Clinical Studies

Beneficial Effects of Mechanical Reperfusion Therapy on Left Ventricular Remodeling and Late Outcome Following Myocardial Infarction

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SUMMARY

The long-term relative benefits of thrombolysis and mechanical reperfusion therapy following acute myocardial infarction (AMI) have not been established. The purpose of this study was to compare left ventricular function, left ventricular remodeling and late outcome after AMI for different reperfusion therapies. Thirty consecutive patients suffering their first anterior wall myocardial infarction with coronary stenoses limited to the left anterior descending coronary artery were studied. They included 10 patients who underwent intracoronary thrombolysis (ICT), 10 who underwent PTCA and 10 who underwent noninterventional medical treatment. All patients underwent coronary angiography (CAG) during the acute phase of AMI and also during the follow-up period, and left ventriculography during the follow-up period and clinical follow-up was performed (mean clinical follow-up period: 53 ± 31 months). No significant difference in global ejection fraction was noted among the groups, although the end-diastolic volume index (EDVI) in the PTCA group (79.4 ± 17.5 ml/m²) was significantly smaller than in the noninterventional (106.1 ± 25.1 ml/m²) and ICT (107.9 ± 28.3 ml/m²) groups (p<0.05). The regional wall motion index (RWMI) for the anterior region in the PTCA group (-2.7 ± 0.8) was greater (p<0.05) than in the noninterventional (-3.4 ± 0.6) and ICT (-3.3 ± 0.6) groups. A significant linear correlation was found between EDVI and % diameter stenosis and also between RWMI and % diameter stenosis following reperfusion (p=0.01). There was no difference in the incidence of cardiac death, nonfatal reinfarction, bypass surgery or congestive heart failure among the groups. Disturbed left ventricular regional wall motion and remodeling benefit most from angioplasty because of prompt restoration of adequate blood flow. However, there was no difference in late outcomes following AMI among the three groups. (Jpn Heart J 1998; 39: 419–433)

Key words: AMI, Reperfusion therapy, ICT, PTCA, Left ventricular remodeling, RWMI, Late outcome

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Rentrop\(^{1}\) performed percutaneous transluminal coronary recanalization for the first time in 1979, as a form of reperfusion therapy for acute myocardial infarction (AMI). Since then, the outcome of patients with AMI has improved because of the rapid restoration of blood flow through the infarct-related artery (IRA). Fifty to seventy percent of patients have normal coronary flow restored by thrombolytic therapy.\(^{2-4}\) In addition, thrombolytic therapy results in an estimated reduction in early mortality of between 20 and 30%.\(^{2,5,6}\) On the other hand, angioplasty, when performed by experienced operators, restores normal blood flow in over 90% of patients. Recently, several trials have compared primary and immediate coronary angioplasty with thrombolytic therapy.\(^{3,7-10}\) The reocclusion rate and residual stenosis of IRA are significantly lower following angioplasty than following thrombolytic therapy.\(^{5,13}\) Left ventricular remodeling following AMI is influenced by the patency and severity of residual stenosis of IRA.\(^{11,12}\) The purpose of this study was therefore to compare left ventricular function, left ventricular remodeling and late outcome after AMI among different reperfusion therapies.

**Methods**

**Patient selection:** Patients were retrospectively selected from patients admitted to our department using the following criteria: (1) clinical and ECG evidence of AMI, (2) coronary angiography (CAG) performed within 48 hours of the acute phase of the AMI and (3) follow-up catheterization performed during the pre-discharge phase. AMI was defined as ischemic chest pain lasting for >30 minutes and ST segment elevation of ≥0.1 mV in at least two contiguous electrocardiographic leads. Inclusion criteria for the study included: (1) the IRA must be the left anterior descending coronary artery with a stenosis proximal to the first septal perforator, (2) TIMI (Thrombolysis in Myocardial Infarction) flow grade of 0 to 2 and (3) absence of significant stenosis (50%) in any other coronary vessels. Exclusion criteria included (1) presence of ≥ grade 3 collateral flow (retrograde collateral flow was scored according to the classification of Rentrop et al.\(^{14}\)), (2) presence of major cardiac complications such as persistent congestive heart failure requiring diuretics, uncontrolled arrhythmias, prior myocardial infarction and other extracardiac complications. Based on these inclusion and exclusion criteria, 30 patients were selected. They included 10 patients who had successful intracoronary thrombolytic therapy performed within 6 hours of the onset of AMI (intracoronary thrombolysis, ICT group), 10 who had successful primary coronary angioplasty performed within 24 hours of the onset of AMI (percutaneous transluminal coronary angioplasty, PTCA group) and 10 who only received medical treatment (noninterventional group). The noninterventional group did
not receive reperfusion therapy either because the time before catheterization exceeded 6 hours from the onset of AMI or the IRA appeared unlikely to benefit from urgent PTCA.

