

Experimental Studies and Clinical Report on the Electrical Alternans of ST Segment during Myocardial Ischemia

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SUMMARY

During myocardial ischemia produced in 43 dogs by occlusion of left coronary artery, electrical alternans developed in 34 experiments. The most common was alternans of ST-T complex.

Surface and intracellular electrograms were recorded simultaneously from contiguous sites in the ischemic area. The alternans of ST-T complex in the surface electrogram corresponded to that of the rate of repolarization of the membrane action potential. The development of this alternans is localized in 2 relatively small area and transient. This may be the reason why electrical alternans of ST-T is clinically rare.

A clinical case showing electrocardiographic changes of electrical alternans of ST-T complex without any change in the QRS complex is reported. Myocardial infarction and hypokalemia is considered as a cause of the alternans.

The present results support the hypothesis that the mechanism of electrical alternans will be an alternation of the rate and extent of the ions transported across the myocardial cell membrane.

Additional Indexing Words:

Coronary ligation Myocardial infarction Surface electrogram
Membrane action potential Alternans of repolarization phase Ions
transport across the membrane Electrolyte imbalance

THE phenomenon of electrical alternans was first described in the experimental animal by Herring¹⁾ in 1909. Subsequently, its occurrence was reported by Lewis²⁾ in man during a bout of paroxysmal atrial tachycardia. It is said that electrical alternans is generally a rare phenomenon in electrocardiography and usually involves QRS complex. Especially, alternans of ST-T alone is a rarity in clinical cardiology.

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A number of investigators³⁾⁻⁵⁾ have produced this phenomenon experimentally and have postulated its mechanism. The theory predicated by Hamburger et al⁶⁾ is that it is a prolongation of refractory phase in some portion of the heart. Brody and Rosman⁷⁾ postulated that electrical alternans might be the result of 2 alternating foci of impulse initiation or 2 alternating paths of conduction from 1 focus. Many investigators⁸⁾⁻¹¹⁾ using the microelectrode technique have suggested that electrical alternans is related to the behavior of individual fiber rather than to alternating refractoriness of some myocardial cells.

In the present experiments, membrane action potential (MAP) and surface electrogram were recorded simultaneously from left ventricle during the electrical alternation following coronary occlusion in dogs.

The purpose of this study is to investigate the mechanism of electrical alternans of ST segment. The nature of ST segment displacement in general was also considered on the basis of the present findings.

Furthermore, we recently observed a patient with electrical alternans of repolarization phase. The mechanism of the development of ST segment alternans in this case will be discussed on the basis of our experiments.

METHODS

Experiments were performed in 43 mongrel dogs weighing 12-21 Kg. Anesthesia was achieved with intravenous pentobarbital sodium at a dose of 25 mg/Kg. With the animal on artificial respiration, the thorax was opened, then the heart and the study areas were exposed. Recording areas were selected on the endocardium and the epicardium of the left ventricle supplied with blood through the anterior descending branch of left coronary artery and on the epicardium of right ventricle.

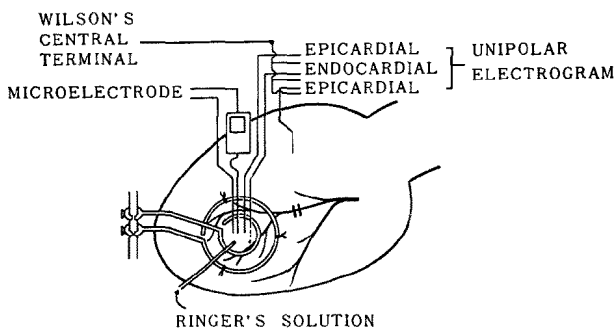


Fig. 1. Schematic illustration of technique for simultaneous recording of unipolar electrogram and MAP. One unipolar and MAP were recorded from contiguous sites in acute myocardial ischemic area. A second unipolar electrogram was recorded from the epicardium of right ventricle or from the endocardium in the ischemic area. Acute myocardial ischemia was produced by ligation of an anterior descending branch of left coronary artery.

The pericardium was removed by dissection. A steel ring covered with polyethylene tubing was affixed to the recording area of left ventricle to minimize movement. To keep the study area moist and warm it was constantly irrigated with Ringer's solution at physiologic temperature (Fig. 1).

