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Original article

Prediction of the filter no-reflow phenomenon in patients with angina pectoris by using multimodality: Magnetic resonance imaging, optical coherence tomography, and serum biomarkers

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ABSTRACT

Background: Although the occurrence of no-reflow during percutaneous coronary intervention (PCI) has been shown to be associated with worse short- and long-term clinical outcomes, the clinical relevance of preventing flow deterioration by using the filter-based distal protection devices (DPDs) is controversial. We investigated predictors of the filter no-reflow (FNR) phenomenon during PCI by using multimodality, such as hyperintense plaques (HIPs) in the coronary artery on T1-weighted imaging (T1WI) non-contrast magnetic resonance, plaque composition by using optical coherence tomography (OCT), and serum biomarkers, in patients with angina pectoris.

Methods and results: Fifty lesions from 50 patients with angina were examined. All patients underwent T1WI within 24 h before invasive coronary angiography was performed, and preinterventional OCT was performed on a native atherosclerotic culprit lesion. The signal intensity of coronary plaque to cardiac muscle ratio (PMR) was calculated on a standard console of the magnetic resonance system. Of the 50 lesions, 20 lesions showed FNR during PCI, while non-FNR was observed in 30 lesions. A cut-off value >1.85 of PMR had a sensitivity of 65%, a specificity of 93%, a positive predictive value of 87%, and a negative predictive value of 80% for identifying lesions with FNR. Multivariate analysis revealed that the presence of HIPs with PMR >1.85 ($p = 0.008$) was the only independent predictor of the FNR phenomenon during PCI.

Conclusions: This study shows that the presence of HIPs with PMR >1.85 on T1WI was a novel independent predictor of the FNR phenomenon during PCI in angina patients. This result may help in identifying high-risk lesions for no-reflow to deploy filter-based DPDs.

Introduction

Percutaneous coronary intervention (PCI) may be complicated by periprocedural myocardial infarction and reduced antegrade flow (“no-reflow”). The occurrence of no-reflow has been shown to be associated with worse short- and long-term clinical outcomes [1]. No-reflow is attributable to the distal embolization of atheromatous or thrombotic materials that results from mechanical fragmentation of the culprit plaque by PCI. However, the clinical relevance of preventing flow deterioration by using distal protection devices (DPDs) is controversial. There are no randomized controlled trials to prove the efficacy of using DPDs in reperfusion therapy for acute myocardial infarction (AMI) [2,3]. On the other hand, some studies showed that DPDs may improve myocardial reperfusion among selected high-risk patient groups [4,5].

Several intravascular ultrasound (IVUS) and optical coherence tomography (OCT) studies have demonstrated that thrombus formation, positive remodeling, and greater lipid plaque burden were independent predictors of the no-reflow phenomenon [6–9]. Moreover, some studies have shown that inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP) are also associated with the no-reflow phenomenon. Magnetic resonance (MR) imaging, on the other hand, enables assessment of the

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morphology of the carotid and coronary atherosclerotic plaques in vivo. It has been reported that hyperintense plaques (HIPs) of the carotid and coronary arteries on MR non-contrast T1-weighted imaging (T1WI) indicate the presence of intraplaque hemorrhage or intracoronary thrombus containing methemoglobin [10–12]. Moreover, Kawasaki et al. reported that coronary HIPs on T1WI were associated with a high incidence of the no-reflow phenomenon [12].

Thus far, to the best of our knowledge, no studies have comprehensively evaluated the prediction of the filter no-reflow (FNR) phenomenon during PCI by using multimodality, such as HIP on T1WI in cardiac MR, plaque composition by using OCT, and biomarkers, in patients with angina pectoris. The present study has been designed for this purpose.

Material and methods

Patients

Seventy-four consecutive angina pectoris patients (74 lesions), who had not undergone previous PCI or coronary artery bypass grafting, were prospectively enrolled in this study between September 2011 and December 2013. Patients eligible for an early invasive strategy according to the American College of Cardiology Foundation/American Heart Association guideline [13] (patients who have refractory angina or hemodynamic or electrical instability and initially stabilized patients who have an elevated risk for clinical events) and those with contraindications for cardiac MR were excluded from the study. All patients underwent cardiac MR and blood sampling within 24 h before the day on which invasive coronary angiography (CAG) and OCT were performed. Of these 74 lesions from 74 patients, 3 lesions that had Thrombolysis in Myocardial Infarction (TIMI) flow grade <2 at baseline, 9 lesions that did not undergo OCT examination before PCI, and 12 lesions that were unsuitable for deployment of the DPD because of small vessels or severe tortuousness, were excluded from this analysis.

