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Coronary Microvascular Resistance Index Immediately After Primary Percutaneous Coronary Intervention as a Predictor of the Transmural Extent of Infarction in Patients With ST-Segment Elevation Anterior Acute Myocardial Infarction

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OBJECTIVES The purpose of this study was to investigate whether microvascular resistance index (MVRI) immediately after primary percutaneous coronary intervention (PCI) can predict the transmural extent of infarction (TEI) defined by contrast-enhanced cardiac magnetic resonance (ce-CMR) in patients with anterior acute myocardial infarction (MI).

BACKGROUND The degree of microvascular damage is an important determinant of myocardial viability and clinical outcomes in acute MI. A novel dual-sensor (pressure and Doppler velocity) guidewire has the ability to evaluate microvascular damage. ce-CMR can accurately discriminate transmural from nontransmural MI, and the TEI by ce-CMR can predict future improvement in contractile function.

METHODS In 27 patients immediately after primary PCI for a first anterior acute MI, MVRI, coronary flow reserve (CFR), deceleration time of diastolic velocity (DDT), and zero flow pressure (Pzf) were measured with a dual-sensor guidewire. TEI was graded from 1 to 4 based on the transmural extent of hyperenhanced tissue (1 = 0% to 25% of left ventricular wall thickness, 2 = 26% to 50%, 3 = 51% to 75%, and 4 = 76% to 100%). Infarct size by ce-CMR was also calculated.

RESULTS Peak creatine kinase-myocardial band values were significantly correlated with MVRI ($r = 0.77$, $p < 0.0001$), CFR ($r = -0.69$, $p < 0.0001$), DDT ($r = -0.75$, $p = 0.0001$), and Pzf ($r = 0.75$, $p < 0.0001$). Also, infarct size by ce-CMR was significantly correlated with MVRI ($r = 0.78$, $p < 0.0001$), CFR ($r = -0.67$, $p < 0.0001$), DDT ($r = -0.70$, $p < 0.0001$), and Pzf ($r = 0.72$, $p = 0.0002$). Receiver-operating characteristic curve analyses of MVRI, CFR, DDT, and Pzf for predicting transmural MI (TEI-grade 4) demonstrated that the area under the curve tended to be higher for MVRI (0.885) than those for CFR (0.848), DDT (0.862), and Pzf (0.853). The best cut-off value for MVRI was 3.25 mm Hg·cm^{-1}·s (sensitivity 75%, specificity 89%). Moreover, increased MVRI was significantly related to increased TEI-grade ($p < 0.0001$).

CONCLUSIONS MVRI measured immediately after primary PCI is a useful predictor for the TEI in patients with anterior acute MI. (J Am Coll Cardiol Img 2009;2:263–72) © 2009 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction is an established reperfusion strategy (1). Primary PCI has been reported to improve clinical outcomes in patients with acute myocardial infarction (MI) (2). However, microvascular perfusion is often impaired after primary PCI, and reperfusion of the epicardial coronary artery will not always guarantee reperfusion at the myocardial tissue level. The aim of current treatment strategies for acute MI is to obtain reperfusion, not only at the level of the epicardial artery but also at the tissue level, but a useful method for assessing coronary microcirculation has not been fully elucidated.

Recently, simultaneous measurement of phasic distal pressure and flow velocity by a single dual-sensor–equipped 0.014-inch guidewire has become possible in daily clinical practice. A previous study reported that using a dual-sensor guidewire, reproducibility of repeated hyperemic resistance parameters derived from distal pressure and velocity measurements in patients with stable angina pectoris was excellent (3). Measurement of distal pressure and flow velocity after reperfusion might provide important information on the state of coronary microvasculature in patients with acute MI. Myocardial necrosis after acute MI progresses as a "wavefront phenomenon" from the endocardium to the epicardium (4). Contrast-enhanced cardiac magnetic resonance (ce-CMR) can accurately discriminate transmural from nontransmural MI at very high spatial resolution (5) and can measure infarct size quantitatively (6–8). The transmural extent of infarction (TEI) defined by ce-CMR allows us to predict future improvement in myocardial contractile function (8,9). The aim of this study was to investigate whether microvascular resistance index (MVRI) measured immediately after primary PCI can predict the TEI in patients with anterior acute MI compared with various indices for assessing coronary microcirculation.

ABBREVIATIONS AND ACRONYMS

ce-CMR = contrast-enhanced cardiac magnetic resonance
CFR = coronary flow reserve
CK-MB = creatine kinase-myocardial band
DDT = diastolic deceleration time
FFR = fractional flow reserve
MI = myocardial infarction
MVRI = microvascular resistance index
PCI = percutaneous coronary intervention
Pzf = zero flow pressure
TEI = transmural extent of infarction
TIMI = Thrombolysis In Myocardial Infarction

METHODS

Patient population. Twenty-seven patients who underwent primary PCI for a first anterior acute MI within 12 h from the onset of symptoms were included. The diagnosis of acute MI was based on chest pain lasting more than 30 min, ST-segment elevation of ≥2 mm (0.2 mV) in at least 2 contiguous leads on electrocardiography, and Thrombolysis In Myocardial Infarction (TIMI) flow grade of 0 or 1 at the initial coronary angiography. We excluded patients with previous myocardial infarction, left main trunk disease, renal insufficiency (serum creatinine >1.5 mg/dl), and cardiogenic shock. Patients were also excluded if they had absolute or relative contraindications to magnetic resonance examination, such as pacemaker, atrial fibrillation, claustrophobia, and so on. Written informed consent was obtained from all patients for participation in this study. The study was carried out according to the Declaration of Helsinki.