Two unipolar electrograms and MAP were recorded simultaneously. One unipolar electrogram and MAR were recorded from left ventricular surface. The other unipolar electrogram was recorded from right ventricular surface or the endocardium of left ventricle just opposite to the recording area of epicardial surface.

The unipolar epicardial surface electrodes were made of tungsten wire about 0.1 mm in diameter. The unipolar endocardial electrodes were made of copper wire coated with enamel, except the tip. The tip of the electrode was sharply bent like a fishhook. The electrode was held inside of a needle. The needle was inserted into ventricular cavity and then only the needle was withdrawn so that the electrode became hooked on the endocardium. The indifferent electrodes for recording unipolar electrograms were connected with Wilson's central terminal.

A mounted flexible glass capillary electrode was used to record intracellular electrogram. The electric resistance of the microelectrode was 10-20 megohms. The indifferent electrode for MAP was placed on the epicardium as close as possible to the microelectrode to minimize the extrinsic factor.

To produce electrical alternans, the anterior descending branch of left coronary artery was ligated for a few minutes. In each experiment, the ligation of coronary artery was made repeatedly.

In 12 cases the electrical stimulation was applied to the endocardium near sinoatrial node at a frequency of about 20 % above the sinus rate.

Two preamplifiers were used to record electrogram and MAP. Output from each amplifier was introduced into a dual beam oscilloscope and into a direct-writing electrograph.

RESULTS

In 43 experimental dogs, myocardial ischemia was produced by occlusion of anterior descending branch of left coronary artery. Electrical alternans developed in 34 of 43 dogs. Fifty cases of alternans were observed. Electrical alternans appeared within 2-3 min after occlusion of coronary artery, and was transient in some cases. Repeated temporary occlusion predisposed to the development of electrical alternans.

A. Alternans in surface electrograms recorded from ischemic areas: Beat-to-beat alternation in the degree of elevation of ST-T complex appeared in all cases (Fig. 2). The average difference in ST segment elevation between alternating complexes was 3.8 mV (1.6-9.6 mV).

In 3 cases, alternans of TQ segment was accompanied by that of ST-T complex (Fig. 3). In the majority of cases, configuration, duration, and amplitude of the QRS complex remained constant during the periods of alternans. In a few cases, however, the alternans of ST-T complex with that of the R wave in amplitude was noted. The R-R intervals did not vary during

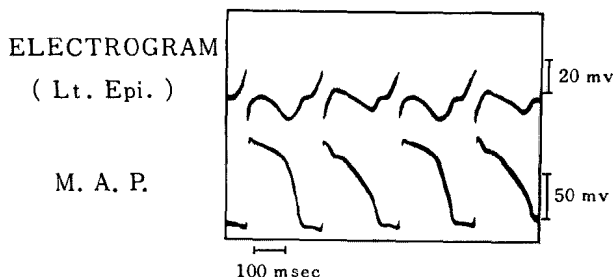


Fig. 2. Electrical alternans of ST-T complex in surface electrogram and electrical alternans of the rate of repolarization in MAP. The ST segment shows alternative displacement without change in TQ level. The configuration, duration and amplitude of QRS complex remained unchanged. The resting level, magnitude and duration of MAP remained unchanged.

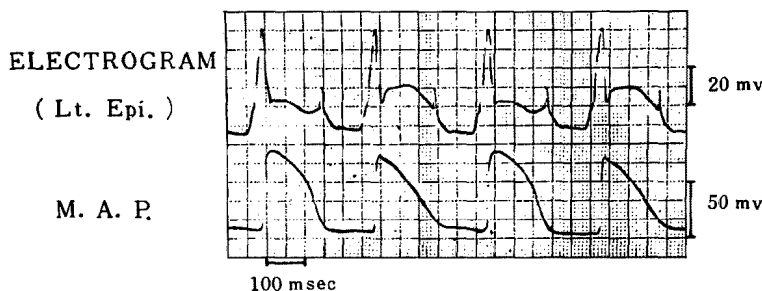


Fig. 3. Electrical alternans of TQ level accompanied by that of ST-T complex. Note that the electrical alternans of resting level is accompanied by that of the rate of repolarization.

alternans in all cases. In 12 cases, in which electrical stimulation was performed, the interval between the artifact of stimulation and the onset of the QRS complex was unchanged.

