THE SIGNIFICANCE OF EXERCISE-INDUCED NORMALIZATION OF INVERTED T WAVE IN PATIENTS WITH OLD MYOCARDIAL INFARCTION

FUMITAKA INOUE[1], TOSHIO HASHIMOTO[1], TAMIO NAKAJIMA[1], SHIROU UEMURA[1], KAZUHIRO DOHI[1] and SHINICHI FUJIMOTO[2]

First Department of Internal Medicine[1]
Department of Clinico-Laboratory Diagnostics[2]
Nara Medical University

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Abstract: The purpose of this study was to investigate the significance of exercise-induced normalization of inverted T wave in patients with old myocardial infarction (MI). The subjects of the present study were eighteen patients with old anterior MI. The treadmill exercise test (TMT) was performed 8±1 months after MI onset. Based on the results of the TMT, these patients were divided into two groups: those who showed normalization of inverted T wave during exercise (Group I), and those who did not show normalization of inverted T wave during exercise (Group II). Between the two groups, the following elements were compared: patient characteristics (age, gender, max CK, coronary risk factor); left ventricular abnormal contraction segment (ACS); and coronary flow reserve (CFR), which represent coronary microvascular circulation as measured by the Doppler guide wire. There were no differences between the two groups in patient characteristics except the max CK. In Group I, the max CK was higher ($p<0.05$), the ACS was higher ($p<0.01$), and the CFR was lower ($p<0.05$), as compared with those of Group II. According to these results, the area of MI was more extensive and the disturbance of coronary microcirculation was more remarkable in Group I in comparison with Group II.

It is suggested that the exercise-induced normalization of inverted T wave can reflect the extent of MI and the disturbance of coronary microvascular circulation.

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Key words: coronary microvascular circulation, inverted T wave, old myocardial infarction, treadmill exercise test

INTRODUCTION

The treadmill exercise test is commonly employed to screen asymptomatic and apparently healthy individuals for subclinical coronary artery disease. Normalization of inverted T wave has been often shown during treadmill exercise test. However, the significance of exercise-induced normalization of inverted T wave has enough been not to clarify in patients with ischemic heart disease. It has been reported that normalization of inverted T wave is a specific sign of exercise-induced myocardial ischemia[1-4]. However, other studies have reported that normalization of inverted T wave is observed in both normal subjects and those with ischemic heart disease[5-7].

Furthermore, to our knowledge, no previous investigation has referred to the relationship between normalization of inverted T wave and assessment of coronary flow reserve. Therefore, we performed coronary flow velocity measurements of patients with old anterior myocardial infarction who showed normalization of inverted T wave during exercise using the Doppler guide wire.

The purpose of this study was to investigate the significance of exercise-induced normalization of inverted T wave in patients with old myocardial infarction.

METHODS

Study groups

Eighteen patients with old anterior myocardial infarction and single vessel disease of the left anterior descending artery (LAD) were the subjects of this study. They underwent direct percutaneous transluminal coronary angioplasty (PTCA) within 6 hours from the onset of acute myocardial infarction (AMI). They showed no evidence of restenosis of the target lesion on coronary angiogram after 8±1 months from onset of AMI. The treadmill exercise test (Case 12, Marquett Inc.) was performed by the Bruce protocol after 8±1 months from onset of AMI. Based on the treadmill exercise test results, the patients were divided into two groups : Group I, those who showed normalization of inverted T wave within leads $V_1 \sim V_6$, and

Table 1. Changes in inverted T wave during treadmill exercise test

Number of patients		Age	Gender	Inverted T wave before exercise	Normalization of inverted T wave during exercise	Follow up period (months)
Group I	1	73	F	V2～V4	V2～V4	8
	2	58	M	V3～V5	V3～V5	7
	3	52	M	V5, V6	V5, V6	8
	4	55	M	V4	V4	10
	5	60	M	V4～V6	V4～V6	8
	6	53	M	V5	V5	8
Group II	1	63	M	not showing	no change	6
	2	68	F	not showing	no change	9
	3	52	F	not showing	no change	6
	4	62	M	not showing	no change	6
	5	40	M	not showing	no change	10
	6	67	F	not showing	no change	9
	7	49	M	not showing	no change	10
	8	64	F	not showing	no change	8
	9	50	M	V3～V6	no change	6
	10	61	M	not showing	no change	8
	11	50	M	not showing	no change	7
	12	69	F	not showing	no change	11

"not showing" ; The inverted T wave did not show in any leads V1～V6.
"no change" ; The normalization of inverted T wave after exercise did not show in any leads V1～V6.

