Plaque Characterization and Atherosclerosis Evaluation by Coronary Angioscopy

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Abstract

When observed by angioscopy, the culprit lesions of acute coronary syndrome (ACS) have a common appearance of a yellow plaque with irregular surface covered by a thrombus. Angioscopy is a powerful device to detect not only the ruptured plaques at ACS lesions but also the yellow plaques in their early stages. The culprit lesions of ACS are sometimes detected by angioscopy even in the angiographically normal segments of coronary arteries. Angioscopy can further classify the culprit lesions of ACS as (1) vasospasm, (2) plaque rupture, or (3) plaque erosion according to the angioscopic definitions. These classifications may be beneficial to determine the treatment strategy. Anti-vasospastic medications rather than stenting may be more suitable for the treatment of vasospasm-induced ACS. Percutaneous coronary intervention (PCI) of ruptured plaque rather than of erosive plaque tends to cause more distal embolization with thrombus and plaque contents. Therefore, distal protection device may be more beneficial for those cases. Although angioscopy may be able to identify vulnerable plaques as the plaques of intensive yellow color, it may be more practical to identify the patients at high risk of suffering ACS by evaluating the extent of coronary atherosclerosis. The process and the time course of plaque formation, maturation, and disruption are left to be clarified, however, the number of yellow plaques or the yellow color intensity of those plaques may be a marker of coronary atherosclerosis. Angioscopy should be useful not only as a diagnostic tool but also as an investigational tool. The effect of medications that regress coronary atherosclerosis may be evaluated by the angioscopically determined markers of coronary atherosclerosis.

Key Words: Angioscopy · Yellow plaque · Thrombus · Acute coronary syndrome · Plaque rupture · Distal protection device

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Evaluation der Arteriosklerose und Plaquecharakterisierung durch koronare Angioskopie

Zusammenfassung

In der angioskopischen Darstellung zeigen Culprit-Läsionen beim akuten Koronarsyndrom eine gelbliche und unregelmäßige, mit Thrombus bedeckte Oberfläche. Die Angioskopie ist eine hervorragende Methode zur Detektion nicht nur der Plaqueruptur beim akuten Koronarsyndrom, sondern auch der „gelben Plaques" in frühen Stadien. Beim akuten Koronarsyndrom können Culprit-Läsionen sogar in angiographisch unauffälligen Koronarsegmenten erkannt werden. Weiterhin wird die Klassifizierung der Culprit-Läsion hinsichtlich 1. Vasospasmus, 2. Plaqueruptur oder 3. Plaqueerosion anhand angioskopischer Kriterien ermöglicht. Diese Klassifizierung kann unter Umständen wichtig für die Festlegung der Behandlungsstrategie sein. Bei Vasospasmus-assoziiertem akuten Koronarsyndrom würde die medikamentöse Therapie gegenüber einer Stentimplantation bevorzugt. Eine Koronarintervention bei Plaqueruptur kann im Vergleich mit der Plaqueerosion zu einer ausgeprägten distalen Embolisierung von Thrombus- und Plaquematerialien führen, weshalb hier unter Umständen ein Embolieschutz-Device eingesetzt werden sollte. Die Angioskopie kann bei intensiver Gelbfärbung eine Identifizierung der vulnerablen Plaque erlauben. Im Einzelfall ist es aber eher praktikabel, das Risiko eines akuten Koronarsyndroms abzuschätzen, indem das Ausmaß der koronaren Atherosklerose evaluiert wird. Es gibt noch eine Reihe offener Fragen zum Verlauf der Plaquebildung und -entwicklung und eventueller Komplikationen wie der Plaqueruptur. Die Anzahl der gelben Plaques oder die Intensität der Gelbfärbung mögen aber Marker der koronaren Arteriosklerose und ihrer Aktivität sein. Die Angioskopie bietet nicht nur als diagnostische Methode, sondern auch für wissenschaftliche Arbeiten mögliche Vorteile. Der Effekt von Medikamenten mit Einfluss auf die Arteriosklerose könnte durch die Analyse der angioskopischen Marker der Arteriosklerose verfolgt werden.