B. Alternans in MAP recorded from ischemic areas: Alternans of the rate of repolarization was observed in all cases (Fig. 2). In the majority of cases, resting level, magnitude and duration of MAP remained unchanged during the period of alternans.

In 3 cases, alternans of resting level accompanying that of the rate of repolarization was observed (Fig. 3). This alternans of MAP corresponded to the alternans of the ST-T complex and that of the TQ segment in surface electrograms.

In 4 cases, alternans of the rate of repolarization with that of the duration of MAP was observed.

C. Unipolar surface electrograms recorded from right ventricle: In 39 cases, unipolar surface electrograms were recorded simultaneously from both right and left ventricles. In spite of the presence of alternans in the

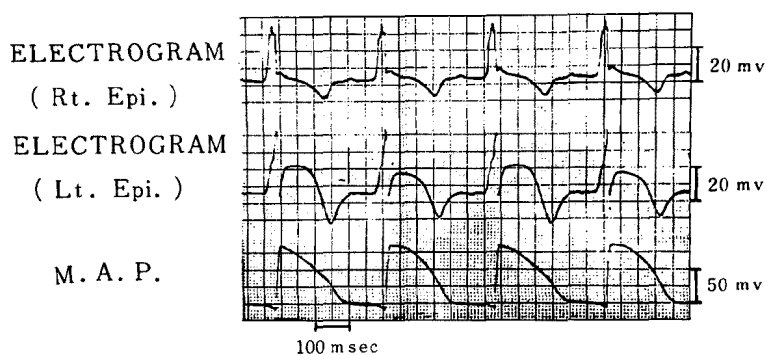


Fig. 4. Electrical alternans of ST-T complex in surface electrogram (middle) and that of the rate of repolarization in MAP (lower) recorded from an ischemic area. Electrical alternans did not occur in surface electrogram (upper) recorded from non-ischemic right ventricle.

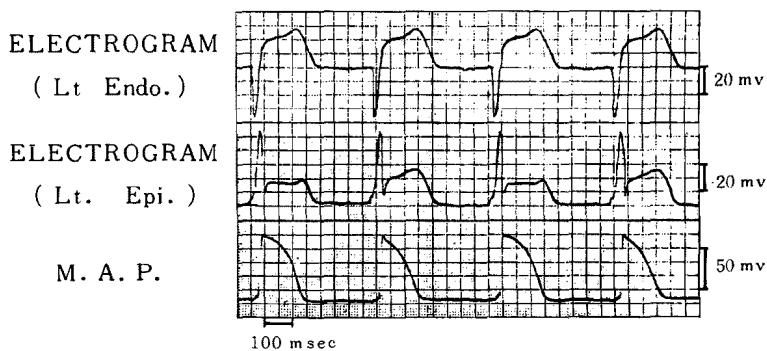


Fig. 5. Endocardial (upper) and epicardial (middle) electrograms and MAP (lower tracing) from an ischemic area. Electrical alternans is confined to epicardial electrogram and MAP.

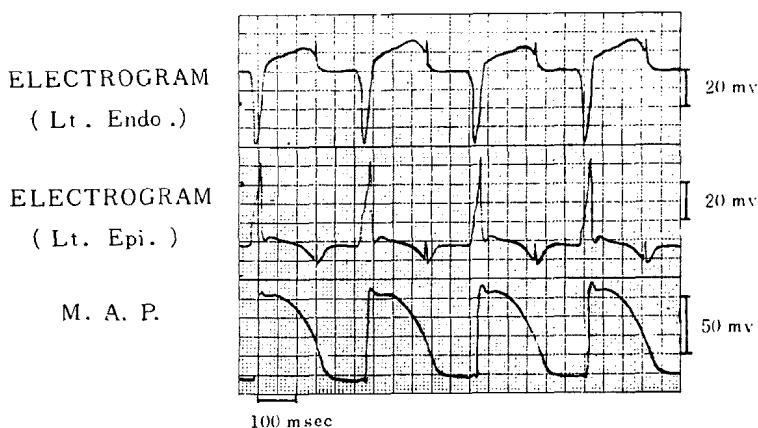


Fig. 6. Endocardial (upper) and epicardial electrograms (middle) and MAP (lower) recorded from an ischemic area. Electrical alternans is confined to endocardial electrogram.

electrogram recorded from the ischemic area of left ventricle, no alternans was observed in the electrogram recorded from right ventricle (Fig. 4).

