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EXPERT CONSENSUS DOCUMENT

Consensus document on the standard of coronary angioscopy examination and assessment from the Japanese Association of Cardiovascular Intervention and Therapeutics

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Abstract
Coronary angioscopy (CAS) is a unique diagnostic device that allows direct visualization of the vascular luminal surface in living patients. CAS contributes to elucidate the pathology of coronary artery disease. This consensus document provides a standard for CAS examination and assessment.

Keyword Coronary angioscopy

Introduction

Coronary angioscopy (CAS) is a unique diagnostic device that allows direct visualization of the vascular luminal surface. It has a role of macropathologic examination in living patients. CAS provides a real-time full-color three-dimensional video image that cannot be presented by any other constructed imaging modalities such as computed tomography, magnetic resonance imaging, intravascular ultrasound (IVUS), or optical coherence tomography (OCT). We can judge not only the shape and color of the target object but also its texture from its movement in the blood flow. CAS image gives us the inspiration of what is happening inside the vessel.

CAS has an extensive role in both research and clinical practice. Numerous novel findings have been reported on acute coronary syndrome (ACS), vulnerable plaques, and vascular response after coronary intervention with or without stent implantation by the experimental and clinical studies with CAS.

In this consensus document, we provide a standard for the examination and assessment by CAS.

Acquisition of angioscopic images

The most important thing for the acquisition of a clear angioscopic image is to clear away the blood from the viewing area. There are two types of angioscopy systems from this point: a balloon occlusion type and a non-occlusion type. A balloon occlusion type CAS is equipped with a compliant balloon to block antegrade blood flow, which makes a clear visual field with smaller amount of flushing fluid. However, since it causes myocardial ischemia, we should be careful not to induce ischemia-related complications. On the other hand, a non-occlusion type CAS can observe coronary lumen for a longer time period without causing myocardial ischemia. Nowadays, a balloon occlusion type CAS is not available for commercial reasons. We can observe coronary lumen continuously from distal are to the ostium of coronary vessels by pulling back the non-occlusion type CAS. Furthermore, we can also observe the same place for a long time to see the movement of the target object, by which we can detect the fracturing of thrombus or the protrusion of plaque debris from the ruptured plaque.

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We should be careful about the focus and color correction (white balance) of CAS image and about keeping the lens of CAS catheter clean when we prepare the system and catheter. After insertion of CAS catheter with guide extension or probing catheter into the distal part of the target lesion, we start observation and acquisition of image by flushing low molecular weight dextran through guiding catheter and/or guide extension catheter/ probing catheter. We continue observation and acquisition of image while pulling back the CAS catheter with guide extension or probing catheter slowly and carefully.

Assessment of angioscopic images

Plaque color

Coronary plaques can be classified into yellow or white. White plaques are commonly observed as the culprit of stable coronary artery disease, whereas yellow plaques are often observed as the culprit of acute coronary syndrome [1]. The yellow plaques are reported to have thinner fibrous cap and larger lipid core than white plaques [2]. Yellow plaques are further classified into grade 0 (white), grade 1 (light yellow), grade 2 (yellow), and grade 3 (intensive yellow) (Fig. 1), and the higher color grade yellow plaques have the higher probability of having thrombus suggesting that the plaque has already been disrupted. There is a significant negative correlation between yellow color grade and fibrous cap thickness assessed by OCT, and grade-3 yellow plaques are regarded as thin-cap fibroatheroma with the cap thickness of less than 65 µm, i.e., vulnerable plaque [3, 4]. Furthermore, the accelerated formation of yellow plaque, i.e., neoatherosclerosis, has been reported after first-generation sirolimus-eluting stent (Cypher stent) implantation [5], and the presence of in-stent yellow plaque (more than grade 2) at 1 year after implantation is a predictor of future stent failure [6]. Therefore, yellow plaque is the major cause of ACS and its detection is clinically very important. Although the lesion with superficial calcium deposition also appears yellow by CAS [7, 8], its cause and clinical implication remains controversial.

