Coronary collateral circulation: Effects on outcomes of acute anterior myocardial infarction after primary percutaneous coronary intervention

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Abstract

**Background** To investigate the effects of collateral coronary circulation on the outcome of the patients with anterior myocardial infarction (MI) with left anterior descending artery occlusion abruptly.

**Methods** Data of 189 patients with acute anterior MI who had a primary percutaneous coronary intervention (PCI) in the first 12 h from the onset of symptoms between January 2004 and December 2008 were retrospective analyzed. Left anterior descending arteries (LAD) of all patients were occluded. LADs were reopened with primary PCI. According to the collateral circulation, all patients were classified to two groups: no collateral group \((n = 111)\), patients without angiographic collateral filling of LAD or side branches (collateral index 0) and collateral group \((n = 78)\), and patients with angiographic collateral filling of LAD or side branches (collateral index 1, 2 or 3). At one year’s follow-up, the occurrence of death, reinfarction, stent thrombosis (ST), target vessel revascularization and readmission because of heart failure were observed.

**Results** At one year, the mortality was lower in patients with collateral circulation compared with those without collateral circulation \((1\% \text{ vs. } 8\%, \text{ } P = 0.049)\), whereas there were no differences in the occurrence of reinfarction, ST, target vessel revascularization and readmission because of heart failure. The occurrence of composite of endpoint was lower in patients with collateral circulation compared with those without collateral circulation \((12\% \text{ vs. } 26\%; \text{ } P = 0.014)\).

**Conclusions** Pre-exist collateral circulation may prefigure the satisfactory prognosis to the patients with acute anterior MI after primary PCI in the first 12 h of MI onset.

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**Keywords:** collateral circulation; myocardial infarction; mortality; left anterior descending artery

1 Introduction

Anterior infarcts often leads to unsatisfactory prognosis because of impaired left ventricular function. Anterior infarcts are associated with a larger enzymatic infarct size and greater reduction in left ventricular ejection fraction (LVEF) compared with nonanterior infarcts.\(^{[1]}\) Reperfusion of the occluded coronary artery early after acute myocardial infarction (AMI) limits infarct size, improves LVEF, and enhances survival.\(^{[2]}\) In some patients, collateral circulations will emerge shortly after the coronary arteries’ occlusion. It is unknown what is the role of collateral circulation in prognosis of the patients with anterior AMI after percutaneous coronary intervention (PCI). The main purpose of the present study was to find the effect of collateral circulation on patients’ outcome in the patients with anterior AMI who had primary PCI within the first 12 h from the onset of symptoms.

2 Methods

2.1 Study patients

We selected patients who fulfilled all the following criteria: (1) admission to the hospital because of anterior wall AMI (continuous ischemic chest pain lasting \(> 30\) min and a minimum of 0.2 mV of ST segment elevation in two contiguous anterior precordial leads); (2) diagnostic coronary angiography showing complete occlusion of the left anterior descending coronary artery (LAD) (Thrombolysis in Myocardial Infarction [TIMI] flow grade 0 or 1); (3) treatment by primary PCI within the first 12 h of the onset of symptoms; and (4) left and right coronary angiograms obtained before the attempted angioplasty of sufficient quality to assess the filling of the LAD and side branches by collateral circulation. Patients with AMI secondary to acute or subacute coronary occlusion after PCI or coronary artery bypass graft surgery (CABG), patients with pulmonary edema, cardiac shock, patients treated by PCI after failed

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thrombolysis (rescue PCI), and, patients with previous anterior infarction were excluded. The patients in this study were classified into two groups: no collateral group, patients without angiographic collateral filling of LAD or side branches (collateral index 0); collateral group, patients with angiographic collateral filling of LAD or side branches (collateral index 1, 2 or 3).\[3\]

2.2 Coronary angiography and primary angioplasty

Patients orally received 600 mg clopidogrel and 300 mg aspirin as soon as possible unless there was a known allergy. Coronary angiography and primary PCI were performed in the first 12 h from the onset of symptoms of AMI. Once the radial or femoral artery was catheterized, 5000 IU of heparin was administered with additional boluses of 2000 IU if needed to achieve an activated clotting time of 250 s to 350 s. Coronary arteriograms were obtained in at least two projections. Flow in the LAD was determined before and after primary PCI and graded as described in the TIMI trial.\[4\] The LAD occlusion was considered proximal if it was located before the origin of the first well developed septal branch, distal if it was located after the origin of the third diagonal branch and mid if located between these limits.\[5\] Primary PCI was performed with conventional catheter balloon technique.\[6\] Stents were used routinely in the target lesion. The policy was to perform angioplasty only to the infarct-related artery, but in exceptional cases additional angioplasty to another vessel was performed because of compromised hemodynamic status. Intraaortic balloon pumping was used in patients with hemodynamic instability or established cardiogenic shock. The primary PCI was considered successful when flow in the infarct-related artery at the end of the procedure was TIMI grade 3 and the residual stenosis was less than 30%.