Study protocol. Cardiac catheterization was performed by a percutaneous femoral approach with a 6-F guiding catheter. All patients received oral aspirin (162 mg) and a bolus of heparin (100 U/kg) before the procedure, and additional heparin was given if the procedure lasted >90 min to maintain an activated clotting time ≥250 s. An intracoronary bolus injection of isosorbide dinitrate (1 to 2 mg) was administered to obtain a high quality angiogram and before hemodynamic measurements. After thrombectomy by Export catheter (Medtronic Japan, Tokyo, Japan), balloon angioplasty was performed, followed by deployment of a single bare metal stent. Balloon size was determined by the angiographically determined dimension of the target vessel. In all patients, intravascular ultrasound-guided upsizing of the stent was performed according to CLOUT (Clinical Outcomes with Ultrasound Trial) criteria (10). After stenting, all patients received ticlopidine (200 mg/day) and aspirin (100 mg/day) for 30 days followed by aspirin alone indefinitely. Procedural success was defined as ≤30% residual stenosis of the culprit lesion by visual assessment. TIMI myocardial perfusion grade was determined from the final angiogram by 2 experienced angiographers blinded to the MVRI result, as described previously (11). Blood samples were obtained on admission and serially every 3 h for the first 24 h after primary PCI, and peak values of creatine kinase (CK) and CK-myocardial band (MB) were determined. ce-CMR was performed 13 ± 2 days after the onset of acute MI.

Hemodynamic measurements and data analysis. Aortic pressure (Pa) was measured through the guiding catheter. Immediately after primary PCI, pressure (Pd) and flow velocity distal to the culprit site were measured simultaneously with a 0.014-inch dual-sensor (pressure and Doppler velocity) guidewire (ComboWire, Volcano Therapeutics, Rancho Cor-

dova, California) (Fig. 1). After the wire was calibrated, advanced through the catheter, and equaled with the Pa in the catheter, it was placed at least 3 to 4 cm distal to the stented segment of the left anterior descending coronary artery and manipulated until an optimal and stable velocity signal was obtained. The position of the tip of the wire was confirmed by fluoroscopy and angiography. The Pa, Pd, instantaneous peak velocity, and electrocardiogram were obtained online at baseline and after induction of maximal hyperemia with 150 μg/kg/min of intravenous adenosine triphosphate via a central venous catheter (ComboMap Pressure and Flow System, Volcano Therapeutics). Twenty minutes after primary PCI, all signals were digitally recorded on a personal computer for offline analysis by an independent investigator who was unaware of patient data. Fractional flow reserve (FFR) was calculated as the ratio of mean Pd to mean Pa during maximal hyperemia. Coronary blood flow velocity reserve (CFR) was calculated as the ratio of time-averaged peak hyperemic to baseline average flow velocity. In 3 consecutive cardiac cycles, the deceleration time of diastolic velocity (DDT, ms) was measured from phasic coronary flow velocity recording as previously described (12) and averaged for the mean value. MVRI was calculated as the ratio of mean Pd to average peak flow velocity during maximal hyperemia (13). We calculated zero flow pressure (Pzf) using the method previously described (14). During maximal hyperemia, the instantaneous peak coronary flow velocity was plotted against the simultaneous measured distal coronary pressure and a pressure-flow velocity loop was displayed by specially designed software. In the phase of diastolic flow decrease, the diastolic pressure-flow relationship was determined by linear regression analysis. The x-intercept of the slope was calculated as the Pzf.

Protocol and image analysis for CMR. All patients were examined at rest in the supine position with a whole body 1.5-T MR scanner (Intera Achieva, Philips Medical Systems, Best, the Netherlands) equipped with a 5-element cardiac phased-array coil for signal reception. All images were gated to the electrocardiogram and obtained during repeated breath-holds. ce-CMR was obtained with contiguous short-axis slices and representative long-axis slices of the left ventricle 10 min after intravenous injection of 0.1 mmol/kg gadolinium-diethylenetriamine penta-acetic acid (Magnevist, Schering AG, Berlin, Germany). We optimized the inversion time (200 to 300 ms) to null the normal myocardium. All analyses were performed by the consensus of the 2 blinded observers on an off-line work station (View-Forum, Philips Medical Systems, Best, the Netherlands). Based on a 17-segment model as previously recommended by the American Heart Association (15), representative short-axis slices of the basal (6 segments), mid-ventricular (6 segments), and apical (4 segments) region of the left ventricle were analyzed. The apex was evaluated from long-axis slices. The TEI was graded from 1 to 4 based on the transmural extent of hyperenhanced tissue within each segment: 1 = 0% to 25% of left ventricular wall thickness; 2 = 26% to 50%; 3 = 51% to 75%; and 4 = 76% to 100% (Fig. 2). The highest grade among 16 segments except apex was defined as the TEI-grade of each case. Infarct size was calculated by automatic summation of all slice volumes of delayed enhanced regions and expressed as a percentage of left ventricular volume. Microvascular obstruction was evaluated qualitatively on delayed enhanced images; it was defined as hypodense regions within the hyperenhanced infarcted area, and was included in the calculation of total infarct size.

