

Collateral Circulation in Total Occlusion of the Left Anterior Descending or Right Coronary Artery

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The functional significance of the collateral circulation was evaluated in 125 patients with total coronary occlusion. Patients were classified into two groups. Group 1: patients with angina pectoris (AP), Group 2: patients with a first transmural myocardial infarction (MI) within 3 months of the symptom onset. Clinical variables, resting and exercise electrocardiogram (EKG) were analyzed with angiographic findings. Collateral fillings were graded from 0 to 3: 0=none; 1=filling of side branches only; 2=partial filling of the epicardial segment; 3=complete filling of epicardial segment. The wall motion of each segment was scored from 1 to 5: 1=normal; 2=mild to moderate hypokinesia; 3=severe hypokinesia; 4=akinesia; 5=dyskinesia. The scores of the 5 segments were added to yield a total LV score. There was a higher prevalence of good collaterals and multi-vessel disease in patients with AP than in those with MI (83% vs 53%, 54% vs 30%, respectively, $p<0.05$). The left ventricular ejection fraction (LVEF), left ventricular end-diastolic pressure (LVEDP) and segmental wall motion score were significantly better in patients with AP than in those with MI ($68.9\pm13.4\%$, vs $50.5\pm12.6\%$, $15.0\pm7.3\text{mmHg}$ vs $20.3\pm8.8\text{mmHg}$, 6.5 ± 2.2 vs 9.6 ± 2.3 , respectively, $p<0.05$). In spite of total coronary occlusion, 61% of AP patients had normal resting EKG but (96% of AP patients who underwent treadmill test proved positive. The proportions of well-developed collaterals in 3 groups divided according to the interval between onset of MI and angiography (within 1 day, 2 to 14 days, 15 days to 3 months) were 13%, 54% and 60%. There were no significant differences in LVEF, segmental wall motion score and LVEDP in MI patients with poorly-developed collaterals and well-developed collaterals ($49.1\pm15.7\%$ vs $46.4\pm10.1\%$, 11.1 ± 2.2 vs 10.9 ± 1.4 and $24.3\pm9.7\text{mmHg}$ vs $20.3\pm7.0\text{mmHg}$, $p=\text{NS}$). The degree of collateral development was higher in MI with right coronary artery occlusion compared with that of left anterior descending artery occlusion (1.1 ± 1.0 vs 2.0 ± 1.0 , $p<0.05$).

In conclusion, collateral circulation can prevent myocardial ischemia and preserve myocardial function in a significant number of patients with AP but do not provide protection against exercise-induced myocardial ischemia in the majority of patients with AP. Well-developed collaterals are uncommonly present within 1 day after MI, but subsequently develop and are generally demonstrable after 2 weeks. Collateral vessels in patients with MI have no beneficial effects on preserving myocardial function.

Key Words: Total coronary occlusion, collateral circulation

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The role of coronary collateral circulation has been a subject of great interest and controversy for many years (Helfant *et al.* 1970; Helfant *et al.* 1971, Levine *et al.* 1973; Carroll *et al.* 1974; Bloor *et al.* 1974; Hamby *et al.* 1976). In spite of total coronary occlusion, a significant number of patients with coronary artery disease (CAD) had no evidence of ischemic in-

jury because of protective effects of collateral vessels to the jeopardized myocardium (Freedman *et al.* 1 (85). Several studies suggested that the presence of collaterals in the early hours of acute myocardial infarction was associated with relatively smaller infarcts and better improvement of the left ventricular function after reperfusion therapy (Saito *et al.* 1 (85). But little information was available in Korea regarding the functional role of collateral vessels in patients with total coronary occlusion.

The purpose of the present study is to evaluate the influence of the collateral circulation on the left ventricular function and its relation to the clinical variables in patients with angina pectoris and in patients with their first transmural myocardial infarction due to total occlusion of the left anterior descending coronary artery (LAD) or the right coronary artery (RCA). Our study was confined to patients with total coronary occlusion to avoid inhomogeneity of patients studied.

