Importance of Collateral Circulation for Prevention of Left Ventricular Aneurysm Formation in Acute Myocardial Infarction

Tadakazu Hirai, MD, Masatoshi Fujita, MD, Hisayoshi Nakajima, MD, Hidetsugu Asanoi, MD, Kazuto Yamanishi, MD, Akira Ohno, MD, and Shigetake Sasayama, MD

The effect of preexistent coronary collateral perfusion on the prevention of left ventricular aneurysm formation was examined in 47 patients undergoing an intracoronary thrombolysis within 6 hours after the onset of a first acute anterior myocardial infarction. Left ventricular aneurysm formation and wall motion were analyzed with cineventriculography. A left ventricular aneurysm was determined as well-defined demarcation of the infarcted segment from normally contracting myocardium. In 25 patients with successful thrombolysis (group A), a left ventricular aneurysm was observed in one patient (4%) during the chronic stage of infarction. In 10 patients who had a significant collateral circulation to the infarct-related coronary artery and unsuccessful reperfusion (group B), the left ventricular aneurysm was observed in only one patient (10%). In the remaining 12 patients with unsuccessful recanalization in the absence of a significant collateral perfusion (group C), there was a higher incidence (seven of 12, 58%) of left ventricular aneurysm formation than in groups A and B (p < 0.05). In group A, both the global ejection fraction and regional wall motion in the infarct areas improved significantly (p < 0.05) between the acute and chronic stages of infarction. By contrast, in groups B and C, these indexes on the ventricular function did not change significantly during the convalescent period. Thus, although the collateral perfusion existing at the onset of acute myocardial infarction may not improve ventricular function, it exerts a beneficial effect on the prevention of left ventricular aneurysm formation. (Circulation 1989;79:791–796)

It is generally accepted that early recanalization of an infarct-related coronary artery in the presence of residual flow resulting from either a subtotal obstruction of infarct-related coronary artery or collateral perfusion exerts a beneficial effect on the regional and global left ventricular wall motion evaluated during the chronic stage of infarction.1–3 However, it is still controversial whether a preexistent coronary collateral circulation contributes to the preservation of jeopardized myocardial function in the case of unsuccessful recanalization.1,3

Left ventricular aneurysm, one of the untoward complications of myocardial infarction, is usually accompanied by absence of residual flow to the myocardium at risk.4–6 Whether collateral circulation already existing at the onset of acute myocardial infarction can prevent the formation of left ventricular aneurysm has not yet been clarified.6

The purpose of our study was to evaluate the relation of significant collateral perfusion to regional myocardial function and left ventricular aneurysm formation in patients with acute myocardial infarction who were treated with intracoronary thrombolysis.

Methods

Study Patients

Over a 4-year period, 47 consecutive patients with a first acute anterior myocardial infarction who had complete occlusion of the proximal part of the left anterior descending coronary artery were referred for intracoronary thrombolysis during the first 6 hours after the onset of symptoms. There were 39 men and eight women with a mean age of 60 years (range, 35–79). The diagnosis of acute myocardial infarction included the presence of persistent ST segment elevation of 2 mm or greater in two or more leads on the standard 12-lead electrocardiogram and severe chest pain lasting for more than 30 minutes.
Cardiac Catheterization