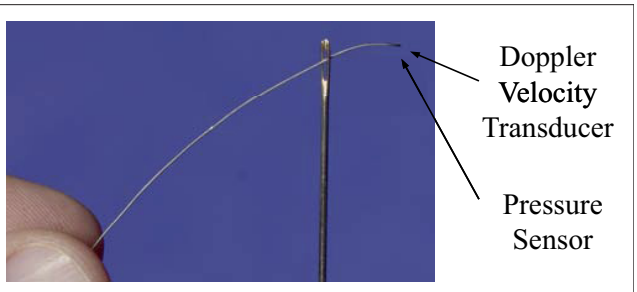

Figure 1. Dual-Sensor Guidewire

The Doppler crystal and pressure sensor are located on the distal tip of the wire.

Statistics. Data were expressed as mean ± SD or n (%). Continuous variables were compared with the use of an unpaired Student *t* test. Categorical variables were compared by the chi-square test or Fisher exact test, as appropriate. Pearson's correlation coefficient test was used to assess correlations between the variables, and linear regression analyses were performed to determine the exact relations between the variables. Spearman's rank correlation test was used to analyze the correlation between MVRI and the TEI grade. Receiver-operating characteristic curve analysis was used to compare the diagnostic performance of coronary physiologic parameters to predict transmural MI. The areas under the curve for MVRI, CFR, DDT, and Pzf

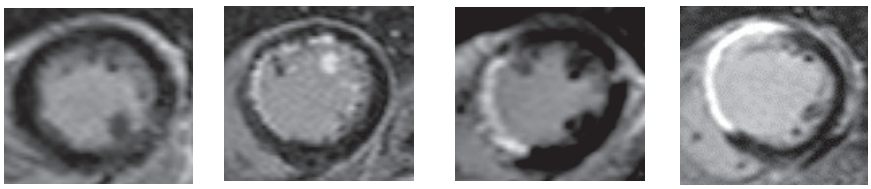

Figure 2. Representative Images of Each TEI-Grade in a Short-Axis View

Transmural extent of infarction (TEI) by contrast-enhanced cardiac magnetic resonance (ce-CMR) was graded from 1 to 4 based on the transmural extent of hyperenhanced tissue: 1 = 0% to 25% of left ventricular wall thickness; 2 = 26% to 50%; 3 = 51% to 75%; and 4 = 76% to 100%.

were compared by using the method of Hanley and McNeil (16). The best cut-off value for MVRI was defined as the value with the highest sum of sensitivity and specificity. Values of $p < 0.05$ were considered statistically significant. All statistical analyses were performed with SPSS software for Windows version 11.0 (SPSS Inc., Chicago, Illinois).

RESULTS

In this study, transmural MI was defined as TEI-grade 4. TEI-grade 4 was observed in 8 (30%) of the 27 patients. These patients were classified as a transmural MI group. The other 19 patients (grade 1, n = 4; grade 2, n = 7; grade 3, n = 8) were classified as a nontransmural MI group.

Patient characteristics are listed in Table 1. There were no differences between the two groups with regard to age, sex, coronary risk factors, history of pre-infarction angina, collaterals, Killip classification, and left ventricular ejection fraction. However, peak CK and peak CK-MB were significantly higher in the transmural MI group than in the nontransmural MI group. Infarct size by CMR was significantly larger in the transmural MI group compared with that in the nontransmural MI group. Microvascular obstruction was present in 5 patients (62%) in the transmural MI group and 3 patients (16%) in the nontransmural MI group ($p < 0.03$). The average time from onset of symptoms to balloon was not different between the 2 groups. The culprit lesion was successfully treated with stent implantation in all patients without procedure-related complications. After primary PCI, TIMI flow grade 2 reflow was observed in 3 (38%) patients in the transmural MI group, and the other 5 (62%) patients demonstrated TIMI flow grade 3 reflow; almost all patients (95%) in the nontransmural MI group had TIMI flow grade 3 reflow in the final coronary angiography. Normal myocardial perfusion (TIMI myocardial perfusion grade 3) was observed in 2 patients (25%) in the transmural MI group and 8 patients (42%) in the nontransmural MI group.

Pressure-flow velocity loop was obtained appropriately in 5 patients in the transmural MI group and 15 patients in the nontransmural MI group. We calculated Pzf in the 20 patients and used them for analysis. Hemodynamic data are summarized in Table 2. In 24 (89%) of 27 patients, the infarct-related artery was treated without significant residual stenosis remaining (mean of the post-procedural FFR measured after primary PCI was 0.89 ± 0.11). The CFR was significantly lower in the transmural MI group than in the nontransmural MI group (1.14 ± 0.19 vs. 1.75 ± 0.48, $p = 0.002$). MVRI (3.70 ± 0.98 mm Hg·cm^{-1}·s vs. 2.17 ± 0.84 mm Hg·cm^{-1}·s, $p = 0.0004$) and Pzf (49.2 ± 11.7 mm Hg vs. 31.9 ± 9.3 mmHg, $p = 0.0033$) were significantly greater in the transmural MI group than in the nontransmural MI group. DDT was significantly shorter in the transmural MI group than in the nontransmural MI group (336 ± 162 ms vs. 632 ± 244 ms, $p = 0.0044$).

