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Original article

Angioscopic differences of coronary intima between diffuse and focal coronary vasospasm: Comparison of optical coherence tomography findings

Daisuke Kitano (MD)[a,b], Tadateru Takayama (MD, FJCC)[b,*], Mitsumasa Sudo (MD)[b], Takaaki Kogo (MD)[b], Keisuke Kojima (MD)[b], Naotaka Akutsu (MD)[b], Toshihiko Nishida (MD)[b], Hironori Haruta (MD)[b], Daisuke Fukamachi (MD)[b], Taro Kawano (MD)[b], Takashi Kanai (MD)[b], Takafumi Hiro (MD, FJCC)[a,b], Satoshi Saito (MD, FJCC)[b], Atsushi Hirayma (MD, FJCC)[a,b]

[a] *Division of Advanced Cardiovascular Imaging, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan*
[b] *Division of Cardiology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan*

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ABSTRACT

Background: Coronary artery vasospasm (CS) can be identified as either a diffuse type or focal type; however, the difference in endothelial characteristics between these spasm types remains unclear. The features of coronary intima associated with diffuse spasm and focal spasm using coronary angioscopy (CAS) were evaluated and the optical coherence tomography (OCT) findings were compared.
Methods: CAS and/or OCT observational analysis was performed in 55 patients (mean age: 61.4 years, 31 men) who had acetylcholine-provoked CS (diffuse CS, 31 patients; focal CS, 24 patients). The yellowness of the intima, presence of thrombus in CAS, and intimal characteristics based on the OCT results were evaluated.
Results: CAS showed more atherosclerotic yellow plaques at the focal spasm segment than at the diffuse spasm segment ($p = 0.032$). Moreover, there were more thrombi at the focal spasm segment ($p = 0.039$). In addition, OCT results revealed that the intima area, maximum intima thickness, and lipid content in the focal CS group were larger than the diffuse CS group ($4.22 \pm 1.67\ mm^2$ vs. $3.45 \pm 2.36\ mm^2$; 0.71 ± 0.29 mm vs. 0.53 ± 0.30 mm; 55.9% vs. 32.0%, $p < 0.001$, respectively).
Conclusions: These results indicate that the presence of atherosclerotic plaques at the spasm site is likely to be related to the occurrence of a focal vasospasm. This may support the difference of features between focal CS and diffuse CS and contribute to precise treatment for each spasm type.

Introduction

Coronary artery vasospasm (CS) is the occurrence of myocardial ischemia that contributes to variant angina, effort angina, myocardial infarction, lethal arrhythmia, and sudden cardiac death [1–5]. CS is not related to the presence or absence of angiographic diseases [6]. It can be identified as two types, diffuse and focal types, which have different aspects [7–9]. There may be some differences regarding the mechanism and clinical features between focal and diffuse CS. However, the precise mechanism of these spasm types remains unknown. In clinical settings, different treatment types may be appropriate for each spasm type. Therefore, it is of interest to distinguish spasm-related atherosclerosis from the unrelated lesion.

Some studies using intravascular imaging modalities, such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT), have displayed the intracoronary features of CS; mild atherosclerotic lesions at the site of focal spasm were found [10–12] and coronary artery segments in diffuse CS showed diffuse intimal thickening with fibrous tissue [13]. These intracoronary imaging

* Corresponding author at: Division of Cardiology, Department of Medicine, Nihon University School of Medicine, 30-1 Oyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan.
E-mail address: takayama.tadateru@nihon-u.ac.jp (T. Takayama).

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modalities provide extensive information on the cross-sectional images of tissues with high-resolution visualization of the vascular wall and plaque morphology. However, it is difficult to detect the superficial appearance of the coronary wall. Coronary angioscopy (CAS) is useful to assess superficial appearances because it allows a direct visualization of the target [14]. However, no previous study reported angioscopic findings on CS. In the present study, we observed coronary arteries of focal CS and diffuse CS with CAS to investigate the differences in intimal appearance of vasospastic coronary arteries between the focal and diffuse types. Furthermore, we compared the findings with the OCT appearance.

Methods

Study subjects

From April 2010 to March 2017, acetylcholine (ACH) provocation tests were performed on 554 patients who had atypical chest pain at rest and/or on exertion. They required coronary angiography (CAG) for the diagnosis of their chest pain, but did not have organic coronary stenosis based on the CAG results. CAS and/or OCT were performed according to the operator's decision on 55 patients (61.4 ± 10.8 years, 31 men) (Fig. 1), who had ACH-provoked CS and agreed for observation using the intracoronary imaging modalities: CAS and/or OCT. All antianginal drugs, except sublingual nitroglycerin, were discontinued at least 12 h before cardiac catheterization. Patients with congestive heart failure, cardiomyopathy, history of fatal arrhythmia, history of myocardial infarction; those who underwent revascularization therapy such as percutaneous coronary intervention and coronary artery bypass grafting surgery; those with chronic renal failure requiring hemodialysis; and those taking β-blockers were excluded from this study at the enrollment. This study protocol was reviewed and approved by the Ethics Committee of Nihon University Itabashi Hospital (RK-170711-9), and written informed consent was obtained from each patient for the study.

