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Plaque morphologies and the clinical prognosis of acute coronary syndrome caused by lesions with intact fibrous cap diagnosed by optical coherence tomography



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ABSTRACT

Background: Pathological studies have suggested that acute coronary syndrome (ACS) may be caused by culprit lesions with intact fibrous cap (IFC), including plaque erosions. This study sought to evaluate the morphological features and clinical outcomes of patients with ACS caused by lesions with IFC.

Methods: A total of 318 patients with ACS who underwent optical coherence tomography (OCT) of a culprit lesion were investigated. The culprit lesions were categorized as follows: those with plaque rupture (PR group), those with an IFC (IFC group), and those with a massive thrombus precluding plaque visualization (MT group). Intravascular ultrasound (IVUS) was performed in 297 patients. Clinical follow-up data were collected regarding adverse cardiac events, including death, myocardial infarction, revascularization, and congestive heart failure requiring hospitalization.

Results: Culprit lesions were categorized into 141 RPs, 131 IFCs, and 46 MTs. IFC group exhibited a smaller remodeling index and less frequently attenuated plaques on IVUS. Three hundred and seven patients (96.5%) were followed for a median follow-up duration of 576 days. Adverse cardiac events were observed in 93 patients (30.3%). Kaplan–Meier analysis demonstrated a significantly lower event rate in IFC group compared with the RP and MT groups. Cox proportional hazard analysis demonstrated that an IFC and multivessel disease were independent predictors of adverse events [hazard ratio 0.57, 95% confidence interval (CI) 0.33–0.98, p = 0.043 and hazard ratio 1.72, 95% CI 1.09-2.73, p = 0.021].

Conclusions: Culprit lesions with IFC showed smaller remodeling indices by IVUS, and were associated with better long-term prognosis compared with those with plaque rupture.

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1. Introduction

Disruption of a fibrous cap overlying a necrotic core, which is generally recognized as plaque rupture, is the major cause of coronary thrombosis resulting in acute coronary syndrome (ACS) [1,2]. The mechanisms and consequences of plaque rupture have been extensively investigated, and therapeutic strategies for ACS have been established with respect to the lesions characterized by plaque rupture. However, pathological studies have suggested that other substrates of coronary thrombosis, such as plaque erosion, have an intact fibrous cap (IFC) without an exposed necrotic core underneath the thrombus. Indeed, postmortem studies have reported that lesions with IFCs account for 30 to

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40% of acute myocardial infarctions that result in cardiac death [3,4]. However, the mechanisms that underlie how lesions with IFCs result in the formation of a coronary thrombus, as well as both the clinical and the morphological features of these lesions in vivo, have not been clarified.

Optical coherence tomography (OCT) is a high-resolution coronary imaging modality that enables clinicians to evaluate plaque characteristics and measure the thickness of the fibrous cap of atheromatous plaque [5]. Recently, studies have noted the potential diagnostic ability of OCT to differentiate among plaque erosion, calcified nodules and plaque rupture [6,7]. Jia et al. reported that OCT-defined erosion and calcified nodules demonstrated prevalences and patient characteristics similar to those included in pathological reports [6]. As suggested by these authors, OCT may represent the best imaging modality with which to examine the pathogenesis of acute coronary syndrome in vivo. However, morphological validation via other imaging modalities, as well as an assessment of the clinical prognoses of these lesions, has not been sufficiently investigated.

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¹ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

In the present study, we sought to assess the morphologies of culprit lesions with IFCs using intravascular ultrasound (IVUS) and to investigate the clinical features and prognoses of ACS patients with culprit lesions with IFCs.

2. Methods

2.1. Study population

From October 2008 to January 2014, a total of 728 patients with ACS, which included 401 patients with ST-elevation myocardial infarction (STEMI), 183 patients with non-ST-elevation myocardial infarction (NSTEMI), and 144 patients with unstable angina pectoris (UAP), were treated with percutaneous coronary intervention (PCI) at Tsuchiura Kyodo General Hospital. Among those patients, 398 consecutive patients (54.7%) who underwent OCT of a culprit lesion at the time of percutaneous coronary intervention (PCI) were included in the present study (Fig. 1). Exclusion criterion for OCT imaging were patients with cardiogenic shock, congestive heart failure, renal insufficiency, significant left main coronary artery disease, and a suboptimal result after thrombectomy with TIMI 0-2 flow. Patients were excluded from the analysis if the culprit lesion could not be identified via electrocardiograms and angiography or if the lesion required balloon angioplasty prior to OCT imaging, whereas thrombectomy was allowed before the imagings. Stent thrombosis and restenosis were excluded because the pathogenesis of ACS is expected to be different from that of de novo lesions. Bypass graft failure or cases with insufficient OCT image quality were also excluded. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's review board.