**ICT procedure:** After the vascular sheath was inserted, heparin (5,000 U) was administered intravenously. Selective coronary angiography was performed after intracoronary infusion of isosorbide dinitrate (2.5 to 5 mg). Urokinase was then infused in the ostial segment of the IRA at a rate of 240,000 U per 15 minutes. Angiography was performed every 15 minutes during the infusion. The infusion was continued until reperfusion was obtained or until a maximum of 720,000 U had been infused. Thrombolytic therapy was considered successful if there was restoration of at least TIMI grade 3 flow in the IRA. After the procedure was completed, the patient was transferred to the intensive care unit and received standard treatment.

**PTCA procedure:** The preinterventional management of patients in the PTCA group was the same as in the ICT group. PTCA was performed by experienced operators. A heparin dose of 10,000 U was administered. A suitable dilation balloon catheter was selected based on the reference coronary diameter of the IRA. The inflation pressure was gradually increased until an optimal result was obtained. If the initial dilation balloon catheter was small, it was replaced by a larger catheter. After an optimal result was obtained, CAG was repeated 10 minutes later to confirm the absence of vessel recoil or reocclusion. Successful PTCA was defined by the presence of <50% residual stenosis and a final TIMI grade 3 flow. After the procedure was completed, the patient received standard treatment.

**Concurrent therapy:** All patients received continuous intravenous heparin at a dose designed to maintain an activated partial-thromboplastin time between 2 and 3 times the normal value until warfarin therapy was initiated. Warfarin was administered at a dose designed to maintain the INR (international normalized ratio) between 2 and 3. All patients received isosorbide dinitrate (15 to 40 mg per day) and aspirin (81 mg per day). Calcium-channel antagonists, β-adrenergic antagonists and ACE inhibitors were given at the discretion of the patient's attending physician. Ninety percent of the patients in the noninterventional group, 50% in the ICT group and 70% in the PTCA group received calcium-channel antagonists. Only one patient received a β-adrenergic antagonist in either the ICT or the PTCA group. ACE inhibitor therapy was administered in only one patient in the PTCA group.

**Follow-up catheterization:** All patients underwent follow-up catheterization before discharge (the mean time from the initial procedure to the follow-up catheterization was 27.5 days). Left ventriculography was employed to analyze global function and measure left ventricular volume using the area-length
Figure 1. Centerline method for regional wall motion analysis. A: The centerline is defined as the point midway between the end-diastolic and end-systolic endocardial contours. Motion is measured along 100 chords constructed perpendicularly to the centerline. B: Motion at each chord is normalized to the end-diastolic perimeter to yield a shortening fraction. Normalized motion for the representative patient is shown by the solid line. The mean motion and one standard deviation above and below the mean for a normal ventriculogram are shown by the dotted line and hatched lines, respectively, for comparison. C: The severity of wall motion abnormality is expressed as the standard deviation away from the normal mean value.

method15,16) from the 30-degree right anterior oblique and 60-degree left oblique projections. Regional wall motion was analyzed using the centerline chord method17) and values are expressed as the number of standard deviations away from the mean value for the normal population. The centerline between the systolic and diastolic contours was generated by computer, and 100 equally spaced perpendicular chords were drawn to the centerline. Chord 1 was drawn
at the intersection of the aortic contour and the anterobasal left ventricular wall, and chord 100 was drawn at the junction of the left ventricular contour and the posterior aortic contour. The motion of each chord was normalized for the heart size by dividing it by the length of the end-diastolic perimeter and expressing the resulting quotient in terms of standard deviation units above or below the normal mean motion of the chords. Normal chord motion in our department was derived from the ventriculograms of 100 patients with normal left ventricular function without coronary arterial, valvular or myocardial disease. In this study, chords 20 to 80 were estimated in order to eliminate differences in individual cardiac shape and the influence of movement of the mitral valve. Therefore, we measured the area of chords 20 to 60 as the anterior region of the infarct related sphere and chords 61 to 80 as the diaphragmatic region of the noninfarct related sphere (Figure 1). CAG was performed in the same projection as the initial procedure in order to estimate the % diameter stenosis of the IRA according to the AHA grading committee classification.

