

Relationship between T-wave normalization on exercise ECG and myocardial functional recovery in patients with acute myocardial infarction

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Background : Several studies suggested that T-wave normalization (TWN) in exercise ECG indicates the presence of viable myocardium. But the clinical implication of this phenomenon in patients with acute myocardial infarction who received proper revascularization therapy was not determined. Precisely the aim of this study was to investigate the relationship between TWN in exercise ECG and myocardial functional recovery after acute myocardial infarction.

Methods : We studied 30 acute myocardial infarction patients with negative T waves in infarct related electrocardiographic leads and who had received successful revascularization therapy. Exercise ECG was performed 10-14 days after infarct onset using Naughton protocol. Patients were divided into 2 groups according to presence (group I; n=14) or not (group II; n=16) of TWN in exercise ECG. Exercise parameters and coronary angiographic findings were compared between groups. Baseline and follow-up (mean 11 months) regional and global left ventricular function was analyzed by echocardiography.

Results : Exercise parameters were similar between groups. There was no difference in baseline ejection fraction and wall motion score between group I and II (EF; $56 \pm 12\%$ vs $52 \pm 11\%$, $p = ns$. WMS; 21 ± 3 vs 23 ± 4 , $p = ns$) and it was improved at the tenth month by similar magnitude (group I/group II, EF % change = $12 \pm 12\%$ vs $7 \pm 6\%$, $p = ns$, WMS % change = $6 \pm 6\%$ vs $7 \pm 5\%$, $p = ns$). The finding of no relation between TWN and functional recovery was observed also when the patients were analysed according to infarct location and presence or absence of Q-waves.

Conclusion : As the exercise-induced TWN in patients with acute myocardial infarction was not related with better functional recovery of dysfunctional regional wall motion and ejection fraction, TWN does not appear to be an indicator of myocardial viability.

Key Words : Myocardial infarction, Exercise test.

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INTRODUCTION

Identification of viable myocardium from the left ventricular area of dysfunctional regional wall motion after acute myocardial infarction is very important because proper revascularization therapy may improve the clinical outcome. In the diagnosis of viable myocardium, 24-hour-delayed redistribution imaging by Thallium-201 scintigraphy, reinjection Thallium-201 scintigraphy, myocardial echocardiography or low dose Dobutamine stress echocardiography are currently applied methods^{1-3, 12)}. Particularly, Positron Emission Tomography is being used as a standard testing because of its high sensitivity⁴⁾. But these testing methods are complicated and expensive, and they require experience to interpret the acute evaluation of viability. Therefore, as a method to identify the presence of viable myocardium with ease, there have been attempts to use exercise ECG performed after myocardial infarction.

Recently, some studies have reported T-wave normalization (TWN), which means normalization of negative T-waves in rest ECG of infarct-related electrocardiography leads or ST-segment elevation may indicate the presence of viable myocardium. Lombardo et al.³⁾ performed low dose Dobutamine stress echocardiography (5-10 $\mu\text{g}/\text{kg}/\text{min}$) in Q-wave myocardial infarction patients and found that contractile reserve was higher in the area with T-wave normalization (TWN) or ST-segment elevation than that of no change of ECG. Margonato et al.⁴⁾ performed Thallium-201 scintigraphy and exercise stress testing and reported that ST-segment elevation and TWN findings in exercise ECG indicate the residual viable myocardium. Also, Mobilis et al.⁶⁾ reported that exercise induced TWN finding is a marker of viable myocardium by comparing ECG changes and positron emission tomography. But Bodi et al.⁷⁾ reported that the ST-segment elevation and TWN findings during exercise testing were not related with functional recovery. It shows that there are still conflicting opinions about the clinical implications of TWN findings and ST-segment elevation induced by exercise stress. Therefore, this study was designed to observe the relation between TWN in exercise ECG and left ventricle functional recovery after acute myocardial infarction to ascertain if T-wave normalization in exercise ECG can detect viable myocardium.

