Effect of Transluminal Coronary Recanalization on Left Ventricular Regional Wall Motion and Clinical Course in Acute Myocardial Infarction

MASAKIYO NOBUYOSHI, M.D.

We performed percutaneous transluminal coronary recanalization (PTCR) in 90 patients within 12 hours of onset of acute myocardial infarction (AMI). Fifty seven patients had total occlusion and 33 patients had subtotal occlusion of the involved coronary artery. Reopening of the occluded coronary artery by injection of isosorbide dinitrate (ISDN) was achieved in 24.4%. Continuous infusion of Urokinase was effective in 82.7%.

Comparison of conventional therapy with PTCR showed that ejection fraction was higher in patients with PTCR than in those with conventional therapy, and that wall motion shortening was better in the former than in the latter.

Relationship of regional wall motion shortening to the time interval from the onset of AMI showed that wall motion shortening was better if recanalized within 3 hours to and was fine within 6 hours, but poor after 6 hours of onset of AMI.

IN recent years, percutaneous transluminal coronary recanalization (PTCR) has been performed shortly after the onset of acute myocardial infarction (AMI) with use of Streptokinase or Urokinase (UK). It is reported that PTCR is effective for the reduction of myocardial necrotic size. Recanalization of the occluded coronary artery by PTCR has been widely recognized. However investigation on reduction of myocardial infarction size, short term prognosis of PTCR and safety of PTCR are still desirable.

Informed consent from patients and immediate relative was obtained in those patients admitted within 12 hours of the onset of AMI (AMI-1) and subjected to PTCR. Those patients admitted after 12 hours of the onset of AMI were treated with conventional therapy in the CCU (AMI-2). AMI-1 group consisted of 90 patients with mean age of 57.2, 72 were male and 18 female. AMI-2 group consisted of 101 patients with a mean age of 68, 69 males and 32 females (Table I).

PATIENTS

Patients with acute myocardial infarction hospitalized between July 14th, 1979 and August 31th, 1982 were the subject of this report.

Key Words:

Acute myocardial infarction
Urokinase
Percutaneous transluminal coronary recanalization
Regional left ventricular wall motion
Coronary spasm

METHOD

1. Emergency Coronary Arteriography and PTCR

Left ventricular pressure and aortic pressure were measured via Sones catheter by brachial approach. The right ventricular hemodynamics were measured with the use of a Swan-Ganz catheter. Left and right coronary arteriography were performed to confirm the infarct-related coronary artery. Isosorbide dinitrate (ISDN) 5 mg was selectively injected into the involved coronary artery through the Sones catheter

Director of Department of Cardiology, Kokura Memorial Hospital, Kitakyushu, Japan

Mailing address: Masakiyo Nobuyoshi, M.D., Department of Cardiology, Kokura Memorial Hospital, 1-1 Kifunemachi, Kokurakita-ku, Kitakyushu 802, Japan

TABLE I CLINICAL CHARACTERISTICS
Patient population (July 14, '79 ~ August 31, '82)

	AMI-1 (ISDN and UK combination therapy)	AMI-2 (conventional therapy)
Number	90 cases	101 cases
Age	57.2 ± 12.0 (31 ~ 88) y.o.	68.0 ± 10.7 (39 ~ 91) y.o.
Sex		
Female	18 cases	31 cases
Male	72 cases	69 cases

AMI = acute myocardial infarction; ISDN = isosorbide dinitrate; UK = urokinase

TABLE II PROTOCOL OF PERCUTANEOUS
TRANSLUMINAL RECANALI-
ZATION

Protocol of ISDN and UK combination therapy

CAG = coronary arteriography; inj. = injection.

and coronary arteriography was repeated. Thereafter one bolus injection of UK (24,000—in the initial 6 patients and subsequently standardized to 120,000 u) into the involved coronary artery was made and repeat coronary arteriography was performed. Then semi or selective infusion of UK 240,000 u into the involved coronary artery was made through the Sones

catheter over a 15 minute period by constant infusion machine (Mark IV). This infusion was repeated 2–3 times and repeat coronary arteriography was obtained each time (Table II).