Group II, those who did not show normalization of inverted T wave (Table 1). The "inverted T wave" was defined as T wave which showed less than −0.2 mV below baseline level in electrocardiography.

Informed consent for this research protocol was obtained from each patient before cardiac catheterization.

Patient characteristics

The age, gender, coronary risk factor, and values of serum max creatinine phosphokinase (CK) were compared between the two groups of patients.

Treadmill exercise test

All patients underwent the treadmill exercise test by the Bruce protocol after 8±1 months from AMI onset. The maximal heart rate (max HR), exercise time, and reason for end point of exercise were compared between the two groups. The target heart rate was set at 90 % of maximal heart rate for the patient's age.

Coronary angiogram and left ventriculogram

After intravenous injection of 100 U/kg of heparin, all patients underwent selective coronary angiogram from femoral approach by Seldinger's technique with 6 French standard catheters.

Left ventriculograms were performed in the 30° right anterior oblique view. The end-diastolic and end-systolic silhouettes were traced and analysed using the centerline method (Cardio 500, Kontron Inc.). The score of regional abnormal wall motion was defined as the abnormal contraction segment (ACS) with motion depressed more than 2 standard deviations (SD) below compared with the normal mean wall motion. This measurement was expressed as the number of chords.

Coronary flow velocity measurements

The Doppler guide wire (FloWire, Cardiometrics Inc.), which is a 175 cm long, flexible, steerable 0.014 inch angioplasty guide wire with a 12-MHz piezoelectric ultrasound transducer at its tip, was used to measure the coronary flow velocity. The forward directed ultrasound beam with a 28° divergent angle can sample a large portion of the flow profile. The coronary flow velocity is determined from the Doppler frequency shift based on the difference between transmitting and returning signals.

The Doppler guide wire did not place in the large side branch. The velocity signals were processed on-line by fast Fourier transform with spectral display. Several velocity parameters can be calculated by analysis of the spectral waveform and have been found to correlate with absolute coronary flow velocity measurements in both in vitro and in vivo validation studies[8,9].

Following diagnostic coronary angiogram, the Doppler guide wire was advanced as far beyond the infarct-related lesion of LAD to the distal as possible, where the spectral waveform could be recorded and the distal baseline average peak velocity (baseline APV, cm/sec) and the distal maximal hyperemic APV induced intracoronary injection of 10 mg of papaverine were measured. The coronary flow reserve (CFR) was calculated as the ratio of the hyperemic APV to the baseline APV.

Statistical analysis

The age, the values of max CK, the max HR, the exercise time, and the parameters of coronary flow using the Doppler guide wire were compared by unpaired Student *t*-test. The gender, coronary risk factors, and reason for end point of exercise were compared by chi-square analysis. The values were expressed as mean±SD, and for all analyses the results were significant at $p<0.05$.

RESULTS

Patient characteristics

There were no differences between the two groups in age and gender. The values of max CK were 4,258±2,119 IU/l in Group I vs 2,069±1,405 IU/l in Group II ($p<0.05$).

For the coronary risk factor, there were no significant differences between the two groups. Hypertension was observed in 33 % (2/6) of the patients in Group I vs 33 % (4/12) in Group II, diabetes mellitus 17 % (1/6) vs 8 % (1/12), hyperlipidemia 17 % (1/6) vs 8 % (1/12), and smoker 67 % (4/6) vs 67 % (8/12) (Table 2).

Treadmill exercise test

The max HR was 145±9/min in Group I vs 139±21/min in Group II, and the exercise time 9±3 min vs 9±4 min, which showed no significant differences between the two groups. The reasons for end point of exercise were target heart rate 17 % (1/6) in Group I vs 25 % (3/12) in Group II, and leg fatigue 83 % (5/6) vs 75 % (9/12) ; there were no significant differences between the two groups (Table 3).