MATERIALS AND METHODS

1. Patients

30 patients with acute myocardial infarction who visited the Korea University Anam Hospital from Jan. 1998 to May 1999 were included for the study. Among patients with acute myocardial infarction during the same period, the patients with heart failure, severe valvular insufficiency and conduction defect, complications related to reperfusion, were excluded. The patients with ventricular hypertrophy with inverted T-wave in rest ECG, left and right bundle branch blocks, Wolff-Parkinson-White syndrome, serious anemia, electrolyte disorders⁸⁾ and patients with poor quality of echocardiographic images were also excluded. Acute myocardial infarction was diagnosed by chest pain lasting for more than 30 minutes which was not relieved by sublingual nitroglycerine, ST-segment elevation on ECG and increase of blood creatinine kinase MB over 10 ng/mL. All the patients underwent coronary angiography; 6 were treated with thrombolytic agent, 16 were treated with mechanical revascularization and 4 with both.

2. Exercise Stress Testing

Low grade exercise stress ECG (Naughton method) with an increasing step at 2-minute intervals during mean 10-14 days after myocardial infarction was performed. 12 lead electrocardiography was continuously monitored, blood pressure was measured and ECG was recorded at every step. Also, exercise time, peak heart rate and metabolic equivalents (METs) were observed. Criteria for TWN were normalization of T-wave after exercise, which was inverted over 0.15 mV at more than 2 infarct-related ECG leads⁹⁾. ST-segment elevation was defined when it was elevated more than 1 mV lasting 0.08 seconds after J-point.

3. Echocardiography

Baseline echocardiography was performed during admission period and a follow-up study was done 11 months later. The changes of left ventricular ejection fraction and regional wall motion were observed for analysis. The ejection fraction was calculated with left ventricular diastolic and systolic volume measured by the modified Simpson's method from the apical four chamber view. The regional wall motion analysis adopted the method recommended by the American Society of Echocardiography, which divides the left ventricle into 16 segments and gives the scores from 1 to 4

according to the contraction of each segment (1=normal, 2=hypokinesia, 3=akinesia, 4=dyskinesia). All the scores of every segment were summed up to get the wall motion score (WMS).

4. Coronary angiography

The standard method by femoral artery approach was used. When the luminal diameter of the coronary artery was reduced by 70%, it was considered as a significant coronary stenosis. The percent stenosis of infarct-related blood vessel, TIMI grade and presence of collateral circulation vessel were recorded. A successful revascularization was defined when the luminal diameter was expanded over 50% and the chest pain vanished.

5. Statistical analysis

For all the statistical results, SPSSWIN 7.5 program was used. Data was expressed as mean value ± SD. For the difference between groups, Mann-Whitney test as the nonparametric method was used for continuous variables, whereas chi-square method was used for non-continuous variables. Changes of baseline and follow-up ejection fraction and regional wall motion were assessed by using Wilcoxin rank test as the nonparametric method. A value of $p < 0.05$ was considered significant.

RESULTS

1. Clinical features

30 patients were divided into group I (14 patients) with TWN and group II (16 patients) without TWN. Table 1 displays the clinical features of the study patients. There were no differences in sex, age, number of risk factors, infarction area, Q-wave infarction rate and revascularization methods between the two groups.

2. Exercise ECG test

Figure 1 shows one example of ECG with TWN observed in exercise ECG. During the exercise ECG testing, there was no difference of total exercise time, metabolic equivalents (METs), peak heart rate and rate of combined ST segment elevation between the two groups (Table 2).

3. Echocardiography

Table 3 indicates baseline and follow-up ejection fraction, wall motion score and its percent changes from

Table 1. Comparison of clinical features between group I and group II.

	Group I	Group II	p-value
Number	14	16	ns
Age (yr)	57 ± 12	62 ± 7	ns
Male	9 (64%)	10 (63%)	ns
Infarction area			
Anterior	8 (57%)	7 (43%)	ns
Inferior	6 (43%)	7 (43%)	ns
Inf-posterior	0	2 (15%)	ns
Q-wave infarction	8 (57%)	9 (56%)	ns
Risk factors			
Diabetes mellitus	5 (36%)	2 (13%)	ns
Hypertension	2 (14%)	2 (13%)	ns
Diabetes & hypertension	1 (7%)	0	ns
Smoking	11 (79%)	12 (75%)	ns
Revascularization			ns
Medical treatment only	1 (7%)	3 (19%)	ns
PTCA and/or STENT	7 (50%)	9 (56%)	ns
Thrombolysis	2 (7%)	4 (25%)	ns
Thrombolysis & PTCA	4 (29%)	0	ns

Table 2. Exercise ECG parameters in patients with and without T-wave normalization

	Group I	Group II	p-value
Exercise time (min)	8 ± 4	11 ± 3	ns
Metabolic equivalents (METs)	5 ± 2	6 ± 1	ns
Peak heart rate (beat/min)	121 ± 13	115 ± 17	ns
Combined ST-segment elevation (%)	5 (36%)	5 (31%)	ns

Table 3. Baseline and follow-up ejection fraction, wall motion score and percent changes between groups.