Catheterization procedure and acetylcholine provocation

After administration of 5000 U of heparin, CAG was performed by the standard Judkins technique using a single-plane or biplane cine angiography system. The absence of luminal narrowing >50% was confirmed by the injection of a contrast medium into the left and right coronary arteries. In the ACH provocation test, under right ventricular pacing back-up, an incremental dose of ACH was injected into the right coronary artery (10, 20, and 50 μg) first, then into the left coronary artery (20, 50, and 100 μg). A standard 12-lead electrocardiogram (ECG) was carefully monitored and recorded every 30 s. Focal CS was defined as localized transient vessel narrowing associated as defined by the American Heart Association [15], with myocardial ischemia including ischemic ST change on the ECG monitor (Fig. 2C and D), and diffuse CS was defined as the observation of severe diffuse vasoconstriction in more than two adjacent coronary segments as evidenced by ischemic ST change (Fig. 3C and D). When chest pain associated with ST elevation was experienced, angiography was immediately performed, and subsequently, nitroglycerin (0.25 mg) was injected into the coronary artery through the catheter to relieve the spasm. We classified that patients who provoked focal CS by ACH with diffuse CS in other coronary segments were included into both the focal and the diffuse CS group.

Angioscopic examination procedure and evaluation

CAS examination was performed using a non-occluded type angioscope (FT-203F or Visible, FiberTech Co., Ltd., Tokyo, Japan). The outer section of the 4-Fr probing catheter (MEDIKIT Co., Ltd., Tokyo, Japan) was used as the guide to insert the optical fiber into the coronary artery. The angioscopic observations were made while the blood was cleared away from the view by the injection of 3% dextran-40 through the probing catheter as previously reported [16]. The optical fiber was placed at the distal segment of the coronary artery and slowly pulled back under angiographic guidance. CAS images were recorded on a digital recorder. The existence of plaque and thrombus was defined under the angiographic guidance and compared with the spasm site angiographically.

We assessed the existence of red thrombi at the site of the spasm and yellow grade of the intima, which we classified as degrees, as previously described [16,17]. Thrombus was defined on the basis of the criteria adopted by the European Working Group on Coronary Angioscopy [18], and the presence of a thrombus was assessed. The plaque color was graded as 0 (white), 1 (light yellow), 2 (yellow), 3 (bright yellow) as previously described [17,19–21]. The maximum yellow grade of the plaques was assessed. Angioscopic

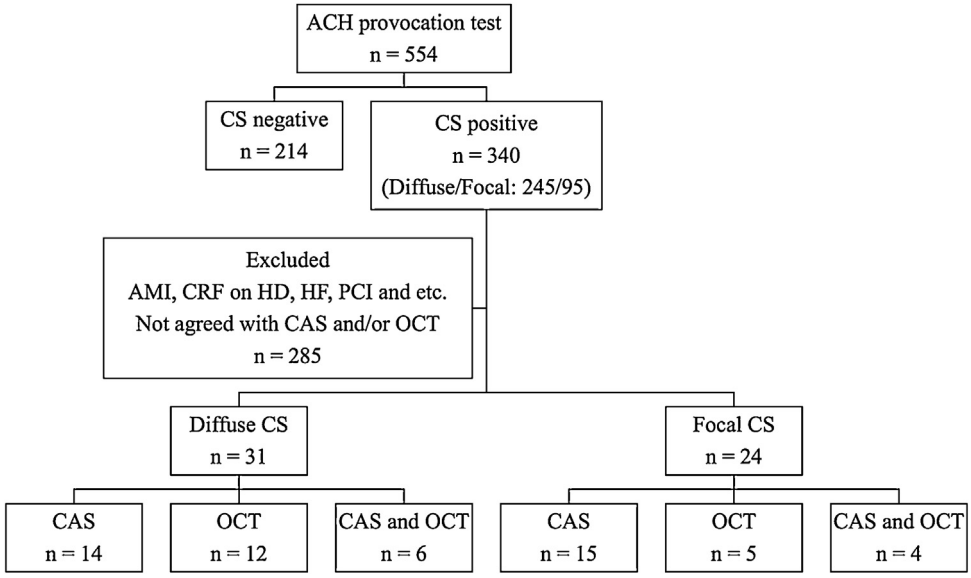

Fig. 1. Study flowchart. ACH, acetylcholine; CS, coronary artery vasospasm; AMI, acute myocardial infarction; CRF, chronic renal failure; HD, hemodialysis; HF, heart failure; PCI, percutaneous coronary intervention; CAS, coronary angioscopy; OCT, optical coherence tomography.

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