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Original article

Relationship between optical coherence tomography-derived morphological criteria and functional relevance as determined by fractional flow reserve

Eisuke Usui (MD), Taishi Yonetsu (MD), Yoshihisa Kanaji (MD), Masahiro Hoshino (MD), Masao Yamaguchi (MD), Masahiro Hada (MD), Tadashi Fukuda (MD), Hiroaki Ohya (MD), Yohei Sumino (MD), Rikuta Hamaya (MD), Yoshinori Kanno (MD), Tadashi Murai (MD), Tetsumin Lee (MD), Tsunekazu Kakuta (MD, PhD)*

Department of Cardiovascular Medicine, Tsuchiura Kyodo General Hospital, Ibaraki, Japan

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ABSTRACT

Background: Although several previous studies have indicated that optical coherence tomography (OCT)-derived minimal lumen area (MLA) correlates with fractional flow reserve (FFR) severity, other morphologic criteria for functionally significant coronary stenosis assessed by FFR have not been fully elucidated. This study aimed to identify OCT-based morphological predictors of physiologically significant ischemia assessed by FFR in angiographically intermediate coronary lesions.

Methods: We investigated 194 de novo intermediate coronary lesions in 178 patients with stable angina pectoris who underwent OCT imaging and FFR measurement. The lesions were divided into two groups according to an FFR threshold: ischemia group, FFR <0.75 ($n = 69$) and non-ischemia group, FFR ≥ 0.75 ($n = 125$). Clinical characteristics, angiographic, and OCT findings were compared between these two groups. Predictors of significant ischemia defined as FFR <0.75 were identified by logistic regression analyses.

Results: Patient age, statin use, lesion in left anterior descending artery (LAD), OCT-derived MLA, and lipid volume index (LVI) (averaged lipid arc multiplied by lipid length) were independent predictors of FFR <0.75 in multivariate logistic regression analysis. Receiver operating characteristic analysis suggested that age <64 years old, OCT-derived MLA ≤ 1.39 mm^2, and LVI ≥ 733 are the best cut-off values for predicting FFR <0.75. Multiple logistic regression models, including the MLA combined with the LAD location, LVI, age, and statin use, provided superior predictive efficacy for physiologically significant ischemia compared with the model that only employed MLA.

Conclusions: Information on OCT-derived LVI and lesion locations facilitates better identification of coronary lesions that cause ischemia than OCT-derived MLA analysis alone.

Introduction

Given the favorable clinical outcomes of fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI), FFR is becoming the standard modality for the assessment of myocardial ischemia caused by epicardial coronary stenosis [1–3]. The advantage of FFR for physiological testing is attributed to its objective assessment of a numerical parameter with a pre-specified threshold. A landmark study by Pijls et al., in which FFR was compared with other non-invasive modalities, demonstrated that an FFR threshold of <0.75 specifically detects reversible myocardial ischemia improved by revascularization [4]. Therefore, FFR <0.75 has been accepted as a specific threshold for myocardial ischemia. It is known that visual-functional mismatches between angiography and FFR are observed in a non-negligible proportion of intermediate stenosis, which is attributed to multiple factors [5]. Although several small-sized studies have demonstrated the capability of coronary angiography for prediction of functionally ischemic lesions, using new

* Corresponding author at: Department of Cardiovascular Medicine, Tsuchiura Kyodo General Hospital, 4-1-1, Otsuno, Tsuchiura, Ibaraki 300-0028, Japan.
E-mail address: kaz@joy.email.ne.jp (T. Kakuta).

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technologies such as 3-dimensional quantitative coronary angiography [6] or computational fluid dynamics modeling [7], the capability is not sufficiently corroborated by sufficient evidence. Also, given the different concepts between the blood flow dynamics in the coronary lumen and morphologic characteristics of vessel wall outside the coronary lumen, prediction of FFR by imaging modalities has been controversial. Nevertheless, it is still conceivable that complexity of plaque including luminal surface irregularity such as plaque rupture may modify the coronary flow dynamics in addition to morphometric parameters such as minimal lumen area (MLA). Intravascular ultrasound (IVUS) provides morphological information about coronary arteries and is utilized as an adjunctive imaging modality to angiograms during PCI. The relationship between FFR severity and IVUS parameters, such as MLA, minimal lumen diameter, and percent stenosis area, has been thoroughly investigated [8,9]. However, the power of IVUS parameters to detect significant FFR values is not sufficient to substitute FFR measurement for an assessment of the physiological significance of coronary stenosis. Optical coherence tomography (OCT) provides higher resolution images than those provided by IVUS, which enables better delineation of the luminal-intima boundary and lumen area measurements with excellent reproducibility [10,11]. Nevertheless, the predictive power of OCT-derived parameters for FFR severity has been investigated only in a few small studies [12–16]; of note, the impact of OCT-derived plaque characteristics on FFR severity has not been demonstrated unlike coronary computed tomography [17,18]. Therefore, the aim of this study was to investigate the morphological predictive factors in OCT for physiologically severe coronary stenosis assessed by FFR in intermediate coronary lesions.