Coronary angiogram and left ventriculogram

No patients showed significant restenosis in the infarct-related artery. Furthermore, the left circumflex arteries and the right coronary arteries did not show significant stenosis. The ACS was 41±12 in Group I vs 7±7 in Group II. The left ventricular regional wall motion decreased significantly more in Group I than in Group II ($p<0.01$) (Fig. 1).

Table 2. Patients characteristics

Variables	Group I	Group II	Statistical significance
Age	59±8	58±9	NS
Gender (M/F)	4/2	5/7	NS
Max CK (IU/l)	4,258±2,119	2,069±1,405	$p<0.05$
Coronary risk factor			
Hypertension	2/6 (33%)	4/12 (33%)	NS
Diabetes mellitus	1/6 (17)	1/12 (8)	NS
Hyperlipidemia	1/6 (17)	1/12 (8)	NS
Smoke	4/6 (67)	8/12 (67)	NS

CK ; creatine phosphokinase.

Coronary flow velocity measurements

The baseline APV in LAD was 14±5.0 cm/sec in Group I vs 24±14 cm/sec in Group II ; there was no significant difference between the two groups. The hyperemic APV was 21±10 cm/sec in Group I vs 49±19 cm/sec in Group II. The hyperemic APV was a significantly lower value in Group I when compared with that of Group II ($p<0.05$). The CFR was 1.7±0.3 in Group I vs 2.5±0.7 in Group II. The CFR was a significantly lower value in Group I when compared with that of Group II ($p<0.05$) (Fig. 2).

Case reports

Case 1

A 58-year old man with anteroseptal AMI was referred to our hospital. The emergency coronary angiogram showed 100 % obstruction in segment 6 of LAD. As a result of direct PTCA, this obstructive lesion was improved to 0 % stenosis. The value of max serum CK was

Table 3. Comparison of the treadmill exercise test between Group I and Group II

Variables	Group I	Group II	Statistical significance
Max HR (bpm/min)	145±9	139±21	NS
Exercise time (min)	9±3	9±4	NS
Reason for exercise end point			
Target heart rate	1/6 (17%)	3/12 (25%)	NS
Leg fatigue	5/6 (83)	9/12 (75)	NS

max HR ; maximal heart rate.

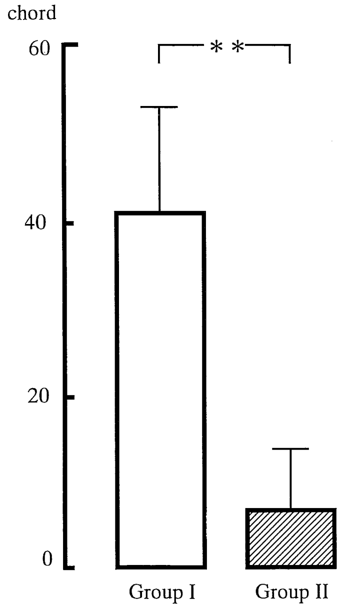


Fig. 1. Comparison of the abnormal contraction segment (ACS) by the centerline method between Group I and Group II. The ACS was 41 ±12 in Group I vs 7±7 in Group II. The left ventricular wall motion was significantly decreased in Group I when compared with that of Group II ($p<0.01$).

4,626 IU/l. The coronary angiogram, which was performed 7 months after AMI onset, did not show significant restenosis. The treadmill exercise test showed that normalization of inverted T wave was observed in leads from V_3 to V_5 (Fig. 3) ; the max HR was 152/min, the exercise time was 10.05 min, and the reason for end point of exercise was leg fatigue. The ACS of the left ventricular was 49. The baseline APV was 17 cm/sec, hyperemic APV was 25 cm/sec, and the CFR was 1.5 (Fig. 4).

