Increased Hyperkinesis in Noninfarcted Areas during Short-term Follow-up in Patients with First Anterior Acute Myocardial Infarction Treated by Direct Percutaneous Transluminal Coronary Angioplasty

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SUMMARY

The time course and clinical significance of hyperkinetic wall motion (HWM) in a noninfarcted area in direct percutaneous transluminal coronary angioplasty (PTCA) has not been clearly demonstrated in patients with acute myocardial infarction (AMI). The objectives of this study were to examine the change in HWM during one-month follow-up after direct PTCA and determine its impact on the recovery of global left ventricular function. A total of 61 patients with first anteroseptal AMI and one vessel disease were evaluated. The paired left ventriculograms in the 30° right anterior oblique view taken both at baseline and follow-up were analyzed by the centerline and area length methods. The severity of hypokinesis was expressed by mean regional wall motion (standard deviation/chord) in most hypocontractile 50% of chords responsible to left anterior descending coronary artery area and HWM by mean regional wall motion in most hypercontractile 50% of chords of noninfarcted area. HWM increased from 0.18 ± 1.07 to 0.48 ± 1.30 ($p = 0.0608$). The delta global ejection fraction (global ejection fraction at follow-up minus global ejection fraction at baseline) was correlated with both delta infarcted wall motion (infarcted wall motion at follow-up minus infarcted wall motion at baseline) and delta HWM (HWM at follow-up minus HWM at baseline) ($r = 0.576$, $p < 0.0001$, $r = 0.383$, $p = 0.0036$, respectively) during follow-up. Further, the delta global ejection fraction showed better correlation with delta

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(HWM + infarcted wall motion) [(HWM plus infarcted wall motion at follow-up) minus (HWM plus infarcted wall motion at baseline)] ($r = 0.593$, $p < 0.0001$). Direct PTCA resulted in the enhancement of HWM, which contributed to the increase in the global ejection fraction with the recovery of infarcted wall motion. (Jpn Heart J 1999; 40: 549–560)

Key words: Myocardial infarction, Direct PTCA, Left ventricular hyperkinesis, Noninfarcted area, Regional wall motion

LEFT ventricular hyperkinetic wall motion in noninfarcted areas is recognized as a very important constituent of left ventricular global function in patients with AMI. This phenomenon has been investigated mainly associated with thrombolytic therapy in the clinical setting.^{1–4)} However, thrombolytic therapy improves global ejection fraction mostly via a dependence on the recovery of infarcted wall motion alone.^{2,4,5)} Although several reports have demonstrated the superiority of direct percutaneous transluminal coronary angioplasty (PTCA) over thrombolytic therapy^{6–8)} in the treatment of AMI, there are no reports concerning the time course and clinical significance of hyperkinesis in direct PTCA. Thus, this study was designed to study the change in left ventricular hyperkinesis during one-month follow-up after direct PTCA and determine its impact on the recovery of global left ventricular function.

METHODS

Patients: A total of 61 consecutive male and female patients with a first acute anteroapical myocardial infarction (AMI) with one vessel disease who were treated by direct PTCA between January 1986 and December 1992 at the National Toyohashi Higashi Hospital were evaluated. Diagnosis of AMI was made in the conventional manner based on clinical history, electrocardiogram (ST segment elevation > 2 mm) in more than two consecutive leads responsible to left anterior descending coronary artery territory, and plasma creatine phosphokinase (CPK) levels more than two-fold greater than the normal level. Multivessel disease, which includes angiographically significant stenosis ($> 50\%$ in % diameter stenosis) in the right coronary artery or left circumflex coronary artery, and cardiogenic shock requiring resuscitation were excluded from this study. All patients gave written informed consent. The study was approved by the Ethics Committee of National Toyohashi Higashi Hospital.