MATERIALS AND METHODS

Study population

One hundred twenty five patients (102 men, 23 women, aged: 31-79) who showed total occlusion of the left anterior descending artery or right coronary artery were selected among 3,647 patients who had a coronary angiographic study at the Yonsei University, Severance Hospital, between February 1982 and August 1992. Of the 125 patients, 79 had their first transmural myocardial infarction within 3 months after symptom onset and the remaining 46 were found to have no myocardial infarction.

Coronary angiography was justified in all patients by the existence of the clinical ischemic symptoms of angina pectoris or myocardial infarction.

The diagnosis of myocardial infarction was based on the presence of a typical history of prolonged chest pain, characteristic electrocardiographic finding, and an increase in the appropriate serum enzyme levels.

We excluded patients who had total occlu-

sions of two or more coronary arteries, total occlusion of the left main coronary artery, history of myocardial infarction older than 3 months, patients who had reperfusion therapy before angiography, previous coronary artery bypass graft, and patients with congenital heart disease. Patients with complete occlusion of the left circumflex artery were also excluded because the left anterior oblique ventriculography is not performed routinely in our laboratory.

Angiographic analysis

Coronary angiography was performed by the Judkins technique. Both coronary angiograms were recorded at 30° frames/sec in multiple projections. After the baseline hemodynamic measurements, left ventriculography was performed in the 30° right anterior oblique projection with the injection of 30cc of contrast medium.

Qualitative assessment of the segmental wall motion was performed visually. Five left ventricular segments in the right anterior oblique projection were indentified: antero-basal, anterolateral, apical, diaphragmatic and posterobasal. The wall motion of each segment was scored from 1 to 5: 1=normal wall motion; 2=mild to moderate hypokinesia; 3=severe hypokinesia, 4=akinesia; and 5=dyskinesia. For each patient, the scores of the five segments were added to yield a total LV score representing the severity of the left ventricular damage. For example, if the anterolateral and apical areas were akinetic and the remaining three segments were normal, the overall LV score would be eleven. Left ventricular ejection fraction was calculated using the area-length method (Sandler *et al.* 1968). Collateral fillings were graded from 0 to 3 according to the criteria of Cohen and Rentrop (1989): 0=none; 1=filling of side branches only; 2=partial filling of the epicardial segment; 3=complete filling of the epicardial segment. For the purpose of this study, the patients were classified into 2 groups according to these collateral criteria: Grade 0 and 1 were considered to have poor collaterals, and grade 2 and 3 were considered to have good collaterals. A significant obstruction

was defined as the luminal narrowing of 50% or more of a major coronary artery branch. The two cardiologists assessed the coronary angiograms and ventriculograms and reached a consensus.

Statistical analysis

All data are expressed as mean \pm standard deviation. The characteristics of the comparable groups were analyzed using the chi-square test for categorical variables, and student's *t* test for continuous variables. A Fisher's exact test was used for nonparametric data. A *p* value <0.05 was considered significant.

RESULTS

Collateral circulation and LV function in patients with angina pectoris (AP) and myocardial infarction (MI)

Forty-four out of 46 patients with AP had collaterals of which good collaterals were observed in 38 (83%) patients. While of the 79 patients who had MI, 17 patients (22%) had no evidence of collateral vessels angiographically and the frequency of good collaterals (42 of 79.53%) was significantly lower than that of the patients with AP ($p < 0.01$). The mean collateral grade in patients with AP was better than that of those with MI (2.2 ± 0.8 vs 1.5 ± 1.0 , $p < 0.05$). LV systolic function and segmental wall motion were significantly well-preserved in patients with AP compared with those with MI. Interestingly, multivessel disease was more frequently involved in patients with AP than in those with MI. Demographic characteristics and distribution of the occluded artery were similar in both groups (Table 1).

Functional significance of collateral circulation in patients with AP (Table 2).