Coronary arteriography was performed by the Judkins technique. After baseline hemodynamic measurements, right and left coronary arteriograms were recorded in multiple projections to identify the infarct-related coronary artery and to evaluate the extent of collateral circulation. Subsequently, intracoronary thrombolysis with high-dose urokinase (240,000–960,000 units) was attempted at an infusion rate of 24,000 units/min. If the infarct-related coronary artery was recanalized with less than 90% residual narrowing in diameter, the procedure was judged successful. Coronary arteriography was repeated after each administration of 240,000 units to identify recanalization. If the obstructed artery was not recanalized after infusion of 960,000 units urokinase, the Judkins coronary catheter was then removed and a pigtail catheter was introduced into the left ventricular cavity. After the left ventricular pressure had returned to baseline, left ventriculography was performed in 30° right anterior oblique projection, with a Toshiba 9-in. (23 cm) image intensification system. Left ventricular opacification was achieved by injecting 30–40 ml radiopaque contrast medium at a rate of 10–14 ml/sec. Films were exposed at a rate of 60 frames/sec with an Ariflex 35 mm cinecamera. After the study, a 1-cm cross-hatched grid was filmed at the same distance from the radiography tube and image intensifier, as was the left ventricular cavity. Thirty-five days (range, 28–40) after the first left ventriculography, a repeat left ventriculogram was obtained in the same manner as the initial one. Coronary artery segments were identified and categorized according to the reporting system proposed by the American Heart Association. The diameter of the coronary arteries was measured with a caliper on adequately magnified 35-mm cineframes at end diastole. A significant coronary stenosis was defined as 75% or more narrowing of a major coronary artery branch.

Grading of Coronary Collateral Filling

Collateral circulation was graded on a scale of 0 to 3 depending on the degree of opacification of the occluded vessel. The score (collateral index, or CI) was based on the injection that best opacified the occluded vessel: 0, none; 1, filling of side branches of the artery to be perfused via collateral vessels without visualization of the epicardial segment; 2, partial filling of the epicardial segment via collateral vessels; and 3, complete filling of the epicardial segment via collateral vessels. The three blinded observers assessed the coronary cineangiograms and reached a consensus.

Assessment of Left Ventricular Aneurysm Formation

A left ventricular aneurysm was diagnosed angiographically with the Coronary Artery Surgery Study protocol. An aneurysm was considered to be present if all of the following three criteria were met: 1) systolic bulging of the involved segment, 2) absence of trabeculation in the involved segment, and 3) well-defined demarcation of the infarcted segment from normally contracting myocardium. It should be emphasized that in addition to abnormalities of systolic wall motion, the presence of diastolic deformity is required.

Analysis of Cineventriculograms

The boundaries of two left ventricular silhouettes (end diastole, end systole) were traced manually by an observer who was unaware of clinical and coronary angiographic data on each patient with use of a sonic digitizing device. End-diastolic frame was determined by the electrocardiogram simultaneously recorded on the cinefilm as the frame nearest the peak of the R wave. The frame of the smallest ventricular volume was taken as end-systolic frame. The area of the ventricular silhouette was calculated from the number of pixels surrounded by the ventricular boundary, and the left ventricular volumes were calculated by a modification of the formula of Kennedy et al. A ventricular silhouette at end systole was superimposed on the end-diastolic frame with two external reference markers. Thirty-six radial grids were drawn from the center of gravity of the end-diastolic silhouette to the endocardial margin. Twenty-five of these 36 radial grids covered the outline of the left ventricular cavity, excluding the area of aortic and mitral valves, which was divided into five sections. Accordingly, five radial grids were included in each section, which roughly corresponded to five areas (anterobasal, anterolateral, apical, diaphragmatic, and posterobasal) defined by a reporting system of the American Heart Association.

The mean value of five grids in the anterolateral area was used as an indication of infarct areas, whereas that in the diaphragmatic area was adopted as the noninfarct areas. The percentage of systolic segment shortening was calculated by: (end-diastolic length–end-systolic length)×100/end-diastolic length.

Serial Creatine Kinase Measurement

Blood samples of creatine kinase were obtained every 2–4 hours for a period of 72 hours after hospitalization. Enzymatic activity of creatine kinase was measured by the method of Rosalki to evaluate the infarct size, and cumulative creatine kinase release was determined by the integrated appearance function curve according to Shell et al and Sobel et al with the individual disappearance constant calculated by the method of Norris et al.

Subgroups

The patients were classified into three groups according to the extent of coronary reperfusion and collateral circulation: group A, patients with successful thrombolysis, independent of collateral cir-
A Group Analysis was extent of the data end-diastolic with the paired infarction, perfusion recanalization calculation; group B, patients who had a significant collateral circulation (CI=2 or 3) to the infarct-related coronary artery and unsuccessful reperfusion; and group C, patients with unsuccessful recanalization in the absence of a significant collateral perfusion (CI=0 or 1).