Peak CK-MB values were significantly correlated with MVRI ($r = 0.77$, $p < 0.0001$), CFR ($r = -0.69$, $p < 0.0001$), DDT ($r = -0.75$, $p = 0.0001$), and Pzf ($r = 0.75$, $p < 0.0001$), respectively (Fig. 3). Correlations between infarct size by ce-CMR and indices of coronary microcirculation were as follows: MVRI ($r = 0.78$, $p < 0.0001$), CFR ($r = -0.67$, $p < 0.0001$), DDT ($r = -0.70$, $p < 0.0001$), and Pzf ($r = 0.72$, $p = 0.0002$) (Fig. 4).

Table 1. Patient Characteristics

	Transmural MI (n = 8)	Nontransmural MI (n = 19)	p Value
Age, yrs	64 ± 12	67 ± 6	0.39
Male, n (%)	6 (75)	16 (84)	0.62
Coronary risk factors, n (%)			
Hypertension	3 (38)	14 (74)	0.10
Diabetes mellitus	3 (38)	5 (26)	0.66
Dyslipidemia	3 (38)	10 (53)	0.68
Smoking	4 (50)	8 (42)	1.00
Family history of coronary artery disease	0 (0)	3 (16)	0.53
History of pre-infarction angina, n (%)	1 (13)	6 (32)	0.63
Killip classification, n (%)			
1	6 (75)	16 (84)	0.62
2	2 (25)	2 (11)	0.56
3	0 (0)	1 (5)	1.00
4	0 (0)	0 (0)	—
Peak CK, IU/l	6,653 ± 2,451	2,776 ± 1,612	<0.0001
Peak CK-MB, IU/l	551 ± 165	247 ± 146	<0.0001
Infarct size by CMR, % of left ventricle	36.6 ± 6.5	19.8 ± 10.9	0.0004
MO present on CMR, n (%)	5 (62)	3 (16)	<0.03
Baseline angiographic characteristics			
Infarct-related artery			
LAD, n (%)	8 (100)	19 (100)	1.00
Number of diseased vessels, n (%)			
1	4 (50)	12 (63)	0.68
2	4 (50)	6 (32)	0.41
3	0 (0)	1 (5)	1.00
Collaterals (Rentrop grade 2 or 3), n (%)	0 (0)	1 (5)	1.00
Onset-to-balloon time, h	4.2 ± 1.4	3.7 ± 2.2	0.56
LVEF, %	44 ± 7	46 ± 8	0.55
Post-procedural outcomes			
Slow flow or no reflow, n (%)	3 (38)	2 (11)	0.14
Side branch occlusion, n (%)	2 (25)	2 (11)	0.56
Distal emobolization, n (%)	0 (0)	0 (0)	—
Mean residual stenosis, %	9 ± 2.2	8.8 ± 2.6	0.85
Final TIMI flow grade, n (%)			
2	3 (38)	1 (5)	0.06
3	5 (62)	18 (95)	0.06
TIMI myocardial perfusion grade, n (%)			
0/1	4 (50)	4 (21)	0.18
2	2 (25)	7 (37)	0.68
3	2 (25)	8 (42)	0.67
Procedure-related complications, n (%)	0 (0)	0 (0)	—

Values are mean ± SD.
CK = creatine kinase; CK-MB = creatine kinase-myocardial band; CMR = cardiac magnetic resonance; LAD = left anterior descending artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MO = microvascular obstruction; TIMI = Thrombolysis In Myocardial Infarction.

MVRI was significantly correlated with CFR ($r = -0.62$, $p = 0.0004$) and DDT ($r = -0.68$, $p < 0.0001$). Also, there was a significant positive correlation between MVRI and Pzf ($r = 0.75$, $p < 0.0001$) (Fig. 5).

Figure 6 shows the receiver operating characteristic curves for the 4 measured hemodynamic parameters. The areas under the curve were 0.885 for MVRI, 0.848 for CFR, 0.862 for DDT, and 0.853 for Pzf. Direct comparison of the receiver operating characteristic analyses by the areas under the curve between MVRI and the other 3 indices did not differ significantly (MVRI vs. CFR, $p = 0.68$; MVRI vs. DDT, $p = 0.80$; MVRI vs. Pzf,

Table 2. Coronary Hemodynamic Data

	Transmural MI (n = 8)	Nontransmural MI (n = 19)	p Value
Heart rate, beats/min	77 ± 7	73 ± 7	0.19
CFR	1.14 ± 0.19	1.75 ± 0.48	0.002
b-APV, cm/s	20 ± 5	22 ± 8	0.52
h-APV, cm/s	23 ± 6	38 ± 14	0.0078
DDT, ms	336 ± 162	632 ± 244	0.0044
FFR	0.89 ± 0.09	0.89 ± 0.12	1.00
b-Pa, mm Hg	89 ± 11	82 ± 17	0.30
h-Pd, mm Hg	79 ± 13	74 ± 21	0.54
MVRI, mm Hg·cm^{-1}·s	3.70 ± 0.98	2.17 ± 0.84	0.0004
Pzf, mm Hg	49.2 ± 11.7 (n = 5)	31.9 ± 9.3 (n = 15)	0.0033

Values are mean ± SD.
APV = average peak flow velocity; b = baseline; CFR = coronary flow reserve; DDT = diastolic deceleration time; h = hyperemia; FFR = fractional flow reserve; MI = myocardial infarction; MVRI = microvascular resistance index; Pa = mean aortic pressure; Pd = mean distal pressure; Pzf = zero flow pressure.

p = 0.47). The best cut-off value of MVRI for the prediction of transmural MI was determined as 3.25 mm Hg·cm^{-1}·s. The sensitivity, specificity, and predictive accuracy for MVRI were 75%, 89%, and 85%, respectively. In Spearman's rank correlation analysis, a significant positive correlation (p < 0.0001) was also observed between MVRI and TEI-grade (Fig. 7).