There was no significant difference in clinical and angiographic characteristics between patients with collateral grade 0, 1 or 2 and grade 3 (Table 2). Sixty-one percent (28 patients) of group 1 patients had normal resting electrocardiogram. Treadmill test was positive in 24 of 25 patients (96%) who underwent the

Table 1. Clinical and angiographic findings in patients with angina pectoris (AP) and with myocardial infarction (MI)

	AP(n=46)	MI(n=79)	P value
Age(yrs)	59.0 \pm 8.0	54.7 \pm 11.5	NS
Male/Female	35/11	67/12	NS
Occluded artery			
LAD	21	40	NS
RCA	25	39	
CAD extent			
1-V	21(46%)	55(70%)	
2,3-V	25(54%)	24(30%)	<0.05
Collateral grade(mean)	2.2 \pm 0.8	1.5 \pm 1.0	<0.05
LVEF(%)	68.9 \pm 13.4	50.5 \pm 12.6	<0.05
LVEDP(mmHg)	15.0 \pm 7.3	20.3 \pm 8.8	<0.05
Wall motion score	6.5 \pm 2.2	9.6 \pm 2.3	<0.05

AP: Angina pectoris, MI: Myocardial infarction, LAD: Left anterior descending artery, RCA: Right coronary artery, CAD: Coronary artery disease, V: vessel, LVEF: Left ventricular ejection fraction, LVEDP: Left ventricular end diastolic pressure, NS: Not significant

Table 2. Clinical and angiographic findings in relation to collateral grades in patients with angina pectoris

Collaterals	Grade 0,1 and 2 (n=26)	Grade 3 (n=20)	P value
Age(yrs)	58.8 \pm 8.9	59.2 \pm 6.9	NS
Male/Female	20/6	15/5	NS
Angina duration(months)	22.9 \pm 30.5	14.1 \pm 21.2	NS
Exercise duration(min)	6.5 \pm 3.2	6.5 \pm 2.4	NS
Occluded artery			
LAD	11	10	
RCA	15	10	NS
CAD extent			
1-V	10	11	
2,3-V	16	9	NS
LVEF(%)	68.0 \pm 13.1	70.0 \pm 14.1	NS
LVEDP(mmHg)	15.9 \pm 7.3	13.4 \pm 7.2	NS
Wall motion score	6.6 \pm 2.0	6.4 \pm 2.5	NS

EKG: electrocardiography

NSRA: nonspecific repolarization abnormality
other abbreviation as in Table 1.

Table 3. Collateral grade in MI patients according to the interval between onset of MI and coronary angiography

Interval	<1D (n=8)	2-14D (n=28)	15D-3M (n=43)
Collateral grade	n(%)	n(%)	n(%)
0	7(88)	5(18)	5(12)
1	0(0)	8(28)	12(28)
2	1(12)	10(36)	15(35)
3	0(0)	5(18)	11(25)
Poor(0~1)	7(88)	13(46)	17(40)
Good(2~3)	1(12)	15(54)	26(60)

D: day, M: month

test (Fig. 2). LVEDP was not significantly different between grade 3 collateral patients with grade 0,1 or 2 collaterals (13.4 ± 7.2 vs 15.9 ± 7.3). The global LV systolic function and segmental wall motion were better in AP patients with grade 3 collaterals compared with those with grade 0,1 or 2 without statistical significance.

Temporal evolution of the coronary collateral circulation after MI (Table 3, Figure 1)

Of the 79 patients with MI, coronary angiography was performed in 8 patients within 1 day (2hr~12hrs) after onset of MI, in 28 patients between 2 days and 14 days, and in 43

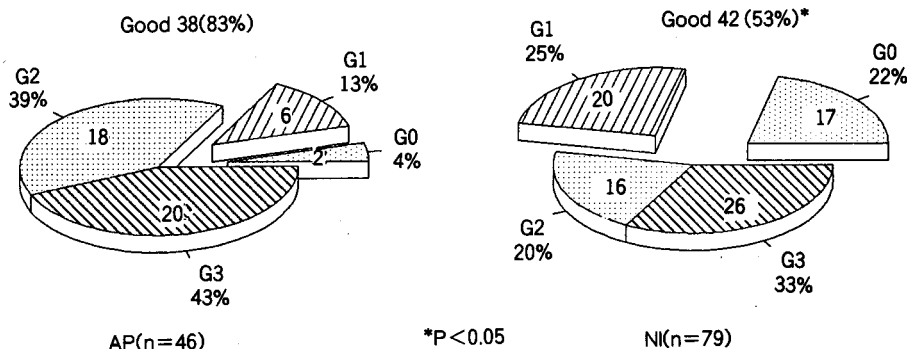


Fig. 1. Collateral grade in AP and MI patients. Note the significantly higher incidence of good collaterals in AP patients. AP: angina pectoris, G: grade, MI: myocardial infarction.

