Shunt Between the Ventricular Chamber and Coronary Arteries Preserves Left Ventricular Function in Acute Myocardial Infarction

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It is controversial whether newly created channels made by transmyocardial laser revascularization are functionally significant, so the present study evaluated the shunt flow from the left ventricular (LV) cavity to the ischemic myocardium in 51 patients with acute myocardial infarction (AMI) caused by complete occlusion of the proximal left anterior descending coronary artery. All patients underwent left heart catheterization within 24 h of onset and all underwent successful coronary reperfusion using primary coronary angioplasty with no angiographic restenosis on follow-up coronary angiography (CAG). The presence of the LV shunt flow was evaluated by selective left CAG after successful reperfusion. The LV global ejection fraction (EF) and regional function (centerline method) were analyzed by ventriculography in both the acute and chronic phases. The patients were divided into the 3 groups (Group A, no LV shunt without collaterals, n=20; Group B, no LV shunt with collaterals, n=24; Group C, LV shunt with collaterals, n=7). There was no difference in the grade of collateral circulation between Groups B and C. The improvements in LVEF and regional function from the acute phase to the chronic phase were significantly greater in Group C than in Groups A and B. Not only collateral circulation but also LV shunt contributes to the functional recovery of infarct myocardium in patients with AMI. (Circ J 2002; 66: 633–638)

Key Words: Acute myocardial infarction; Collateral circulation; Myocardial stunning; Shunt; Transmyocardial laser revascularization

Patients with severe, symptomatic coronary artery disease (CAD) not amenable to percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting surgery present a difficult clinical problem. An option for the management of these patients is transmyocardial laser or ultrasound revascularization (TMLR). Frazier et al used 201TI single photon emission computed tomography to demonstrate that myocardial perfusion at rest and after dipyridamole administration showed a significant improvement among the treated ischemic segments in patients with angina who were not considered suitable for standard revascularization. On the other hand, Allen et al concluded that the symptomatic benefit of TMLR (holium laser) did not improve myocardial perfusion in the laser-treated areas. However, other studies have shown that TMLR relieves angina by causing myocardial sympathetic denervation. Al-Sheikh et al reported that TMLR does not significantly affect resting or stress myocardial perfusion, but does increase the extent of sympathetic denervation observed on positron emission tomography (decreased myocardial [11C]hydroxyephedrine uptake). Thus, the functional role of newly created channels as a result of TMLR has not been elucidated, and it also remains unclear whether the channels formed in reptile hearts, which permit a substantial amount of myocardial perfusion from the ventricular chamber, are created in the presence of severe coronary stenoses in human patients with CAD. The purpose of this study was twofold: to characterize the incidence of channels and to evaluate their functional significance in patients with acute myocardial infarction (AMI).

Methods

Patient Population

Between April 1997 and March 2000, we successfully performed primary PTCA for an acutely occluded proximal left anterior descending coronary artery (LAD) within 24 h of the onset of symptoms in 60 consecutive patients with their first anterior AMI. Of this group of patients, we studied 51 patients who did not have angiographic restenosis, which was defined as stenosis ≥50%, at follow-up coronary angiography (CAG) performed 2 weeks after the onset of AMI. There were 44 men and 7 women with a mean age of 60 years (range, 34–81).

Treatment Protocol

All patients were administered 5,000 U of heparin intravenously and transported promptly to the catheterization laboratory. A second 5,000 U bolus of heparin was administered intravenously after circulatory access was obtained. Coronary angiography was first performed in the non-infarct-related artery to evaluate the extent of collateral circulation to the area perfused by the completely occluded infarct-related artery. Angioplasty was performed in a routine manner with the use of appropriately sized angio-
plasty balloon catheters. Repeated balloon inflations were performed in an attempt to decrease the residual stenosis to 50% or less. Intracoronary urokinase at a dose of up to 480,000 U was administered after angioplasty if there was definitive angiographic evidence of a persistent intracoronal thrombus. A continuous intravenous infusion of heparin and nitroglycerin was given for 24 to 72 h after the procedure. Written informed consent was obtained from each patient. The angiographic restenosis, defined as restenosis ≥50%, was evaluated 2 weeks after an initially successful procedure.