DISCUSSION

The present study demonstrated that MVRI estimated immediately after primary PCI was strongly correlated with enzymatic infarct size and infarct size as defined by ce-CMR (Figs. 3 and 4), and was able to distinguish between nontransmural and transmural MI immediately after primary PCI at the cardiac catheterization laboratory. Moreover, increased MVRI was significantly related to higher TEI-grade (Fig. 7). These findings may lead us to the concept that MVRI is a useful variable for direct assessment of microcirculatory function.

The distinction between reversible and irreversible injury early after reperfusion is an important and challenging clinical question. However, early after primary PCI, it is difficult to evaluate true infarct size

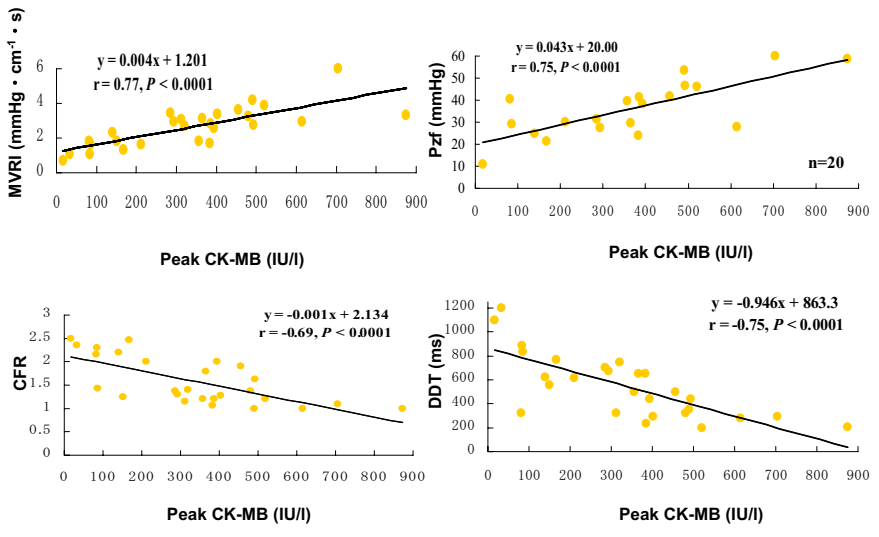

Figure 3. Correlations Between Each Index and Enzymatic Infarct Size

Peak creatine kinase-myocardial band (CK-MB) values were significantly correlated with microvascular resistance index (MVRI) (r = 0.77, p < 0.0001), coronary flow reserve (CFR) (r = −0.69, p < 0.0001), diastolic deceleration time (DDT) (r = −0.75, p = 0.0001), and zero flow pressure (Pzf) (r = 0.75, p < 0.0001).

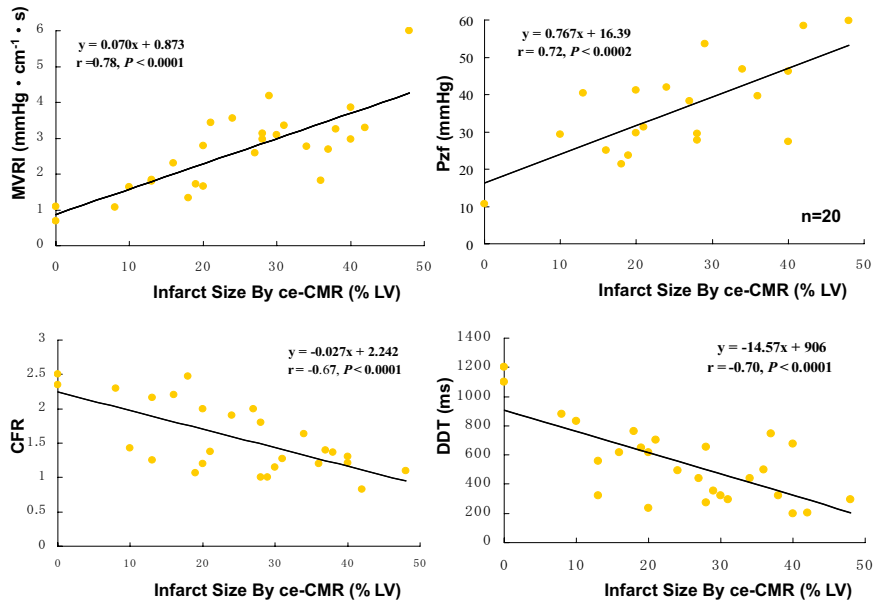

Figure 4. Correlations Between Each Index and Infarct Size by ce-CMR

Infarct size by contrast-enhanced cardiac magnetic resonance (ce-CMR) was significantly correlated with MVRI ($r = 0.78$, $p < 0.0001$), CFR ($r = -0.67$, $p < 0.0001$), DDT ($r = -0.70$, $p < 0.0001$), and Pzf ($r = 0.72$, $p = 0.0002$). LV = left ventricle; other abbreviations as in Figure 3.

and residual myocardial viability because of stunned myocardium and advancing reperfusion injury. For this purpose, CMR with contrast-enhancement may be more sensitive than echocardiography and single-photon emission computed tomography (5). Using ce-CMR, Choi et al. (8) reported that in patients within 1 week after onset of MI, a decrease in the TEI was associated with greater long-term improvement in