**Measurement of peak creatine kinase MB isozyme activity:** Blood samples used for the measurement of creatine kinase MB (CK-MB) isozyme activity were collected every 3 hours for the first 24 hours and every 6 hours for the next 24 hours.

**Late outcome:** The mean clinical follow-up period was 53 ± 31 months. The endpoint for the study was a composite outcome including cardiac death, nonfatal reinfarction, coronary bypass surgery and congestive heart failure requiring hospitalization.

**Statistical analysis:** Results are expressed as the mean ± SD. Multiple comparisons among groups were performed using a one-way ANOVA combined with Fisher's PLSD. The chi-square test or Fisher's exact test was used to analyze categoric variables among the three groups. Continuous variables were analyzed using Student's t test. Differences were considered significant when \( p < 0.05 \). Event free ratios were calculated using the Kaplan-Meier product limit. The log-rank test was applied for evaluating differences in the event free ratio among each group.

**Results**

**Baseline characteristics:** Patient age was significantly greater in the ICT and PTCA groups than in the noninterventional group \( (p < 0.05) \). No significant differences were observed among groups with regard to gender, presence of preinfarction angina, peak CK-MB activity, the sum of ST elevations in electrocardiographic leads and the number of electrocardiographic leads with abnormal Q waves on admission, or the degree of anterograde and retrograde flow in the
IRA before reperfusion therapy. The time to reperfusion tended to be longer in the PTCA group than in the ICT group, although the difference was not significant (Table I).

**Clinical findings in the chronic phase**: The number of electrocardiographic leads with abnormal Q waves was greater in the noninterventional group than in the ICT and the PTCA groups ($p < 0.05$). Systolic blood pressure and left ventricular end-diastolic pressure did not differ significantly among the groups (Table II).

**Findings at predischarge CAG**: The change in the % diameter stenosis of the IRA from the postreperfusion period to follow-up CAG is shown in Figure 2. The % diameter stenosis in the postreperfusion period was 100%, 91.5% and 20.0% in the noninterventional, ICT and PTCA groups, respectively. At the time of the second CAG, the % diameter stenosis was 92.3%, 73.9% and 35.0% in the

### Table I. Clinical Characteristics of the Patients at Base Line

<table>
<thead>
<tr>
<th></th>
<th>Noninterventional</th>
<th>ICT</th>
<th>PTCA</th>
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<tr>
<td></td>
<td>$n = 10$</td>
<td>$n = 10$</td>
<td>$n = 10$</td>
</tr>
<tr>
<td>Age (y)</td>
<td>$52.0 \pm 10.6$</td>
<td>$61.7 \pm 8.2^*$</td>
<td>$60.9 \pm 7.8^*$</td>
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<tr>
<td>Gender, male</td>
<td>8 (80)</td>
<td>9 (90)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Preinfarctional angina</td>
<td>7 (70)</td>
<td>7 (70)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Time to reperfusion (hr)</td>
<td>...</td>
<td>$4.3 \pm 1.6$</td>
<td>$8.3 \pm 7.7$</td>
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<tr>
<td>ΣST on admission (mV)</td>
<td>$1.76 \pm 0.91$</td>
<td>$2.03 \pm 1.43$</td>
<td>$1.52 \pm 0.53$</td>
</tr>
<tr>
<td>Number of Q wave leads</td>
<td>$3.3 \pm 2.7$</td>
<td>$1.8 \pm 2.2$</td>
<td>$2.8 \pm 1.9$</td>
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<tr>
<td>TIMI grade flow</td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>8</td>
<td>7</td>
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<td>Collateral flow</td>
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<td>Peak CK-MB (IU/L)</td>
<td>$211.4 \pm 155.2$</td>
<td>$207.1 \pm 170.5$</td>
<td>$248.5 \pm 175.2$</td>
</tr>
</tbody>
</table>

*$p < 0.05$ vs. noninterventional. Data are presented as the mean ± SD or number (%) of patients.

