Prognostic Value of Transthoracic Doppler Echocardiography Coronary Flow Velocity Reserve in Patients with Nonculprit Stenosis of Intermediate Severity Early after Primary Percutaneous Coronary Intervention

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Background: Treatment of nonculprit coronary stenosis during primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction may be beneficial, but the mode and timing of the intervention are still controversial. The aim of this study was to examine the significance and prognostic value of preserved coronary flow velocity reserve (CFVR) in patients with nonculprit intermediate stenosis early after primary percutaneous coronary intervention.

Methods: Two hundred thirty patients with remaining intermediate (50%–70%) stenosis of non-infarct-related arteries, in whom CFVR was performed within 7 days after primary percutaneous coronary intervention, were prospectively enrolled. Twenty patients with reduced CFVR and positive results on stress echocardiography or impaired fractional flow reserve underwent revascularization and were not included in further analysis. The final study population of 210 patients (mean age, 58 $\pm$ 10 years; 162 men) was divided into two groups on the basis of CFVR: group 1, CFVR > 2 (n = 174), and group 2, CFVR $\leq$ 2 (n = 36). Cardiac death, nonfatal myocardial infarction, and revascularization of the evaluated vessel were considered adverse events.

Results: Mean follow-up duration was 47 $\pm$ 16 months. Mean CFVR for the whole group was 2.36 $\pm$ 0.40. There were six adverse events (3.4%) related to the nonculprit coronary artery in group 1, including one cardiac death, one ST-segment elevation myocardial infarction, and four revascularizations. In group 2, there were 30 adverse events (83.3%, P < .001 vs group 1), including two cardiac deaths, two ST-segment elevation myocardial infarctions, and 26 revascularizations.

Conclusions: In patients with CFVR > 2 of the intermediate nonculprit coronary lesion, deferral of revascularization is safe and associated with excellent long-term clinical outcomes. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Myocardial infarction, STEMI, Nonculprit coronary stenosis, Coronary flow velocity reserve, Primary percutaneous coronary intervention

In patients presenting with ST-segment elevation myocardial infarction (STEMI), the prevalence of multivessel disease approaches 40%,[1] and these patients are at greater risk for adverse cardiac events following primary percutaneous coronary intervention (pPCI).[2] According to current guidelines, only treatment of the infarct-related lesion is recommended, whereas coronary stenosis of non-infarct-related arteries should be treated during other procedures, if objective evidence of residual myocardial ischemia is documented.[3,4] However, recent randomized trials showed that stenting of nonculprit stenosis during the acute phase of STEMI reduces the risk for further adverse cardiac events.[5,6] However, performance of percutaneous coronary intervention (PCI) during STEMI of residual stenosis in a non-infarct-related artery without evidence of ischemia is controversial.[4-8] In fact, recent data showed beneficial effects of invasive

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Abbreviations

CABG = Coronary artery bypass grafting

CFVR = Coronary flow velocity reserve

FFR = Fractional flow reserve

LAD = Left anterior descending coronary artery

PCI = Percutaneous coronary intervention

pPCI = Primary percutaneous coronary intervention

RCA = Right coronary artery

SE = Stress echocardiography

STEMI = ST-segment elevation myocardial infarction

TDE = Transthoracic Doppler echocardiographic

functional testing immediately after pPCI for evaluation of nonculprit lesions,[7,8] but this approach may be compromised by prolongation of the procedure in the clinical setting of STEMI with frequently disturbed hemodynamics and microcirculation.

Coronary flow velocity reserve (CFVR) by transthoracic Doppler echocardiographic (TDE) imaging can provide useful quantitative information on the functional status of coronary artery circulation.[9-19] TDE CFVR has been extensively validated in prognosis of patients with stable coronary artery disease, but the significance and possible specific role of evaluation of CFVR in nonculprit intermediate coronary stenosis early after STEMI and pPCI has not been specifically investigated.

The aim of this study was to examine the significance and prognostic value of preserved CFVR (CFVR > 2) in patients with nonculprit intermediate stenosis early after pPCI.

METHODS

Study Population

We prospectively included 210 patients (162 men, 48 women; mean age, 58 ± 10 years) from December 2007 to August 2014, at the Clinic of Cardiology, Clinical Center of Serbia, who fulfilled the following criteria: (1) culprit lesion responsible for acute myocardial infarction treated successfully with pPCI, (2) presence of intermediate coronary stenosis (50%–70% diameter stenosis) in a proximal segment of the left anterior descending coronary artery (LAD) or right coronary artery (RCA), other than the infarct-related artery (nonculprit stenosis), (3) stable hemodynamic status at the time of CFVR testing, and (4) follow-up.