Clinical Variables
The presence or absence of a history of preinfarction angina before the acute infarction was documented. Preinfarction, long-standing stable angina was defined as typical anginal chest pain occurring at least 1 week before the onset of AMI. Preinfarction unstable angina was defined as typical anginal chest pain occurring less than 1 week before the onset of AMI. A history of hypertension was defined as a systolic pressure greater than 160 mmHg, a diastolic pressure greater than 95 mmHg or currently undergoing treatment for hypertension. The diagnosis of diabetes mellitus was established based on any one of the following 3 factors: history of taking insulin or an oral hypoglycemic agent, abnormal preinfarction fasting glucose levels (≥120 mg/100 ml) and positive results on a 75-g oral glucose tolerance test.

Coronary Angiographic and Procedural Characteristics
The infarct-related artery, the severity of CAD and the extent of residual stenosis were determined with CAG at the onset of AMI. We also documented complications related to the primary angioplasty procedure, such as coronary dissection or hemodynamic instability requiring the use of intraaortic balloon pumping. Follow-up CAG was conducted using the Judkins technique in 51 patients, 14 days (range, 10–17) after the onset of AMI. Quantitative analysis of the percent lumen diameter stenosis of the infarct-related artery was performed using a caliper on adequately magnified 35-mm cine frames at the end-diastolic phase in multiple projections. The projection showing the most severe coronary narrowing was selected.

Analysis of Ventriculograms
Left ventriculography was performed using a power injection with the patient in the 30° right anterior oblique position. The endocardial contours of the left ventricle at the end-diastolic and end-systolic frames of the left ventriculograms were traced independently by 3 different observers. In 51 patients, left ventriculography was also performed before the completion of reperfusion therapy and analyzed by the procedure used during the chronic phase. The left ventricular (LV) volume was calculated by the area-length method and used to determine the ejection fraction (EF). Regional wall motion was calculated by the centerline method. A computer generated the centerline between the systolic and diastolic contours, and 100 equally spaced chords were drawn perpendicular to the centerline. Chord 1 was drawn at the intersection of the aortic contour and the anterobasal LV wall, and chord 100 was drawn at the junction of the LV contour and the posterior aortic contour. The measured motion of each chord was normalized for heart size by dividing it by the length of the end-diastolic perimeter and then expressed in terms of standard deviation units (SD) above or below the normal mean motion of chords. Normal chord motion in our laboratory was derived from the ventriculograms of 50 patients with normal LV function without coronary artery or valvular heart disease.

Abnormalities in wall motion were calculated by 2 approaches. First, the severity of hypokinesis in the infarct region was calculated as the mean of the chord lying in the hypokinetic area and expressed as SD per chord. Second, the circumferential extent of hypokinesis was also calculated as the set of contiguous chords whose motion was depressed more than 2 SD below the normal mean and expressed as a percentage of the endocardial contour length.

Measurement of Peak Creatine Kinase Activity
Blood samples for the measurement of creatine kinase activity were drawn every 3 h for the first 24 h and every 6 h for the next 24 h of AMI. Serum creatine kinase activity was determined spectrophotometrically using Rosalki’s method.

Collateral Circulation
Collateral circulation was graded on a scale of 0 to 3, depending on the degree of opacification of the occluded vessel. The score of the collateral index was based on the injection that best opacified the occluded vessel: 0 = no opacification; 1 = filling of side branches of the artery to be perfused by way of collateral vessels without visualization of the epicardial segment; 2 = partial filling of the epicardial segment by way of collateral vessels; and 3 = complete filling of the epicardial segment by way of collateral vessels.

LV Shunt
The LV shunt was defined as transmural channels from the LAD into the ventricular chamber over the LAD territory (anterior and anterolateral region of the heart). Using selected left CAG, we examined whether or not such channels existed after successful reperfusion of the acutely occluded artery in the acute phase. We defined LV shunt (+) if angiographic contrast medium appeared directly into the LV cavity as multiple jets, and its absence as LV shunt (−) (Fig 1). Three blinded observers assessed the coronary angiograms for collateral circulation and LV shunt, and reached a consensus.