D. Unipolar electrograms recorded from endocardium in ischemic areas: In 11 cases, unipolar electrograms were recorded simultaneously from both endocardial and epicardial surfaces of ischemic area. Four cases showed alternans confined to epicardial surface and 2 cases showed alternans confined to endocardial surface (Figs. 5, 6).

In the remaining 5 cases, alternans of ST segment was observed simultaneously in both epicardial and endocardial electrograms (Fig. 7A). In 2 of these, the direction of ST segment deviation in epicardial electrograms was different from that in the corresponding endocardial electrograms (Fig. 7B).

E. Relationship between alternans in surface electrogram and MAP: The alternans of the rate of repolarization in MAP corresponds to the alternans of ST-T complex in surface electrograms.

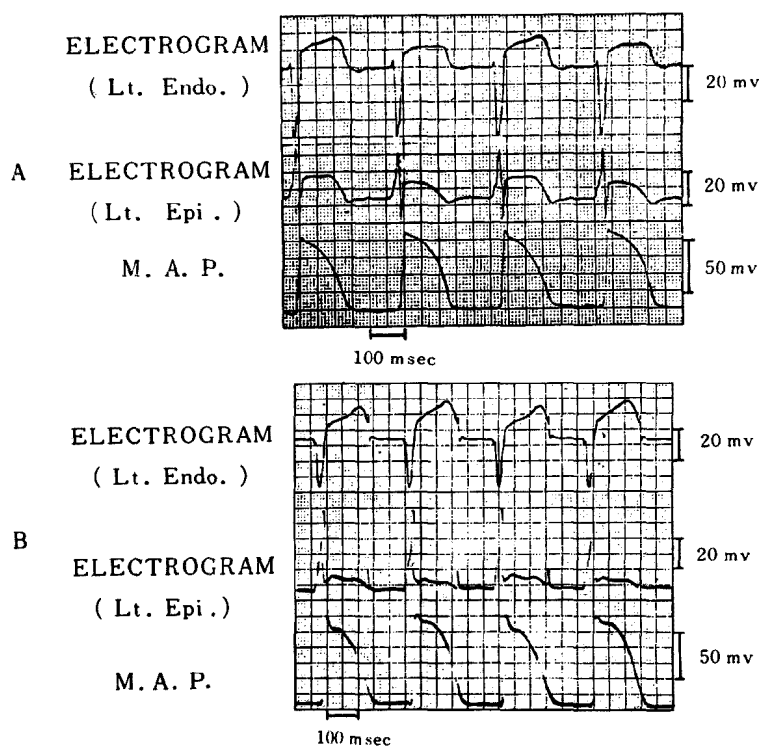


Fig. 7. Endocardial and epicardial electrograms and MAP from an ischemic area. Electrical alternans of ST segment occurs simultaneously in epicardial and endocardial electrograms. (A) The direction of ST segment deviation in epicardial electrogram is the same as in the corresponding endocardial electrogram. (B) The direction of ST segment deviation in epicardial electrogram is different from that in the corresponding endocardial electrogram.

The quantitative relationship between the difference of ST-T displacement in alternating surface electrograms and that of the corresponding displacement of repolarization phase in MAP was studied in the same manner as described by Prinzmetal et al.¹²⁾ Basically the procedure consisted of computing the correlation coefficient (r) of the regression line. The regression line is represented by the following equation:

$$v_2 - v_1 = -C(V_2 - V_1).$$

In the above equation, $v_2 - v_1$ is the difference of displacement of ST-T complex in alternating surface electrogram, $V_2 - V_1$ is the difference of displacement of repolarization phase in the corresponding MAP, and C is proportionality constant. In all cases, the value of r was more than 0.95. The proportionality constant (C) ranged from 0.25 to 0.90.