Thus, 50 lesions from 50 patients, who had angiographically documented narrowing of at least 50% of the luminal diameter of a major coronary artery on CAG, were examined in this study. Unstable angina pectoris was diagnosed in 32 patients, according to Braunwald's criteria. Stable angina pectoris, defined as chest pain typical of cardiac ischemia on exertion, was diagnosed in another 18 patients. Oral aspirin (100 mg) and clopidogrel (75 mg) were administered on admission. Moreover, high-risk patients were also treated with intravenous heparin, but no one received thrombolytic agents.

The study was approved by the hospital ethics committee, and informed consent was obtained from all patients before the study.

MR coronary plaque image acquisition

Coronary plaque imaging was performed by using a 1.5-T MR imager (Achieva, Philips Medical Systems, Best, The Netherlands) with a 5-element cardiac coil. Nitroglycerin (0.3 mg) was administered sublingually immediately before taking images to obtain high-quality MR images. Initial survey images were focused around the heart, and the reference images were then obtained for sensitivity of parallel imaging. Transaxial cine MR images were then acquired by using a steady-state free precession sequence with breath holding to determine the trigger delay time when the motion of the right coronary artery was minimal.

First, to obtain detailed anatomic information, free-breathing steady-state free precession whole-heart coronary MR angiographic images were acquired [repetition time, 3.7 ms; echo time, 1.8 ms; flip angle, 80°; SENSE factor, 2.0; number of excitations, 1; navigator gating window of ±2.0 mm with diaphragm drift correction; field of view, 300 × 255 × 120 mm (rectangular field of view, 85%); acquisition matrix, 240 × 240; reconstruction matrix, 512 × 512 × 160, resulting in an acquired spatial resolution of 1.25 × 1.25 × 1.5 mm reconstructed to 0.6 × 0.6 × 0.75 mm].

Next, coronary plaque images were obtained when patients were breathing freely by using a three-dimensional T1WI inversion-recovery gradient-echo sequence with black-blood condition with a Look Locker sequence, fat-suppressed and radial k-space sampling in Y–Z plane [repetition time, 4.4 ms; echo time, 2.0 ms; flip angle, 20°; SENSE factor, 2.5; number of excitations, 2; navigator gating window of ±1.5 mm with diaphragm drift correction; field of view, 300 × 240 × 120 mm (rectangular field of view, 80%); acquisition matrix, 224 × 224; reconstruction matrix, 512 × 512 × 140, resulting in an acquired spatial resolution of 1.34 × 1.34 × 1.7 mm reconstructed to 0.6 × 0.6 × 0.85 mm] [10–12].

MR coronary plaque image analysis

First, when the target lesion was confirmed in the coronary MR angiography, the areas corresponding to the above site in the coronary T1WI obtained were carefully matched according to the surrounding cardiac and chest wall structures. Then, the signal intensity of coronary plaque to cardiac muscle ratio (PMR; PMR was defined as the highest signal intensity of the coronary plaque divided by the signal intensity of the left ventricular muscle near the coronary plaque), measured by placing a free-hand circular region of interest on a standard console of the clinical MR system, was calculated. Coronary plaque image analysis was performed by a single experienced cardiologist who was blinded to clinical information and the OCT findings. The interobserver and intraobserver coefficients of variation for measurement of the PMR were reported in our previous study [11].

Angiographic, OCT, and interventional procedures

CAG was performed by using the standard femoral or radial approach. All patients received intravenous heparin (5000 IU) before the procedure. This was followed by an intravenous bolus injection of 2000 IU every hour during the procedure. After administration of 0.2 mg of intracoronary nitroglycerin, diagnostic CAG was performed. Preinterventional OCT imaging was performed on a native "de novo" atherosclerotic lesion considered to be the culprit lesion. Thrombolysis or thrombectomy was not performed for any patient. The culprit vessel was identified based on clinical, scintigram stress test, and angiographic data. The culprit lesion site selected for analysis was the image slice with the smallest lumen cross-sectional area. Almost all patients underwent direct stenting. Pre-dilatation was performed when stent delivery was expected to be difficult, and post-dilatation with a non-compliant balloon was performed at the operator's discretion.

The OCT images were acquired by using a commercially available time-domain (M2 Cardiology Imaging system, LightLab Imaging, Inc, Westford, MA, USA) or frequency domain (ILUMIEN/ILUMIEN OPTIS OCT Intravascular Imaging System, St Jude Medical, St Paul, MN, USA) OCT system, as previously described [14].

Following OCT, the filter-based DPD (Filtrap, Nipro, Japan) was delivered through a low-profile, 3.2-Fr exchange sheath that allows free rotational movement of the guidewire component. The guidewire component then served as the rail over which other catheters and stents were advanced to the target lesion. After positioning the DPD across the stenosis, the delivery-retrieval sheath was removed, and balloon dilatation and stent implantation were then performed according to routine practice. Then, DPD was recaptured with a 4-Fr retrieval sheath, and removed from the native vessel.