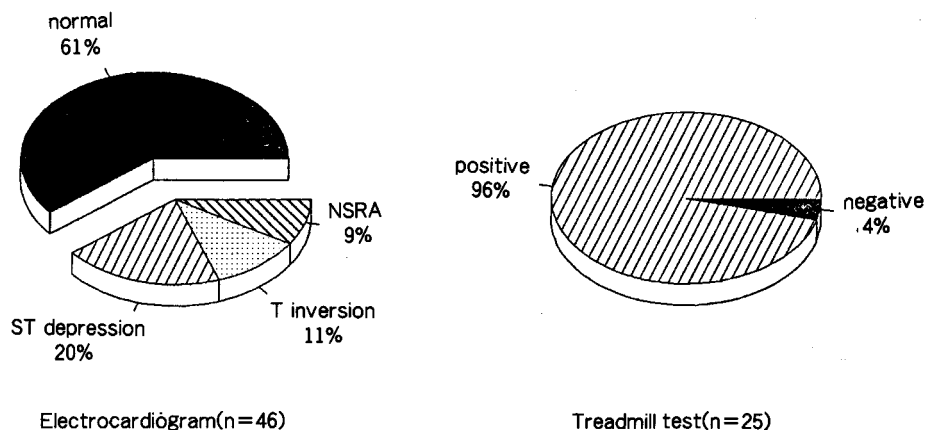


Fig. 2. Electrocardiogram and treadmill test in AP patients.

NSRA: nonspecific repolarization abnormality. Other abbreviation as in Fig 1.

patients between 15 days to 3 months after onset of acute MI symptoms. Of the 8 patients studied within 1 day after MI, 7 (88%) had no demonstrable collaterals and 1 patient had grade 2 collateral vessels. Of the 28 patients studied between 2 days and 14 days after MI, 5 patient (18%) had no visible collat-

erals, 8 (29%) had grade 1, 10 (36%) had grade 2, and 5 (18%) had grade 3. Of the 43 patients studied between 15 days to 3 months after MI, 5 patient (12%) had no collaterals while 12 (28%) had grade 1, 15 (35%) had grade 2 and 11 (26%) had grade 3 collateral channels (Table 3). By combining grade 2 and 3 collaterals, the proportions with good coronary collateral vessels in each subgroup divided according to interval between onset of MI and angiography was 13%, 54% and 60%. These differences in incidence of good collaterals

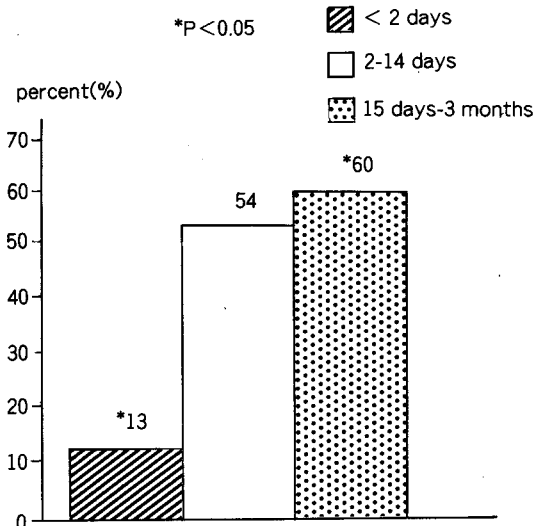


Fig. 3. Incidence of good collaterals in MI patients according to the interval between the onset of MI and coronary angiography. Note the higher incidence of good collaterals in late angiography group compared with early angiography group. Abbreviation as in Fig 1.