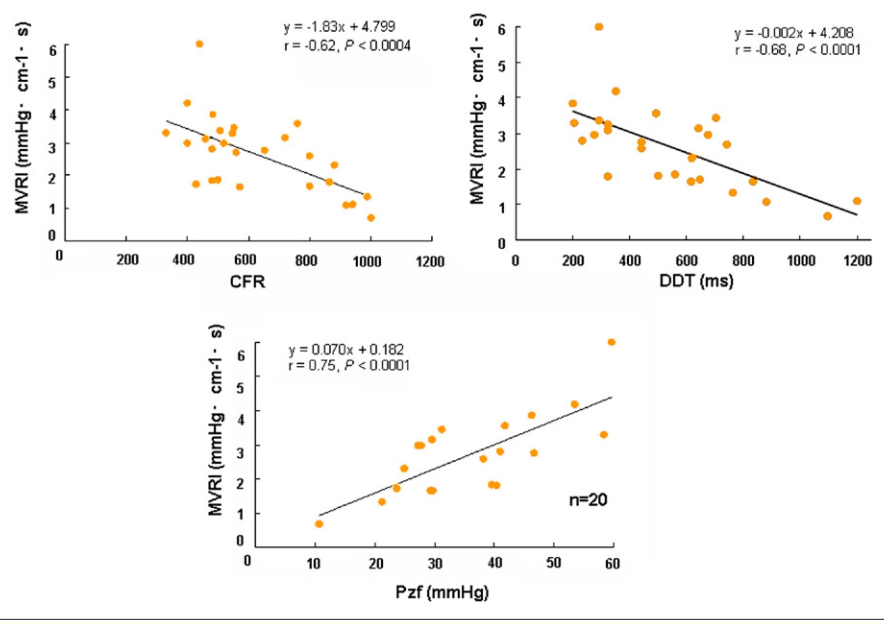

Figure 5. Correlations Between MVRI and the Other 3 Indices

MVRI was significantly correlated with CFR ($r = -0.62$, $p = 0.0004$) and DDT ($r = -0.68$, $p < 0.0001$). Also, there was a significant positive correlation between MVRI and Pzf ($r = 0.75$, $p < 0.0001$). Abbreviations as in Figure 3.

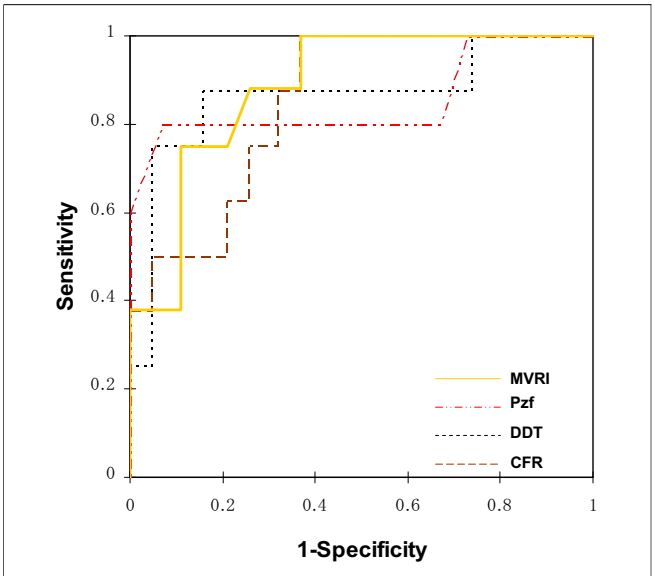

Figure 6. ROC-Analysis for the 4 Measured Hemodynamic Parameters

The areas under the curve (AUC) for predicting transmural extent of infarction grade 4 of MVRI, CFR, DDT, and Pzf were 0.885, 0.848, 0.862, and 0.853, respectively. In direct comparison of the AUCs, there were no significant differences between MVRI and the other 3 hemodynamic variables (MVRI vs. CFR, p = 0.68; MVRI vs. DDT, p = 0.80; MVRI vs. Pzf, p = 0.47). The best cut-off value for MVRI was determined as 3.25 mm Hg·cm^{-1}·s (sensitivity 75%, specificity 89%). Abbreviations as in Figure 3.

contractile function, and only 5% of myocardial segments with 76% to 100% TEI improved in the chronic state. Therefore, in the present study, we used the TEI-grade by ce-CMR to evaluate residual myocardial viability and defined the TEI-grade 4 as transmural MI. We also used various indices, including MVRI, to evaluate microvascular integrity, and we investigated the relations between the TEI and those indices. In this study, the receiver operating characteristic analysis showed that not only MVRI, but also CFR, DDT, and Pzf, were useful hemodynamic variables for predicting transmural MI immediately after primary PCI in patients with anterior acute MI. However, direct comparison of the areas under the curve between MVRI and the other 3 indices did not reveal significant differences. Further investigations will be required to establish which of these measures has the highest clinical relevance for predicting transmural necrosis in the post-infarct setting.