	Group I	Group II	p-value
Number	14	16	ns
EF: base (%)	56 ± 12	52 ± 11	ns
EF: f/u (%)	61 ± 7	55 ± 9	ns
EF: % change (%)	13 ± 7	15 ± 11	ns
WMS: base	23 ± 4	25 ± 5	ns
WMS: f/u	21 ± 3	23 ± 4	ns
WMS: %change	11 ± 3	12 ± 8	ns

EF, ejection fraction; WMS, wall motion score; base, baseline; f/u, follow up.

baseline to follow-up between group I and group II. The ejection fraction and wall motion score were significantly

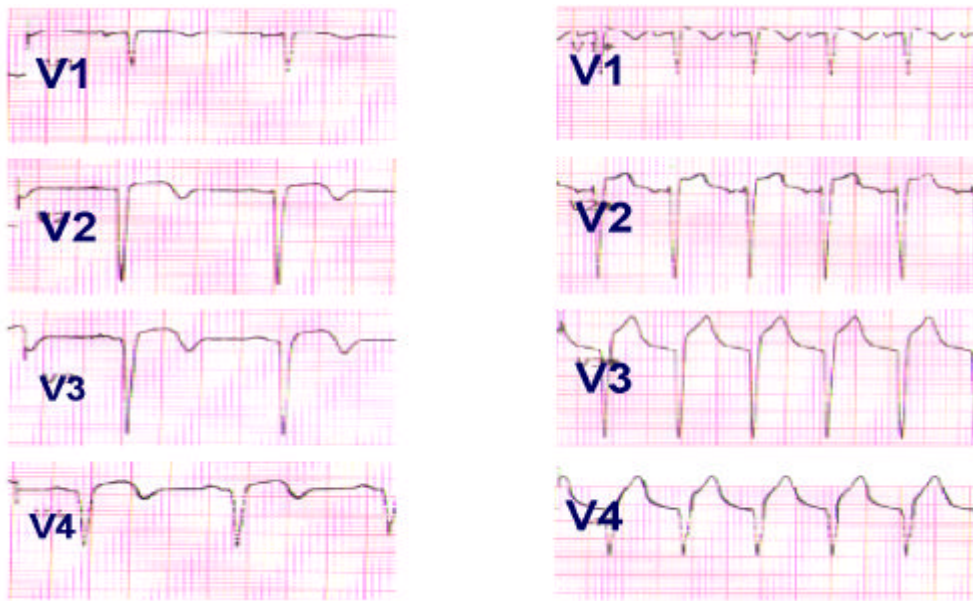
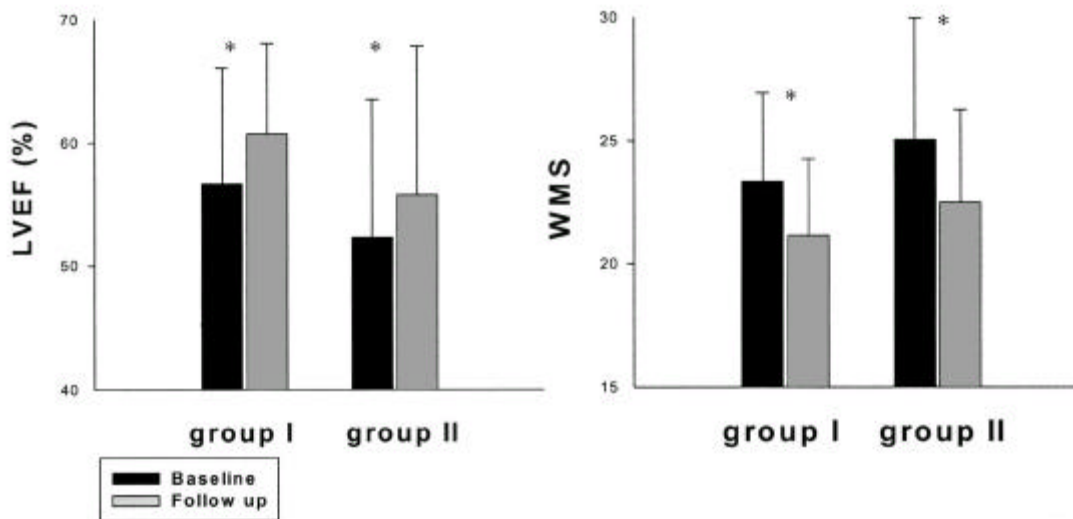