Table 4. Clinical and angiographic findings in relation to collateral grades in patients with MI

Collaterals	Poor (n=37)	Good (n=42)	P value
Age	54.8±12.0	54.5±11.1	NS
Male/Female	33/4	34/8	NS
CAD extent			
1-V	29	26	NS
2,3-V	8	16	
MI site			
Anterior	28	15	<0.05
Inferior	9	27	
Interval(days)	24.2±27.9	30.2±28.6	NS
LVEF(%)	50.1±14.2	50.7±11.1	NS
LVEDP(mmHg)	22.6± 8.9	18.4± 8.3	NS
Wall motion score	10.3± 2.4	9.0± 2.1	<0.05

Abbreviation as in Table 1.

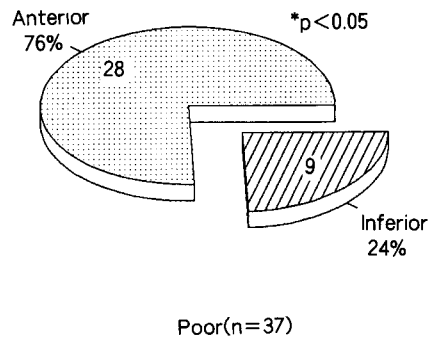
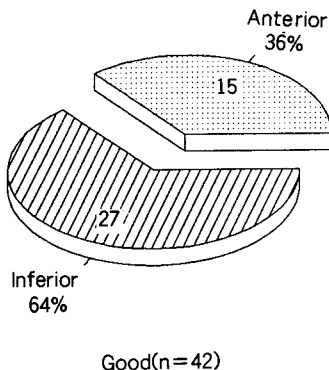


Fig. 4. Collateral grade and infarct site. Note the higher incidence of inferior MI in patients with good collaterals. Abbreviation as in Fig 1.

Table 5. Comparison of clinical and angiographic findings between patients with anterior MI and those with inferior MI

	Anterior (n=43)	Inferior (n=36)	P value
Age	55.8±10.5	53.3±12.5	NS
Male/Female	34/9	33/3	NS
CAD extent			
1-V	32	23	
2,3-V	11	13	NS
Interval(days)	25.9±28.6	29.9±28.1	NS
Collateral grade	1.1± 1.0	2.0± 1.0	<0.05
LVEF(%)	48.1±13.9	53.2±10.4	NS
LVEDP(mmHg)	22.9± 8.9	17.3± 7.8	<0.05
Wall motion score	11.0± 1.9	8.0± 1.7	<0.05

Abbreviation as in Table 1.

were statistically significant ($p<0.05$) between early angiographic group (<1day) and late angiographic group (15 days~3 months) (Fig. 3).

Functional significance of coronary collateral circulation in patients with MI

Of the 79 patients with MI, 37 (47%) had poor and 42 (53%) had good collaterals. There were 43 patients with occlusion of the LAD and anterior MI and 36 patients with occlusion of the RCA and inferior MI. LVEDP was lower in patients with good collaterals than in those with poor collaterals without statistical significance. Segmental wall motion score of the LV was significantly lower in patients with good collaterals than in those with poor collaterals (Table 4). But these differences in LV function between two comparable groups have been attributed to the difference in the frequency of the anterior MI rather than the beneficial effect of good collaterals. When we compared patients with anterior MI to those with inferior MI, there was no significant differences in demographic characteristics, the extent of CAD, and the interval between the onset of MI and angiography. But patients with inferior MI had a significantly higher collateral grade than those with anterior MI (2.0 ± 1.0 vs 1.1 ± 1.0 , respectively, $p<0.05$). LVEDP and segmental wall motion score

Table 6. Clinical and angiographic findings in relation to collateral grades in patients with anterior MI

Collaterals	Poor (n=28)	Good (n=15)	P value
Age(yrs)	55.3±11.9	56.8± 7.5	NS
Male/Female	24/4	10/5	NS
CAD extent			
1-V	22	10	
2,3-V	6	5	NS
Interval(days)	24.1±27.6	29.3±31.0	NS
LVEF(%)	49.1±15.7	46.4±10.1	NS
LVEDP(mmHg)	24.3± 9.7	20.3± 7.0	NS
Wall motion score	11.1± 2.2	10.9± 1.4	NS

Abbreviation as in Table 1.