2.2. Cardiac enzyme assessment

Creatinine kinase (CK), creatinine kinase myocardial band (CK-MB), and troponin-I were each measured on admission. CK and CK-MB were each measured every 3 h following the PCI procedures until the values decreased; the highest values were considered the peak values.

2.3. Coronary angiography

The baseline coronary angiograms before any interventional procedure were analyzed by off-line quantitative coronary angiography (QCA-CMS, Medis, Netherlands). The reference diameter, minimum



Fig. 1. Patient population. Among a total of 398 patients with acute coronary syndrome who underwent optical coherence tomography, 318 de novo culprit lesions were observed by OCT and investigated in the present study. The lesions were divided into the following 3 groups according to the OCT findings: RP, demonstrating plaque rupture; IFC, demonstrating intact fibrous caps; and MT, demonstrating a massive thrombus.

lumen diameter, diameter stenosis, and lesion length were measured for each culprit lesion. Thrombolysis In Myocardial Infarction (TIMI) flow grade was determined for the culprit vessel. Multivessel disease was defined as having angiographical stenoses with more than 50% diameter stenosis in two or three major epicardial coronary arteries.

2.4. OCT image acquisition

OCT imaging was performed before any interventional procedures for lesions showing TIMI 3 flow without angiographically suspected thrombi, otherwise thrombectomy was performed using aspiration catheter (Eliminate, Terumo, Tokyo, Japan) and repeated up to 3 times until TIMI 3 flow was obtained before the OCT imaging. Either the time-domain (M2/M3 Cardiology Imaging System, LightLab Imaging, Inc., Westford, MA) or the frequency-domain OCT system (C8-XR™ OCT Intravascular Imaging System, St. Jude Medical, St. Paul, Minnesota) was used in this study. The technique of intracoronary OCT imaging has been described previously [8–11]. In brief, using an M2/M3 system, an occlusion balloon (Helios, LightLab Imaging Inc. Westford, MA) was advanced proximal to the lesion and inflated up to 0.4–0.6 atm, according to the vessel's size, during image acquisition. The imaging wire was advanced at least 40 mm distal to the lesion in order to acquire the images of the target lesion and proximal and distal reference segments, subsequently automated pulled-back was started from distal to proximal at 1.0 mm/s while saline was continuously infused from the tip of the occlusion balloon. With the C8 system, a 2.7-F OCT imaging catheter (Dragonfly JP, LightLab Imaging Inc., Westford, MA) was advanced distal to the lesion via the angioplasty guide wire. Guiding catheter was coaxially positioned into coronary ostium and contrast media was injected using a power injector at the flush rate of 3.0 to 4.0 ml per second through the guiding catheter, subsequently pullback was started as soon as the blood was cleared.

2.5. OCT analysis

The OCT analysis included either the presence or the absence of intraluminal thrombus and fibrous cap disruption. An intraluminal thrombus was defined as a mass attached to the lumen surface or floating within the lumen [11,12]. Plaque rupture was defined as a discontinuity of the fibrous cap overlying a necrotic core, with or without cavity formation (Fig. 2) [11,12]. Culprit lesions were divided into the following three categories according to the OCT findings: lesions characterized by plaque rupture at the culprit lesion (RP group) (Fig. 2); lesions demonstrating no plaque rupture, with sufficient plaque visualization behind the thrombus (IFC group) (Fig. 3); and lesions with massive thrombi precluding the assessment of plaque morphology over 90° of circumferences (MT group) (Fig. 4).

The calcified nodules were evaluated separately because they theoretically have a disrupted fibrous cap overlying nodular calcium, which may confuse the definition of "intact fibrous cap" in the present study. The calcified nodules were defined as lesions exhibiting disruptions in the fibrous caps over a calcified plaque, characterized by superficial and protruding calcium accompanied by substantial calcium deposition both proximal and distal to the lesion (Fig. 5) [6]. The OCT images were digitally stored and analyzed offline by two independent investigators who were unaware of the corresponding patients' clinical information. In case of a disagreement between the two observers, a consensus reading was obtained.

2.6. IVUS image acquisition

IVUS was successfully performed in 297 patients in order to examine the culprit lesion immediately after OCT imaging. A 40-MHz IVUS catheter (Boston Scientific, Natick, MA) was used throughout the study. The catheter was advanced distal to the target lesion, Download English Version:

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