Schlüsselwörter: Angioskopie · Gelbe Plaque · Thrombus · Akutes Koronarsyndrom · Plaqueruptur · Embolieschutz-Device

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Introduction

The culprit lesions of coronary artery diseases have been evaluated by coronary angiogram, and some kinds of lesion characterization have also been done by angiography, e.g., concentric/eccentric lesions, smooth/irregular contour, thrombus, and dissection. However, the sensitivity of the angiogram to detect thrombus is extremely low compared with angioscopy, and the risk of suffering acute coronary syndrome (ACS) has never been successfully evaluated by angiography. Therefore, new diagnostic devices such as intravascular ultrasound (IVUS) and angioscopy were expected to analyze the coronary arteries and atherosclerotic plaques more precisely and to evaluate their risk of causing ACS. Many studies with these devices are trying to detect vulnerable plaques that may cause ACS in the near future. However, the characteristics of really vulnerable plaques have not been determined and are still being sought for by many investigators. We have observed various coronary arteries of stable and unstable diseases angioscopically and found coronary angioscopy to be a useful diagnostic and investigational tool in various situations, although our effort to detect vulnerable plaques is still under way.

Culprit Lesions of ACS

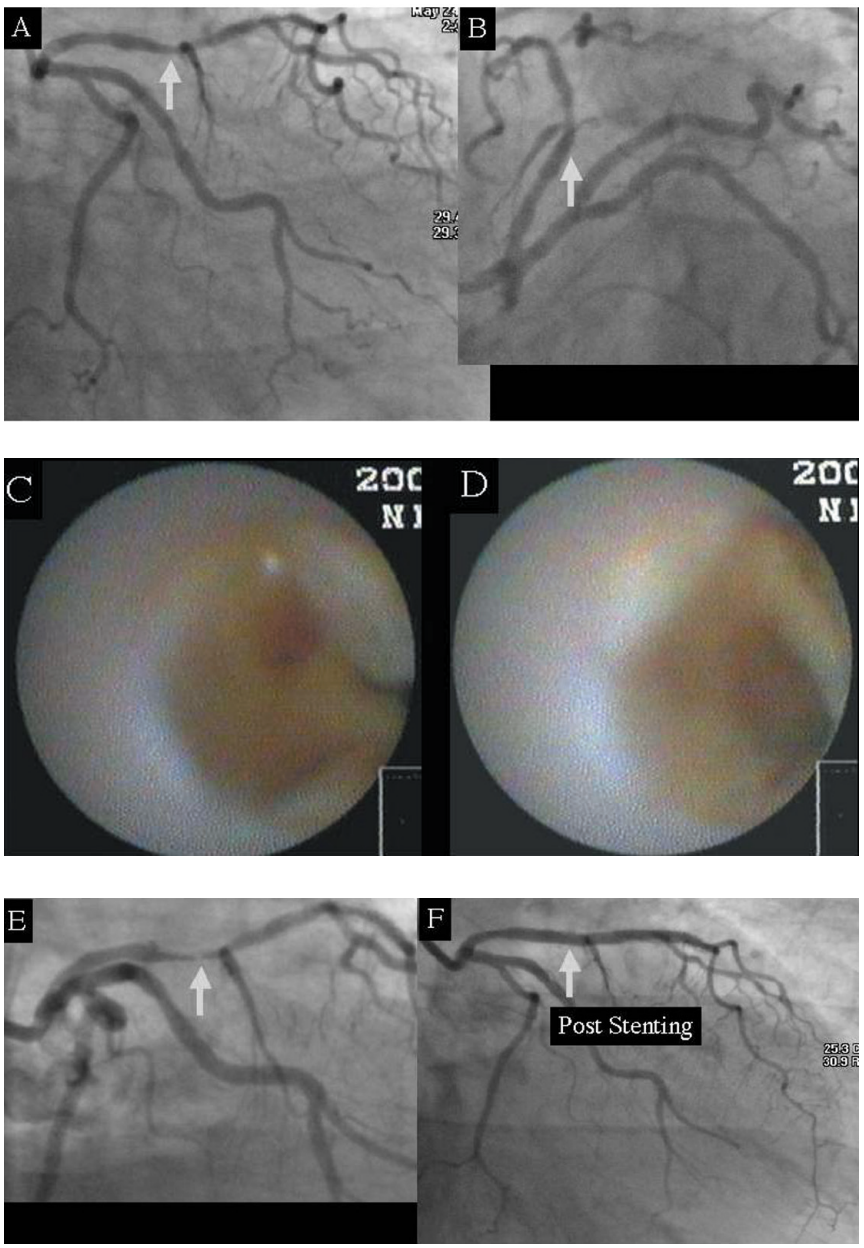
The culprit lesions of ACS have a common appearance of yellow plaques with a mixture of red and white thrombi, although predominantly white [1–3]. Culprit lesions of acute myocardial infarction tend to have more reddish thrombus than those of unstable angina, which sometimes have purely white thrombus. The surface of those plaques is usually irregular, and a protrusion of plaque contents is often observed. The mixture of plaque contents and white thrombus appears as "yellow thrombus". The thrombus and protruded plaque contents are easily fragmented and washed away into the distal arteries. The protrusion is often observed even after angiographically successful plain old ballon angioplasty (POBA). The culprit plaques of ACS usually have an intensive yellow color in the acute phase. However, the yellow color intensity of the plaque gradually decreases by 6–18 months after onset, and the prevalence of the plaque to have a thrombus also diminishes accordingly [4]. Thrombus on the culprit plaque of acute myocardial infarction is observed in 45% of patients without diabetes mellitus at 1 month, but in 78% of diabetic patients.