CASE REPORT

A 66-year-old Japanese woman was admitted to Anjo Kosei Hospital on March 20, 1976 in a state of unconsciousness, high fever and frequent convulsions. The temperature was 39.5°C, the pulse rate 120/min, and the blood pressure 116/82 mmHg. An ECG showed sinus tachycardia, low voltage in limb leads and non-specific myocardial damage (Fig. 8A). An X-ray film of the chest disclosed cardiac enlargement and calcification in the aortic arch (CTR: 57 %). No congestion was observed in either of the lung fields. Laboratory findings were as follows: Na 147 mEq/L; K 3.5 mEq/L; Cl 96 mEq/L; cholesterol 201 mg/100 ml; β -lipoprotein 570 mg/100 ml; BUN 32 mg/100 ml; creatinine 1.2 mg/100 ml; GOT 33U; GPT 33U; LDH 523U; WBC 10,800; RBC 484×10^4 ; Hb 15.0 Gm/100 ml; Ht 45.0 %.

A few days after admission the temperature dropped near to normal and the frequency of convulsions decreased, but the patient was still unconscious. Thereafter the patient made no satisfactory progress maintained on the artificial forced feeding, and the serum electrolytes imbalance progressed gradually.

In the morning of May 20, respiration became irregular like the Cheyne-Stokes respiration. An ECG showed the pattern of acute anterolateral myocardial infarction; the ST segments elevated in leads V_2 through V_6 , the R wave in lead V_2 poorly progressed, the QS waves appeared in leads V_2 through V_6 , and the Q waves in leads V_5 through V_6 (Fig. 8B). The serum potassium level lowered to 2.7 mEq/L. The blood pressure was 96/68 mmHg, and the heart rate 114/min.

On the following day, the respiration was still irregular, and the general condition was unchanged. The ECG taken at 3:00 p.m. showed a short run of ventricular premature beats and the monophasic wave. The marked elevation of ST segment was seen in leads V_3 through V_6 (Fig. 8C). The blood pressure was 118/74 mmHg and the heart rate 108/min.

The serum potassium level remained at 2.7 mEq/L in spite of administration of potassium chloride (Table I). Two hours later the electrical alternans of ST segment appeared (Fig. 8D). It continued about 2 hours. Then the elevation of ST segment gradually returned to normal level, and wide negative T wave with

bizarre QRS appeared (Fig. 8E). During this course the patient was in a deep comatous state, and now under the persistent vegetative condition. The recent ECG showed only the pattern of myocardial damage; negative T waves were in leads V_2 through V_6 (Fig. 8F)

