



## 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% vs. 8%,  $P = 0.049$ ), 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% vs. 26%;  $P = 0.014$ ). **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.<sup>[1]</sup> Reperfusion of the occluded coronary artery early after acute myocardial infarction (AMI) limits infarct size, improves LVEF, and enhances survival.<sup>[2]</sup> 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).<sup>[3]</sup>

## 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.<sup>[4]</sup> 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.<sup>[5]</sup> Primary PCI was performed with conventional catheter balloon technique.<sup>[6]</sup> 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.<sup>[3]</sup> 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  $\geq 30$  min duration with ST segment elevation of  $\geq 0.1$  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  $\pm$  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 categorical variables between groups unless expected values were less than 5, in which case we used the Fisher 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 fulfilled 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 $\pm$ SD	57 $\pm$ 11	55 $\pm$ 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  $392 \pm 160$  min and the elapsed time between the onset of symptoms suggestive of AMI and the opening of LAD was  $402 \pm 160$  min in no collateral group, which were significantly shorter as compared with that in collateral group ( $472 \pm 154$  min and  $482 \pm 154$  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  $\pm$  SD or n(%).

	No collateral (n = 111)	Collateral (n = 78)	P Value
Symptom to angiography time (min)	392 $\pm$ 160	472 $\pm$ 154	0.001
Symptom to balloon time (min)	402 $\pm$ 160	482 $\pm$ 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.

Table 3. Results of follow-up.

	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.

[12%],  $P = 0.014$ ).

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 identified without collateral circulation (hazard ratio[HR] = 2.916, 95%CI: 1.291–6.586;  $P = 0.010$ ) and the proximal LAD occlusion (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.<sup>[7-8]</sup> 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.<sup>[9]</sup> 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,<sup>[10]</sup> preinfarction angina,<sup>[5]</sup> history of angina pectoris,<sup>[11]</sup> time from onset to cardiac catheterization.<sup>[12]</sup> 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.<sup>[13]</sup> 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.<sup>[1]</sup> 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.<sup>[13]</sup> In other study, collateral circulations were visible in nearly 40% of patient with AMI.<sup>[14]</sup> 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.<sup>[15]</sup> Time to reperfusion is important for survival with thrombolytic therapy.<sup>[16,17]</sup> 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.<sup>[18]</sup> 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 treatment with thrombolytic therapy.<sup>[19]</sup> In contrast, TIMI 3 flow was achieved in a high percentage of patients regardless of time to treatment with primary PCI. Second, in patients treated with thrombolytic therapy, mortality rates from myocardial rupture increased progressively with increasing time to treatment. In contrast, mortality rates due to myocardial rupture after primary PCI are very low.<sup>[20]</sup> Third, the incidence of intracranial hemorrhage after thrombolytic therapy increased with increasing time to treatment.<sup>[17]</sup> The occurrence of intracranial hemorrhage with primary PCI is rare.<sup>[21]</sup> In our study, collateral circulation was an dependent factor for the composite endpoint, and the

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<sup>[22–23]</sup> and prevent ventricular remodeling,<sup>[24]</sup> thereby improving prognosis independent of coronary reperfusion therapy.<sup>[25]</sup> 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.<sup>[26]</sup>

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.

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## Book Review

**Long-term care medicine: A pocket guide.** Fenstemacher PA and Winn P Eds; Humana Press: Secaucus, USA, 2010 (351 pp). ISBN: 978-1-60761-141-7. Paperback Price: \$39.95

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With people aged over 65 years as the most rapidly growing population within the United States as well as much of the rest of the world, there is a corresponding need for growth of greater understanding and better management of them. Fenstemacher and Winn together with 20 knowledgeable contributors have produced this splendid, concise, inexpensive little book to thoroughly improve both. It is divided into four sections: Introduction, Common Medical Conditions, Psychosocial Features, and Special Issues in Continuing Care. The book address all the varied components of the long-term care system whether for remaining at home or for living within institutions, maintaining their happiness, self-respect, and quality of life, all the way through.