Case 2

A 64-year-old woman with anteroseptal AMI was referred to our hospital. The emergency coronary angiogram showed 99 % stenosis in segment 7 of LAD. As a result of direct PTCA, this lesion was improved to 0 % stenosis. The value of max serum CK was 1,990 IU/l. The coronary angiogram, which was performed 6 months after AMI onset, did not show significant

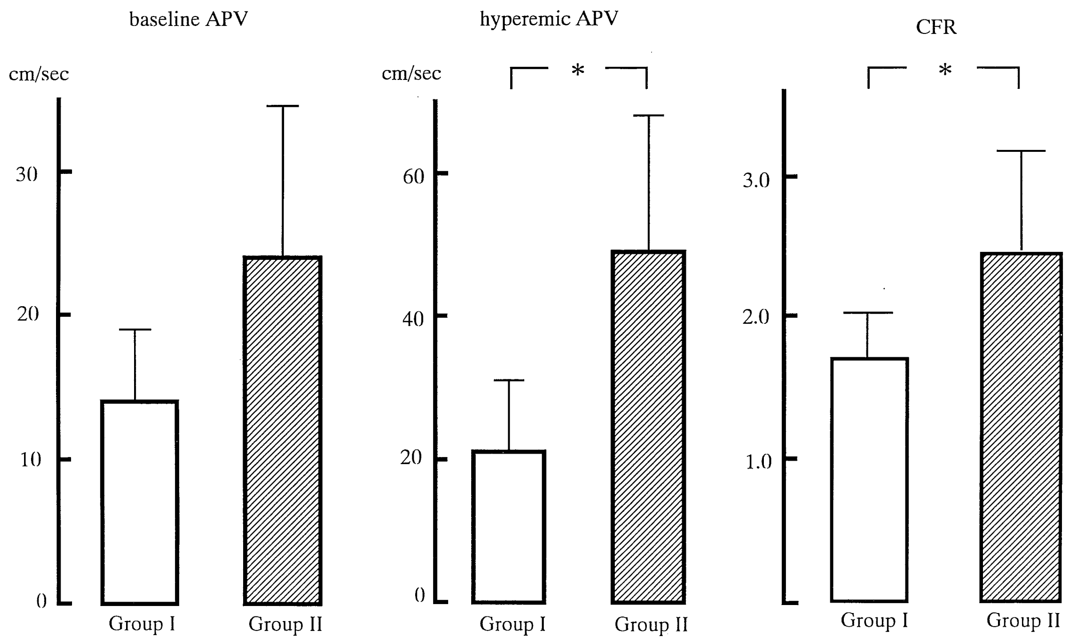


Fig. 2. Comparison of coronary flow velocity measurements between Group I and Group II. The baseline average peak velocity (APV) in distal LAD artery was 14±5.0 cm/sec in Group I vs 24±14 cm sec in Group II, there were no significant difference between the two groups. The hyperemic APV was 21±10 cm/sec in Group I vs 49±19 cm/sec in Group II. The hyperemic APV was a significantly lower value in Group I when compared with that of Group II ($p<0.05$). The coronary flow reserve (CFR) was 1.7±0.3 in Group I vs 2.5±0.7 in Group II. The CFR was a significantly lower value in Group I when compared with that of Group II ($p<0.05$).

