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

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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-
nique for studying collateral circulation, may not be accurate in assessing collateral circulation because most collaterals are too small to visualize angiographically. Intracoronary pressure measurement is a new technique for providing accurate and quantitative information about the collateral circulation, 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. 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%. Angiographic collateral vessels (0 to 3) were graded according to Rentrop’s classification. Grade 2 or 3 and grade 0 or 1 by Rentrop’s classification were defined as angiographically sufficient and insufficient collaterals, respectively.

**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 single-element 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 \(100 \times \left[ \frac{P+M \text{ CSA}}{EEM \text{ CSA}} \right]\). 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 \(\left( \frac{\text{lesion}}{\text{proximal reference segment}} \right) \times \left( \frac{\text{EEM CSA}}{\text{P+M CSA}} \right)\) pre-intervention EEM CSA. Positive remodeling was defined as a \(\text{RI} > 1.0\) and non-positive remodeling as a \(\text{RI} \leq 1.0.\)\(^{16}\)

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.

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 (\(p=0.722\)).
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). 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. 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. Likewise, positive remodeling might be associated with the removal of the stimulus for the development of collaterals. The collateral development and positive remodeling were more
frequently observed in the patients with acute myocardial infarction than in those without. 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. These previous findings on coronary artery disease 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. 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, 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. 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. Most acute myocardial infarctions occur in the lesions of angiographic diameter stenosis <50%. 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.

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