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The Effects of Coronary Artery Remodeling on the Developments of Collateral Blood Flow in Patients with Acute Myocardial Infarction Treated with Primary Angioplasty

Jae-Hyeong Park, MD[1], Myeong-Ki Hong, MD[1], Cheol Whan Lee, MD[1], Young-Hak Kim, MD[1], Seung Whan Lee, MD[1], Yong He, MD[2], Jong-Min Song, MD[1], Ki-Hoon Han, MD[1], Duk-Hyun Kang, MD[1], Jae-Kwan Song, MD[1], Jae-Joong Kim, MD[1], Seong-Wook Park, MD[1] and Seung-Jung Park, MD[1]

[1]Department of Medicine, University of Ulsan College of Medicine, Cardiac Center, Asan Medical Center, Seoul, Korea, [2]Department of Cardiology, Si Chuan Univerisity, Chengdu, Si Chuan, China

ABSTRACT

Background: The relation between pressure-derived fractional collateral flow (PDCF) and coronary arterial remodeling remains uncertain in acute myocardial infarction. **Methods**: We evaluated the effect of arterial remodeling on the development of PDCF in 72 patients with first acute myocardial infarction (pain onset <12 h) treated with primary angioplasty. Intravascular ultrasound study was performed before intervention. The remodeling index (RI) was defined as a ratio of (lesion/proximal reference) external elastic membrane area. Positive remodeling was defined as a RI >1.0 and nonpositive remodeling as a RI ≤1.0. Using a 0.014-in. fiber optic pressure monitoring guide wire, the PDCF index was measured by simultaneous measurement of mean aorta pressure (Pao), distal coronary pressure during the balloon occlusion (Pocc), and central venous pressure (CVP): PDCF index= 100×(Pocc-CVP)/(Pao-CVP). Sufficient collateral was defined as PDCF index >24% and insufficient collateral as PDCF index ≤24%. **Results**: The RI was 1.04±0.15 in the lesions with sufficient collateral and 1.03±0.16 in the lesions with insufficient collateral (p=0.812). There was no significant difference in the frequency of positive remodeling between the 2 groups (55% vs. 54%, respectively, p=0.966). The PDCF index was 20±11% and 20±9% in positive and nonpositive remodeling, respectively (p=0.891). There was no significant correlation between RI and PDCF index (r=0.027, p=0.823). **Conclusions**: The pattern of coronary arterial remodeling might not influence the development of collateral blood flow in patients with acute myocardial infarction treated with primary angioplasty. **(Korean Circulation J 2004;34(1):47-52)**

KEY WORDS: Ultrasonography, interventional; Myocardial infarction; Collateral circulation.

Introduction

Adaptive remodeling of the vessel wall occurs in parallel with the accumulation of atherosclerotic plaque, delaying the development of functionally important lumen stenosis.[1-5] On average, lumen compromise is delayed until the atherosclerotic lesion occupies more than an estimated 40% to 50% of the potential area within the internal elastic lamina (40% to 50% cross-sectional narrowing). Arterial remodeling may be a heterogeneous response, ranging from positive to negative remodeling.[2-5]

The coronary collateral circulation is an alternative source of blood supply to a myocardium jeopardized by abruptly occluded vessels and prevents myocardial death. Coronary angiography, the most commonly used tech-

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Correspondence : Seung-Jung Park, MD, Department of Medicine, University of Ulsan College of Medicine, Cardiac Center, Asan Medical Center, 388-1 Poongnap-2dong, Songpa-gu, Seoul 138-736, Korea
Tel : 82-2-3010-4818, Fax : 82-2-475-6898
E-mail : sjpark@ amc.seoul.kr

nique for studying collateral circulation, may not be accurate in assessing collateral circulation because most collaterals are too small to visualize angiographically.[6] Intracoronary pressure measurement is a new technique for providing accurate and quantitative information about the collateral circulation,[7-10] and it can be easily applied during the coronary intervention.

Positive remodeling prevents angiographic stenosis despite significant histologic stenosis. However, prevention of the development of a flow-limiting stenosis by positive remodeling unfortunately also removes the stimulus for the development of collaterals.[11] The relation between coronary collateral blood flow and coronary arterial remodeling remains uncertain in acute myocardial infarction. We hypothesize that positive remodeling is associated with less development of coronary collateral blood flow in acute myocardial infarction. The aim of this study was to evaluate the effect of arterial remodeling on the development of pressure-derived fractional collateral flow (PDCF) in patients with first acute myocardial infarction treated with primary angioplasty.