2. Post PTCR Treatment

The patients were given drip infusion of UK 240,000 u and Heparin 10,000–15,000 u a day for 2 or 3 days. Warfarin was administered to maintain thrombotest at about 20%.

3. Coronary arteriography at the chronic stage

About one month after the AMI, hemodynamics were measured by use of Swan-Ganz catheter and coronary arteriography was performed by the Sones technique. Left ventriculography was performed in RAO 30° and LAO 60° with 76% Urographin 35 ml at the rate of 6 ml per second. Coronary arteriograms and left ventriculograms were analyzed with a Tagarno Viewer by more than 2 observers.

4. Effect of PTCR

Narrowing of infarct-related coronary artery was divided into 1) total obstruction, and 2) subtotal obstruction: The latter group was subdivided into: a) 99% narrowing with severely delayed filling (contrast medium did not reach the peripheral artery) b) 99% narrowing with moderately delayed filling (contrast medium reached the peripheral artery but very slowly) c) 99% narrowing with mildly delayed filling (contrast medium reached the peripheral artery slowly) d) 99% narrowing without delayed filling e) less than 90% narrowing. PTCR was considered effective when improvement of one grade or more was recognized (Table IV).

Fig.1. Measurement of left ventricular wall motion shortening according to Pujadus method in RAO 30°.

5. Effect of PTCR on Improvement of Left Ventricular Function

The patients were divided into recanalized group when final arteriographic finding revealed any antegrade flow after PTCR, and nonrecanal-

ization group when total occlusion remained after PTCR.

i) Ejection fraction

Recanalized, nonrecanalization and conventional treatment groups were compared by ejection fraction obtained from left ventriculography at RAO 30°.

ii) Analysis of regional left ventricular wall motion

Regional percent wall shortening was calculated from the modified hemiaxis shortening methods according to Pujadus¹ in which the left ventricular wall is divided into 5 segments to evaluate infarct-related myocardial wall motion (Fig. 1). Measurement was made in one cardiac cycle but cardiac cycles before and after premature beat were excluded. For this analysis, the patients with reinfarction, significant narrowing of noninfarcted coronary artery affecting regional wall motion, or infarct-related circumflex artery were excluded. Statistical

Ejection fraction in chronic stage

Fig.2. The left ventricular ejection after about 4 weeks from the onset of acute myocardial infarction studied in three groups UK (-): conventional treatment group.

TABLE III

Combination of ISDN and UK treatment	
ISDN alone	9 (10.0%)
ISDN and UK bolus	29 (32.2%)
ISDN and UK cont.	52 (57.8%)
Main lesion of ISDN and UK combination therapy group	
RCA	32 (35.6%)
LAD	40 (44.4%)
LCX	17 (18.9%)
LMT	1 (1.1%)
Examination time after onset	
Acute stage	4.1 ± 2.7hr.
~ 3hr.	44 cases
~ 6hr.	30 cases
~ 12hr.	16 cases
Chronic stage	29.6 ± 7.7D

Upper column shows the descriptions of patient population treated by percutaneous transluminal recanalization.

Middle column shows percentage of related coronary arteries.

RCA = right coronary artery; LCA = left coronary artery; LCX = left circumflex artery; LMT = left main trunk

Lower column shows the time interval from the onset of acute myocardial infarction to emergency coronary arteriography

hr = hours

analysis was made by χ^2 test, Student t test and paired t test.

RESULTS

1. Involved Coronary Artery and Time Elapsed before PTCR

Ninety patients received PTCR within 12 hours after onset of AMI. Nine patients received ISDN only, 29 ISDN and one bolus of UK injection, and 52 ISDN, one bolus UK injection and continuous UK infusion (Table III). The involved coronary artery was the RCA in 32 patients, the LAD in 40, the LCX in 17 and the left main trunk in one patient. Time interval

TABLE IV RELATIONSHIP BETWEEN FINDINGS OF INITIAL ARTERIOGRAM AND THOSE AFTER ISOSORBIDE DINITRATE INJECTION

Control	Total occlusion	After ISDN				
		99	99	99	99	≤ 99
Before ISDN						
Total (57 cases)	46	4	5	0	1	1
a) 99 (2 cases)	0	0	1	1	0	0
b) 99 (24 cases)	6	0	11	1	4	0
c) 99 (4 cases)	1	0	0	1	2	2
d) 99 (3 cases)	0	0	0	0	3	0

Encircled groups were considered to be effective by administration of isosorbide dinitrate.