Figure 1. Exercise ECG : Normalization of T-wave was observed in leads from V1 to V4.

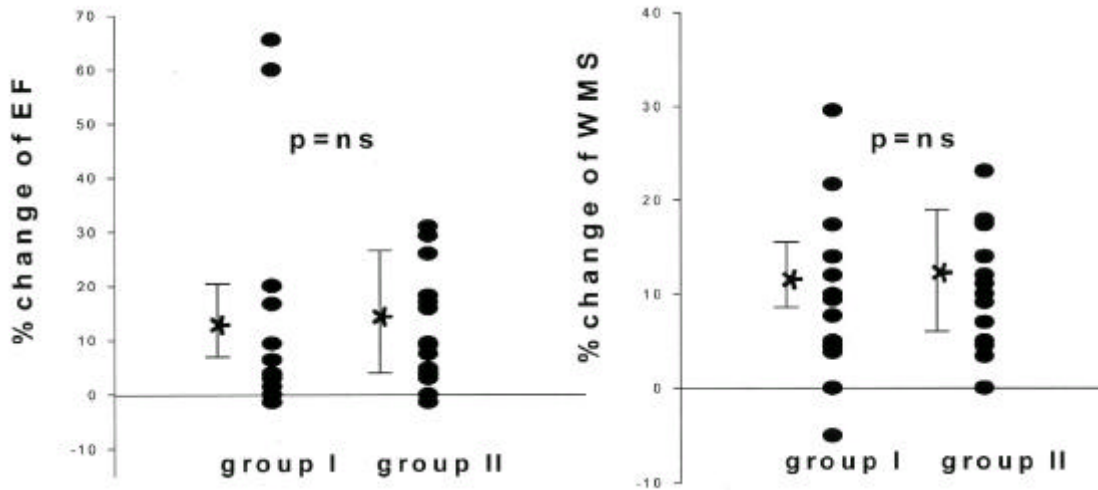


LVEF, left ventricular ejection fraction; WMS, wall motion score; TWN, T-wave normalization. * $p < 0.05$

Figure 2. Changes of ejection fraction and wall motion score in each group.

improved in the follow-up test compared to baseline ($p < 0.05$) in each group. There was no difference in percent changes of ejection fraction and wall motion score indicating the degree of improvement (Figure 2, 3)

between group I and II. The patients were divided according to the presence or absence of Q wave in ECG and still similar trends between Q wave and non Q wave myocardial infarction patients group were found



EF, ejection fraction; WMS, wall motion score

Figure 3. Percent change of ejection fraction and wall motion score

Table 4. Baseline and follow-up ejection fraction, wall motion score and percent changes between groups according to Q-wave.

	Group I	Group II	p-value
Q wave			
Number	6	7	ns
EF: base (%)	53 ± 13	62 ± 5	ns
EF: f/u (%)	57 ± 11	64 ± 5	ns
EF: % change (%)	12 ± 12	7 ± 6	ns
WMS: base	24 ± 6	22 ± 3	ns
WMS: f/u	23 ± 4	20 ± 2	ns
WMS: % change	6 ± 6	7 ± 5	ns
Non-Q wave			
Number	8	9	ns
EF: base (%)	51 ± 7	51 ± 14	ns
EF: f/u (%)	56 ± 8	58 ± 8	ns
EF: % change (%)	11 ± 9	20 ± 27	ns
WMS: base	26 ± 4	25 ± 4	ns
WMS: f/u	22 ± 4	22 ± 4	ns
WMS: % change	12 ± 7	12 ± 11	ns

EF, ejection fraction; WMS, wall motion score; TWN, T-wave normalization; base, baseline; f/u, follow up.

