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Brief Clinical Perspective

Coronary Angiography Provides Considerable *in vivo* Pathophysiological Information on Coronary Artery Disease

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Abstract

Coronary cineangiography (CAG) has various limitations and pitfalls, but is widely accepted for evaluating coronary circulation. The interpretation of CAG focuses mainly on the extent and location of coronary artery disease. However, CAG can also provide considerable and varied *in vivo* pathophysiological information on coronary artery disease as follows:

Certain *in vivo* angiographic coronary morphologies are indicative of histological findings, such as ruptured atheromatous plaque with/without overlying thrombus. Such morphologies are commonly found in patent ischemia- or infarct-related arteries of patients with acute coronary events in both the acute phase and one month after standard medication, and the diseased portion with the morphology is highly specific to the culprit site. The rupture of plaque and overlaid thrombus is just as important in patients with acute coronary events who survive as in patients who die. Diseased sites with complex lesions are prone to progress toward clinical ischemic episodes. The severity of coronary narrowing immediately after acute coronary events does not influence later left ventricular function if antegrade coronary blood flow without distal filling delay is preserved. Coronary stenosis induced by plaque rupture and superimposed thrombus is likely to improve or disappear with time and/or anticoagulant administration with/without antiplatelet therapy.

Such information derived from CAG may improve the understanding and suggest optimal therapeutic strategies of coronary artery disease for individual patients.

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Key Words

■ **Angiography (coronary cineangiography)** ■ **Coronary artery disease** ■ **Plaque**
■ **Angioscopy** ■ **Diagnostic techniques** ■ **Atherosclerosis**

Coronary cineangiography (CAG) is widely accepted for the evaluation of coronary circulation (**Table 1**)[1]. However, CAG provides only a silhouette of the internal edges of the coronary artery, and the resolution is affected by many factors, mainly the resolving power of the equipment, and the conditions of exposing and developing the cinefilm. Consequently, small structures beyond the resolution of the equipment and certain anatomical findings such as slit-like, membranous or band-like obstructions, and intracoronary thrombus can hardly be detected. Dynamic phenomena that are inac-

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Table 1 Diseases requiring examination by coronary angiography

1. Coronary atherosclerosis
   1) Ischemic heart disease with transient/persistent supply and demand imbalance including thrombosis, superimposed spasm
   2) Sequential observation during coronary intervention including follow-up study/evaluation after coronary intervention
   3) Chronic atherosclerosis with change in myocardial substrate
2. Congenital abnormalities of coronary arteries
   1) Anomalous origin from pulmonary artery
   2) Other coronary arteriovenous-fistula
   3) Origin of coronary artery not from ordinal sinus of Valsalva
   4) Hypoplastic or aplastic coronary arteries
   5) Coronary-intracardiac shunt
3. Coronary artery embolism
   1) Aortic or mitral endocarditis
   2) Prosthetic aortic or mitral valves
   3) Abnormal native valves or left ventricular mural thrombus
   4) Platelet embolism
4. Coronary arteritis
   1) Polyarteritis nodosa, progressive systemic sclerosis, giant cell arteritis
   2) Mucocutaneous lymph node syndrome (Kawasaki disease)
   3) Syphilitic coronary ostial stenosis
5. Miscellaneous mechanical obstruction of coronary arteries
   1) Coronary artery dissection in Marfan syndrome, pregnancy or unknown etiology
   2) Prolapse of aortic valve myxomatous polyps into coronary ostia
   3) Dissection or rupture of sinus of Valsalva
6. Functional obstruction of coronary arteries
   1) Coronary artery spasm with/without atherosclerosis
   2) Myocardial bridges

Source: adapted with modifications from reference 1 [Myerburg RJ, Castellanos A: Cardiac arrest and sudden death. *in* Heart Disease: A Textbook of Cardiovascular Medicine (ed by Braunwald E), 5th Ed. WB Saunders, Philadelphia, 1997; p 748].

Selected abbreviations and acronyms

CAG = coronary cineangiography

tive at the time of CAG study cannot be detected by CAG. These include "Hit and run"[2] events such as coronary embolization or thrombosis with subsequent resolution, and coronary artery spasm. Furthermore, there are a number of problems with CAG. For example, eccentric obstructions may easily be underestimated or even overlooked while some are alleviated by minimal foreshortening and orthogonal view without overlapping.

Thus, the information obtained from CAG is limited, and the interpretations of CAG focus mainly on the extent and location of coronary artery disease. However, CAG includes and can provide considerable *in vivo* pathophysiological information if interpreted based on the following concepts. First, CAG findings are dynamic in nature, only demonstrating the angiographic profile of an individual patient at a specific point in time (**Fig. 1**). Second, both quantitative and qualitative assessment of each lesion with recognition and special attention to reconstructing the three dimensional structure of the diseased site may facilitate better understanding of the CAG findings as well as the pathophysiology in each patient.

Certain *in vivo* angiographic coronary morphologies are indicative of histological findings, such as ruptured atheromatous plaque with/without overlying thrombus[3-8]. We have shown occasional development of morphologies indicative of ruptured plaque at the site of occlusion, with recanalization and/or reduction of intraluminal narrowing after progressive removal of overlying thrombus and plaque content by thrombolytic therapy[5]. Recently, the diseased portion with such morphology was demonstrated to be highly specific to the culprit site[9], and the morphology is also commonly found in patent ischemia- or infarct-related arteries one month after acute coronary events in patients receiving standard medication without thrombolytic agents[9].