Diagnostic catheterization and direct PTCA: Diagnostic catheterization was performed routinely in all patients just before direct PTCA. Direct PTCA was consistently and without exception a first strategy for recanalizing the (sub) occluded coronary arteries during this study and was performed via the femoral

approach. PTCA was started just after the diagnostic catheterization (within 30 minutes after entry into the catheterization laboratory). Initial success was defined as % diameter stenosis < 50% according to the Thrombolysis in Myocardial Infarction Criteria⁹⁾ 2 or 3 flow without major complications (death, recurrent AMI, or repeat PTCA) during the hospital stay. Follow-up catheterization was performed before discharge (one month after recanalization) in all eligible patients. The restenosis was defined as a % diameter stenosis > 50% at follow-up. Blood samples were obtained to measure CPK levels every four hours for 24 hours after admission.

Angiographic analysis: The paired coronary angiograms taken at baseline and follow-up were reviewed by two independent and experienced physicians. Antegrade coronary flow and collateral flow from the opposite coronary arteries were evaluated by the Thrombolysis in Myocardial Infarction criteria⁹⁾ and the Rentrop score,¹⁰⁾ respectively. The % diameter stenosis was calculated from the reference diameter (mean of the proximal and distal references) and minimal lumen diameter measured by a caliper method at baseline and one-month follow-up. The paired left ventriculograms in the right anterior oblique view were also analyzed by two independent and experienced physicians. Left ventricular end-diastolic and end-systolic contours were manually traced on paper and digitized into a computer. Regional wall motion and left ventricular volume at baseline and one-month follow-up were evaluated using the centerline and area length methods, respectively. Global ejection fraction (GEF) was calculated from left ventricular volume at the end-diastolic and end-systolic phases. Only normal sinus beats were analyzed. The centerline method has been described in detail elsewhere.^{2,11)} Briefly, it calculates regional wall motion along 100 chords drawn perpendicular to a centerline constructed midway between the end-diastolic and end-systolic contours and expresses abnormality in units of standard deviation from the normal mean as determined in a group of 64 normal patients. The regions indicated by chord numbers 0 to 10 and 81 to 100 in the centerline method were excluded from wall motion analysis because they should be considered as aortic and mitral valve regions.

Definition of hypokinesis in infarcted area (infarcted wall motion) and hyperkinesis in noninfarcted area (HWM): The severity of hypokinesis was expressed by mean regional wall motion (standard deviation/chord, average of standard deviations from the normal mean) in most hypocontractile 50% chords responsible to left anterior descending coronary artery area (chord number 11–66) (infarcted wall motion)²⁾ and the extent of hypokinesis was defined as the number of chords with regional wall motion < -1. Hyperkinesis was also expressed by mean regional wall motion in most hypercontractile 50% chords of a noninfarcted area (67–80) (HWM).²⁾ When a patient had $HWM \geq 0.5$ standard

deviation/chord, hyperkinesis in the patient was considered to be positive dichotomously. The number of chords in a noninfarcted area with regional wall motion > 1 was used to determine the extent of hyperkinesis. The paired parameters of left ventricular function were compared between baseline and one-month follow-up in patients with successful direct PTCA.

Statistical methods: All values are expressed as mean $\pm$ standard deviation. Chi-square analysis was used to compare categorical variables. The paired *t*-test was used to analyze the serial changes in the left ventricular functional variables. A probability level < 0.05 was considered to be statistically significant.

RESULTS

Clinical demographics and hemodynamic data: Sixty one of 517 patients

Table I. Clinical and Hemodynamic Data on Admission in Patients with First Acute Anterior Myocardial Infarction

		Overall
Patient number		61
Mean age (years)		65 $\pm$ 13
Males (%)		44 (72.1)
Time of coronary artery occlusion (hrs)		6.0 $\pm$ 6.0
Forrester subset	1 (%)	15 (24.6)
	2 (%)	24 (39.3)
	3 (%)	9 (14.8)
	4 (%)	13 (21.3)
Cardiogenic shock (%)		4 (6.6)
Use of IABP (%)		5 (8.2)
Peak CPK (IU/l)		3577 $\pm$ 2401
Occluded site	proximal (%)	30 (49.2)
	mid (%)	30 (49.2)
	distal (%)	1 (1.6)
TIMI flow	0 (%)	49 (80.3)
	1 (%)	5 (8.2)
	2 (%)	7 (11.5)
Collateral flow	— (%)	33 (54.1)
	1+ (%)	21 (34.4)
	2+ (%)	7 (11.5)
MR	— (%)	19 (31.1)
	1+ (%)	24 (39.3)
	2+ (%)	16 (26.2)
	3+ (%)	2 (3.3)
Global ejection fraction (%)		45 $\pm$ 10
LVEDVI (ml/m ²)		84 $\pm$ 18
Systolic blood pressure (mmHg)		126 $\pm$ 29
Heart rate (/min)		79 $\pm$ 16
LVEDP (mmHg)		25.5 $\pm$ 7.3