Methods

Study population

We prospectively studied 72 patients with first acute myocardial infarctions who were referred to the Asan Medical Center for emergency primary angioplasty with intravascular ultrasound (IVUS) and 0.014-in. pressure monitoring guide wire between October 2000 and December 2001. The criteria for selection were as follows: 1) chest pain >30 min in duration and occurring within 12 h after the onset of symptoms, 2) ST-segment elevation >0.1 mV in two contiguous electrocardiographic leads, 3) total occlusion of the infarct-related artery, and 4) lesion length <15 mm. Patients with experience of cardiogenic shock, severe heart failure, previous bypass surgery, atrial fibrillation or valvular heart disease, among other criteria, were excluded from the study. The infarct-related artery was determined from the entry electrocardiogram, ventriculographic contraction abnormalities, and coronary angiographic findings. During the same study period, primary angioplasty was performed in 98 patients. Eight patients who had either experienced cardiogenic shock or who were hemodynamically unstable and 18 patients with lesion length >15 mm were excluded from this study. All patients received conventional drug therapy in accordance with standard clinical practice. Written informed consent was obtained from all patients, and our institutional review board approved the study protocol.

Measurements of collateral blood flow

Left and right coronary angiography was performed in all patients, followed by primary angioplasty according to the study protocol of our institution. A 0.014-in. (0.036 cm) fiber optic pressure monitoring guide wire (RADI Medical Systems, Uppsala, Sweden) was set at 0, calibrated, advanced through the guiding catheter, and positioned distal at the occlusion site to be dilated, and balloon inflation at the occlusion site was performed to measure the collateral flow. Pressure-derived fractional collateral flow (PDCF) was determined by simultaneous measurement of aortic pressure (Pao, mm Hg, obtained from the guiding catheter), the distal coronary pressure during balloon occlusion (Pocc, mm Hg), and central venous pressure (CVP, mm Hg): PDCF index=100×(Pocc-CVP)/(Pao-CVP). Sufficient collateral was defined as PDCF index >24% and insufficient collateral as PDCF index ≤24%.[7] Angiographic collateral vessels (0 to 3) were graded according to Rentrop's classification.[12] Grade 2 or 3 and grade 0 or 1 by Rentrop's classification were defined as angiographically sufficient and insufficient collaterals, respectively.[13]

IVUS imaging protocol

Pre-intervention IVUS study was performed after intracoronary administration of 0.2 mg nitroglycerin. The ultrasound catheter was advanced approximately 10 mm beyond the target lesion, and an imaging run was performed from beyond the target lesion to the aorto-ostial junction. Studies were performed with a commercially

available system (Boston Scientific Corporation/Cardiovascular Imaging System, Inc.) with a 30 MHz singleelement beveled transducer mounted on the end of flexible shaft and rotated at 1,800 rpm within a 3.2 F short monorail imaging sheath. With this system, the transducer was withdrawn automatically at 0.5 mm/sec to perform the imaging sequence. Ultrasound studies were recorded on 1/2-in high-resolution s-VHS tape for off-line analysis.

Quantitative IVUS measurements

Cross-sectional area (CSA) measurements of external elastic membrane (EEM), lumen, and plaque+media (P+M) by IVUS have been previously validated.[14)15)] The EEM CSA (that represents total arterial CSA) was measured by tracing the leading edge of the adventitia. The P+M CSA (that represents atherosclerotic plaque) was calculated as EEM CSA minus lumen CSA. The plaque burden was measured as 100×[P+M CSA/EEM CSA]. The target lesion and proximal reference segments were assessed quantitatively. The pre-intervention lesion site was the image slice with the smallest lumen CSA, and among image slices with the same minimum lumen CSA, the one with the largest plaque burden (and therefore, the largest P+M CSA) was measured. The lumens of all the lesions measured 0.9 mm^2, due to totally occluded lesions and lumens of the lesions smaller than the size of the IVUS catheter (3.2F=1.07 mm). The proximal reference segment was the most normal-looking segment within 5 mm of the lesion. At each image slice, EEM and lumen CSA were measured with a commercially available program for computerized planimetry.

The remodeling index (RI) was defined as (lesion/proximal reference segment) pre-intervention EEM CSA. Positive remodeling was defined as a RI >1.0 and non-positive remodeling as a RI ≤1.0.[16)]

Statistical analysis

Statistical analysis was performed with the SPSS software program. Categorical data were presented as frequencies, and continuous data were presented as mean±SD. Comparisons were performed with Chi-square tests and unpaired t-tests. The linear regression analysis was performed to evaluate the relationship between PDCF and RI. A $p<0.05$ was considered statistically significant.