Serial or longitudinal *in vivo* observations can show that the rupture of plaque and overlaid thrombus is just as important in patients with acute coronary events who survive as in patients who die[6,7,10]; diseased sites with complex lesions are prone to progress toward clinical ischemic episodes[10-16]; the severity of coronary narrowing immediately after acute coronary events does not influence later left ventricular function if antegrade coronary flow without distal filling delay is preserved[17]; and coronary stenosis induced by plaque rupture and superimposed thrombus is likely to improve or disappear with time and/or anticoagu-

lant administration with/without antiplatelet therapy[6,18-20]. Intracoronary angioscopic observations have recently supported some of these findings[21,22].

Thus, CAG includes considerable *in vivo* information about coronary artery disease, although the interpretation of CAG is not definitive and CAG cannot identify the instability of plaques[23]. However, such *in vivo* morphologies found at the time of CAG examination have not yet been correlated with histological examination except in a few patients[6,7]. Clarification of what each morphology actually represents by means of histological correlation, and *in vivo* intravascular angioscopic and ultrasonic observations, the time course of the morphological changes, how this time course is modified by pharmacological interventions, and individual differences in the clinical course will improve the understanding of the CAG findings as well as the pathophysiology and may suggest the optimal treatment for individual patients. At present, anticoagulation with warfarin and/or antiplatelet therapy with aspirin is a common non-invasive strategy[6,18-20]. Antiangiogenetic and anti-inflammatory therapy and/or lipid lowering are also promising treatments[24-28].

No uniform relationship between clinical symptoms and CAG findings has yet been recognized, possibly because a broad spectrum of patients with coronary artery occlusion, varying widely in cause, are classified together under the single diagnosis of "coronary artery disease." The lack of a uniform relationship is also attributable to the types of studies performed, the patient populations studied, and definitions used. In addition, the time interval between the onset of symptoms and CAG study may also be very important, since the CAG study is often performed late after symptoms manifest.

CAG includes considerable *in vivo* pathophysiological information on coronary artery disease, which may provide better understanding and optimal therapeutic strategies of the disease for individual patients. CAG could be useful for evaluating the clinical features of coronary artery disease and selecting treatment.

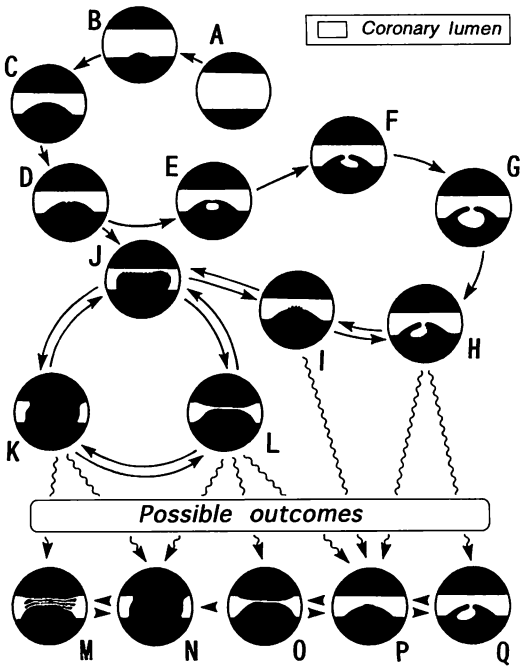

Fig. 1 Sequential changes in angiographic coronary morphology in patients with acute coronary events, based on previous observations[3,6,7,9,10,15-18]
The sequence has 3 stages. In the first stage, the atheromatous plaque becomes larger but the coronary lumen is not so severely occluded to reduce blood flow (A–C). In the second stage, the fibrous cap is disrupted, and the plaque content or atheromatous debris extrudes into the blood stream (D–G). In the third stage, thrombus overlies the disruption causing variable grades of reduction in the coronary lumen (H–L). In certain patients, thrombus accumulates at the site of intimal damage without plaque disruption[14-16], reducing the lumen (D to J–L). Possible outcomes are also presented (M–Q).

要　約

虚血性心疾患の診断における冠動脈造影の役割

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冠動脈造影は広く臨床に供用されている．しかし，多くの場合，読影は狭窄病変の有無とその部位診断，および狭窄度の判定が中心になっているように思われる．一方，造影像の一部は破裂粥腫や潰瘍形成，付着血栓などの組織所見を示唆することや，ある疾患には特有な造影像があることなども報告されている．更に，組織学的検討から示唆されたとおり，粥腫の破裂と血栓付着が急性心

事故の機序であること，一部の症例の造影所見は考えられていたよりも，はるかに短時間内に変化することがあることなども示されてきた．

今後，造影像と組織学的所見の関係が血管内視鏡や血管内エコー，組織学的検索などにより解明され，かつ造影像の経時的推移が明らかにされ，また，当該症例の病歴や臨床像，臨床データとの対比が行われれば，冠動脈造影は当該症例が予測される臨床経過の中のどのような断面に位置するのか，予後はどのように考えられるのか，どのような治療法が適切かなど，虚血性心疾患の病態の解明のみならず，治療法の確立，当該症例に対する治療法の選択やその効果の判定などに結び付く重要な情報を提示する検査法に発展しうる．

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