CPK = creatine phosphokinase; TIMI = thrombolysis in myocardial infarction trial; MR = mitral regurgitation; LVEDVI = left ventricular end diastolic pressure; IABP = intra aortic balloon pumping

with AMI admitted during the study period were enrolled as subjects. Table I lists the clinical demographics and hemodynamic data of the study population. There were 44 male (72.1%) and 17 female subjects. The mean age of the subjects was 65 ± 13 years. Forrester subset III or IV was found in 36.1% and cardiogenic shock in 6.6%. Coronary angiography revealed the proximal left anterior descending coronary artery was occluded in approximately half of the patients. Spontaneous recanalization (The Thrombolysis in Myocardial Infarction criteria 2) was recognized in 11.5%. Collateral circulation was found in 45.9%.

Initial and short-term follow-up results of direct PTCA: The initial success rate of direct PTCA was 98.4% (60/61) and the mean final % diameter stenosis was $37 \pm 14\%$. In one patient, a guide wire could not be passed beyond the occlusion so conservative treatment was performed. Four patients died during the hospital stay, 3 due to chronic heart failure and 1 due to ventricular septal rupture. The remaining 56 patients, excluding the unsuccessful case and 4 deaths, underwent one-month follow-up catheterization which demonstrated a mean % diameter stenosis of $38 \pm 27\%$ and a restenosis rate of 18% (10/56).

Changes in left ventricular function and hyperkinesis in noninfarcted area: Changes in left ventricular function are shown in Table II. GEF and left ventricular end-diastolic volume index improved significantly during follow-up. Regional wall motion showed significant improvement in infarcted area. HWM increased slightly from 0.18 ± 1.07 to 0.48 ± 1.30 . As shown in Figure 1A and 1B, delta GEF (GEF at follow-up minus GEF at baseline) was correlated with both delta infarcted wall motion (infarcted wall motion at follow-up minus infarcted wall motion at baseline) and delta HWM (HWM at follow-up minus HWM at baseline) ($r = 0.576$ $p < 0.0001$, $r = 0.383$ $p = 0.0036$, respectively). In addition, delta GEF showed better correlation with delta (HWM + infarcted wall

Table II. Changes in Left Ventricular Function

	Baseline	After one month	<i>p</i> value
GEF (%)	45 ± 11	56 ± 11	< 0.0001
LVEDVI (ml/m ²)	85 ± 18	80 ± 16	< 0.0001
Number of chords with RWM ≤ -1	55 ± 7	42 ± 17	0.0270
Number of chords with RWM >1	2 ± 4	4 ± 6	0.0064
IWM	-3.96 ± 0.45	-2.72 ± 1.00	< 0.0001
HWM	0.18 ± 1.07	0.48 ± 1.30	0.0608
HR (/min)	80 ± 15	77 ± 14	0.4947
LVEDP (mmHg)	25.5 ± 7.3	17.3 ± 5.5	0.0001
% diameter stenosis	37 ± 14	38 ± 27	0.4693

GEF = global ejection fraction; LVEDVI = left ventricular end diastolic volume index; RWM = regional wall motion; HWM = hyperkinetic wall motion; IWM = infarcted wall motion; HR = heart rate; LVEDP = left ventricular end diastolic pressure

Figure 1. Delta global ejection fraction (GEF) during one-month follow-up after direct percutaneous transluminal coronary angioplasty (PTCA) was correlated with delta infarcted wall motion (IWM) and delta hyperkinesis (HWM) ($r=0.576$, $p<0.0001$, $r=0.383$, $p=0.0036$, respectively) (**1A** and **1B**). Delta GEF showed a good correlation with delta (IWM and HWM) ($r=0.593$, $p<0.0001$) (**1C**).