Plaque rupture

Plaque rupture is a major mechanism of ACS [9–11]. CAS can easily identify the ruptured plaque (Fig. 2) by detecting the protrusion of yellow intra-plaque material into lumen accompanied by thrombus, which often contains sparkling materials suggesting the presence of cholesterol crystals.

Plaque erosion

Plaque erosion is another mechanism of ACS [10, 12–14]. Eroded plaque by CAS is defined by the presence of thrombus without protrusion of yellow intra-plaque material (Fig. 2). Although it may possibly be a ruptured plaque with a very small rupture, we can usually judge if there is the protrusion of intra-plaque material into the lumen, i.e., plaque rupture, since CAS can provide a fine full-color three-dimensional video image of the vascular surface.

Thrombus

Thrombus is detected as a material adhering to the luminal surface or protruding into the lumen. Thrombus is classified into red, white, or mixed according to its color (Fig. 3). White thrombus is composed of platelets and fibrin, while red thrombus contains abundant erythrocytes in the fibrin network [15]. Reddish thrombi are often observed as the culprit of acute myocardial infarction where blood flow

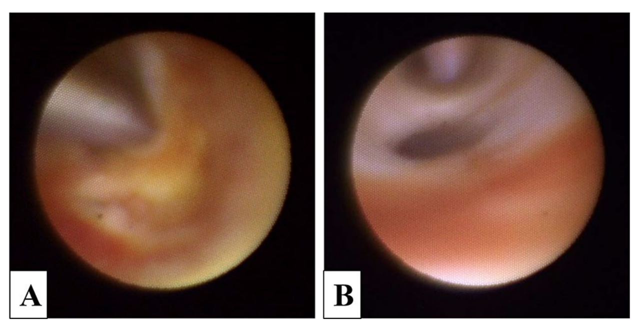
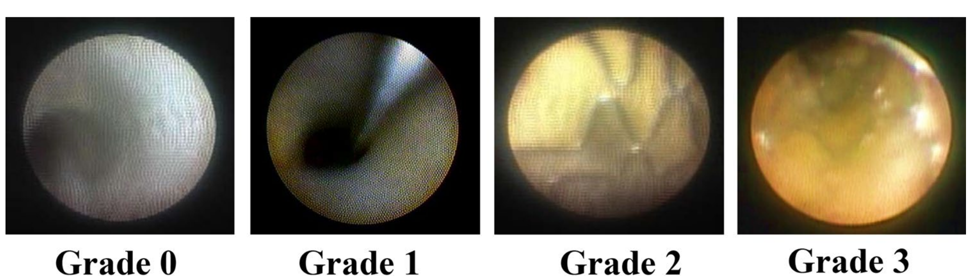


Fig. 2 Plaque rupture and erosion. **a** Plaque rupture, perforation of a fibrous cap overlying lipid core. **b** Plaque erosion., redding without trans-cap ruptures

Fig. 1 Grading of yellow color. Grade 0: white, grade 1: light yellow, grade 2: yellow, grade 3: intensive yellow



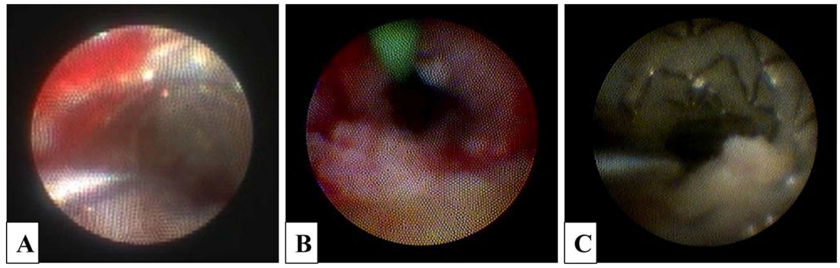


Fig. 3 Thrombus images. **a** Red thrombus, **b** mixed thrombus, **c** white thrombus

is significantly reduced, whereas white thrombi are often observed as the culprit of unstable angina or non-ST elevated myocardial infarction where blood flow is adequately preserved [10, 16].