(Table 4).

When they were analysed by infarct location, baseline ejection fraction (55 ± 13% vs 43 ± 8%, $p=0.06$) and follow-up ejection fraction (61 ± 9 vs 52 ± 10, $p=0.06$) were higher in patients with TWN than without TWN among anterior

Table 5. In anterior myocardial infarction, baseline and follow-up ejection fraction, wall motion score and percent changes between groups.

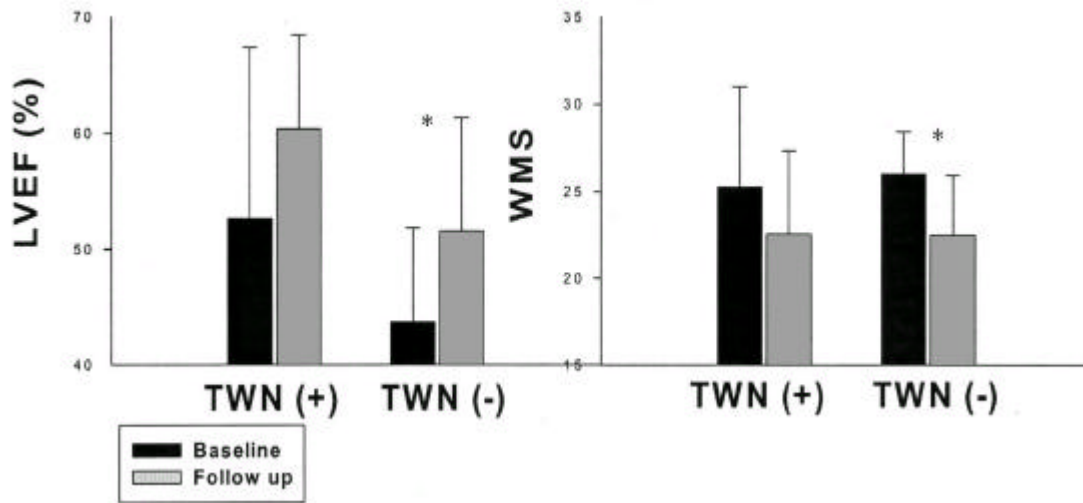
	Group I	Group II	p-value
Number	7	7	ns
EF: base	55 ± 13	43 ± 8	0.06
EF: f/u	61 ± 9	52 ± 10	0.06
EF: % change	15 ± 4	19 ± 10	ns
WMS: base	24 ± 5	29 ± 4	ns
WMS: f/u	21 ± 4	24 ± 4	ns
WMS: % change	14 ± 7	16 ± 9	ns

EF, ejection fraction; WMS, wall motion score; TWN, T-wave normalization; base, baseline; f/u, follow up; * $p < 0.05$.

Table 6. In inferior myocardial infarction, baseline and follow-up ejection fraction, wall motion score and percent changes between groups.