Diagnosis of ACS

Angiographically, severe coronary stenosis is not always detected in patients with suspected unstable angina who present with chest pain. In those cases, angioscopy is supposed to be a powerful device to confirm the diagnosis of an ACS. The culprit lesions of ACS show an appearance extremely different from the culpurit lesions of stable angina or from the normal coronary segments as described above and can easily be detected by angioscopy. The culprit lesions of ACS usually have angiographically detectable stenosis, also its severity varies widely. However, we have seen some patients in whom an ACS lesion was detected in the angiographically normal coronary segment. In ACS lesions with ruptured plaque, the vessel lumen is often narrowed by protruded plaque contents and thrombus without presenting angiographic stenosis, not only before percutaneous coronary intervention (PCI) but even after successful dilatation by POBA. Therefore, it is not surprising that the culprit lesion of ACS can occlude abruptly even after angiographically successful dilatation by POBA. If, angiographically, no severe stenosis and, angioscopically, no ACS lesions are detected in patients with unstable angina, vasospastic angina must be suspected. In general, the culprit lesions of vasospastic angina are angioscopically white and no yellow plaques are observed.

Classification of ACS Lesions

The culprit lesions of ACS can be classified into three groups by the angioscopic findings: (1) ruptured yellow plaque with its contents protruded into the lumen mixed with massive thrombus (plaque rupture group), (2) mural thrombus over yellow plaque without obvious protrusion (plaque erosion group), and (3) no yellow plaque or adhering thrombus after reperfusion (secondary thrombosis after vasospasm may play a role, vasospasm group). According to our data, slow-flow phenomenon, abrupt closure after POBA, and large infarct size are more often observed in the plaque rupture group than in the plaque erosion group. Embolic substances are collected by distal protection device in the plaque rupture group rather than in the plaque erosion group. Therefore, the suppression of protruded material by stent or the prevention of distal embolization by distal protection device should be more effective in patients belonging to the plaque rupture group. For patients of the vasospasm group, calcium antagonist and nitrate may be effective to prevent recurrence and



Figures 1A to 1F. Patient with ruptured plaque and thrombus in the angiographically normal segment presenting no symptoms. Follow-up angiography was performed 6 months after PCI at the distal LAD (A, B). Angioscopically, a ruptured plaque with thrombosis (C, D) was observed in the proximal LAD where no stenosis was detected by angiography (A, B, arrow). The patient suffered unstable chest pain symptoms about 1 week later. At this time, angiography revealed severe stenosis (E, arrow) in the segment where the ruptured plaque had previously been detected. Stenting was successfully performed (F, arrow).