Table III. Comparison of Clinical and Hemodynamic Data between Groups with and without Hyperkinesis at Baseline in Acute Anterior Myocardial Infarction

	HWM (+)	HWM (-)	<i>p</i> value
Patient number	21	40	
Means (years)	66 ± 12	65 ± 14	0.7465
Malcs (%)	14 (66.7)	30 (75.0)	0.7954
Duration of coronary occlusion (hrs)	7.35 ± 7.75	5.20 ± 4.63	0.2188
Forrester subset			0.8107
1 (%)	6 (28.6)	8 (20.0)	
2 (%)	9 (42.8)	18 (45.0)	
3 (%)	3 (14.3)	5 (12.5)	
4 (%)	3 (14.3)	9 (22.5)	
Cardiogenic shock (%)	2 (9.5)	0 (0)	0.2148
Peak CPK (IV/l)	2573 ± 1614	4077 ± 2587	0.0249
Occluded site			0.2611
proximal (%)	8 (38.1)	23 (57.5)	
mid (%)	13 (61.9)	16 (40.0)	
distal (%)	0 (0)	1 (2.5)	
TIMI flow			0.0871
0 (%)	19 (90.5)	27 (67.5)	
1 (%)	0 (0)	8 (20.0)	
2 (%)	2 (0.5)	5 (12.5)	
Collateral flow			0.3253
— (%)	14 (66.7)	20 (50.0)	
1 + (%)	5 (23.8)	15 (37.5)	
2 + (%)	2 (9.5)	5 (12.5)	
MR			0.4579
— (%)	7 (33.3)	11 (27.5)	
1 + (%)	10 (47.6)	14 (35.0)	
2 + (%)	4 (19.1)	13 (32.5)	
3 + (%)	0 (0)	2 (5.0)	
Global ejection fraction (%)	51 ± 6	43 ± 11	0.0023
LVEDVI (ml/m ²)	79 ± 17	87 ± 19	0.1270
IWM	-3.92 ± 0.40	-3.96 ± 0.56	0.7860
HWM	1.18 ± 0.70	-0.45 ± 0.79	0.0001
Number of chords with RWM < -1	52 ± 5	57 ± 8	0.0001
LVEDP (mmHg)	23.3 ± 9.2	26.9 ± 5.8	0.0433

CPK = creatine phosphokinase; TIMI = thrombolysis in myocardial infarction trial; MR = mitral regurgitation; LVEDVI = left ventricular end diastolic volume index; LVEDP = left ventricular end diastolic pressure.

motion) [(HWM plus infarcted wall motion at follow-up) minus (HWM plus infarcted wall motion at baseline)] ($r = 0.593$, $p < 0.0001$. Figure 1C) compared with delta infarcted wall motion and delta HWM.

Predictive factors of hyperkinesis at baseline and follow-up: At baseline, the peak CPK level and left ventricular end-diastolic pressure were lower and the extent of the infarcted wall region was less in the HWM positive group than in the HWM negative group (Table III). The same patterns were observed during follow-up, although the peak CPK level was not significantly different between the two groups. The left ventricular end-diastolic volume index was smaller and mitral regurgitation tended to be less frequent in patients with hyperkinesis compared with patients without hyperkinesis at follow-up (Table IV).