Table 7. Clinical and angiographic findings in relation to collateral grades in patients with inferior MI

Collaterals	Poor (n=9)	Good (n=27)	P value
Age(yrs)	53.2±12.9	53.3±12.6	NS
Male/Female	9/0	24/3	NS
CAD extent			
1-V	7	16	
2,3-V	2	11	NS
Interval(days)	24.4±30.4	30.8±27.7	NS
LVEF(%)	53.2± 8.5	53.1±11.1	NS
LVEDP(mmHg)	17.3± 2.3	17.3± 9.0	NS
Wall motion score	8.1± 1.7	8.0± 1.7	NS

Abbreviation as in Table 1.

were significantly higher in patients with anterior MI compared with the inferior MI patients (Table 5). Poor LV function in patients with anterior MI might be due to a larger infarct size rather than the effect of poor collateral development in anterior MI. Therefore, we also examined the relation between the degree of collateral development and LV function in patients with anterior MI. Of the 43 patients with anterior MI, there was no significant differences in LVEF, LVEDP, and segmental wall motion score between patients with poor collaterals (n=28) and those with

good collaterals (n=15)(Table 6). In 36 patients with inferior MI, there were no significant relation between the presence of good or poor collateral vessels and LV function(Table 7).

DISCUSSION

The functional significance of the human coronary collateral circulation has been controversial for many years. In spite of total coronary occlusion,a significant number of patients with coronary artery disease had no evidence of ischemic injury because of protective effects of collateral vessels to the jeopardized myocardium. A totally obstructed coronary artery perfused by well-developed collaterals has been shown to be hemodynamically comparable to an artery with a 91% to 99% diameter stenosis (Flameng *et al.* 1978).

Collateral circulation and left ventricular function in AP and MI

Although considerable controversy surrounds the functional significance of coronary collaterals,there is general agreement that collateral blood flow may protect the heart from transmural infarction, preserve wall motion, and prevent pathologic infarction in areas of myocardium supplied by totally occluded vessels (Levin *et al.* 1974; Hamby *et al.* 1976; Hecht *et al.* 1975). Freedman *et al.* (1985) reported that collateral flow was present in all patients with an occluded artery without Q wave, whereas all patients with a totally occluded artery without collateral flow had Q wave infarctions. In our study,similar findings were observed 96% of patients with angina pectoris alone showed angiographically demonstrable collateral flows and those patients without infarction showed better left ventricular function than those with MI. There were significantly higher incidence of good collaterals and better LV function in non-infarct group than those of the infarct group. Our findings of good collateral filling and better LV function in patients without myocardial infarction suggests the possible role of collateral circulation in total coronary occlusion.

Functional significance of collateral circulation in patients with angina pectoris

Prior data showed severity of coronary arterial stenosis and longer duration of previous angina pectoris allowed collateral development before coronary occlusion thereby limiting myocardial damage (Piek *et al.* 1991; Juilliere *et al.* 1990). All patients included in our study were of totally occluded coronary arteries and there was no statistically significant correlation between duration of angina and development of collateral circulation. But in our study,we analyzed duration of angina only in patients without infarction as a factor of collateral development. In a significant number of patients with total coronary occlusion without infarction demonstrate normal electrocardiograms at rest but almost 96% of patients who underwent treadmill exercise test proved positive. These findings are similar with the observation by Martinez-Rios *et al.* (1970) that patients with coronary artery disease who have collaterals are more likely to have normal resting electrocardiograms than their counterparts who do not have collaterals. Also, these findings may suggest that collateral circulation can prevent myocardial ischemia at rest but do not provide protection against exercise-induced ischemia. Several investigators revealed that the presence of collateral flow did not prevent exercise-induced ischemia as judged by thallium imaging and reversible thallium defects were almost invariably present after exercise in the patients with collateral flow (Freedman *et al.* 1985; Berman *et al.* 1977). But although collaterals do not apparently prevent or delay the development of exercise-induced ischemia, they can limit its duration by allowing a faster recovery (Bonetti *et al.* 1992).