Before March 2007, most of patients were implanted with bare-metal stents (BMS) and since then drug-eluting stent (DES) was extensively used. Postinterventional antiplatelet therapy consisted of clopidogrel (150 mg/d for two weeks, continued for three months for BMS or one year for DES) and aspirin (300 mg/d for one month and continued indefinitely).

2.3 Coronary collateral circulation

Collateral circulation to the occluded LAD was assessed in coronary cineangiograms by two experienced coronary angiographers who had no knowledge of patient data. Collateral circulation was graded by using a semiquantitative scale from 0 to 3 (collateral index) depending on the degree of angiographic opacification of the occluded LAD in the best injection: 0 = no collateral circulation; 1 = collateral filling of LAD side branches without visualization of any epicardial segment; 2 = collateral partial filling of the epicardial segment, and 3 = collateral filling of the complete epicardial segment.\[3\] In case of noncoincidence, the angiographers reached a consensus.

2.4 Follow-up

All patients in the study were follow-up for one year. The occurrence of death, reinfarction, stent thrombosis (ST), target vessel revascularization and readmission because of heart failure were observed. The follow-up information was obtained by a phone call at one year. Reinfarction was defined as the recurrence of ischemic chest pain after primary PCI of ≥ 30 min duration with ST segment elevation of ≥ 0.1 mV over the previous ST segment in two contiguous leads and the MB fraction of creatine kinase (CK-MB) profile consistent with the diagnosis. ST was defined as thrombosis in stent by angiography. Target vessel revascularization was defined as PCI or coronary artery bypass graft due to restenosis or reocclusion of the target lesion in association with objective evidence of ischemia or viable myocardium. Historical angina pectoris was defined as typical chest pain episode(s) persisting < 30 min either at rest or with effort before 24 h before onset of AMI.

2.5 Statistical analysis

Continuous variables followed a normal distribution is expressed as mean ± SD. For comparisons of continuous variables between both groups the Student t test for unpaired observations was used. We used the chi-square test to compare categoric variables between groups unless expected values were less than 5, in which case we used the Fischer exact test. The Cox proportional hazards model was used to assess the association between the composite endpoint and coronary collateral circulation. All results were analyzed by using a two-sided significance level of 0.05. Data analyses were performed by using the statistical software SPSS 11.0 from SPSS Inc. (USA).

3 Results

3.1 Baseline characteristics of patients

From January 2004 to December 2008, 456 patients with anterior wall AMI within the first 12 h of the onset of symptoms were treated in our center by primary PCI. For the present analysis, we selected 189 of these patients who fulfilled the above mentioned criteria. The 267 patients who did not fulfill the criteria were excluded. Of the 189 patients included, 111 (59%) did not have angiographically visible collateral circulation to the LAD, 78 (41%) patients,
were found some collateral circulation of the LAD (collateral index 1 in 60 patients, index 2 in 16 patients and index 3 in 2 patient).

The baseline clinical characteristics of groups are summarized in Table 1. There were no significant differences in age, gender or prevalence of the main cardiovascular risk factors between the two groups.

### Table 1. Baseline clinical characteristics of study groups.

|                | No collateral (n = 111) | Collateral (n = 78) | P Value |
|----------------|-------------------------|---------------------|---------|
| Age (yr), mean ± SD | 57 ± 11                 | 55 ± 12             | 0.583   |
| Female          | 21 (19%)                | 11 (14%)            | 0.385   |
| Hypertension    | 44 (40%)                | 32 (40%)            | 0.989   |
| Hypercholesterolemia | 23 (21%)          | 14 (18%)            | 0.537   |
| Cigarette smoking | 70 (63%)               | 45 (58%)            | 0.698   |
| Diabetes mellitus | 16 (14%)               | 11 (14%)            | 0.952   |
| History of angina pectoris | 67 (60%)        | 56 (72%)            | 0.104   |

### 3.2 PCI procedure results

The angiographic finding and the results of primary PCI in the two groups are presented in Table 2. The elapsed time between the onset of symptoms suggestive of AMI and the angiography was 392 ± 160 min and the elapsed time between the onset of symptoms suggestive of AMI and the opening of LAD was 402 ± 160 min in no collateral group, which were significantly shorter as compared with that in collateral group (472 ± 154 min and 482 ± 154 min, P = 0.001).