### Table II. Clinical Parameters before Hospital Discharge

<table>
<thead>
<tr>
<th></th>
<th>Noninterventional</th>
<th>ICT</th>
<th>PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n = 10$</td>
<td>$n = 10$</td>
<td>$n = 10$</td>
</tr>
<tr>
<td>Number of Q wave leads</td>
<td>$4.8 \pm 1.5$</td>
<td>$3.2 \pm 2.1^*$</td>
<td>$2.4 \pm 1.4^*$</td>
</tr>
<tr>
<td>Syst. BP (mmHg)</td>
<td>$97.8 \pm 10.8$</td>
<td>$102.2 \pm 16.9$</td>
<td>$122.1 \pm 18.1^*$</td>
</tr>
<tr>
<td>LVEDP (mmHg)</td>
<td>$11.2 \pm 5.9$</td>
<td>$10.6 \pm 5.7$</td>
<td>$13.1 \pm 5.9$</td>
</tr>
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*$p < 0.05$ vs. noninterventional. **$p < 0.05$ vs. noninterventional, ICT. Data are presented as the mean ± SD. Syst. BP = systolic blood pressure; LVEDP = left ventricular end-diastolic pressure.
noninterventional, ICT and PTCA groups, respectively. A significant difference was noted for each group between the two time points. In six patients from the noninterventional group, spontaneous recanalization was noted during the follow-up period. In the ICT and PTCA groups, no patients developed re-occlusion during the follow-up period. The % diameter stenosis decreased significantly from the postreperfusion period to the time of second CAG in the noninterventional and ICT groups. However, there was significant progression of the % diameter stenosis in the PTCA group.

**Left ventricular volume and global function:** As shown in Figure 3-A no significant difference in the global ejection fraction (EF) among the three groups
was observed (noninterventional group, 42.4 ± 7.1%; ICT group, 43.9 ± 5.9%; and PTCA group, 49.2 ± 12.6%). However, the end-diastolic volume index (EDVI) in the PTCA group (79.4 ± 17.5 ml/m²) was significantly less than in the noninterventional (106.1 ± 25.1 ml/m²) and ICT (107.9 ± 28.3 ml/m²) groups (p < 0.05).

**Regional wall motion index:** The regional wall motion index (RWMI) for the anterior wall in the PTCA group (−2.7 ± 0.8) was significantly greater (p < 0.05) than in either the noninterventional (−3.4 ± 0.6) or ICT (−3.3 ± 0.6) groups. The RWMI for the diaphragmatic region did not differ significantly among the three groups, although the RWMI for the diaphragmatic region in the PTCA group (−1.8 ± 1.0) tended to be greater than in the other groups (noninterventional: −2.3 ± 1.2; ICT: −2.2 ± 0.9). In addition, no difference in RWMI between the noninterventional and ICT groups was noted (Figure 3-B).

**Influence of residual stenosis on global EF, EDVI and regional wall motion following reperfusion and during the follow-up period:** The global EF, EDVI and RWMI for the infarct zone were plotted against % diameter stenosis
Figure 4. Relationship between residual % diameter stenosis at the postreperfusion and follow-up periods and global EF, EDVI and regional wall motion.
during the postreperfusion and follow-up periods (Figure 4). Significant linear correlations were found between the EDVI and the % diameter stenosis and between the RWMI and the % diameter stenosis during the postreperfusion period ($p = 0.01$). However, during the follow-up period, this correlation did not exist (Figure 4).

**Six year clinical event rate:** The mean clinical follow-up period was $53 \pm 31$ months. Two (6.7%) of the 30 patients died due to reinfarction. Both patients who died were in the ICT group, and death occurred between 24 and 42 months after the initial infarction. As shown in Figure 5-A, there was no difference in the

![A](image)

![B](image)

**Figure 5.** Five year Kaplan-Meier survival curves for patients free from cardiac death, nonfatal reinfarction and coronary bypass surgery (A) and congestive heart failure (B).
incidence of the endpoints composed of cardiac death, nonfatal reinfarction and coronary bypass surgery among the three groups. In addition, the incidence of congestive heart failure requiring hospitalization was also similar among the three groups (Figure 5-B).