Table 1. Baseline clinical characteristics

	Total patients (n=72)
Age (years)	55+13
Male gender (%)	61 (85)
Risk factors	
Hypertension (%)	17 (24)
Diabetes mellitus (%)	13 (18)
Hypercholesterolemia (%)	12 (17)
Cigarette smoking (%)	21 (29)
Number of diseased vessel	
One (%)	48 (67)
Two (%)	14 (19)
Three (%)	10 (14)
Dilated coronary arteries	
Left anterior descending (%)	36 (50)
Left circumflex (%)	9 (13)
Right coronary (%)	27 (37)

Results

The baseline clinical characteristics of 72 patients are presented in Table 1. Sufficient collateral existed in 22 lesions by PDCF and in 20 lesions by angiography. IVUS findings between the lesions with sufficient collateral and those with insufficient collateral according to PDCF and angiography are shown in Table 2. There were no significant differences in the IVUS variables of the two groups. Positive remodeling was observed in 39 lesions (54%).

The RI was 1.04±0.15 in the lesions with sufficient collateral and 1.03±0.16 in the lesions with insufficient collateral by PDCF (p=0.812). The frequency of positive remodeling was in 55% (12/22) vs. 54% (27/50), respectively (p=0.966). The RI was 1.03±0.13 in the lesions with sufficient collateral and 1.04±0.17 in the lesions with insufficient collateral by angiography (p=0.722).

Table 2. Intravascular ultrasound findings (%)

Pressure-derived fractional collateral flow	Sufficient (n=22)	Insufficient (n=50)	p
Proximal reference segment			
EEM CSA (mm^2)	15.3 ±4.1	15.9 ±4.7	0.555
Lumen CSA (mm^2)	9.0 ±2.1	9.6 ±3.3	0.377
P+M CSA (mm^2)	6.3 ±2.3	6.3 ±2.0	0.961
Plaque burden (%)	41 ±6	40 ±6	0.548
Lesion segment			
EEM CSA (mm^2)	15.8 ±3.8	16.2 ±4.4	0.671
Lumen CSA (mm^2)	0.9 ±0.0	0.9 ±0.0	
P+M CSA (mm^2)	14.9 ±3.8	15.3 ±4.4	0.671
Plaque burden (%)	94 ±2	94 ±2	0.739
Remodeling index	1.04±0.15	1.03±0.16	0.812
Angiographic collateral flow	**Sufficient (n=20)**	**Insufficient (n=52)**	**p**
Proximal reference segment			
EEM CSA (mm^2)	15.6 ±3.9	15.8 ±4.8	0.827
Lumen CSA (mm^2)	9.2 ±2.1	9.5 ±3.3	0.640
P+M CSA (mm^2)	6.4 ±2.1	6.3 ±2.1	0.904
Plaque burden (%)	41 ±5	40 ±6	0.826
Lesion segment			
EEM CSA (mm^2)	15.8 ±3.4	16.2 ±4.6	0.672
Lumen CSA (mm^2)	0.9 ±0.0	0.9 ±0.0	
P+M CSA (mm^2)	14.9 ±3.4	15.3 ±4.6	0.672
Plaque burden (%)	94 ±1	94 ±2	0.819
Remodeling index	1.03±0.13	1.04±0.17	0.722

EEM: external elastic membrane, CSA: cross-sectronal area, P+M: plaque+media

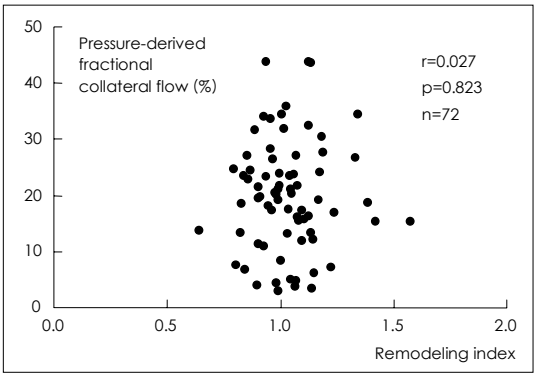

Figure 1. The relation between remodeling index and pressure-derived fractional collateral flow index.