Statistical Analysis
All values are expressed as mean±SEM. For comparison of the data in the acute and chronic stages of infarction, the paired t test was used. Proportions for patients with and without aneurysm formation were compared among three groups with the χ² test with Freeman and Halton’s method. Results were considered significant at the 5% critical level.

Results
Extent of Coronary Vessel Disease
In group A (age, 59±2 years), the proportion of patients showing one-, two-, and three-vessel disease was 14 of 25 (56%), six of 25 (24%), and five of 25 (20%), respectively. Of 10 patients in group B (age, 58±3 years), four patients (40%) had one-vessel disease, three (30%) had two-vessel disease, and the remaining three (30%) had three-vessel disease. In group C (age, 63±2 years), the proportion of one-, two-, and three-vessel disease was four of 12 (33%), five of 12 (42%), and three of 12 (25%), respectively. There were no statistical differences in the extent of coronary vessel disease among the three groups.

Data on Thrombolysis and Collateral Circulation
Of 47 patients, 25 (53%) had successful thrombolysis (group A). Twenty-two patients with unsuccessful thrombolysis included seven patients with subtotal stenosis. The overall reperfusion rate was 68%. Among the 22 patients with unsuccessful thrombolysis, 10 had well-developed collateral circulation (CI, grade 2 or 3) (group B), and the remaining 12 patients had inadequate collateral circulation (CI, grade 0 or 1) (group C). There were no intergroup differences in the time from the onset of symptoms to intracoronary thrombolysis (group A, 4±1 hours; group B, 4±1 hours; group C, 4±1 hours). On the initial angiogram before thrombolysis, a total occlusion of the left anterior descending coronary artery was seen in all patients.

Coronary Angiographic Findings at Second Cardiac Catheterization
The reocclusion rate in patients with successful thrombolysis (group A) was 8% (two of 25 patients). Of the 22 patients who had an occluded artery on the initial angiograms (groups B and C), seven had totally occluded vessels, nine had subtotally occluded vessels, and the remaining six patients had a patent infarct-related coronary artery. In group C, five patients showed late collateralization to the myocardium at risk, and three of the five patients had a well-developed collateral circulation.

Hemodynamics
The heart rate decreased in the chronic phase compared with in the acute phase (group A, 84±2 compared with 74±2 beats/min, p<0.05; group B, 82±4 compared with 76±4 beats/min; group C, 91±5 compared with 74±4 beats/min, p<0.05). No significant changes in left ventricular peak systolic pressure were observed in all the three groups. In group A, the left ventricular end-diastolic pressure decreased significantly from 18±1 mm Hg in the acute phase to 13±1 mm Hg in the chronic phase. In other two groups B and C, the differences in left ventricular end-diastolic pressure were not significant between the acute and chronic phases (Table 1).

Overall Left Ventricular Function
In group C, the cardiac index tended to decrease during the convalescent period (2.9±0.2 compared with 2.6±0.2 l/min/m²). In the patients of this group, the left ventricular end-diastolic volume index increased from 75±3 to 85±4 ml/m² (p<0.05) as did the left ventricular end-systolic volume index (42±2 to 49±3 ml/m²). The global ejection fraction during the acute phase was 49±2%, 48±3%, and 43±3% in groups A, B, and C, respectively (NS); during the chronic phase, it was 56±2%, 55±4%, and 42±3%, respectively. Thus, the global ejection fraction was