Materials and methods

Study population

The institutional registry data of consecutive patients who underwent intracoronary OCT at Tsuchiura Kyodo General Hospital between October 2011 and June 2016 was queried to identify the patients with intermediate stenosis for whom OCT imaging and FFR measurement were performed during the same procedure. OCT imaging was performed at the operators' discretion based on the institutional protocol of OCT which excluded significant left main disease, congestive heart failure, and renal insufficiency. From the database, patients who satisfied the following criteria were selected for the present study: >20 years old; stable angina pectoris; physiological assessment by pressure wire for de novo coronary lesions that indicate intermediate stenosis, which is defined as 40% to 80% diameter stenosis on an angiogram; and well-visualized OCT imaging performed for the intermediate lesions. A total of 205 patients with 217 lesions were identified. Of those 217 lesions, one intermediate lesion at left-main trunk was excluded because of incomparable physiological impact of left-main trunk lesion even with left anterior descending artery (LAD) lesions. Another patient, who underwent OCT imaging irrespective of congestive heart failure based on the operator's discretion, was excluded with consideration of the increased end-diastolic pressure of left ventricle which may affect FFR. A patient with creatinine level >2.0 g/dL underwent OCT with use of low-molecular weight dextran. This patient was also excluded because of potential error in morphometric analysis caused by different osmolarities. Tandem lesions ($n = 5$) and previous myocardial infarction-related arteries ($n = 15$) were also excluded from the analysis (Fig. 1). Baseline patient characteristics were collected by reviewing medical charts. The study protocol was approved by the institutional review board, and all patients provided written informed consent prior to catheterization.

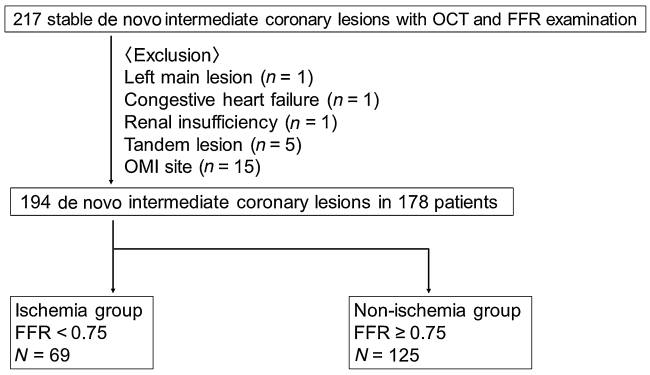

Fig. 1. Patient population. A total of 217 intermediate coronary lesions in 205 patients with stable angina pectoris undergoing OCT and FFR examination were selected from the institutional database. After exclusion, 194 de novo intermediate coronary lesions were included in the analysis. The lesions were divided into two groups based on the FFR cut-off value: an ischemia group (FFR <0.75, $n = 69$) and a non-ischemia group (FFR ≥0.75). FFR: fractional flow reserve, OCT: optical coherence tomography.

Catheterization protocol and angiographic analysis

Catheterization was performed according to the standard protocol at the institution. In brief, coronary angiography was performed via radial or femoral artery with a 6 French system prior to PCI procedures, OCT imaging, and FFR measurements. Patients received a bolus infusion of unfractionated heparin (5000 IU) as soon as a sheath was introduced into the artery, and an additional bolus of 2000 IU was administered every hour as needed to maintain an activated clotting time >250 s. Nitroglycerin (0.2 mg) was administered into the coronary artery prior to coronary angiography. Quantitative coronary angiography (QCA) was performed using offline software (CMS-MEDIS, Medis Medical Imaging Systems, Inc., Leiden, Netherlands). The minimum lumen diameter, reference diameter, and lesion length were measured in diastolic frames from orthogonal projections. Angiographic lesion complexity was assessed according to the Ambrose classification [19,20]. Simple coronary lesions were concentric or eccentric and characterized by a smooth surface and a broad neck. Complex coronary lesions were eccentric with a narrow neck, overhanging edges, or irregular borders, or had several multiple irregularities. The OCT imaging and FFR measurements were performed prior to PCI for the target lesion or after the PCI procedure for non-target intermediate lesions.

FFR measurements

For FFR measurements, a RadiAnalyzer Xpress console with Pressure Wire Certus (St. Jude Medical, St Paul, MN, USA) was used throughout the study. After the guiding catheter was engaged with the coronary artery, the pressure wire was introduced, zeroed, and equalized to the catheter-tip pressure before crossing the lesion. Afterward, the pressure sensor was positioned a minimum of 3 cm distal to the lesion in the distal third of the artery. Baseline pressures were recorded for a minimum of 20 s. Thereafter, FFR was measured at steady-state maximal hyperemia induced by intravenous infusion of adenosine 5′-triphosphate at the rate of 160 $\mu g\ kg^{-1}\ min^{-1}$.

OCT image acquisition and analysis

OCT imaging was acquired prior to any interventional procedures using frequency-domain OCT systems (ILUMIEN®, St. Jude Medical Inc., or LUNAWAVE®, Terumo, Tokyo, Japan). The technique of OCT image acquisition has been described elsewhere

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