Coronary collateral circulation after MI

The incidence of patients with well-developed coronary collateral vessels in the first few hours after clinical infarction was disappointingly small and this paucity of collateral vessels was not observed 1 to 13 days after myocardial infarction. Our observation on the incidence of well-developed collaterals in the

early hours of myocardial infarction was consistent with the findings of prior reports (Nitzberg *et al.* 1985; Schwartz *et al.* 1984). Collateral circulation was more frequent in inferior infarct patients with RCA occlusion than in anterior infarct patients with LAD occlusion. Stadius *et al.* (1985) suggested the presence of the two different myocardial resistance beds in the RCA might explain why collateral circulation was more common with RCA than with LAD occlusion. LVEDP and segmental wall motion score were significantly higher in patients with anterior MI compared to inferior MI patients. Poor LV function in patients with anterior MI might be due to a larger infarct size rather than the effect of poor collateral development in anterior MI. Postmortem study has demonstrated approximately two-thirds of the left ventricular myocardium received its blood supply from the LAD (Kalbfleisch *et al.* 1977) and location of the infarct-related occlusion in the LAD was associated with the greatest decrease in ejection fraction and with the longest hypokinetic and abnormally contracting segment lengths (Stadius *et al.* 1985). Schwartz *et al.* (1984) reported the preservation of ischemic myocardium by well-developed coronary collateral vessels at the time of myocardial infarction might be an uncommon occurrence. These findings are consistent with our observations that the incidence of good collaterals in early hours of myocardial infarction is not frequent. Our results showed there was no statistically significant difference in LV function between patients with poor collaterals and good collaterals in infarct patients thus were in good agreement with prior reports.

Coronary angiography, the most frequently used technique for studying the coronary circulation in humans, can only visualize vessels more than 100 μm in diameter, however, most arterial collaterals are smaller. Furthermore, identification of epicardial conduits on angiography does not correlate the extent of the myocardium supplied by them. Although radionuclide perfusion imaging techniques can provide an assessment of relative perfusion to the myocardium but they are limited by their spatial and temporal resolution. A study using

myocardial contrast echocardiography demonstrated that myocardial contrast echocardiography can be used to measure collateral flow in patients with recent MI and this technique may be suited for the assessment of collateral perfusion in patients undergoing cardiac catheterization. Recently, development of an angioplasty guidewire with a Doppler tip permits quantitative measurement of coronary blood flow velocity beyond severe and totally occluded arterial segments (Kern *et al.* 1993).

Limitation of the study

Our study has certain limitations. First, it is a retrospective assessment of patients with total coronary occlusion. Our results need to be confirmed by a properly performed prospective study. Second, the grading system for collateral circulation employed in this study was subjective and qualitative. Third, optimally, serial angiograms in a single study group would be more definite in documenting the temporal changes of coronary collateral growth and its influence to LV function. In consideration of the factors related to the development of collateral circulation, presence and duration of angina were not evaluated in patients with myocardial infarction in our study.

CONCLUSION

Although there were some limitations in patient selection and qualitative assessment of collateral circulation and LV function in this study, it is summarized and concluded that: (1) There is a higher prevalence of good collaterals and multivessel disease in patients with AP than in those with MI; (2) The collateral circulation can prevent myocardial ischemia and preserve myocardial function at rest in a significant number of patients with AP, but do not provide protection against exercise-induced myocardial ischemia in a majority of patients with AP; (3) Well-developed collaterals are uncommonly present within 1 day after MI. But they subsequently develop and are generally demonstrable within 2

weeks. But collateral vessels in patients with MI have no beneficial effects on preserving myocardial function; (4) Good collateral flow is more prevalent in MI patients with RCA occlusion compared to LAD occlusion.

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