<table>
<thead>
<tr>
<th>Group</th>
<th>HR (beats/min)</th>
<th>LVPSP (mmHg)</th>
<th>LVEDP (mmHg)</th>
<th>CI (l/min/m²)</th>
<th>LVEDVI (ml/m²)</th>
<th>LVESVI (ml/m²)</th>
<th>EF (%)</th>
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<tbody>
<tr>
<td>Group A (n=25)</td>
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<tr>
<td>Acute</td>
<td>84±2</td>
<td>127±5</td>
<td>18±1</td>
<td>3.1±0.2</td>
<td>76±3</td>
<td>38±2</td>
<td>49±2</td>
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<tr>
<td>Chronic</td>
<td>74±2*</td>
<td>134±4</td>
<td>13±1*</td>
<td>3.1±0.2</td>
<td>75±3</td>
<td>33±2</td>
<td>56±2*</td>
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<td>Group B (n=10)</td>
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<tr>
<td>Acute</td>
<td>82±4</td>
<td>133±7</td>
<td>13±2</td>
<td>2.6±1.2</td>
<td>65±4</td>
<td>33±3</td>
<td>48±3</td>
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<tr>
<td>Chronic</td>
<td>76±4</td>
<td>126±8</td>
<td>14±2</td>
<td>2.9±0.2</td>
<td>68±3</td>
<td>30±2</td>
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<td>Group C (n=12)</td>
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<tr>
<td>Acute</td>
<td>91±5</td>
<td>130±7</td>
<td>17±2</td>
<td>2.9±0.2</td>
<td>75±3</td>
<td>42±2</td>
<td>43±3</td>
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<tr>
<td>Chronic</td>
<td>74±4*</td>
<td>128±6</td>
<td>17±1</td>
<td>2.6±0.2</td>
<td>85±4*</td>
<td>49±3</td>
<td>42±3</td>
</tr>
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Values are mean±SEM. CI = cardiac index; EF = ejection fraction; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; LVPSP = left ventricular peak systolic pressure. Comparison was made between the acute and chronic phases in each group. *p<0.05.
augmented in groups A and B, but only the former reached a statistical significance (Figure 1).

**Regional Myocardial Function**

The percentage segment shortening in the infarct areas during the acute phase was 3.9±1.3%, 6.2±1.7%, and 0.8±2.9% in groups A, B, and C, respectively (NS). In the chronic phase, the percentage segment shortening was 14.3±2.9%, 13.8±3.7%, and −0.4±2.5% in groups A, B, and C, respectively. The changes in the percentage segment shortening are depicted in Figure 2. Only patients in group A had a significant improvement (*p*<0.05) in regional segment shortening in the infarct areas. In the non-infarct segments, the percentage segment shortening in the acute stage was 30.0±6.0%, 41.3±5.7%, and 28.4±3.4% in groups A, B, and C, respectively (NS). In the chronic stage, the percentage segment shortening was 30.9±1.8%, 40.4±5.7%, and 29.0±3.5% in groups A, B, and C, respectively. There were no significant changes in regional segment shortening of the noninfarct areas from the acute to chronic stage of infarction in all the three groups.

**Left Ventricular Aneurysm**

The prevalence of left ventricular aneurysm formation in each group is shown in Figure 3. Among the 47 patients, nine (19%) had suffered from left ventricular aneurysm formation. Of the 12 patients who had poorly developed collateral circulation associated with unsuccessful recanalization (group C), seven had left ventricular aneurysm formation (58%). By contrast, only one of the 25 patients (4%) with successful thrombolysis (group A) and one of the 10 patients (10%) who had well-developed collateral circulation despite unsuccessful recanalization (group B) had left ventricular aneurysm. The incidence of aneurysm formation in group C was significantly higher than in groups A and B.

**Creatine Kinase**

Cumulative creatine kinase release in each group is shown in Figure 4. There were no significant differences in cumulative creatine kinase release among the three groups (group A, 2,584±350 units/l; group B, 3,026±551 units/l; group C, 4,036±770 units/l).

