COMPARATIVE EFFECTS OF EARLY AND LATE REPERFUSION OF THE INFARCT-RELATED CORONARY ARTERY AND COLLATERAL CIRCULATION WHICH DEVELOPS AFTER INFARCTION ON LEFT VENTRICULAR SIZE AND FUNCTION

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This study assesses the effects of early and late reperfusion of the infarct-related coronary artery and collateral circulation developed after infarction on left ventricular morphology and function in 22 patients with a first acute anterior myocardial infarction and without long-standing preinfarction angina. The patients were categorized into 4 groups: group A—5 patients with successful reperfusion within 6 h after the onset of infarction; group B—6 patients with late patency of the infarct-related coronary artery; group C—6 patients without recanalization of the infarct-related coronary artery who had good collateral circulation (collateral index (CI)=2 or 3); and group D—5 patients without recanalization who had either poor or no collateral circulation (CI=0 or 1). The left ventricular size and function were evaluated by means of contrast left ventriculography during the chronic stage of infarction. The left ventricular global and regional functions were preserved better ($p<0.05$) in group A than in the other three groups. Although there was no difference in regional wall motion of the infarct area among groups B, C and D, the ejection fraction was greater ($p<0.05$) and the percentage perimetric circumference was smaller ($p<0.05$) in groups B and C than in group D. Among the 4 groups, the left ventricular end-diastolic volume index tended to be greater in group D. Thus, these results suggest that blood supply to the infarct area is essential for the preservation of left ventricular size and function regardless of the timing and route.

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THROMBOLYTIC therapy within 6 h after the onset of acute myocardial infarction has been demonstrated to reduce infarct size, preserve left ventricular function and improve survival rate!^{1–3} However, whether late reperfusion of the infarct-related coro-

nary artery is similarly effective has yet to be determined.⁴ The functional role of collateral circulation which develops after infarction also has yet to be clarified.⁵

The purpose of the present study was to evaluate the effects of early and late reperfusion of the infarct-related coronary artery and collateral circulation which develops after acute myocardial infarction on left ventricular morphology and function during

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TABLE I HEMODYNAMICS AND GLOBAL LEFT VENTRICULAR FUNCTION

	HR (beats/min)	LVPSP (mmHg)	LVEDP (mmHg)	CI (l/min·m ²)
Group A (n=5)	81±10	148±18	8±5	4.0±1.5
Group B (n=6)	68±12	127±20	16±5	2.7±0.5
Group C (n=6)	66±8*	121±17*	14±5	3.0±0.4
Group D (n=5)	78±8	118±15*	17±10	2.7±0.4

HR=heart rate; LVPSP=left ventricular peak systolic pressure; LVEDP=left ventricular end-diastolic pressure; CI=cardiac index

*: $p < 0.05$ vs Group A.

the chronic stage of infarction.

METHODS

Study Patients

The study included 22 patients with a first acute anterior myocardial infarction as a result of complete occlusion of the proximal part to the first major diagonal branch of the left anterior descending coronary artery who had no long-standing preinfarction angina. The 19 men and 3 women had a mean age of 54 ± 7 (SD) years. The diagnosis of acute myocardial infarction was based on the presence of persistent ST segment elevation of 2 mm or greater in 2 or more leads on a standard 12-lead electrocardiogram and severe chest pain lasting for more than 30 min.

Cardiac Catheterization

The time interval from acute myocardial infarction to the present study was 29 ± 7 days. All medications were withheld for at least 24 h before the study. Cardiac catheterization was performed with patients in a fasting state after premedication with 5 mg of oral diazepam. After conventional diagnostic catheterization of the right and left sides of the heart, both coronary arteriograms were recorded by means of the Judkins technique in multiple projections to identify coronary artery stenosis and to evaluate the extent of collateral circulation. After left ventricular pressures, as measured with a Statham P23 Db external strain gauge, had returned to baseline levels, left ventricular cineangiography was performed in a 30-degree right anterior oblique projection with a Toshiba 9-inch (23 cm) image-intensification system. Left ventricular opacification was achieved by injection of 30 to 40

ml of radiopaque contrast medium at a rate of 10 to 14 ml/sec. Films were exposed at a rate of 60 frames/sec with a 35 mm Arriflex cinecamera. Two lead markers were placed on the image intensifier as fixed references for superimposition of the images. After the study, a 1 cm cross-hatched grid was filmed at the same distance from the x-ray tube and image intensifier as was the left ventricular cavity.