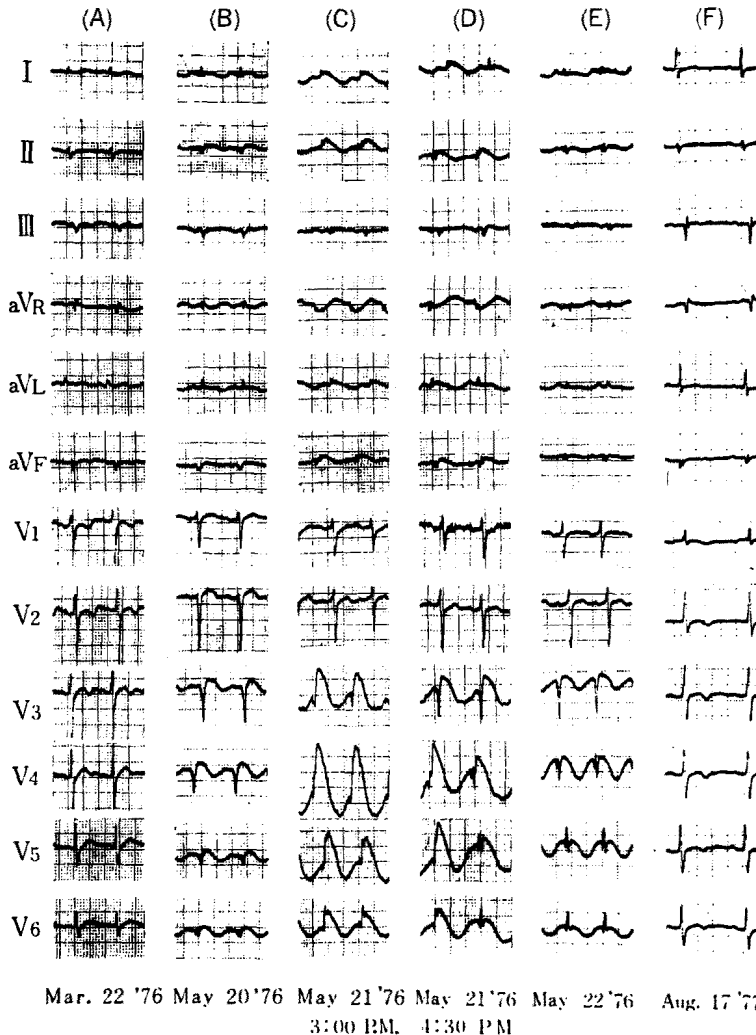


Fig. 8. (A) The ECG of March 22, 1976, shows sinus tachycardia and low voltage in limb leads. (B) On May 20, elevation of ST segment in V_{2-6} , regression of R in V_2 , QS in V_{3-5} and Q in V_2 appeared. (C) The ECG at 3:00 p.m. of May 21, shows monophasic waves in I, II, aV_L , aV_F , and V_{3-6} . (D) At 4:30 p.m. of the same day, electrical alternans of ST-T segment appeared. (E) On May 22, wide negative T in V_{3-6} were shown. Elevation of ST disappeared. (F) On August 17, 1977, coronary T in V_{3-6} appeared.

Table I. Data of ECG and Corresponding Serum
Electrolytes Values

Date	Serum Electrolyte			ECG (Manifestations)
	Na	K	Cl	
March 20	147	3.5	96	Fig. 8A
May 20	137	2.7	87	Fig. 8B
May 21	139	2.7	92	Fig. 8C, 8D
May 22	133	3.0	89	Fig. 8E
May 24	127	3.7	86	Fig. 8F

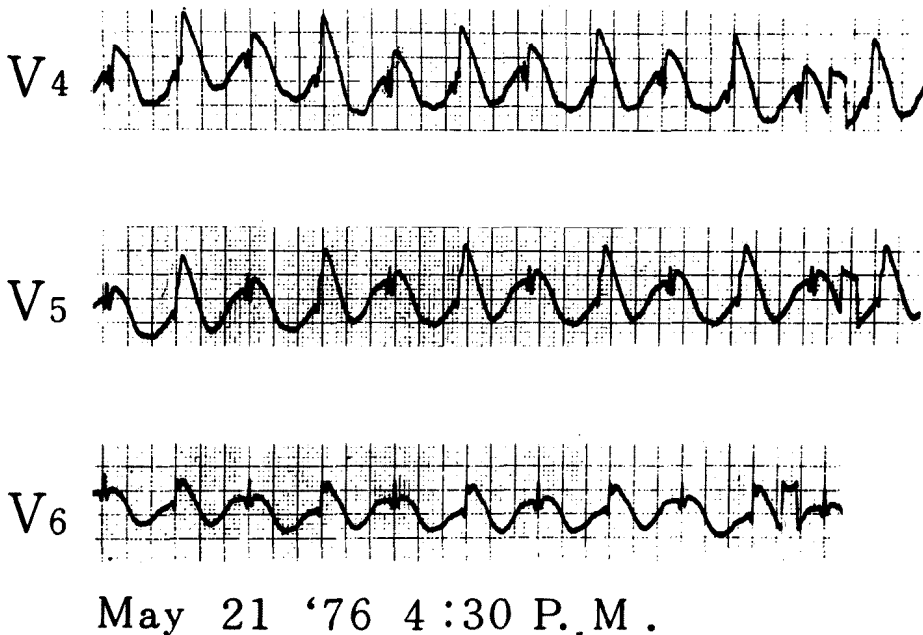


Fig. 9. Longer records of Fig. 8D.

DISCUSSION

In 34 of 43 experiments, beat-to-beat alternation in surface electrogram occurred during myocardial ischemia by occlusion of coronary artery. The most common alternans was that of ST-T complex. Hellerstein and Liebow³⁾ observed an alternans of ST segment in 8 of 9 dogs following occlusion of coronary artery. During myocardial insufficiency in 7 dogs, Roselle and associates⁵⁾ observed alternans of ST segment in all cases. Consequently, the high incidence of electrical alternans following coronary occlusion may be stressed.

In the present experiments, however, electrical alternans in both epi-

cardial and endocardial electrograms recorded from ischemic areas did not always appear simultaneously. In some cases, it occurred only in the epicardial electrogram. In other cases, it occurred only in the endocardial electrogram. These findings indicate that the area of alternans is not extensive but is limited to a relatively small area. Furthermore, electrical alternans was transient in some cases. These may be the reasons why electrical alternans is considered to be a clinically rare phenomenon in electrocardiography.