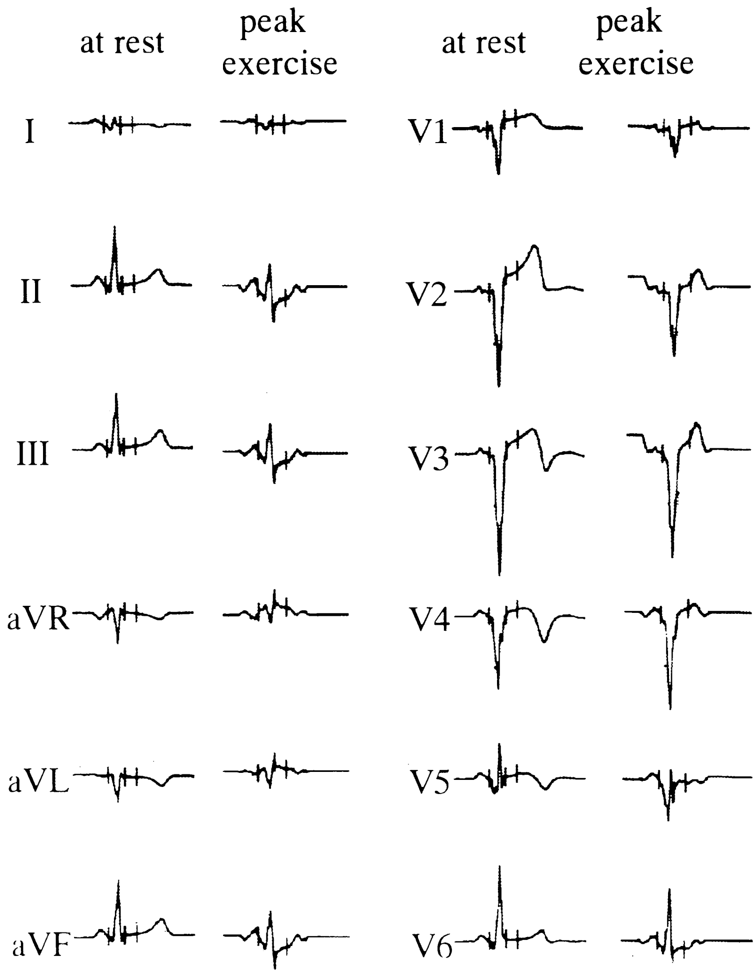
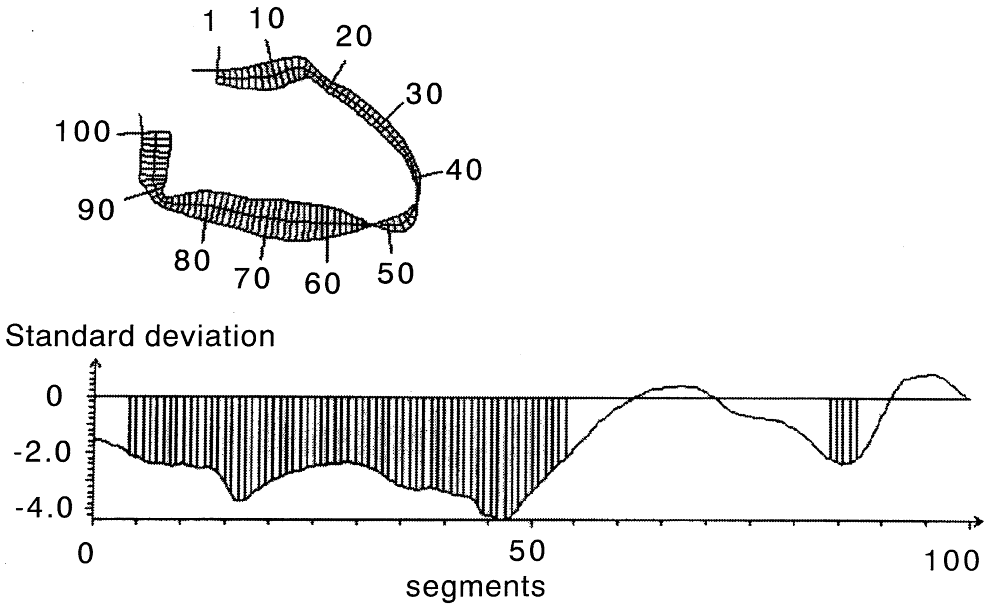


Fig. 3. The treadmill test in the case of a 58-year-old man after 7 months from AMI onset (Case 1). The normalization of inverted T wave was shown in leads from V3 to V5.

restenosis. The treadmill exercise test did not show normalization of inverted T wave (Fig. 5) ; the max HR was 166/min, the exercise time was 6.57 min and the reason for end point of exercise was target heart rate. The ACS of the left ventricular was 8. The baseline APV was 38 cm/sec, hyperemic APV was 88 cm/sec, and the CFR was 2.3 (Fig. 6).