Informed consent was obtained from each patient, and there were no complications related to the present study.

Analysis of Data

The boundary of the two left ventricular silhouettes (end diastole and end systole) was delineated by an observer who was unaware of the results of coronary angiography using an OSCON computer-assisted image-processing system. The end-diastolic frame was determined using the ECG which was simultaneously recorded on the cinefilm, and was taken to be the frame nearest the peak of the R wave. The frame of the smallest ventricular volume was taken to be the end-systolic frame. The left ventricular volumes were calculated by a modification of the formula of Kennedy et al.⁶ The end-systolic frame was superimposed on the end-diastolic frame by means of two external reference markers. Thirty-six radial grids were drawn from the center of gravity of the end-diastolic silhouette to the endocardial margin. Of these 36 radial grids, 25 covered the outline of the left ventricular cavity, which was divided into five sections.⁷ The area of the aortic and mitral valves was not included in this study. Accordingly, five radial grids covered each section, which roughly corresponded to the five sections (1=anterobasal, 2=antero-

Fig. 1. Comparison of left ventricular volume among the 4 groups. EDVI=end-diastolic volume index; ESVI=end-systolic volume index; ER=early recanalization; LR=late recanalization; R(-)=no recanalization; coll(+)=well-developed collateral circulation (collateral index 2 or 3); coll(-)=poor or no collateral circulation (collateral index 0 or 1).

Fig. 2. Ejection fraction in the 4 groups. All abbreviations are the same as in Fig. 1.

lateral, 3=apical, 4=diaphragmatic, and 5=posterobasal) described by the reporting system of the American Heart Association⁸

In the present study, the mean values of the five grids in the anterolateral segment were evaluated as the infarct region perfused by collateral circulation. The percentage of systolic segment shortening was calculated by the formula: (end-diastolic length-end-systolic length) $\times$ 100/end-diastolic length⁷

As an index of the extent of myocardial infarction, the percentage perimetric circumference was calculated as the ratio of that part which showed segment shortening of less than 20% to the entire left ventricular wall in the end-diastolic frame⁹

Grading of Collateral Circulation

The extent of coronary collateral circulation to the region supplied by the occluded coronary artery was classified into four grades (collateral index [CI]): 0=no visible filling of any collateral channels, 1=collateral filling of branches of the occluded arteries without any dye reaching the epicardial segments of the distal arterial segments, 2=partial collateral filling of the epicardial segments of the distal arterial segments, and 3=complete collateral filling of the distal segments¹⁰. The extent of collateral circulation was based on the consensus of three blinded observers.

Subgroups

The patients were divided into 4 groups: group A—5 patients with successful reperfusion within 6 h after the onset of infarction; group B—6 patients with late patency of the infarct-related coronary artery; al-

Fig. 3. Segmental shortening in infarct areas in the 4 groups. All abbreviations are the same as in Fig. 1.

though these patients had unsuccessful thrombolysis, the infarct-related coronary artery was patent during the chronic stage of infarction; group C—6 patients without recanalization of the infarct-related coronary artery who had good collateral circulation (collateral index (CI)=2 or 3); and group D—5 patients without recanalization who had either poor or no collateral circulation (CI=0 or 1). Successful thrombolysis was defined as recanalization with a residual stenosis of $\leq 90\%$.

Statistical Analysis

The unpaired Student's *t* test was used to compare data. A probability (*p*) value of less than 0.05 was considered significant. All results are expressed as mean $\pm$ standard deviation.

RESULTS

Extent of Coronary Vessel Disease

In group A (age, 59 ± 5 years), 2, 1, and 2 patients showed one-, two-, and three-vessel disease, respectively. In group B (age, 46 ± 2 years), all 6 patients had one-vessel disease.

In group C (age, 57 ± 6 years), 5 patients had one-vessel disease and 1 patient had three-vessel disease. Of the 5 patients in group D (age, 56 ± 9 years), 2 had one-vessel disease and the remaining 3 had two-vessel disease. There were no significant differences between the extent of coronary vessel disease among the 4 groups.