**DISCUSSION**

Previous studies have demonstrated that reperfusion therapy for AMI, including thrombolysis and coronary angioplasty, can improve short-term survival and preserve left ventricular function. However, there have been no angiographic studies confirming coronary artery patency at the acute phase or long-term outcome studies demonstrating improved survival for reperfusion therapies. In our study, we determined coronary artery patency by CAG and monitored patient outcome for a mean period of 53 months. In previous studies, the longest follow-up period was 3 years. In this study, we specifically wanted to determine the importance of reperfusion therapy on global and regional left ventricular function, left ventricular remodeling and long-term prognosis.

**Baseline characteristics:** There were no significant differences in the baseline characteristics among the three groups except that patients in the ICT and PICA groups were older than patients in the noninterventional group. Cardiovascular disease is the most common cause of death and disability in the elderly. In fact, nearly 50% of patients who die during hospitalization for an AMI are > 75 years of age. Further, advanced age is the most important adverse long-term prognostic factor following AMI. However, the mean age of the patients in our study was 58.2 years (38–74 years). Therefore, we believe that the results of this study were not influenced by the difference in the three groups.

**Infarct size:** We used two indices to estimate infarct size: peak CK-MB activity and the number of electrocardiographic leads with abnormal Q waves. There was a tendency toward a higher CK-MB activity in the PTCA group than in the others. In contrast, the number of abnormal Q waves in the noninterventional group was greater than in either the ICT or PTCA groups before discharge. The discordance between peak CK activity and infarct size may be explained by the washout of CK during reperfusion. The infarct size estimated by scintigraphic defects on radionuclide studies is smaller in patients who achieve early reperfusion (< 6 hr) than in nonreperfused patients, although there is no significant difference in infarct size between thrombolysis and mechanical reperfusion. Our data agree with these previous reports.

**Change in the % diameter stenosis of the IRA:** According to previous studies, early re-occlusion of the IRA occurs in < 5% of patients undergoing angioplasty and in 10 to 20% of patients undergoing thrombolysis. In our study,
there was no evidence of reocclusion at the time of the second CAG in either the ICT or PTCA groups. Furthermore, spontaneous recanalization was noted in six patients from the noninterventional group at the time of the second CAG. This spontaneous recanalization rate is similar to previously reported rates.21,34) The present study has indicated that the residual % diameter stenosis was significantly greater in the noninterventional group than in the ICT and PTCA groups at both the first and second CAG.

**Left ventricular volume and function:** No significant differences were observed in the global left ventricular ejection fraction among the three groups, in keeping with most previous studies.35-37) A few reports13,37) have shown that patients undergoing PTCA have a better global ejection fraction than patients undergoing thrombolysis, although the incidence of prior infarction and the patency rate of the IRA were not matched in those studies. EDVI and regional wall motion in the infarct zone before the discharge period were preserved to a greater extent in the PTCA group in our study. Similar findings have been reported by Ward et al.37) and O'Neill et al.13) However, the most important determinants of post-infarction left ventricular volume and left ventricular function are thought to be a history of previous infarction, IRA patency, the severity of the residual stenosis in the IRA and the location of the infarction.11,13,37,38) Our study suggests that RWMI and EDVI had a good correlation with the degree of residual stenosis immediately following reperfusion. Previous studies11,13) reporting a strong correlation between the minimal lumen diameter of the IRA and cardiac function support our findings.

**Prognosis:** The GUSTO IIb trial findings39) suggest that angioplasty provides a small to moderate, short-term clinical advantage over thrombolytic therapy in certain situations. However, some earlier studies8,40,41) could not provide evidence that long-term mortality was lower in patients undergoing immediate or primary angioplasty than in patients receiving thrombolytic therapy. In our study, there was no difference in the incidence of cardiac death, nonfatal reinfarction, need for coronary bypass surgery or congestive heart failure among the three groups. Therefore, we hypothesize that the most important determinants of long-term prognosis following myocardial infarction are prior myocardial infarction, the presence of heart failure and the presence of residual severe ischemia in a different coronary territory.

**Conclusion:** The prevention of disturbed left ventricular regional wall motion and remodeling are greatest with the use of angioplasty because of the prompt restoration of blood flow through the infarct-related artery. However, there is no difference in the outcome several years after AMI irrespective of selecting angioplasty, thrombolysis or conservative medical therapy, if initial major complications do not occur.
REFERENCES


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