The frequency of positive remodeling was 50% (10/20) vs. 56% (29/52), respectively (p=0.660). The PDCF index was 20±11% and 20±9% in positive and nonpositive remodeling, respectively (p=0.891). The angiographic collateral grade was 0.9±0.9 and 1.1±1.0 in positive and nonpositive remodeling, respectively (p=0.312). There was no significant correlation between RI and PDCF index (r=0.027, p=0.823, Figure 1).

Discussion

A postmortem study revealed that the lesions with positive remodeling might be associated with more plaque vulnerability compared with the lesions with negative remodeling.[17] This may be related to the remodeling paradox that positive remodeling delays luminal narrowing on the one hand, but is associated with vulnerable plaques on the other.[17] Likewise, positive remodeling might be associated with the removal of the stimulus for the development of collaterals.[11] The collateral development and positive remodeling were more

frequently observed in the patients with acute myocardial infarction than in those without.[16)18)19)] There was no published data to elucidate the relationship between the pattern of coronary remodeling and collateral development in the patients with acute myocardial infarction. Therefore, it was hypothesized that positive remodeling was associated with less development of coronary collateral blood flow in acute myocardial infarction. However, the results of the current study suggested that the pattern of coronary arterial remodeling did not influence the development of collateral blood flow in patients with acute myocardial infarction treated with primary angioplasty.

Using angiography to evaluate the collateral flow, there were no significant differences in the frequency of positive remodeling and the RI between the lesions with sufficient collateral and those with insufficient collateral in coronary artery disease.[16)] These previous findings on coronary artery disease[16)] were similar to what we found in this study using angiography in acute myocardial infarction. However, angiographically visible collaterals represent only a fraction of the total collateral vessels because collaterals are angiographically demonstrable only when they reach 100 μm.[20)] Moreover, angiography may not detect most collaterals situated intramurally, whereas intracoronary pressure measurements provide the opportunity to measure the contribution of total collateral flow in humans,[7-10)20)] allowing quantitative assessment of collateral flow in acute myocardial infarction. Therefore, we evaluated the relation between coronary remodeling and the development of collateral by PDCF as well as angiography. There was no significant correlation between the pattern of coronary remodeling and the development of collateral vessel by PDCF in acute myocardial infarction in the current study.

Pohl et al.[21)] reported that coronary lesion severity was the only independent pathogenic variable related to collateral flow in a study with a large number of patients and quantitative means for collateral assessment. Therefore, angiographically mild or intermediate degree of narrowing (up to 40% to 50% cross-sectional narrowing) is not an adequate stimulus for the development of collateral vessels. However, in lesions with up to 40% to 50% cross-sectional narrowing, lumen compromise is delayed by positive remodeling.[1)5)] Most acute myocardial infarctions occur in the lesions of angiographic diameter stenosis <50%.[22)23)] Sudden thrombotic occlusion from ruptured plaque resulted in subsequent disaster : sudden changes of lumen from diameter stenosis <50% to total occlusion. These findings may indicate no significant relation between coronary remodeling and the development of collateral vessel in acute myocardial infarction in the current study. When acute myocardial infarction occurs in the lesion of diameter stenosis <50%, it is in an intermediate state between maximal degree of positive remodeling and minimal degree of collateral development.

Limitations

One difficulty was differentiating between low echogenic thrombus and low echogenic soft plaque. Therefore, when the P+M CSA was calculated as EEM CSA minus lumen CSA, P+M included the thrombus as well as the atheromatous plaque. However, the major concern of the current study was the remodeling pattern and comparison of the vessel size (EEM CSA) between the lesion segment and proximal reference segment. Therefore, they did not help to validate the initial hypothesis of this study.

REFERENCES

1) Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis G. *Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371-5.*
2) Pasterkamp G, Borst C, Post MJ, Mali WP, Wensing PJ, Gussenhoven EJ, et al. *Atherosclerotic arterial remodeling in the superficial femoral artery: individual variation in local compensatory enlargement response. Circulation 1996;93: 1818-25.*
3) Nishioka T, Luo H, Eigler NL, Berglund H, Kim CJ, Siegel RJ. *Contribution of inadequate compensatory enlargement to development of human coronary artery stenosis: an in vivo intravascular ultrasound study. J Am Coll Cardiol 1996; 27:1571-6.*
4) von Birgelen C, Mintz GS, de Vrey EA, Kimura T, Popma JJ, Airiian SG, et al. *Atherosclerotic coronary lesions with inadequate compensatory enlargement have smaller plaque*

and vessel volume: observation with three dimensional intravascular ultrasound in vivo. Heart 1998;79:137-42.