Exclusion criteria were (1) all significant valvular diseases, (2) poor acoustic window (for CFVR and echocardiographic assessment), (3) second- and third-degree atrioventricular block, (4) chronic obstructive pulmonary disease, (5) primary hypertrophic or dilated cardiomyopathy, (6) nonculprit stenosis of the left circumflex coronary artery, and (7) poor life expectancy because of other concomitant disease. Informed consent was obtained from all patients, and the local ethical committee approved the study protocol.

Initially, the study population consisted of 258 patients, but four patients were excluded from follow-up because of cancer diagnosed during hospitalization and seven patients because of an inability to obtain technically adequate CFVR (overall feasibility, 97%). Also, 13 patients with proximal nonculprit intermediate stenosis of the left circumflex coronary artery, one patient with second-degree atrioventricular block, two patients with severe aortic stenosis and mitral regurgitation, and one patient with severe chronic obstructive pulmonary disease were excluded from the CFVR examination.

A CFVR value of 2.0 was considered as the cutoff point,[9-14] and the patients were divided into two groups: those with preserved CFVR > 2 (group 1, 174 patients) and those with impaired CFVR ≤ 2 (56 patients). Because CFVR testing cannot discriminate truly significant stenosis from microvascular dysfunction,[12,16,20-22] additional stress echocardiography (SE) or fractional flow reserve (FFR) assessment was performed in all patients with impaired CFVR. Twenty of 56 patients with CFVR ≤ 2 who had positive results on SE in the region of a nonculprit vessel ($n = 15$) or FFR < 0.80 ($n = 5$) were immediately referred for PCI or coronary artery bypass grafting (CABG) and excluded from further analysis (Figure 1) in order not to be biased in analysis by SE- or FFR-guided revascularization, which are, per se, already recommended by the guidelines. The remaining 36 patients with impaired CFVR and normal findings on SE ($n = 32$) or FFR ($n = 4$) represented group 2 (Figure 1) and were referred for further medical treatment. In the final study population, CFVR was evaluated in single, proximal intermediate stenosis of the LAD ($n = 193$ patients) or RCA ($n = 17$).

The culprit stenosis responsible for STEMI was identified according to electrocardiographic changes and angiographic images. pPCI of the culprit stenosis was done routinely according to current recommendations. After successful recanalization of the culprit lesion, in cases of residual nonculprit intermediate stenosis of the LAD or RCA, patients were referred for noninvasive TDE CFVR evaluation. In all patients, TDE CFVR evaluation was performed within 7 days of pPCI, while FFR assessment was done during additional coronary angiography before hospital discharge.

Further clinical management of the patients was carried out at the discretion of the treating cardiologists, including angiographic findings, all functional testing, and clinical symptom assessment.

Echocardiographic Examination and CFVR

Echocardiographic studies were performed using the available digital ultrasound system (Acuson Sequoia C256; Siemens Medical Solutions USA, Mountain View, CA) with a 3V2C multifrequency transducer using second-harmonic technology. Standard two-dimensional, M-mode, left ventricular ejection fraction (Simpson biplane method) measurements were done according to American Society of Echocardiography guidelines.[23] Standard echocardiographic examination and TDE CFVR were performed in the first 7 days after STEMI. The distal part of the LAD and the right posterior descending coronary artery were evaluated using a 4-MHz transducer. For color Doppler flow mapping, the velocity range was set in the range of 16 to 24 cm/sec. Visualization of the distal segment of the LAD artery was done in a modified three-chamber view. Evaluation of right posterior descending coronary artery flow for RCA stenosis was done in the apical two-chamber view. From this position, the probe was slightly rotated anticlockwise and tilted anteriorly, until the coronary blood flow in the posterior interventricular groove was identified by color Doppler. Blood flow velocity was measured using pulsed-wave Doppler echocardiography with a sample volume 3 to 5 mm wide. Alignment of the ultrasound beam direction with distal LAD and right posterior descending flow was as parallel as possible, with the stable transducer position at rest and during maximal hyperemia. Peak diastolic coronary flow velocity was measured in basal conditions and during maximal hyperemia, which was induced with adenosine (0.14 mg/kg/min intravenously, during 2 min).Three optimal diastolic flow profiles at rest and during hyperemia were obtained, and results were averaged. CFVR was calculated as the ratio of hyperemic to basal peak diastolic flow velocities, as