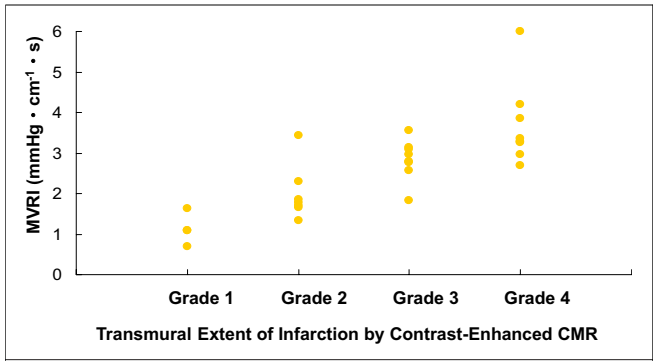

Figure 7. Relationship Between MVRI and TEI-grade

In Spearman's rank correlation analysis, there was a significant positive correlation between MVRI and the transmural extent of infarction grade ($p < 0.0001$). CMR = cardiac magnetic resonance; other abbreviation as in Figure 3.

Several previous clinical studies have reported that CFR assessed early after reperfusion is a good predictor of left ventricular wall motion recovery and remodeling (17–19). Several mechanisms, such as distal microembolism during primary PCI, compression by tissue edema, platelet plugging, neutrophil adhesion, damage from oxygen free radicals, thrombus formation in the microvasculature itself, and microvascular vasoconstriction, may contribute to increased microvascular resistance in the infarct area. Because the combination of 2 or more of these mechanisms immediately after primary PCI may result in reduced CFR, CFR measured immediately after primary PCI does not accurately reflect residual myocardial viability. Also, Pzf may reflect microvascular tone and increase after acute MI. In a recent study, Pzf was shown to be a better predictor of residual myocardial viability than CFR (20). These may explain why the correlation between CFR and infarct size was weaker than that with Pzf.

A previous study showed that using a Doppler guidewire offers a better quantitative assessment of coronary flow velocity and microvascular damage in patients with reperfused MI (21). It has been demonstrated that the coronary flow velocity pattern, including DDT, immediately after primary PCI can predict in-hospital complications and mortality after acute MI, left ventricular functional recovery, and long-term cardiac events (22–25). In this study, the DDT correlated well with infarct size by CMR and peak CK-MB values. This finding may provide new support for clarifying the correlation between DDT and microvascular integrity as well.

In the present study, MVRI correlated well with CFR ($r = -0.62$, $p < 0.0004$), DDT ($r = -0.68$, $p < 0.0001$), and Pzf ($r = 0.75$, $p < 0.0001$) (Fig. 5). All correlations between MVRI and other indices of myocardial tissue level perfusion may suggest that microvascular malperfu-

sion after primary PCI is likely due to increased microvascular resistance.

Study limitations. Several limitations of our study must be considered. First, our study population was limited to only 27 patients with anterior acute MI undergoing primary PCI to the left anterior descending artery. A large number of examinations including other coronary arteries will be required to determine the clinical usefulness of our results. Second, although the analysis of hemodynamic measurements was blinded, measurements were performed by an angiographer, so it is not possible to exclude entirely the influence of investigator bias in our results. Third, MVRI, CFR, and Pzf are limited by their reliance on the achievement of maximal hyperemia. Failure to achieve peak hyperemia, by not achieving maximal reduction in microvascular resistance, may result in overestimation of MVRI and Pzf and underestimation of CFR. For these reasons, we used intravenous adenosine triphosphate to induce steady-state maximal hyperemia. Finally, coronary flow velocity measured within a few minutes after reperfusion may reflect a hyperemic reaction after direct angioplasty. In this study we performed all hemodynamic measurements 20 min after primary PCI to obtain a standardized value, as described previously (25).

Clinical implications. Despite early successful reperfusion, some patients with acute MI have inadequate myocardial perfusion in the absence of angiographic evidence of mechanical epicardial artery obstruction. This inadequate myocardial perfusion may be associated with higher microvascular resistance and larger myocardial infarcts than in patients with adequate perfusion. Some therapeutic agents have shown improvement in coronary microcirculatory perfusion. One pilot trial reported that administration of low-dose intracoronary streptokinase immediately after primary PCI improved myocardial reperfusion (26). In a randomized trial of intracoronary verapamil in patients with acute MI, there was improvement of perfusion at the tissue level, using myocardial contrast echocardiography, compared with placebo (27). The agent nicorandil, an adenosine triphosphate-sensitive K^+ channel opener with vasodilating action, was also shown to improve coronary microcirculatory perfusion in the infarct area (28). Therefore, in patients with high microvascular resistance immediately after primary PCI, it may be necessary to think about pharmacologic strategies such as intracoronary streptokinase, verapamil, nicorandil, or a combination of these agents as an adjunct to primary PCI. Measuring MVRI, given its simplicity and high reproducibility of measurement (3), may allow us to determine the efficacy of those therapeutic strategies for microvascular protection in patients with acute MI.

CONCLUSIONS

Simultaneous measurement of distal pressure and flow velocity immediately after reperfusion may provide additional insight into the management of patients with acute MI. Coronary microvascular resistance index measured immediately after primary PCI is a useful coronary physiologic parameter for predicting the TEI in patients with anterior acute MI.