Abbildungen 1A bis 1F. Asymptomatischer Patient mit Plaqueruptur und Thrombusbildung im Bereich eines angiographisch normalen Koronarsegments. Nach einer Intervention im Bereich des distalen RIVA (A, B) erfolgte nach 6 Monaten eine erneute Angiographie. Angioskopisch zeigte sich eine Plaqueruptur mit Thrombusauflagerung im proximalen RIVA (C, D), die angiographisch stumm blieb (A, B, Pfeil). 1 Woche später entwickelte der Patient eine instabile Angina. Jetzt zeigte sich eine angiographisch hochgradige Stenose (E, Pfeil) im Bereich der Plaqueruptur, die zuvor angioskopisch dargestellt worden war. Die Stenose wurde erfolgreich mittels Stentimplantation behandelt (F, Pfeil).

stenting may not be necessarily required. Thus, angioscopic observation and classification of ACS lesions should be useful to decide on the treatment strategy.

Vulnerable Plaques and Atherosclerosis

The characteristics of vulnerable plaques have been speculated about from the appearance of ACS lesions, but have not been clarified yet. Angioscopically, yellow lesions are considered more vulnerable than white ones. Furthermore, the intensity of the yellow color is known to be associated with the size of lipid core and the thickness of fibrous cap and is supposed to be a marker of vulnerability. We classified the color of plaques as 0 (white), 1 (slight yellow), 2 (yellow), or 3 (intensive yellow) [4], and showed that the incidence of thrombosis and of positive remodeling at the plaque was higher for plaques of a higher yellow color grade. Therefore, the plaques of intensive yellow color are supposed to be vulnerable, although their risk of causing ACS events has not been clarified. We have observed coronary arteries of > 1,000 patients by angioscopy, but rarely experienced ACS occurring at the previously observed vessel segment. Therefore, it can be stated that a grade 3 yellow plaque may be more vulnerable than a grade 1 yellow plaque, but not vulnerable enough to require urgent treatment.

We have previously reported that multiple yellow plaques are detected both in the infarct-related and non-infarct-related coronary arteries, and suggested that the formation of yellow plaques is a pan-coronary process [5]. Therefore, we hypothesized that the extent of coronary atherosclerosis could be evaluated by

(1) the number of yellow plaques (NYP) in a coronary artery, (2) their maximum yellow color grade (MCG), (3) their sum of yellow color grade (SCG), or (4) the index calculated as NYP × MCG. These angioscopic parameters of atherosclerosis were determined in 85 patients with acute myocardial infarction, and a comparison was made between those who suffered a secondary ACS event and those who did not during 5 years of follow-up [5]. The parameters were higher in patients who suffered a secondary ACS event, suggesting that angioscopically determined parameters of atherosclerosis reflect the risk of suffering ACS events. Therefore, we think it is more practical and beneficial to evaluate a patient's risk to suffer an ACS event than to find vulnerable plaques that cause such an event.

However, we experienced some interesting cases (Figures 1A to 1F) where ruptured plaque with massive thrombus was accidentally detected in the angiographically normal coronary segment. The patients had no symptoms on detection of the ruptured plaque. However, they suffered unstable angina within 1 week, and a severe stenosis emerged in the segment where the ruptured plaque had previously been detected. In our opinion, it takes some time from the onset of plaque rupture to the onset of unstable symptoms, at least in some patients. Therefore, an angioscopically detected ruptured plaque with massive thrombus in a patient without any symptoms or signs of myocardial ischemia might require PCI (especially stenting), although further investigation is necessary.

Future Directions of Angioscopy

It is now possible to evaluate the amount of lipid deposition or thinning of the fibrous cap only by the subjective classification of yellow color and the extent of atherosclerosis by the aforementioned simple parameters. Therefore, more objective and systematic methods to evaluate the color of plaques and the extent of lipid deposition in all coronary arteries would be required to improve the reliability of the judgment. The process of plaque maturation, rupture, thrombosis, and the onset of unstable symptoms must be clarified to identify really vulnerable plaques.

To treat intracoronary lesions more delicately, intracoronary observation by means of angioscopy may become a useful guide for the intervention. Removal of the ruptured plaque may represent an ideal treatment for culprit lesions of ACS to prevent abrupt closure, acute thrombosis, distal embolization, or even restenosis. Since angioscopy can easily detect the residual plaque, it is supposed to be a useful guide for this intervention.

After establishing the angioscopic evaluation of coronary atherosclerosis, angioscopy can be used as an investigational tool to evaluate the effect of drugs that target the regression of coronary atherosclerosis or the prevention of ACS events. Smaller-sized clinical trials may become possible when using the angioscopic parameters of atherosclerosis as an endpoint.

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