### 3.3 Follow-up

The follow-up results of one year were presented in Table 3. Nine patients in no collateral group after PCI died. Five of them died in hospital, one died of refractory ventricular fibrillation, three died of cardiogenic shock, one died of heart rupture. Four of them died after discharge, one died of refractory heart failure, one died of reinfarction, one died of heart rupture and one died of sudden death. One patient died of refractory heart failure after discharge in collateral group. The mortality in no collateral group was 9/111 (8%) was significantly higher than that in collateral group (1/78 [1%], P = 0.049). The occurrence of reinfarction, ST, TVR and readmission because of heart failure was similar in the 2 groups. The composite endpoint was higher in no collateral group (29/111 [26%] vs. 9/78

### Table 2. Angiographic findings and primary PCI results. Data are presented as mean ± SD or n(%).

|                | No collateral (n = 111) | Collateral (n = 78) | P Value |
|----------------|-------------------------|---------------------|---------|
| Symptom to angiography time (min) | 392 ± 160          | 472 ± 154           | 0.001   |
| Symptom to balloon time (min)     | 402 ± 160           | 482 ± 154           | 0.001   |
| Collateral circulation            |                       |                     |         |
| 0                             | 111                    |                     |         |
| 1                             | 60 (77%)               |                     |         |
| 2                             | 16 (21%)               |                     |         |
| 3                             | 2 (3%)                 |                     |         |
| Level of LAD occlusion          |                       |                     | 0.870   |
| Distal segment                  | 0                      | 0                    |         |
| Middle segment                  | 54 (46%)               | 37 (50%)             |         |
| Proximal segment                | 57 (54%)               | 41 (51%)             |         |
| TIMI flow in LAD after PCI      |                       |                     | 0.838   |
| Grade 0                        | 1 (1%)                 | 0 (0%)               |         |
| Grade 1                        | 1 (1%)                 | 2 (3%)               |         |
| Grade 2                        | 2 (2%)                 | 1 (1%)               |         |
| Grade 3                        | 107 (96%)              | 75 (96%)             |         |
| IABP in PCI                     | 7 (6%)                 | 2 (3%)               | 0.202   |
| Successful primary PCI          | 109 (98%)              | 75 (96%)             | 0.405   |
| DES used                       | 56 (50%)               | 40 (52%)             | 0.840   |

PCI: percutaneous coronary intervention; IABP: intra-aortic balloon pump; DES: drug eluting stent; LAD: Left anterior descending arteries.
The association between the composition of endpoint and coronary collateral circulation (with or without), the LAD occlusion location (proximal or non-proximal), sex, smoking, history of angina pectoris, diabetes mellitus, hypertension, hypercholesterolemia, symptom to balloon time was tested with the Cox proportional hazards model. The model indentified without collateral circulation (hazard ratio[HR] = 2.196, 95%CI: 1.073– 4.492; P = 0.031) were independent predictors of one year composite endpoint.

The occurrence of composite endpoint in patients with collateral coronary circulation was lower than that in patient without collateral coronary circulation in those patients received PCI within six hours of symptoms (0/19 [0%] vs. 16/53 [30.2%], P = 0.008), but not in those received PCI between 6 to 12 h after symptoms (9/59 [15.5%] vs. 13/58 [22.4%], P = 0.353). For patients with collateral coronary circulation, the occurrence of composite endpoint in those who received PCI between 6 h and 12 h after symptom onset was lower than that in patients without collateral coronary circulation but received PCI within six hours of symptoms (9/59 [15.5%] vs. 16/53 [30.2%], P = 0.023).

4 Discussion

The coronary collateral circulation is an alternative source of blood supply to a myocardium jeopardized by abruptly occluded vessels, preventing myocardial death and favoring myocardial recovery after reperfusion therapy. However, the functional significance of collateral circulation in AMI has been a matter of debate for many years. It has been traditionally assumed that coronary arteries are functional end arteries in the absence of stenoses, but it also was reported that there are functional collateral vessels to the extent in humans with angiographically normal coronary arteries. Factors that may influence the presence of collaterals after the onset of AMI have been demonstrated in previous clinical studies. The recruitment of collateral circulation is affected by the presence of multivessel disease, preinfarction angina, history of angina pectoris, time from onset to cardiac catheterization. It was reported that collateral circulation did not exert a protective effect in patients who underwent primary PCI. In that paper, the author didn’t analyse the outcome of patients with anterior AMI and only chose the patients with AMI in the first six hours of AMI onset. The patients with LAD-related infarcts had a worse prognosis compared with the patients with non-LAD-related infarcts because of a lower residual LVEF. So, the study for collateral circulation to the LAD-related infarcts may be important.