Table IV. Comparison of Clinical and Hemodynamic Data between Groups with and without Hyperkinesis One Month after Recanalization in Acute Anterior Myocardial Infarction

		HWM (+)	HWM (-)	p value
Patient number		28	28	
Mean age (years)		66 ± 12	62 ± 13	0.2220
Males (%)		21/28 (75.0)	20/28 (71.4)	0.7628
Duration of coronary occlusion (hrs)		5.7 ± 5.7	5.9 ± 5.9	0.9537
Forrester subset at follow-up	1 (%)	27 (96.4)	22 (78.6)	0.1647
	2 (%)	1 (3.6)	2 (7.1)	
	3 (%)	0 (0)	3 (10.7)	
	4 (%)	0 (0)	1 (3.6)	
Cardiogenic shock (%)		2 (7.1)	1 (3.6)	0.9999
Peak CPK (IV/l)		2952 ± 1676	4015 ± 2818	0.1081
Occluded site	proximal (%)	12 (42.9)	17 (60.7)	0.2301
	mid (%)	16 (57.1)	10 (35.7)	
	distal (%)	0 (0)	1 (3.6)	
TIMI flow	0 (%)	21 (75.0)	21 (75.0)	0.6836
	1 (%)	4 (14.3)	2 (7.1)	
	2 (%)	3 (10.7)	5 (17.9)	
Collateral flow	— (%)	15 (53.6)	14 (50.0)	0.9197
	1 + (%)	9 (32.1)	10 (35.7)	
	2 + (%)	4 (14.3)	4 (14.3)	
MR at follow-up	— (%)	20 (71.4)	14 (50.0)	0.0983
	1 + (%)	8 (28.6)	12 (42.9)	
	2 + (%)	0 (0)	2 (7.1)	
GEF at follow-up (%)		61 ± 7	51 ± 13	0.0012
LVEDVI at follow-up		72 ± 11	88 ± 17	0.0002
IWM		-2.30 ± 1.20	-2.73 ± 1.01	0.1234
HWM		1.50 ± 0.72	-0.54 ± 0.87	0.0001
Number of chords with RWM < -1		35 ± 16	48 ± 17	0.0085
LVEDP (mmHg)		17.8 ± 6.4	16.8 ± 4.3	0.5598

TIMI = thrombolysis in myocardial infarction trial; MR = mitral regurgitation; LVEDVI = left ventricular end diastolic volume index; IWM = infarcted wall motion; HWM = hyperkinetic wall motion; RWM = regional wall motion; LVEDP = left ventricular end diastolic pressure.

DISCUSSION

The results of the present study have demonstrated that hyperkinesis in a noninfarcted region was identified in 34.4% of patients with one-vessel first anterior AMI at baseline, and that its incidence increased to 50.0% one month after revascularization by direct PTCA. The mean HWM increased slightly from 0.18 ± 1.07 standard deviation/chord at baseline to 0.48 ± 1.30 standard deviation/chord one month after direct PTCA. This enhancement of HWM in the noninfarcted areas significantly contributed to the improvement in GEF (11%) and the recovery of infarcted wall motion.

Mechanism and incidence of hyperkinesis in AMI: Thus far, three mechanisms of hyperkinesis in acute coronary artery occlusion have been suggested, 1) an intraventricular regional interaction between infarcted and noninfarcted myo-

cardium due to mechanical unloading of the remote myocardium,^{12,13} 2) the Frank-Starling mechanism,¹⁴⁻¹⁶ and 3) the release of additional catecholamines after acute coronary occlusion.¹⁷ However, the exact mechanism is still a matter of controversy because acute ischemia is usually accompanied by compensatory operation of the Frank-Starling mechanism and myocardial function is regulated by various neurohumoral mechanisms in clinical situations. The incidence of hyperkinesis differs among previous reports^{1,18-21} that have been designed to estimate the effect of reperfusion therapy with streptokinase or tissue plasminogen activator for AMI on left ventricular function and late clinical outcomes. Because they experienced difficulties in defining hyperkinesis dichotomously, these studies reported a wide range of incidences (4% to 68%). Meanwhile, these data on the incidence of and change in hyperkinesis are based on thrombolytic therapy only, so the impact of successful direct PTCA on hyperkinesis is not well known.