5) Mintz GS, Kent KM, Pichard AD, Satler LF, Popma JJ, Leon MB. *Contribution of inadequate arterial remodeling to the development of focal coronary artery stenoses: an intravascular ultrasound study. Circulation 1997;95:1791-8.*
6) Gensini GG, Bruto da Costa BC. *The coronary collateral circulation in living man. Am J Cardiol 1969;24:393-400.*
7) Pijls NH, Bech GJ, el Gamal MI, Bonnier HJ, de Bruyne B, van Gelder B, et al. *Quantification of recruitable coronary collateral blood flow in conscious human and its potential to predict future ischemic events. J Am Coll Cardiol 1995;25:1522-8.*
8) Pijls NH, van Son JA, Kirkeeide RL, de Bruyne B, Gould KL. *Experimental basis of determining maximum coronary, myocardial and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation 1993;87:1354-67.*
9) Seiler C, Fleisch M, Garachemani A, Meier B. *Coronary collateral quantitation in patients with coronary artery disease using intravascular flow velocity or pressure measurements. J Am Coll Cardiol 1998;32:1272-9.*
10) van Liebergen RA, Piek JJ, Koch KT, de Winter RJ, Schotborgh CE, Lie KI. *Quantification of collateral flow in humans: a comparison of angiographic, electrocardiographic and hemodynamic varaibles. J Am Coll Cardiol 1999;33:670-7.*
11) Ward MR, Pasterkamp G, Yeung AC, Borst C. *Arterial remodeling: mechanisms and clinical implications. Circulation 2000;102:1186-91.*
12) Rentrop KP, Cohen M, Blanke H, Phillips RA. *Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. J Am Coll Cardiol 1985;5:587-92.*
13) Nakae I, Fujita M, Fudo T, Iwase T, Tanaka T, Tamaki S, et al. *Relation between preexistent coronary collateral circulation and the incidence of restenosis after successful primary coronary angioplasty for acute myocardial infarction, J Am Coll Cardiol 1996;27:1688-92.*
14) Tobis JM, Mallery J, Mahon D, Lehmann K, Zalesky P, Griffith J, et al. *Intravascular ultrasound imaging of human coronary arteries in vivo: analysis of tissue characteristics with comparison to in vivo histologic specimens. Circulation 1991;83:913-26.*
15) Nishimura RA, Edwards WD, Warnes CA, Reeder GS, Holmes DR Jr, Tajik AJ, et al. *Intravascular ultrasound imaging: in vitro validation and pathologic correlation. J Am Coll Cardiol 1990;16:145-54.*
16) Nakamura M, Nishikawa H, Mukai S, Setsuda M, Nakajima K, Tamada H, et al. *Impact of coronary artery remodeling on clinical presentation of coronary artery disease: an intravascular ultrasound study. J Am Coll Cardiol 2001;37:63-9.*
17) Pasterkamp G, Schoneveld AH, van der Wal AC, Haudenschild CC, Clarijs RJ, Becker AE, et al. *Relation of arterial geometry to lumen narrowing and histologic markers for plaque vulnerability: the remodeling paradox. J Am Coll Cardiol 1998;32:655-62.*
18) Schoenhagen P, Ziada KM, Kapadia SR, Crowe TD, Nissen SE, Tuzcu EM. *Extent and direction of arterial remodeling in stable versus unstable coronary syndromes: an intravascular ultrasound study. Circulation 2000;101:598-603.*
19) Helfant RH, Vokonas PS, Gorlin R. *Functional importance of the human coronary collateral circulation. N Engl J Med 1971;284:1277-81.*
20) Lee CW, Park SW, Cho GY, Hong MK, Kim JJ, Kang DH, 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;35:949-55.*
21) Pohl T, Seiler C, Billinger M, Herren E, Wustmann K, Mehta H, et al. *Frequency distribution of collateral flow and factors influencing collateral channel development; functional collateral channel measurement in 450 patients with coronary artery disease. J Am Coll Cardiol 2001;38:1872-8.*
22) Ambrose JA, Tannenbaum MA, Alexopoulos D, Hjemdahl-Monsen CE, Leavy J, Weiss M, et al. *Angiographic progression of coronary artery disease and the development of myocardial infarction. J Am Coll Cardiol 1988;12:56-62.*
23) Little WC, Constantinescu M, Applegate RJ, Kutcher MA, Burrows MT, Kahl FR, et al. *Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? Circulation 1988;78:1157-66.*