99 = 99% narrowing with severe delayed filling;

99 = 99% narrowing with moderate delayed filling;

99 = 99% narrowing with mild delayed filling

from the onset of AMI to coronary arteriography was within 3 hours in 44 patients, 3 to 6 in 30, 6 to 12 in 16, for an average time interval of 4.1 hours. Chronic phase coronary arteriography was performed after a mean of 29.6 days, subsequent to the AMI.

2. Effects of ISDN and UK on Recanalization

a) Treatment of ISDN

Coronary arteriographic findings before and after ISDN were compared (Table IV). Fifty seven patients had total occlusion in the initial arteriography, 9 patients improved to 99% and delay occlusion, and 2 patients to less than 99% narrowing. Of 30 patients with delayed filling in the control arteriography, 11 patients improved by one degree or more, and 8 patients to 99% narrowing without delayed filling. Nine patients progressed from subtotal occlusion to total occlusion. Three patients with less than 99% narrowing in the control arteriography remained unchanged. Effect of ISDN on the recanalization on the whole was 24.4%.

b) Treatment of combined therapy

Fifty two patients received combined therapy (ISDN, one bolus UK injection and continuous UK infusion) and their coronary arteriographic findings before and after the combined therapy were compared. Of 35 patients with total occlusion in the control arteriography, 20 patients improved to 99% narrowing with delayed filling, and 10 patients to less than 99%

TABLE V

Effective		
<i>Relationship between latency and recanalization with ISDN and UK</i>		
~ 3 hr.	23/26	88.5%
~ 6 hr.	13/16	81.3%
~ 12 hr.	8/10	80.0%
<i>Relationship between involved coronary artery and recanalization with ISDN and UK</i>		
RCA	15/17	88.2%
LAD	22/24	91.7%
LCX	7/11	63.6%

narrowing. Of 15 patients with subtotal occlusion in the control arteriography, one patient improved to 99% narrowing with delayed filling, and 10 patients improved to 99% narrowing without delayed filling; 2 patients with 99% narrowing improved to less than 99% narrowing. Overall improvement was 82.7%.

c) Effect of PTCR by the time interval

Effect of PTCR by the time interval after the onset of AMI was studied in 52 patients of continuous UK infusion (Table V). Recanalization was observed in 88.5% of the patients treated within 3 hours of infarction, 81.3% in those treated between 3 to 6 hours of AMI, and 80% when treated 6 to 12 hours after the onset of MI. In other words, the shorter the interval between the onset and PTCR, the better the

Fig. 3. Regional wall motion shortening of the involved right coronary artery (RCA)

Regional wall shortening with recanalized group was significantly better in the inferior wall (seg. 4), as compared with non-recanalized and conventional treatment group.

UK (-) = conventional treatment group; UK (A) = non-recanalized group; UK (B) = recanalized group; cont. = control.

The shaded area in the figure shows normal ranges of regional wall shortening.

Fig.4. Regional wall motion shortening of the involved left anterior descending artery (LAD)

Regional wall shortening in the recanalized group was significantly better in the anterior wall (seg. 2) as compared with non-recanalized and conventional treatment groups.

UK (-) = conventional treatment group; UK (A) = non-recanalized group; UK (B) = recanalized group; cont. = control group.

The shaded area in the figure shows normal ranges of regional wall shortening.

recanalization rate was, but the difference was statistically non-significant. Good recanalization was obtained in the LAD in 91.7%, and in the RCA (88.2%), but only 63.6% in the LCX. These differences were non-significant.

3. Ejection Fraction

Ejection fraction was compared between the recanalized group, nonrecanalized group and conventional therapy group. Significantly better ejection fraction ($p < 0.01$) was recognized in the recanalized group ($60.1 \pm 12.4\%$) as compared with nonrecanalized group ($47.6 \pm 16.6\%$) and conventional group ($52.8 \pm 11.5\%$).