DISCUSSION

1. The relationship between exercise-induced normalization of inverted T wave and abnormality of the epicardial coronary artery



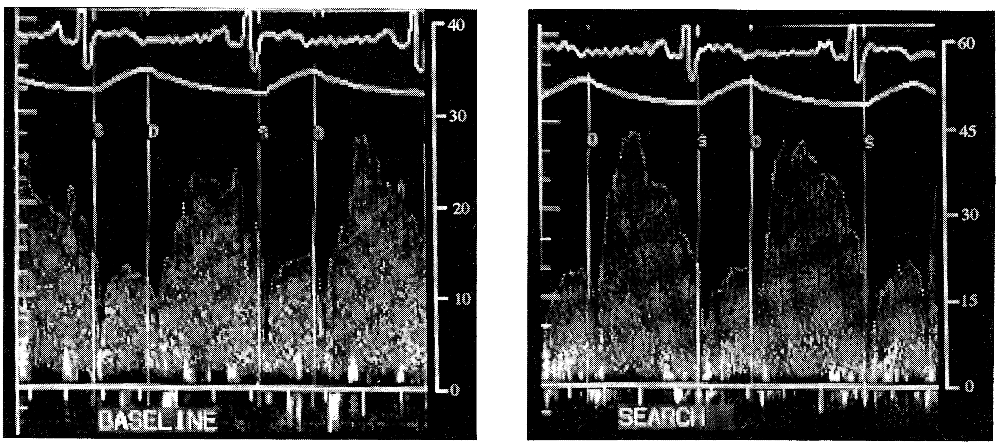


Fig. 4. The left ventricular regional wall motion and the coronary flow velocity measurements in the Case 1. Upper panell : The digitigated left ventricular wall motion curve of right anterior oblique (RAO) 30° view, and standard deviation curve of RAO 30° view. Dark shading area showed the ACS by the centerline method. It was 35.
Lower panell : left ; The baseline APV was 17 cm/sec. right ; The hyperemic APV was 25 cm/sec. The CFR was 1.5.

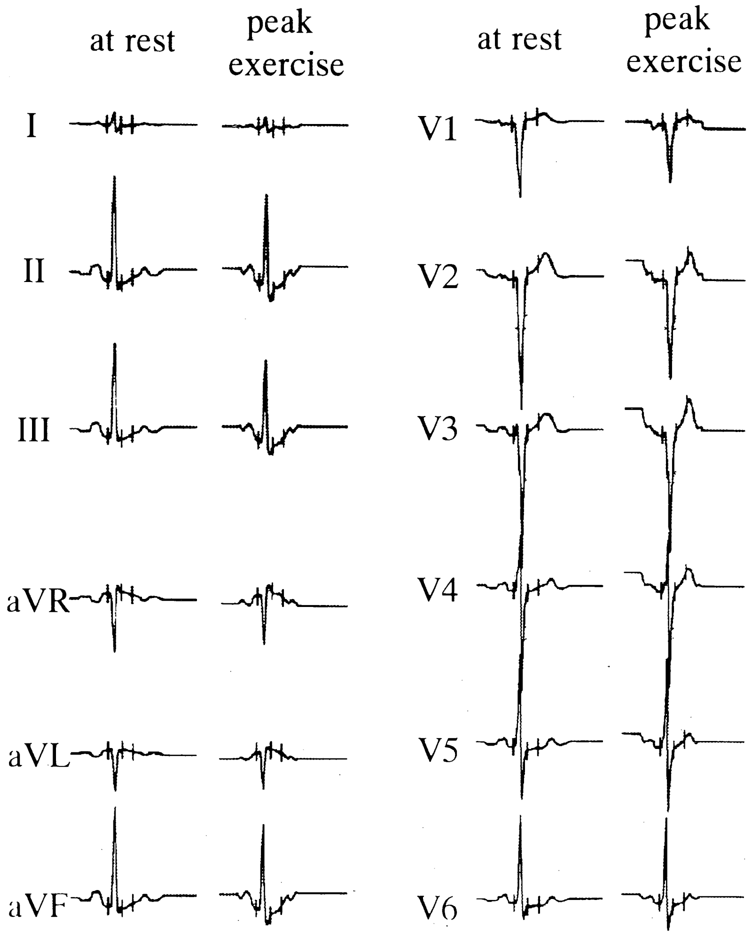


Fig. 5. The treadmill test in the case of a 64-year-old woman after 6 months from AMI onset (Case 2).
The normalization of inverted T wave was not shown in any leads from V1 to V6.