In the first six hours of AMI onset, 17% of patients with anterior AMI were found angiographic collateral circulation. In other study, collateral circulations were visible in nearly 40% of patient with AMI. In the present study, collateral circulation to the occluded LAD is found by angiography within the first 12 h of AMI onset in 41% of patients with anterior AMI. The percent of the patients with collateral circulation in the first six hours of AMI was 24%. The pressure-derived fractional collateral flow was measured in 70 patients with AMI onset in the first 12 h. It was found that the left ventricular recovery after reperfused AMI was primarily determined by pressure-derived fractional collateral flow and was less dependent on time to reperfusion in patients with collaterals. Time to reperfusion is important for survival with thrombolytic therapy. Improvement in ejection fraction was substantial with reperfusion at less than two hours but was relatively independent of time to reperfusion after two hours. The mortality was independent of time to reperfusion. It has been suggested that some reasons why time to treatment may be less important with primary PCI than thrombolytic therapy might be possible. First, TIMI 2 to 3 flow is achieved less often with increasing time to reperfusion after two hours. The mortality was independent of time to reperfusion. In contrast, TIMI 3 flow was achieved less often with increasing time to treatment with thrombolytic therapy. In our study, collateral circulation was an dependent factor for the composite endpoint, and the

| Composite endpoint | No collateral (n = 111) | Collateral (n = 78) | P Value |
|--------------------|------------------------|--------------------|---------|
| Death              | 9 (8%)                 | 1 (1%)             | 0.049   |
| ST                 | 4 (4%)                 | 1 (1%)             | 0.312   |
| Reinfarction       | 5 (5%)                 | 1 (1%)             | 0.210   |
| TVR                | 10 (9%)                | 3 (4%)             | 0.137   |
| PCI                | 9                      | 3                  |         |
| CABG               | 1                      | 0                  |         |
| Readmission because of heart failure | 9 (8%) | 4 (5%) | 0.312 |
| Composite endpoint | 29 (26%)               | 9 (12%)            | 0.014   |

CABG: coronary artery bypass graft surgery.
symptom to treatment time was not an dependent factor. It was suggested that the time to reperfusion was a crucial factor for the prognosis of patient with AMI in the first hours onset (possible two hours or six hours or other) and the benefit of reperfusion would decrease after the first hours AMI onset. The presence of collateral circulation at this time point may improve myocardial salvage and prevent ventricular remodeling and prevent ventricular remodeling, thereby improving prognosis independent of coronary reperfusion therapy. In the present study, the patients with collateral coronary circulation had better prognosis than it in the patient without collateral coronary circulation when the patients with AMI accepted primary PCI in the first six hours of syndrome to treatment time. The patients with AMI with collateral coronary circulation accepted primary PCI between 6 h and 12 h of syndrome to treatment time had a better prognosis tendency compared with the patients without collateral coronary circulation. The patients with collateral coronary circulation accepting primary PCI between 6 h and 12 h of syndrome to treatment time had better prognosis than it in the patients without collateral coronary circulation accepting primary PCI in the first 6 h of syndrome to treatment time. These results suggest that finding a way to gaining the collateral coronary circulation earlier might give a better prognosis to the patients with AMI. It has been found that basic fibroblast growth factor enhances collateral development, reduces infarct size and improves cardiac function. Some potential limitations need to be addressed. First, the sum of sample is not a larger number. Second, some data, such as peak creatine kinase myocardial band and left ventricular ejection fraction at one year were not collected completely. So, the infarction area and the function of left ventricle were not evaluated accurately.