4. Left Ventricular Regional Wall Motion

Reduction of myocardial infarction size by PTCR was considered to be the mechanism of

better ejection fraction in the recanalized group (Fig. 5). Regional percent wall shortening was studied in those patients with the lesion localized to the LAD or the RCA only. The shaded areas in the figure show regional percent wall shortening in 10 normal patients as control. Regional wall shortening in the recanalized group was significantly better in the anterior wall (Segment 2) in the LAD lesion group and inferior wall (seg 4 and 5) in the RCA lesion group as compared with the nonrecanalized and conventional therapy group (Figs. 3, 4). No patients in non-recanalized group and conventional therapy group had normal wall motion in the anterior wall (seg 2) and in the inferior wall (seg 4), while 15 of the 38 patients (39.5%) in the recanalized group had normal segmental wall motion of the affected areas. However, many patients in the

Fig. 5. Relationship of regional wall shortening to the time elapsed between the onset of acute myocardial infarction and percutaneous transluminal recanalization and degree of recanalization

If recanalization occurs within 6 hours of the onset of acute myocardial infarction, left ventricular wall motion shortening will remain fairly good, but even though recanalization occurs after 6 hours of the onset of acute myocardial infarction, left ventricular wall motion shortening will remain poor.

The upper band shows the range of percent wall motion shortening of normal control group and the lower band shows the range of that of patients with total occlusion even after PTCR. Closed circle shows patients with moderate delay by PTCR. Open circle shows the patients with mild or without delay by PTCR.

recanalized group showed poor wall shortening. Although not shown in the figure, averages of regional percent wall shortening in the noninfarct related areas of the left ventricle were within the normal range.

5. Relationship of Regional Wall Shortening to the Time Elapsed between the Onset of AMI and PTCR, and Degree of Recanalization

Regional wall motion in the chronic phase depended on the degree of recanalization and the time involved in reestablishing flow (Fig. 5). Poor regional wall motion were observed in

patients with late or poor recanalization. The patients who improved from total occlusion to less than subtotal occlusion were grouped by time interval and their segmental wall shortening were studied. The normal average for the inferior wall (seg 4) and anterior wall (seg 2) were considered to be 100%; the study subject's segmental wall motion was shown as % of the average. Normal range of segmental wall shortening was observed in 10 of 16 patients (62.5%), recanalized within 3 hours of AMI; in 5 of 14 patients (35.7%), if recanalized within 3–6 hours and in none beyond 6 hours. Between the last group (more than 6 hours) and the

TABLE VI

<i>Cinical course and complications</i>				
<i>A: In the catheterization room in acute stage</i>				
<i>I.</i>	<i>Death</i>	<i>1/102(LOS)</i>		
<i>II.</i>	<i>Arrythmia due to reperfusion injury</i>			
	<i>Frequent VPC</i>	<i>10/53</i>		
	<i>Ventricular tachyarrythmia</i>	<i>3/53</i>		
	<i>Conduction disturbance</i>	<i>3/53</i>		
	<i>Total</i>	<i>16/53 (30.2%)</i>		
<i>B: Subacute ~ chronic stage</i>				
<i>I.</i>	<i>Death</i>	<i>AMI-1 recanal.</i>	<i>AMI-1 non-recanal.</i>	<i>AMI-2 convent.</i>
	<i>LOS, CHF</i>	<i>0</i>	<i>1</i>	<i>12</i>
	<i>Rupture</i>	<i>1</i>	<i>2</i>	<i>6</i>
	<i>Arrythmia</i>	<i>0</i>	<i>0</i>	<i>3</i>
	<i>noncardiogenic</i>	<i>0</i>	<i>1</i>	<i>4</i>
	<i>Total</i>	<i>1/53</i>	<i>4/49</i>	<i>25/101</i>
<i>II.</i>	<i>Re-infarction</i>		<i>5/53 (all alive)</i>	
<i>III.</i>	<i>Infarctectomy</i>		<i>1 (alive)</i>	

other two groups (within 6 hours) significant statistical difference was observed. The relationship between the degree of recanalization and percent segmental wall shortening in those patients on whom recanalization was achieved within 6 hours was studied. Twelve of 19 patients (63.2%) of recanalization with less than mildly delayed filling had normal wall motion, while only 3 of 11 patients (29.3%) with recanalization of 99% narrowing with more than moderately delayed filling had normal wall motion.