Clinical Follow-up
During the in-hospital convalescent period, aspirin (81
mg orally) was administered daily. Oral calcium channel antagonists, nitrates, angiotensin converting enzyme inhibitors (Group A: B: C = 45% : 25% : 14%, p=NS) and β-adrenergic blocking agents (Group A: B: C = 45% : 25% : 14%, p=NS) were given at the discretion of the attending physician.

### Patient Subgroups

The 51 patients, who underwent follow-up CAG, were classified into 3 major subgroups according to the extent of collateral circulation. Group A comprised 20 patients who had no LV shunt without collaterals, Group B comprised 24 patients who had no LV shunt with collaterals, and Group C comprised 7 patients who had an LV shunt with collaterals.

### Statistical Analysis

Data are expressed as the mean±SD. Multiple comparisons among groups were performed by one-way ANOVA combined with Scheffe’s test. Parametric comparisons were performed using unpaired Student t test. Results were considered significant at p<0.05.

### Results

#### Patient Population

The characteristics of the 51 patients undergoing follow-up angiography who did or did not have well developed collateral circulation and/or LV shunt at the onset of AMI are summarized in Table 1. The 3 groups were well balanced with respect to all cardiovascular risk factors, coronary angiographic and procedural characteristics. There was a significant difference in male predominance among the 3 groups. Neither the incidence of stable preinfarction angina nor that of unstable preinfarction angina significantly differed among the 3 groups. During the follow-up period, clinical events, including recurrent ischemia, reinfarction, death from any cause and treatment with repeated coronary angioplasty or bypass grafting, did not occur in the 51 patients.

### Hemodynamics

The heart rate decreased in the chronic phase compared with the acute phase (Group A, 68±12 vs 84±15 beats/min; Group B, 66±10 vs 75±14 beats/min; Group C, 63±6 vs 75±11 beats/min, p<0.05). No significant changes in the LV peak systolic pressure were observed in the 3 groups. In Groups B and C, the LV end-diastolic pressure decreased significantly from 23±9 mmHg in the acute phase to 13±4 mmHg in the chronic phase and from 24±10 mmHg in the acute phase to 11±3 mmHg in the chronic phase. In Group A, the differences in LV end-diastolic pressure were not significant between the acute and chronic phases (Table 2).

### Overall LV Function

In Group A, the cardiac index tended to decrease during the convalescent period (3.1±0.6 vs 2.3±0.5 L·min⁻¹·m⁻²). In all 3 groups, the differences in the LV end-diastolic and end-systolic volume indices were not significant between the acute and chronic phases. The global EF during the acute phase was 44±9%, 45±7%, and 45±5% in Groups A, B, and C, respectively. The global EF during the chronic phase was 38±7%, 36±5%, and 32±4% in Groups A, B, and C, respectively.
B, and C, respectively (NS); during the chronic phase, it was 39±9%, 48±7%, and 54±7%, respectively. Thus, the global EF was significantly augmented in Groups B and C (Fig 2). The improvements in EF from the acute phase to the chronic phase were significantly greater in Group C than in Groups A and B (9.7±4.0% vs –4.4±4.2%, p<0.01).

Regional Myocardial Function

The chord shortening in the infarct areas during the acute phase was 2.2±2.1%, 1.0±1.5%, and –0.5±1.9% in Groups A, B, and C, respectively (p<0.05). In the chronic stage, the chord shortening was 0.2±1.8%, 2.8±1.4%, and 4.7±1.7% in Groups A, B, and C, respectively (p<0.05). The changes in the chord shortening are depicted in Fig 3. Patients in Groups B and C had a significant improvement (p<0.05) in chord shortening in the infarct areas. The extent of improvements was significantly greater in Group C than in Groups A and B (5.1±1.7% vs –2.0±1.3% and 1.8±1.2%, p<0.01).

Creatine Kinase

Peak serum creatine kinase concentrations in each group are shown in Table 3. There were no significant differences among the groups (A: 4,401±3,345 U/L; B: 4,228±2,622 U/L; C: 2,742±1,239 U/L).

Discussion

Our results from 51 patients with anterior AMI and successful primary PTCA demonstrate that patients with well-developed preexistent collateral circulation and channels from the ventricular chamber to the myocardial vascular network of the LAD perfusion territory benefit most from revascularization. In contrast, in those patients with well-developed collateral circulation only, the beneficial effect of early reperfusion of the LAD is relatively small.