Hemodynamics and Global Left Ventricular Function

Hemodynamics are shown in Table I. The left ventricular end-diastolic pressure was lower in group A than in groups B, C and D, but this difference was not significant. The cardiac index in group A was also greater than those in groups B, C and D (*p*=NS). The left ventricular end-diastolic volume index was smallest in group A (group A, 80 ± 14 ml/m²; group B, 91 ± 16 ml/m²; group C, 88 ± 6 ml/m²; group D, 109 ± 35 ml/m²), but no significant differences were observed (Fig. 1). The left ventricular end-systolic volume index in group A (34 ± 9 ml/m²) was significantly smaller than those in the other 3 groups (group B, 54 ± 11 ml/m²; group C, 52 ± 8 ml/m²; *p*<0.01 vs group A, group D,

Fig.4. Perimetric circumference in the 4 groups. All abbreviations are the same as in Fig. 1.

79 ± 28 ml/m²; $p < 0.05$ vs group A)(Fig. 1). The left ventricular ejection fraction in group A ($58 \pm 5\%$) was significantly higher than those in the other 3 groups (group B, $40 \pm 3\%$; group C, $42 \pm 7\%$; group D, $29 \pm 5\%$; $p < 0.05$ vs group A). The ejection fraction in group D was significantly lower than those in groups B and C ($p < 0.01$)(Fig. 2).

Regional Left Ventricular Function

Segmental shortening in the infarct areas was significantly better preserved in group A ($15.0 \pm 5.9\%$) than in the other 3 groups (group B, $-3.0 \pm 3.2\%$; group C, $-3.2 \pm 3.1\%$; group D, $-4.7 \pm 3.0\%$; $p < 0.05$ vs group A)(Fig. 3). The percentage perimetric circumference was lower in group A ($28 \pm 6\%$) than in the other groups (group B, $48 \pm 8\%$; group C, $45 \pm 7\%$; group D, $63 \pm 11\%$; $p < 0.01$ vs group A). The percentage perimetric circumference in group D was significantly higher than those in groups B and C ($p < 0.01$)(Fig. 4). All of the aforementioned parameters were comparable between groups B and C.

DISCUSSION

A salient finding of this study was that,

regardless of the timing and route, significant blood flow to the infarct area contributed to the reduction of infarct size, the prevention of ventricular enlargement and the preservation of left ventricular global function in patients with acute anterior myocardial infarction.

Effect of Late Reperfusion of the Infarct-Related Coronary Artery

Our results are in agreement with earlier reports on the beneficial effect of late recanalization of the infarct-related coronary artery. Siu et al⁴ reported that late recanalization of the infarct-related coronary artery, even days after thrombolysis, can prevent infarct expansion and ventricular remodeling.

Role of Collaterals in the Preservation of Left Ventricular Function

In the present study, angiographically demonstrable collaterals were associated with better preservation of wall motion in the region perfused by the infarct-related coronary artery. Previous studies have emphasized the importance of collateral blood flow to the infarct zone upon acute coronary occlusion to salvage myocardium which is to be rendered ischemic, to protect against car-

diogenic shock¹¹ and to preserve regional myocardial function¹². Our findings demonstrated that collateral circulation which develops after infarction also plays a crucial role in preserving jeopardized myocardium and preventing ventricular enlargement.

The relative contributions of preexisting collateral channels and those which develop after acute myocardial infarction to the preservation of left ventricular integrity deserve comments. Although previously established collateral channels have been shown to prevent the formation of left ventricular aneurysm,¹³ collateral circulation which develops after infarction does not prevent the formation of a left ventricular aneurysm. This difference may be explained, at least in part, by the amount of viable myocardium in the infarct area. In patients without preexisting well-developed collateral channels, acute coronary occlusion would result in transmural necrosis with a minimal viable myocardium. In these 6 patients (group C), regional myocardial hypertrophy as a result of subsequent collateral development may be insufficient to maintain tensile strength and prevent aneurysm formation.

Limitations

In interpreting our findings, some limitations must be considered. First, the number of patients in this study was relatively small, because only those with an occlusion of the proximal left anterior coronary artery were analyzed. More studies with a large number of patients would be necessary before we could reach the definitive conclusion that a blood supply to the infarct area is essential for the preservation of left ventricular size and function regardless of the timing and route. Second, in our patients in groups C and D no information was available on various indexes related to the size of the infarct during the acute stage. Therefore, it may be difficult to compare the data on left ventricular function among the 4 groups. In future studies, it would be preferable to focus only on patients about whom precise information on the acute stage of infarction is available.

Clinical Implications

The results of this study suggest that any attempts to provide significant blood flow to the infarct area are beneficial as a therapeutic

strategy for acute myocardial infarction, even when such intervention is applied late after the infarction episode.

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