6. Clinical Course

One patient, 88 years old female admitted to our hospital in shock, died during emergency coronary arteriography. She had a new anterior infarction over an old inferior infarction; coronary arteriography revealed total obstruction of the LAD; following the injection of ISDN, the blood pressure fell and died (Table VI). Reperfusion arrhythmias were recognized in 16 of 53 patients with recanalization but these were

transient. Ventricular fibrillation occurred in 2 patients but successfully cardioverted. A patient with ventricular tachycardia was controlled with intravenous injection of xylocaine. Temporary pacing was effective for complete AV block. Only one patient in the recanalization group died in the CCU. A patient, 77 years old female had 99% narrowing with delay of the LAD 2 hours after the onset of infarction and coronary arteriographic findings remained unchanged after PTCR. After returning to CCU, frequent ventricular premature contraction occurred and she died of cardiac rupture. Three of 49 patients in nonrecanalized group died. One died of heart failure and two of cardiac rupture. Twenty one of 101 patients in conventional group died, twelve died of heart failure or shock, 6 of cardiac rupture, 3 of arrythmia. Reinfarction occurred in 5 patients in recanalized group, but no patient died. Coronary arteriography in the chronic phase showed total occlusion of the same site as in the acute phase. One patient underwent a successful emergency left ventricular infarctectomy for frequent ventricular fibrillation.

DISCUSSION

1. Recanalization Rate

PTCR has been effective therapy for acute myocardial infarction since Rentrop et al.² Ganz et al.³ and Weinstein et al.⁴ made their reports. These authors reported a recanalization rate ranging from 40 to 90%. The PTCR was performed by combining nitroglycerin, mechanical recanalization with guide wire, and super selective infusion with a small gauged catheter of Streptokinase. We performed PTCR⁵ by combining one bolus injection of 5 mg ISDN, one bolus injection of 120,000 u UK and continuous semi or selective infusion of 240,000 to 720,000 u UK. The improvement of antegrade flow of the occluded coronary artery by injection of ISDN suggested that coronary spasm may be primarily or secondarily involved in the site of occluded coronary artery in acute myocardial infarction. Coronary thrombus was observed in the site of occluded coronary artery in many patients. Lysis of the coronary thrombus was observed with one bolus injection of UK and/or continuous infusion of UK. Recanalization rate was 82.7% on the whole, but the extent of recanalization differed. In 5 of 52 patients the occlusion remained complete. In 15 patients moderately delayed filling, and in 10 mildly

delayed filling were achieved. In seventy five percent of patients studied in the chronic phase had further improvement in the narrowing compared with that in the acute phase; 16% remained unchanged and 10% progressed to total occlusion. The ratio of complete occlusion before and after PTCR were 48% and 12.2% respectively. These findings suggest that lysis of coronary thrombus by UK is still in progress even after PTCR. Spann et al⁶ reported that 7 of 13 patients showed early recanalization by large amount of Streptokinase injection intravenously when administered within one hour of the onset of infarction. These findings suggest the importance of intravenous infusion of UK in the CCU after PTCR. Superselective infusion of UK or SK into the involved coronary artery has been reported as most effective in reestablishing blood flow at the site of the involved coronary artery but technical difficulties might occur. The danger of inducing coronary spasm and/or causing mechanical intimal injury by the catheter are ever present. Our semiselective infusion technique allows similar recanalization rate with less risks than superselective infusion.

2. *Involvement of Coronary Spasm in the Acute Phase*

Oliva and Breckinridge⁷ reported that patency returned in 9 of 15 patients who received nitroglycerin within 12 hours after the onset of myocardial infarction. In our study, recanalization was observed in only 22 of 90 patients (24.4%) after injection of ISDN into the coronary artery.