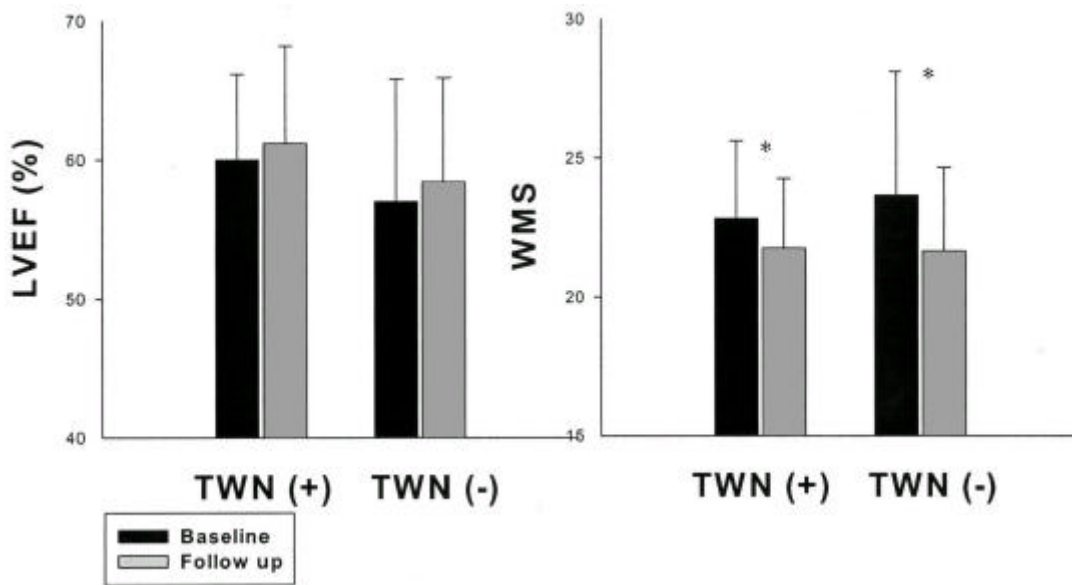
	Group I	Group II	p-value
Number	7	9	ns
EF-base	56 ± 11	57 ± 9	ns
EF-f/u	60 ± 11	58 ± 8	ns
EF-%change	6 ± 13	3 ± 4	ns
WMS-base	23 ± 3	24 ± 4	ns
WMS-f/u	21 ± 3	22 ± 3	ns
WMS-%change	7 ± 5	8 ± 6	ns

EF, ejection fraction; WMS, wall motion score; TWN, T-wave normalization; base, baseline; f/u, follow up; * $p < 0.05$.



LVEF, left ventricular ejection fraction; WMS, wall motion score; TWN, T-wave normalization; * $p < 0.05$.

Figure 4. Changes of ejection fraction and wall motion score in anterior myocardial infarction.



LVEF, left ventricular ejection fraction; WMS, wall motion score; TWN, T-wave normalization; * $p < 0.05$.

Figure 5. Changes of ejection fraction and wall motion score in inferior myocardial infarction.

infarction patients. In the group of anterior wall infarction, the left ventricular function improved significantly in follow-up test in patients without TWN ($EF_{\text{base/follow up}}$:

$43 \pm 8\% / 52 \pm 10\%$, $p = 0.03$, $WMS_{\text{base/follow up}}$: $29 \pm 4 / 24 \pm 4$, $p = 0.02$), whereas patients with TWN did not show a significant improvement ($EF_{\text{base/follow up}}$: $55 \pm 14\% / 61 \pm 9\%$,

$p=ns$, $WMS_{base/follow\ up} : 24\pm 5 / 21\pm 4$, $p=ns$, Table 5).

In inferior myocardial infarction patients, the left ventricular function was not different from baseline and follow-up testings in both groups (Table 6).

4. Coronary angiographic finding

There was no difference in number of stenotic coronary vessel, location of infarction related vessel and grade of collateral circulation between two groups. But after revascularization therapy, the percent of patients with >70% residual stenosis of infarction related coronary artery was higher in the TWN group (Table 7).

Table 7. Angiographic comparison between patients with and those without TWN

	Group I	Group II	p value
Diseased vessel (I/2)	9 / 5 (64 / 36%)	11 / 5 (69 / 31%)	ns
IRA (LAD/RCA/LCX)	7 / 6 / 1 (50 / 43 / 7%)	7 / 7 / 2 (44 / 44 / 12%)	ns
Collateral vessel (grade>1)	2(14%)	5(30%)	ns
Luminal narrowing >70% in IRA	0(0%)	4(16%)	0.03

IRA, infarction related artery;

LAD, left anterior descending artery;

RCA, right coronary artery; LCX, left circumflex artery

DISCUSSION

In this study, the association of exercise induced normalization of T-wave, which was inverted in rest ECG in patients after myocardial infarction with late functional recovery, was not found.

Dysfunctional but viable myocardium is generally divided into hibernating myocardium and stunning myocardium. The former is defined as temporary dysfunctional myocardium by the reduction of coronary flow and the latter condition is induced by repeated myocardial ischemia or reversible ischemic myocardial damage¹⁰⁻¹¹. There are several testing methods to detect this viable myocardium. Recently, the finding of T-wave normalization during exercise ECG has been reported as an indicator of viable myocardium. Previous studies have suggested the relation between viable myocardium and TWN mostly by imaging diagnostic methods¹⁻⁵. There were a few data comparing left ventricular function recovery with the findings of T-wave normalization but

their results are controversial¹³⁻¹⁵. Therefore, this study was designed to investigate whether TWN on exercise ECG was related with late functional recovery among acute myocardial infarction patients after revascularization therapy. As a result, the left ventricular function was recovered at follow-up in both groups but, regardless of the presence of TWN, the degree of left ventricular functional recovery was similar in both groups and made this result different from previous studies by explaining that positive TWN finding indicates the viable myocardium.