References
1 Elsman P, van’t Hof AW, de Boer MJ, et al. Impact of infarct location on left ventricular ejection fraction after correction for enzymatic infarct size in acute myocardial infarction treated with primary coronary intervention. Am J Heart J 2006; 151: e1239–1214.
2 Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists’ (FTT) Collaborative Group. Lancet 1994; 343: 311–322.
3 Rentrop KP, Feit F, Sherman W, et al. Serial angiographic assessment of coronary artery obstruction and collateral flow in acute myocardial infarction. Report from the second Mount Sinai-New York University Reperfusion Trial. Circulation 1989; 80: 1166–1175.
4 Chesbrow JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987; 76: 142–154.
5 Perez-Castellano N, Garcia EJ, Abeyta M, et al. Influence of collateral circulation on in-hospital death from anterior acute myocardial infarction. J Am Coll Cardiol 1998; 31: 512–518.
6 Han YL, Wang B, Wang XZ, et al. Comparative effects of percutaneous coronary intervention for infarct-related artery only or for both infarct- and non-infarct-related arteries in patients with ST-elevation myocardial infarction and multi-vessel disease. Chin Med J (Engl) 2008; 121: 2384–2387.
7 Nicolau JC, Nogueira PR, Pinto MA, et al. Early infarct artery collateral flow does not improve long-term survival following thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1999; 83: 21–26.
8 Sabia PJ, Powers ER, Jayaweera AR, et al. Functional significance of collateral blood flow in patients with recent acute myocardial infarction. A study using myocardial contrast echocardiography. Circulation 1992; 85: 2080–2089.
9 Wustmann K, Zbinden S, Windecker S, et al. Is there functional collateral flow during vascular occlusion in angiographically normal coronary arteries? Circulation 2003; 107: 2212–2220.
10 Vytssoulis G, Kyriakidis M, Karpanou E, et al. A prospective angiographic study of the coronary collateral circulation in coronary arterial disease. Int J Cardiol 1990; 27: 187–191.
11 Nakagawa Y, Ito H, Kitakaze M, et al. Effect of angina pectoris on myocardial protection in patients with reperfused anterior wall myocardial infarction: retrospective clinical evidence of "preconditioning". J Am Coll Cardiol 1995; 25: 1076–1083.
12 Rentrop KP, Cohen M, Blanke H, et al. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. J Am Coll Cardiol 1985; 5: 587–592.
13 Antoniucci D, Valenti R, Moschi G, et al. Relation between preintervention angiographic evidence of coronary collateral circulation and clinical and angiographic outcomes after primary angioplasty or stenting for acute myocardial infarction. Am J Cardiol 2002; 89: 121–125.
14 de Boer MJ, Reiber JH, Suryapranata H, et al. Angiographic findings and catheterization laboratory events in patients with primary coronary angioplasty or streptokinase therapy for acute myocardial infarction. Eur Heart J 1995; 16: 1347–1355.
15 Lee CW, Park SW, Cho GY, et al. Pressure-derived fractional collateral blood flow: a primary determinant of left ventricular recovery after reperfused acute myocardial infarction. J Am Coll Cardiol 2000; 35: 949–955.
16 Goldberg RJ, Mooradd M, Gurwitz JH, et al. Impact of time to treatment with tissue plasminogen activator on morbidity...
and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). Am J Cardiol 1998; 82: 259–264.

17 Newby LK, Rutsch WR, Califf RM, et al. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-I Investigators. J Am Coll Cardiol 1996; 27: 1646–1655.

18 Brodie BR, Stone GW, Morice MC, et al. Importance of time to reperfusion on outcomes with primary coronary angioplasty for acute myocardial infarction (results from the Stent Primary Angioplasty in Myocardial Infarction Trial). Am J Cardiol 2001; 88: 1085–1090.

19 Bode C, Smalling RW, Berg G, et al. Randomized comparison of coronary thrombolysis achieved with doublebolus reteplase (recombinant plasminogen activator) and front-loaded, accelerated alteplase (recombinant tissue plasminogen activator) in patients with acute myocardial infarction. The RAPID II Investigators. Circulation 1996; 94: 891–898.

20 Brodie BR, Stuckey TD, Hansen CJ, et al. Timing and mechanism of death determined clinically after primary angioplasty for acute myocardial infarction. Am J Cardiol 1997; 79: 1586–1591.

21 Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997; 278: 2093–2098.

22 Habib GB, Heibig J, Forman SA, et al. Influence of coronary collateral vessels on myocardial infarct size in humans. Results of phase I thrombolysis in myocardial infarction (TIMI) trial. The TIMI Investigators. Circulation 1991; 83: 739–746.

23 Hirai T, Fujita M, Yoshida N, et al. Importance of ischemic preconditioning and collateral circulation for left ventricular functional recovery in patients with successful intracoronary thrombolysis for acute myocardial infarction. Am Heart J 1993; 126: 827–831.

24 Hirai T, Fujita M, Nakajima H, et al. Importance of collateral circulation for prevention of left ventricular aneurysm formation in acute myocardial infarction. Circulation 1989; 79: 791–796.

25 Hirayama A, Adachi T, Asada S, et al. Late reperfusion for acute myocardial infarction limits the dilatation of left ventricle without the reduction of infarct size. Circulation 1993; 88: 2565–2574.

26 Zhang C, Yang J, Feng J, et al. Short-term administration of basic fibroblast growth factor enhances coronary collateral development without exacerbating atherosclerosis and balloon injury-induced vasoproliferation in atherosclerotic rabbits with acute myocardial infarction. J Lab Clin Med 2002; 140: 119–125.