The significance of exercise-induced normalization of inverted T wave has not been sufficiently clarified. Since Master's report[1] concluded that normalization of inverted T wave represented myocardial ischemia, reports with similar conclusions have been published[2-4]. On the other hand, Cohn's[5] and Linhart's reports[6] concluded that normalization of inverted T wave was not correlated with abnormality of the coronary artery. Aravindaksham showed that the normalization of inverted T wave did not relate with the myocardial ischemia, but with the

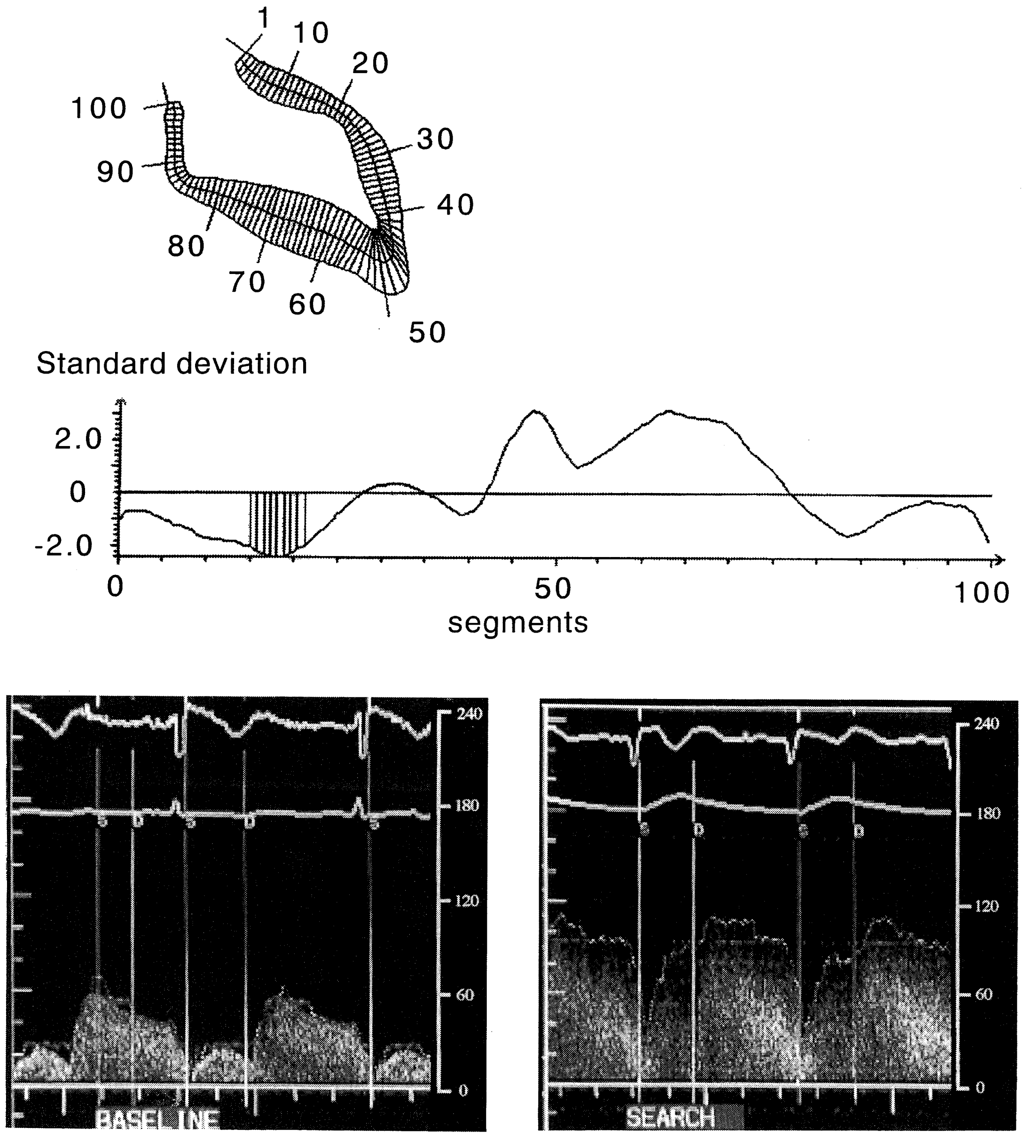


Fig. 6. The left ventricular regional wall motion and the coronary flow velocity measurements in the Case 2. Upper panall : The digitigated left ventricular wall motion curve of RAO 30° view, and standard deviation curve of RAO 30° view. Dark shading area showed the ACS. It was 5.
Lower panall : left ; The baseline APV was 38 cm/sec. right ; The hyperemic APV was 88 cm/sec. The CFR was 2.3.

sympathetic nervous system[7]. The patients enrolled in this study showed 1)old anterior myocardial infarction with a single vessel disease of LAD ; and that 2)they underwent direct PTCA and had no evidence of restenosis. So exercise-induced normalization of inverted T wave is not correlated with abnormality of the epicardial coronary artery in this study.