The mechanism of exercise induced T-wave normalization has not been clarified yet, but it can be explained by several reasons. In cases with coronary diseases, exacerbation of myocardial ischemia or passive stretching of the infarction area by the tension being developed by normal contracting myocardium or presence of viable myocardium¹⁸ were reported to be related with T-wave normalization. From this study, the mechanism of T-wave normalization on exercise appears to be related with either exaggerated abnormal infarction area wall motion or myocardial ischemia. Every myocardial infarction patient included in this study took a proper revascularization therapy before exercise ECG and showed no ST depression or chest pain during exercise. But 4 patients among group II who did not have TWN exercise ECG showed a significant stenosis (>70%) of infarction related vessel by angiography. But on coronary angiography, all of these patient showed TIMI III coronary flow and exercise ECG showed no ST depression. When the data was analysed after the 4 patients had been excluded, there was no difference in baseline and follow-up left ventricular function and left ventricular functional recovery. Thus, it is unlikely that myocardial ischemia may induce T-wave normalization during exercise test.

67% of the patients in this study showed left ventricular ejection fraction over 50%. The mean baseline ejection fraction and wall motion score between group I and II was not different. But in patients with anterior infarction, patients with TWN tended to have higher ejection fraction and wall motion score at baseline. This result was different from previous studies that suggested a relation between TWN finding and viable myocardium. They explained that baseline ejection fraction of patients with TWN was lower than that of patients without TWN and the left ventricular function did not recover or, rather, reduced even after revascularization in the group without TWN^{16, 22}. But the result is the opposite in this study. The explanation for this difference is not clear. All the

patients in this study received proper revascularization therapy and did not show inducible ischemia in exercise ECG. Thus the findings of TWN in exercise ECG appear to be related with exaggerated dysfunctional regional wall motion caused by increased myocardial contraction on exercise in normal area.

In diagnosing viable myocardium with exercise ECG, the intensity of exercise stress testing and location of infarction was reported to be important to consider. Mobilis et al.⁽⁶⁾ presented that detection rate of viable myocardium be higher when a lower intensity of exercise test is used, or when the patient has anterior myocardial infarction. The exercise protocol in this study was the Naughton method which is a low intensity exercise protocol. Also, when compared by infarction areas of anterior and inferior, the left ventricular functional recovery did not show any difference in degree.

Like TWN, there are various opinions about the implication of ST-segment elevation in exercise stress testing in patients with myocardial infarction. Dyskinesia, aneurysm, coronary spasm and serious proximal constriction are known to be related and there are some recent reports that ST-segment elevation indicates viable myocardium⁽¹⁷⁻²¹⁾. But this has not been clearly explained so far and interaction with TWN is not well known, either. Saito et al.⁽²³⁾ performed positron emission tomography and presented that there was viable myocardium in only 10% of patients in case of exercise induced ST-segment elevation without TWN after myocardium infarction, which explained their correlation. But it is considered that TWN finding and combined ST-segment implications require further studies.

This study was subject to some limitations. First, most patients were administered an antianginal drug, except beta blocker, during exercise stress testing, which might mask induction of ischemia. Second, combined ST-segment elevation was seen in 10 patients that may interfere interpretation of the genuine relation between TWN group and viable myocardium. But ST-segment elevation mechanism has not been known so far and there was no difference of frequency between the groups which would affect the study result much. Third, the range of follow-up period was relatively uneven, from 2.2 months, so to 20 months that it can affect the rate of the left ventricular functional recovery. In some patients there could be reocclusion of revascularized infarct related artery.

In conclusion, this study confirmed that exercise stress testing induced TWN finding is not related to the

myocardial functional recovery in patients with acute myocardial infarction after revascularization and that TWN finding on exercise stress electrocardiography does not indicate myocardial viability.

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