Study Design

In an attempt to precisely evaluate the effect of residual blood flow to the territory perfused by the occluded infarct-related coronary artery on the regional ventricular function, the present investigation was conducted from the following view points. Because the extent of regional wall motion observed on contrast left ventriculography differs greatly among the various areas of the ventricular wall,13 only patients with anterior AMI caused by occlusion of the proximal LAD were selected for analysis. Only patients with a complete occlusion of the LAD before primary PTCA were included in this study. Because incomplete occlusion of the receiving coronary artery of collateral circulation decreases the pressure gradient across the collateral network, leading to an underestimation of the collateral perfusion,12,14 Regional wall motion is also modified by restenosis of the dilated LAD.15 Accordingly, patients with significant restenosis on follow-up left ventriculography were excluded from subsequent analysis.

Effect of Preexistent Coronary Collateral Circulation on LV Function

Our investigation revealed that preexistent well-developed coronary collateral circulation plays an important role in the LV functional recovery of patients who undergo early reperfusion, findings that were in agreement with those of earlier studies16–18 in which the LV function has been shown to improve during the convalescent period of infarction if patients had early reperfusion in the presence of well-developed collateral circulation.

Effects of Channels From the Ventricular Chamber to the Myocardial Vascular Network of the LAD on LV Function

Our study demonstrated that in the presence of a well-developed collateral circulation, blood flow to the jeopardized myocardium through channels from the ventricular chamber contributes to further restoration of the LV function after reperfusion in patients with AMI. These findings suggest that the channels may serve as blood conduits in humans. Although it is well-known that the naturally occurring channels of reptile hearts permit a substantial amount of myocardial perfusion directly from the ventricular...
Ischemic preconditioning affected the difference in the LV functional recovery between Groups B and C. Finally, the ischemic preconditioning affected the difference in the LV functional recovery between Groups B and C.

Possible Mechanisms of New Channel Creation
Although it is well appreciated that a high-grade coronary stenosis causes collateral vessel growth,

limited information is available regarding the triggers for the growth of human collateral vessels. A severe coronary stenosis induces myocardial ischemia,

and without an LV shunt. Accordingly, it is unlikely that information is available regarding the triggers for the growth of human collateral vessels. A severe coronary stenosis induces myocardial ischemia,

transcollateral pressure gradient associated with increased wall shear stress at the site of preexistent collateral vessels and increased concentrations of several angiogenic growth factors,

which are all important stimuli for collateral vessel growth. The previously mentioned mechanical and biochemical factors associated with high-grade coronary stenosis could be also a stimulus for the formation of new channels from the ventricular cavity to the vascular network in the myocardium perfused by an occluded coronary artery. Collateral vessels and channels from the ventricular cavity to the vascular network in the myocardium may be progressively augmented as the severity and duration of coronary stenosis increases.

We are now using CAG as a gold standard for the assessment of collateral circulation in the catheterization laboratory. However, conventional CAG cannot visualize the collateral vessels with a diameter less than 100um, so contrast echocardiography or coronary wedge pressure or flow measurement may be more appropriate. In the present study, Rentrop's collateral index was similar in Groups B and C, but if the aforementioned collateral flow index had been utilized, Group C patients may have had a higher collateral flow index than Group B patients. This well-developed collateral circulation in Group C may have contributed to the improved LV functional recovery irrespective of the presence of the channels from the LV cavity to the coronary network in the jeopardized region.

Study Limitations
First, because direct visualization of the shunt flow from the LV cavity to the ischemic region during the LAD occlusion was difficult

we used selective left CAG for this purpose. Although it is unclear whether the reversely visualized channels function as significant blood conduits, the favorable effect of these channels on LV functional recovery strongly supports their significance as direct blood flow from the LV chamber to ischemic myocardium. Second, although the importance of ischemic preconditioning for functional recovery of stunned myocardium is still controversial,

in our study the prevalence of preinfarction unstable angina was comparable between patients with and without an LV shunt. Accordingly, it is unlikely that ischemic preconditioning affected the difference in the LV functional recovery between Groups B and C. Finally, the presence of an LV shunt should be directly confirmed with a histologic examination.

References

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