2. The relationship between exercise-induced normalization of inverted T wave and extent of myocardial infarction

There have been no previous studies that investigated the relationship between exercise-induced normalization of inverted T wave and left ventricular wall motion. In our study, although the left ventricular regional wall motion was significantly reduced in Group I when compared with that of Group II, it could not be clarified that exercise-induced normalization of inverted T wave would be induced by regional wall motion abnormality.

After early recanalization therapy in patients with AMI, the peak plasma CK has been shown within 24 hours. In Vater's report[10] there was significant correlation between the max CK and the infarct size. In this study, the max CK was a higher value in Group I when compared with that of Group II.

According to these results of left ventricular regional wall motion and max CK, it is suggested that the area of myocardial infarction is more extensive in Group I when compared with that of Group II. Therefore, it is suggested that the extent of myocardial infarction correlates with exercise-induced normalization of inverted T wave in patients with old myocardial infarction.

3. The relationship between exercise-induced normalization of inverted T wave and coronary microvascular circulation

Recently, the developed Doppler guide wire has been used to estimate not only proximal coronary flow velocity, but also distal velocity. The CFR is defined as the ratio of maximal vasodilative coronary flow velocity to basal flow velocity[11]. The maximal coronary blood flow is obtained by intracoronary administration of papaverine at doses from 10 to 15 mg in human coronary circulation[12]. The CFR is useful for estimating 1)functional assessment of coronary stenosis of intermediate severity ; 2)determination of the need for lesion-specific interventional therapy ; and 3)assessment of coronary microvascular circulation[11]. Abnormal CFR is observed not only in cases with stenosis of the epicardial coronary artery, but also in cases with impaired coronary microvascular circulation, such as diabetes mellitus, hypertension, cardiomyopathy and myocardial infarction[13-16]. According to these studies, the CFR represented disturbance of coronary microvascular circulation without significant stenosis in the epicardial coronary artery. The disturbance of the coronary microvascular circulation is based on impaired blood flow in the small intramural arteriolar resistance vessels ($<200\ \mu m$) or in the coronary capillary system[17]. In this study, the CFR was a lower value in Group I when compared with that of Group II. According to the ACS and max CK in this study, the area of myocardial infarction is more extensive in Group I when compared with that of Group II. All patients showed no significant stenosis of epicardial coronary arteries. Furthermore, there were no significant differences between the two groups concerning hypertension and diabetes mellitus as factors for reduced CFR. It is suggested that the reduced CFR reflects the disturbance of the coronary microvascular circulation due to myocardial infarction. To our knowledge, no previous studies had investigated the relationship between exercise-induced normalization of inverted T wave and coronary microvascular circulation.

We therefore cannot deny the possibility that normalization of inverted T wave is induced by impaired coronary microvascular circulation.

Limitation of this study

The patients enrolled in our study were restricted to those with old anterior myocardial infarction with no evidence of significant restenosis in the epicardial coronary artery. To investigate the significance of exercise-induced normalization of inverted T wave in more detail, it is desirable that the subjects of the study should include patients with significant restenosis in the epicardial coronary artery. Furthermore, the patients for Group II should show inverted T wave before exercise and not show normalization of inverted T wave during exercise. However, patients did not show inverted T wave before exercise except for one case.

It was not possible to investigate the coronary flow dynamics during exercise. This may clarify the direct evidence of the relationship between normalization of inverted T wave and coronary flow. Furthermore, experimental study using a dog model may be useful to evaluate the mechanism of normalization of inverted T wave.

In conclusion, from this study, the exercise-induced normalization of inverted T wave can reflect the extent of myocardial infarction and the disturbance of coronary microvascular circulation.

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