrical stability.

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References

FIGURE 3. Isopotential maps of amplitude of ST alternans recorded just before occurrence of ventricular fibrillation (Vf) (right side) or 7 minutes after ligation in dogs without Vf (left side). Dotted areas show area of ST elevation. Isopotential contour lines are drawn in increments of 0.5 mV.
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