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REFERENCES

1. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). J Am Coll Cardiol 2004;44:671–719.
2. Stone GW, Brodie BR, Griffin JJ, et al. Clinical and angiographic follow-up after primary stenting in acute myocardial infarction: The Primary Angioplasty in Myocardial Infarction (PAMI) stent pilot trial. Circulation 1999;99:1548–54.
3. Siebes M, Verhoeff B-J, Meuwissen M, de Winter RJ, Spaan JAE, Piek JJ. Single-wire pressure and flow velocity measurement to quantify coronary stenosis hemodynamics and effects of percutaneous interventions. Circulation 2004;109:756–62.
4. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. 1. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation 1977;56:786–94.
5. Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002.
6. Thiele H, Kappl MJE, Conradi S, Niebauer J, Hambrecht R, Schuler G. Reproducibility of chronic and acute infarct size measurement by delayed enhancement-magnetic resonance imaging. J Am Coll Cardiol 2006;47:1641–5.
7. Ichikawa Y, Sakuma H, Suzawa N, et al. Late gadolinium-enhanced magnetic resonance imaging in acute and chronic myocardial infarction. Improved prediction of regional myocardial contraction in the chronic state by measuring thickness of nonenhanced myocardium. J Am Coll Cardiol 2005;45:901–9.

8. Choi KM, Kim RJ, Gubernikoff G, Vargas JD, Paker M, Judd RM. Transmural extent of acute myocardial infarction predicts long-term improvement in contractile function. Circulation 2001;104:1101–7.
9. Beek AM, Kühl HP, Bondarenko O, et al. Delayed contrast-enhanced magnetic resonance imaging for the prediction of regional functional improvement after acute myocardial infarction. J Am Coll Cardiol 2003;42: 895–901.
10. Stone GW, Hodgson JM, St Goar FG, et al. Improved procedural results of coronary angioplasty with intravascular ultrasound-guided balloon sizing: the CLOUT pilot trial. Circulation 1997;95:2044–52.
11. Gibson CM, Cannon CP, Murphy SA, et al. Relationship of TIMI myocardial perfusion grade to mortality after administration of thrombolytic drugs. Circulation 2000;101:125–30.
12. Yamamuro A, Akasaka T, Tamita K, et al. Coronary flow velocity pattern immediately after percutaneous coronary intervention as a predictor of complications and in-hospital survival after acute myocardial infarction. Circulation 2002;106:3051–6.
13. Meuwissen M, Chamuleau SAJ, Siebes M, et al. Role of variability in microvascular resistance on fractional flow reserve and coronary blood flow velocity reserve in intermediate coronary lesions. Circulation 2001;103: 184–7.
14. de Bruyne B, Bartunek J, Sys SU, Pijls NH, Heyndrickx GR, Wijns W. Simultaneous coronary pressure and flow velocity measurements in humans. Feasibility, reproducibility, and hemodynamic dependence of coronary flow velocity reserve, hyperemic flow versus pressure slope index, and fractional flow reserve. Circulation 1996; 94:1842–9.
15. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105:539–42.
16. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1983; 148:839–43.
17. Suryapranata H, Zijlstra F, MacLeod DC, van den Brand M, de Feyter PJ, Serruys PW. Predictive value of reactive hyperemic response on reperfusion on recovery of regional myocardial function after coronary angioplasty in acute myocardial infarction. Circulation 1994;89:1109–17.
18. Beygui F, Feuvre CL, Helft G, Maunoury C, Metzger JP. Myocardial viability, coronary flow reserve, and in-hospital predictors of late recovery of contractility following successful primary stenting for acute myocardial infarction. Heart 2003;89:179–83.
19. Garot P, Pascal O, Simon M, et al. Impact of microvascular integrity and local viability on left ventricular remodelling after reperfused acute myocardial infarction. Heart 2003;89: 393–7.
20. Shimada K, Sakanoue Y, Kobayashi Y, et al. Assessment of myocardial viability using coronary zero flow pressure after successful angioplasty in patients with acute myocardial infarction. Heart 2003;89:71–6.
21. Kawamoto T, Yoshida K, Akasaka T, et al. Can coronary blood flow velocity pattern after primary percutaneous transluminal coronary angioplasty predict recovery of regional left ventricular function in patients with acute myocardial infarction? Circulation 1999;100:339–45.
22. Akasaka T, Yoshida K, Kawamoto T, et al. Relation of phasic coronary flow velocity characteristics with TIMI perfusion grade and myocardial recovery after primary percutaneous transluminal coronary angioplasty and rescue stenting. Circulation 2000;101: 2361–7.
23. Yamamuro A, Akasaka T, Tamita K, et al. Coronary flow velocity pattern immediately after percutaneous coronary intervention as a predictor of complications and in-hospital survival after acute myocardial infarction. Circulation 2002;106:3051–6.
24. Furber AP, Prunier F, Nguyen HCP, Boulet S, Delépine S, Geslin P. Coronary blood flow assessment after successful angioplasty for acute myocardial infarction predicts the risk of long-term cardiac events. Circulation 2004;110:3527–33.
25. Wakatsuki T, Nakamura M, Tsunoda T, et al. Coronary flow velocity immediately after primary coronary stenting as a predictor of ventricular wall motion recovery in acute myocardial infarction. J Am Coll Cardiol 2000;35: 1835–41.
26. Sezer M, Oflaz H, Gören T, et al. Intracoronary streptokinase after primary percutaneous coronary intervention. N Engl J Med 2007;356: 1823–34.
27. Taniyama Y, Ito H, Iwakura K, et al. Beneficial effect of intracoronary verapamil on microvascular and myocardial salvage in patients with acute myocardial infarction. J Am Coll Cardiol 1997;30:1193–9.
28. Ito H, Taniyama Y, Iwakura K, et al. Intravenous nicorandil can preserve microvascular integrity and myocardial viability in patients with reperfused anterior wall myocardial infarction. J Am Coll Cardiol 1999;33: 654–60.

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