**Discussion**

In the present study, the importance of collateral circulation in preventing the left ventricular aneurysm formation after acute myocardial infarction was documented by the finding that the prevalence of left ventricular aneurysm in patients with poor collateral circulation (group C) is much higher than those with a significant collateral circulation (group B). This may be explained, at least in part, by the fact that the well-developed collateral circulation increases the number of islands of viable heart muscle amidst the infarct area, hereby enforcing its tensile strength and preventing the aneurysm formation. Indeed, earlier studies revealed a beneficial effect of persistent islands of residual subepicardial cells in the infarct zone on infarct expansion. In the present study, there was a tendency toward smaller infarct sizes in group B compared with group C, evaluated by the cumulative creatine kinase release. This finding is consistent with the prevalence of aneurysm formation in group C (significantly higher than in group B). These results are in agreement with data by Weisman et al showing that a beneficial effect of reflow in the acute stage of infarction may be preservation of shape rather than the quantity of myocardial salvage.
Patients who had good collaterals during the acute stage of infarction (group B) showed a considerable improvement in regional and global left ventricular function during the convalescent period, although the changes were not statistically significant. These findings are consistent with an earlier observation of others that in patients with well-developed collateral circulation, depressed myocardial function was ameliorated during the convalescent period despite unsuccessful intracoronary thrombolysis. Thus, the preservation of myocardial function in the infarct area after acute coronary occlusion may be achieved by the well-developed collateral perfusion.

Other determinants related to left ventricular aneurysm formation must be considered. Arvan and Badillo have emphasized a crucial role of the preserved contractile property of the myocardium in the noninfarct areas for the aneurysm formation. They have demonstrated with two-dimensional echocardiography that the percentage fractional shortening of the noninfarct segments was significantly greater in patients with aneurysm than in those without aneurysm. In the present study, regional wall motion in the noninfarct areas was well maintained and comparable among all the three groups.

Accordingly, it is unlikely that the extent of contraction of the noninfarct myocardium affected the prevalence of left ventricular aneurysm formation. Hemodynamic parameters such as the ventricular peak systolic and end-diastolic pressures that may be related to the pathogenesis of aneurysm formation were also quite comparable among the three groups during the acute phase of infarction. Thus, it is more likely that the regional blood flow supply to the infarct areas is the most important determinant of the destiny of the jeopardized myocardium, especially in terms of infarct expansion.

In five patients (42%) in group C, left ventricular aneurysm formation was not observed, despite the absence of visualized flow to the infarct areas in acute stages of infarction. Three of these five patients revealed a recanalized infarct-related coronary artery on coronary cineangiograms obtained during the chronic stage of infarction. In the remaining two patients, repeat coronary cineangiography disclosed a well-developed (CI, 3) collateral circulation to the area perfused by the completely obstructed left anterior descending coronary artery. When the above-mentioned spontaneous recanalization or collateral development occurs before the completion of left ventricular aneurysm formation, patients may be free from the aneurysm. Indeed, there is a report on the time course required for aneurysm formation. The slow development of aneurysm from about 24 hours to 4 weeks after the onset
of acute myocardial infarction may give a possibility of favorable effects of the delayed flow supply to the infarct zone on the prevention of aneurysm formation.\textsuperscript{18,20,21} By contrast, a left ventricular aneurysm was formed in one patient in group A. In this patient, reocclusion of the recanalized coronary artery was strongly suspected by the postinfarction angina and double peak in the curve of creatine kinase release.

In interpreting our findings, several limitations must be considered. First, angiographically visible collateral vessels represent only a fraction of the total collateral network because the angiographic techniques are able only to visualize collateral channels more than 100 μm in diameter. Moreover, angiography may not detect the majority of collaterals situated intramurally. Therefore, the collateral channels visualized by angiography may not accurately quantify collateral circulation. Second, the differences among the study groups could be related to baseline differences such as size of region at risk or occlusion time until thrombolysis. Although the time from the onset of symptoms to intracoronary thrombolysis was similar among three groups, it was impossible to compare the original risk region in each patient. Finally, the small numbers in each group may bias the interpretation of results.

In conclusion, our results indicate that the well-developed collateral circulation could prevent the left ventricular aneurysm formation after acute myocardial infarction, although it may not contribute to the preservation of regional wall motion and reduction in the infarct size.

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References


KEY WORDS • intracoronary thrombolysis • left ventricular function • creatine kinase • cineventriculography
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