Possible factors influencing the occurrence of hyperkinesis: Historically, the clinical significance of hyperkinesis in AMI patients has focused on the relationship with the clinical or hemodynamic severity of AMI. First, uncomplicated infarction resulted in a greater incidence of hyperkinesis in noninfarcted areas compared with complicated cases.²⁰ Second, hyperkinesis was detected more often or in a higher degree in one vessel disease than in multivessel disease.^{3,19} The infarct related artery did not affect the incidence of hyperkinesis.^{1,19} In this study, only patients with angiographically documented one vessel stenosis in the left anterior descending coronary artery were included for analysis in order to eliminate the influence of additional hypoperfusion or infarction due to a second diseased vessel. In this study, the peak CPK level and left ventricular end-diastolic pressure were lower and the extent of the infarcted wall motion was less in patients with hyperkinesis than in those without hyperkinesis at baseline. These results indicate that, in contrast to previous studies, the hyperkinesis did not depend on the large size or hemodynamic severity of AMI. This tendency was also recognized at follow-up. In spite of the more stable hemodynamic condition at one-month follow-up, the incidence of hyperkinesis increased and hyperkinesis contributed to the increase in GEF. Our data suggest that hyperkinesis is synergistic with infarcted wall motion^{12,13} but is not a compensatory mechanism.^{19,22}

Time course of hyperkinesis: Several reports have described the change in hyperkinesis after reperfusion therapy in patients with AMI.^{2,4, 5,11,18,21,23} In almost all studies in which intracoronary or intravenous STK alone or no thrombolytic therapy was performed, hyperkinesis decreased^{2,4,5,11,24} or had disappeared²¹ at follow-up. However, additional mechanical revascularization resulted in good maintenance of hyperkinesis at follow-up.^{11,18,23} Sheehan *et al.*¹¹ reported that the degree of hyperkinesis decreased 6-7 weeks after reperfusion therapy in all 3 groups (streptokinase + coronary artery bypass grafting group, streptokinase

alone group, and non-revascularized group) studied. However, the loss was less in the bypass grafting group. Grine *et al.*¹⁸⁾ demonstrated that after 7 days hyperkinesis remained at the same level as baseline in a thrombolytic study using intravenous tissue plasminogen activator, in which emergent PTCA or bypass grafting was added in 55% of the cases. Our study not only confirmed this maintenance of hyperkinesis but also showed an increase in hyperkinesis after direct PTCA. The increase in hyperkinesis might be the result of better recovery of infarcted wall region and not a separate compensation of the infarcted wall motion.

Efficacy of direct PTCA over thrombolytic therapy in AMI patients: In several randomized studies, direct PTCA has been shown to be more efficient in reducing the mortality rate and non-fatal reinfarction rate and preserving left ventricular function, at least until discharge or within 30 days after AMI, compared with thrombolytic therapy.^{6,7,25)} With regard to the difference in recovery of left ventricular function between direct PTCA and thrombolytic therapy, several reasons could be considered, such as more rapid restoration of the Thrombolysis in Myocardial Infarction criteria grade 3 flow after revascularization, a higher patency rate, and lower residual stenosis²⁶⁾ that lead to sustained optimal blood flow through the infarct-related vessel before discharge in the direct PTCA group. These might have contributed to the greater degree of improvement in left ventricular function⁷⁾ in our study. The absence of or less hemorrhagic extension to non-infarcted areas of myocardial tissue recognized after thrombolytic therapy⁷⁾ also may partly explain the higher incidence of hyperkinesis at one-month in the present study compared with previous results of thrombolytic therapy with and without PTCA. This certain amount of sustained or newly developed hyperkinesis at follow-up contributed to the increase in GEF (11%), and might lead to the longer -term benefit.

Study limitations: Use of a single-plane, right anterior oblique ventriculogram may underestimate hyperkinesis of the noninfarct zone. Nevertheless, because the ejection fraction was calculated from a right anterior oblique projection, hyperkinesis of a magnitude sufficient to maintain the ejection fraction should be apparent in the same view.^{18,27)} In addition, previous studies have shown that the severity of hypokinesis in the infarct region could be detected with greater sensitivity in the right anterior oblique projection.²⁸⁾ The only exception was in patients with left circumflex artery occlusion²⁷⁾ who were excluded from this study.

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