Regarding the occurrence of different kinds of electrical alternans in endocardium and epicardium (Fig. 7B), endocardial alternans may be a reciprocal phenomenon of the epicardial alternans. However, the phenomenon depicted in Fig. 7A does not support this possibility. Another possibility is that different kinds of electrical alternans occurred simultaneously in each area. To solve this problem, additional recording of MAP from the endocardium would be necessary. The result suggests that surface electrograms are derived from the membrane action potentials in the adjacent area and that the cause of electrical alternans is in the cell itself rather than in the large muscle bundles.

There are many theories regarding the nature of ST segment shift. One of them is that diastolic injury current causes a TQ segment shift, resulting in a relative ST segment shift.^{13),14)} Another theory is that systolic injury current causes a true ST segment shift.^{15),6)} Some investigators^{17),18)} have postulated the combination of these 2 theories. The bases for these theories are as follows: The myocardial cells in the injured area lack the ability to polarize normally in resting stage and lack the ability to depolarize normally in activation. Abnormal polarization causes diastolic injury current and abnormal depolarization causes systolic injury current. Relative ST segment shift due to TQ segment shift has been explained by hypopolarization or hyperpolarization of myocardial cells. True ST segment shift without TQ segment shift has been explained by hypodepolarization or hyperpolarization of cardiac muscle cells.

In the present results, alternation of ST segment was not associated with alternation of TQ segment. This alternation of ST segment corresponds to the alternation of the rate of repolarization in MAP, supporting the idea that electrical alternans is due to a alternation in the rate and quantity of ionic movements across the cell membrane. The amplitude and resting level of membrane action potential remained unchanged. In addition, there is a strong correlation between the difference of ST-T displacement in alternating surface electrograms and that of the corresponding displacement of repolarization phase in MAP. These results suggest that only the changes of phase 2 in membrane action potential may contribute to the true shift of ST segment

in surface electrogram. This idea is consistent with the suggestion of Samson et al¹⁹⁾ that the true ST elevation is a manifestation of earlier repolarization of cardiac muscle cells. It is well known that the plateau phase of action potentials is the consequence of increase in slow inward current which is predominantly carried by Ca^{++} .²⁰⁾⁻²²⁾ The change of the plateau phase of action potentials accompanied by the ST segment alternans is similar to a change induced by the variation of Ca^{++} concentration.²³⁾ The changes in electrocardiogram observed in the present study are similar to that induced by administration of Ca^{++} .²⁴⁾ Bass²⁵⁾ studied the electrical restitution following an action potential in cat papillary muscle by interpolation of test extrasystoles at various delays in the interval between 2 action potentials, and suggested a causal relationship between membrane Ca content and the configuration of action potential. These facts suggest that the alternans of ST segment may be due to the alternation of the Ca^{++} flow during the plateau phase of action potentials. Further investigation of the mechanism of electrical alternans will offer additional evidence concerning the mechanism of ST segment displacement.

Clinically, electrical alternans has been observed in patients with paroxysmal tachycardia, acute coronary occlusion, severe angina pectoris, valvular heart disease, hyperkalemia, hypocalcemia, and pericarditis with effusion. Toxic dose of digitalis and propylthiouracil have initiated this phenomenon. Most cases reported to date showed alternation of the QRS amplitude either with or without T wave alternans, while only several cases of isolated T-U alternans can be found in the literature.¹⁶⁾⁻²⁹⁾ Our present case shows the alternation of repolarization phase alone. This patient had suffered from anterior myocardial infarction, and the alternans of repolarization phase was developed only in the ischemic area (V_{3-6}). The duration was very short. It is thus considered that ischemic condition probably plays a major role in the development of ST-T alternans in this case. Because it has been reported that the K^+ concentration also affect the plateau phase of action potentials,³⁰⁾ and Ishikawa et al¹⁶⁾ have found the electrical alternans in a patient with hypokalemia, it is probable that hypokalemia played a role in the development of the alternans. Unfortunately, Ca content of the blood was not examined. Since the present study indicates that alternation of the rate of repolarization in action potentials is accompanied by ST-T alternans, effort is now under way to study the relationship between the slow inward Ca^{++} currents and ST-T alternans.

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