Neointimal coverage after stent implantation

CAS is a useful tool to evaluate the time course of vascular response after coronary intervention. Novel findings such as delayed neointimal coverage and accelerated yellow plaque formation after drug-eluting stents (DES) implantation have been reported by many studies with angioscopy [5, 6, 17–21]. These findings would contribute to the development of new DES with better biocompatibility. Furthermore, early CAS findings on new DES would give us a caution on the bad later clinical outcomes as in the case of Cypher stent, in which a high incidence of very late stent thrombosis was suspected from the early CAS findings.

The degree of neointima coverage over the stent is usually classified into 4 grades: grade 0 (fully visible without coverage), grade 1 (stent with very thin neointima coverage), grade 2 (stent is completely embedded under neointima but seen translucently), and grade 3 (stent is invisible under neointima) (Fig. 4), although it is sometimes classified into 3 grades combining grade 2 and 3 as grade 2 [6, 20, 22]. Several studies demonstrated that the intra-stent thrombus adhesion is more frequently observed at the site of neointima coverage grade 0/1 than at the site of neointima coverage grade 2/3 [17–19, 23], suggesting that neointima coverage grade is correlated with the degree of re-endothelization. The neointima coverage grade is generally heterogeneous to some extent; therefore, the neointima coverage grade of a stent would be determined by the dominant grade or by the minimum and maximum grade in the stent. Furthermore, the heterogeneity of the grade is presented by the heterogeneity index calculated by maximum–minimum grade [24–26].

A yellow plaque newly formed inside the stent is recognized as neoatherosclerosis [5, 27], which would be accelerated by poor re-endothelization and prolonged inflammatory reaction [28]. First-generation sirolimus-eluting Cypher stent is known to accelerate the formation of yellow plaque in the stented site [5]. Yellow plaque is more frequently observed after first-generation bioresorbable vascular scaffolds (ABSORB) implantation than after everolimus-eluting stent implantation [29]. The presence of yellow plaque after stent implantation is a predictor of future stent failure [6]; therefore, CAS should be a useful tool to detect high risk patients of future stent failure.

Observation of other vessels by angioscopy

If blood is cleared away from the viewing area , angioscopy can observe any vessel including aorta [30, 31], carotid artery [32], pulmonary artery [33, 34], and lower extremity peripheral artery [35, 36]. There would be a new world in those vessels to which we are blinded. Angioscopic observations of those vessels would give us much new inspiration to clarify the pathophysiology of various vascular diseases.

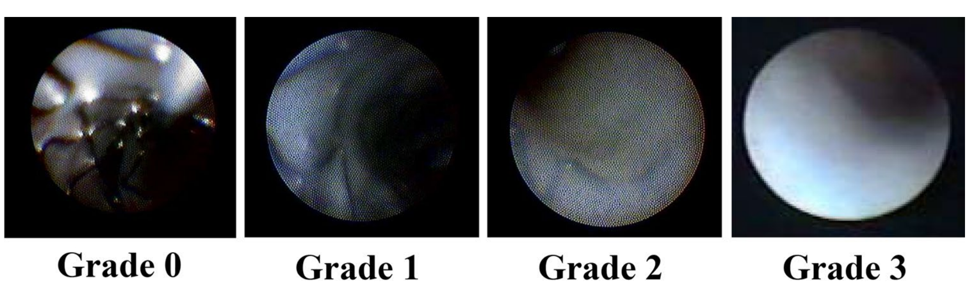


Fig. 4 Grade of neointimal coverage. Grade 0: fully visible stent struts similar to immediately after stent implantation, Grade 1: stent struts with very thin neointima, but protruded into the lumen and transparently visible, Grade 2: stent struts embedded by neointima but seen translucently, Grade 3: stent struts fully embedded and not visible

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Declarations

Conflict of interest All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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