The question arises as to whether or not coronary spasm plays a role in the development of myocardial infarction. Although ISDN or nitroglycerin induce recanalization, it might be difficult to draw a conclusion as to whether coronary spasm is the cause of myocardial infarction.

The pressure applied during intracoronary injection of a contrast medium alone may remove the coronary thrombus and possibly induce recanalization. One case in our study recovered patency after injection of the contrast medium only. In the vast majority, however, recanalization resulting from injection of a contrast medium was not observed. Relief of obstruction in these cases was observed only after ISDN injection. The fact that mechanical recanalization rarely follows the injection of contrast medium only and that recanalization is induced

by ISDN in some cases suggests that coronary spasm is in some way involved in the production of myocardial infarction^{8,9}

3. *Effect of UK on Reduction in Myocardial Infarction Size*

The prevention of progressive myocardial necrosis by reperfusion of the occluded coronary artery in the early stage of acute myocardial infarction has been investigated by use of hemodynamics, cardiac enzyme, cardiac scintigraphy, and RI angiography.¹⁰⁻¹² Examination of ejection fraction and regional wall motion revealed that wall motion of the jeopardized area of myocardium depends on the presence or absence of recanalization. This finding suggests that early reperfusion reduces the myocardial necrosis. In most successful cases, CPK elevation is minimal and ECG shows no myocardial infarction pattern. Cardiac scintigraphy revealed no defect in the affected myocardium immediately after PTCR. The wall motion of affected myocardium in the chronic phase depends on the time interval from the MI onset to the recanalization, degree of recanalization, presence or absence of collaterals and size of infarction area. Total occlusion of coronary artery for 3 hours induced irreversible change of myocardium in animal experiments.¹³ We obtained good wall motion in more than a half of patients given PTCR within 6 hours. Rentrop et al.¹⁴ reported reduction of myocardial necrotic size by recanalization within 4 hours. Smalling et al.¹⁵ reported that wall motion of the affected myocardium was reversible by recanalization within 18 hours. If good collaterals exist in the occluded coronary territory, myocardium of these area was reversible when recanalization occurs even after many hours. We had few patients on whom recanalization was achieved after 6 hours of onset of AMI but improvement of wall motion was not recognized. However segmental wall motion improvement was obtained in patients recanalized within 6 hours. Recanalized patients with delayed filling of occluded coronary artery after PTCR show further recanalization, no change, or reocclusion of their involved coronary artery. Not only reoccluded patients but also patients with no improvement of delayed filling showed very poor wall motion in the chronic phase and the rise of CPK was identical to those with totally occluded patients. The early occurrence of antegrade coronary blood flow reduces myocardial necrotic size and is reflected on the

different mortality of patients with AMI. These findings suggest the need for emergency A-C bypass surgery for patients with delayed filling. Cardiac death in the CCU occurred, in one of 53 patients with recanalization, and 21 of 101 patients with conventional treatment. IABP was necessary in 3 patients undergoing PTCT, and they all fell into the nonrecanalized group. These findings suggest the need for emergency A-C bypass surgery in those patients with poor PTCT results.

4. Safety or Side Effect

The most serious side effect of PTCT may be reperfusion injury. Transient arrhythmia was recognized in 30.2% of our patients immediately after recanalization. One patient showed reelevation of the ST segment but neither was fatal. In animal experiments reperfusion after 6 hours of ligation of the left circumflex artery caused hemorrhage of myocardium in 75% of the animals.¹⁶ No patient had deterioration of left ventricular function. Use of large amount of UK did not result in hemorrhage complications and no patient had coronary angiography related complication.

5. Mortality Before and After PTCT

Mortality in the CCU was reduced to about 5% by PTCT. Reduction to 5% mortality in the CCU is very important because 2-3% reduction in mortality by conventional therapy is extremely difficult to achieve. Furthermore, very low mortality in the recanalized group indicates that every effort should be made to obtain recanalization by PTCT. In the future, introduction of combined therapy of PTCT and PTCA is necessary for the acute myocardial infarction.

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