For the past several decades, the central hypothesis underlying acute coronary event and sudden cardiac death (SCD) risk has involved the concept of the “vulnerable” plaque, defined as an unstable plaque harboring high-risk features that is prone to spontaneous rupture. Yet, current diagnostic approaches, angiography in particular, can readily detect obstructive coronary artery disease (CAD) but remain unable to reliably identify individuals or lesions at risk for future plaque rupture and SCD. Furthermore, mildly stenotic plaques visualized on angiography have been linked to future cardiovascular events, secondary to positive remodeling with large extraluminal plaque constituents that are angiographically invisible. Here, we present a case of acute thrombotic coronary occlusion of a previously identified mildly stenotic plaque only 3 days prior, providing a frank illustration of the limitations of coronary angiography to identify high-risk plaque phenotypes.

A 73-year-old dyslipidemic, non-diabetic man was admitted to hospital complaining of progressively worsening chest pain associated with dyspnea while walking his dog over the past 3 weeks. He was an ex-smoker with a history of stage IA gastric cancer currently in remission, treated with local endoscopic control 4 months earlier. Electrocardiography showed terminal T-wave inversions in leads V5 and V6, and on laboratory testing the cardiac enzymes were negative. Based on clinical presentation, he was diagnosed with unstable angina (UA), and treated...
with oral aspirin 100 mg, clopidogrel 75 mg, and rosuvastatin 2.5 mg daily. Four days later, coronary angiography indicated severe stenosis (90%) in the proximal left anterior descending artery (LAD; Figure 1A Left). In addition, there was a mildly stenotic lesion in the proximal segment of the right coronary artery (RCA; Figure 2A). The LAD lesion was presumed to be the cause of the UA symptoms, and therefore percutaneous coronary intervention (PCI) of the LAD stenosis was carried out. In consideration of the potential need for future invasive procedures to treat gastric cancer, a bare metal stent (BMS) was used (3.5×15 mm; Multi-Link8; Abbott Vascular) followed by post-dilatation with a 3.25-mm non-compliant balloon (NC Quantum, Boston Scientific; Figure 1A Right). Following PCI, the UA completely resolved and he was discharged 2 days after the procedure. On the first day after discharge, however, the patient presented with severe persistent chest pain at rest lasting for 4 h. Electrocardiography showed ST elevation in leads II, III, aVF (3 mm) accompanied by reciprocal ST depression in leads I and aVL. He was thus diagnosed with acute inferior ST-elevation myocardial infarction, and emergency coronary angiography showed a thrombotic occlusion of the proximal RCA (Figure 2B), which had appeared as a non-significant, mild stenosis only 3 days earlier (Figure 2A). Primary PCI was carried out, restoring antegrade flow following manual thrombectomy and initial lumen expansion with a 2-mm semi-compliant balloon (Laxa, Goodman). Intravascular ultrasound (IVUS) showed plaque rupture at the culprit lesion site (Figure 2C Left). Positive vessel remodeling was more significant surrounding the RCA rupture site (Figure 2C Right), compared with the LAD lesion (remodeling index: 1.41 in RCA and 0.92 in LAD; Figure 1B). BMS (3.5×18 mm, Multi-Link8, Abbott Vascular) was deployed followed by post-dilatation using a 3.5-mm non-compliant balloon (Hiryu Plus, Terumo). Peak creatinine kinase was 841 IU/L. After clinical stabilization, the patient was discharged home without symptoms.

While major efforts have been undertaken to define strategies to identify specific lesions or individuals at heightened risk of future acute coronary events, as yet there are no reliable diagnostic approaches to identify such vulnerable plaques or individuals. Serial angiography suggests that most lesions causing future acute coronary syndrome (ACS) were only mildly stenotic before clinical onset,¹ and a prospective IVUS-based landmark study indicated that mildly stenotic atherosclerotic plaques on angiography responsible for future ACS had plaque burden that was significantly more advanced.² Despite the relatively poor predictive ability of IVUS-based studies to date, future multimodality intravascular imaging approaches may play an important complementary role in the identification and characterization of patients and plaques at elevated future cardiovascular risk. In order to identify high-risk coronary lesions, new technologies are being developed to characterize high-risk plaque biological signatures beyond structural plaque composition, such as molecular imaging.³ One promising new strategy involves intravascular near-infrared fluorescence molecular imaging, a high-resolution biological imaging approach to characterize high-risk coronary plaque features such as vascular inflammation and fibrin deposition.⁴

In the present case, while the mild RCA lesion may have been a second culprit stenosis at the time of initial PCI,
given that the pathology of ACS often involves multiple cycles of plaque rupture and healing as a mechanism of plaque growth, this phenomenon is not detectable on angiography, although high-sensitivity C-reactive protein significantly increased up to 21.6 mg/L at the day of initial PCI, compared to baseline (0.226 mg/L), suggesting vascular inflammation with plaque disability. Invasive IVUS or optical coherence tomography may have been able to visualize subclinical plaque rupture in the RCA, but intra-coronary imaging has its own inherent risks and is generally not advised in non-culprit vessels. Therefore, this case highlights the severe limitations of current clinical coronary imaging to provide critical information on the potential for subsequent critical coronary events. With the development of new multimodality imaging technologies that include plaque biological readouts, identification of high-risk plaque features that may predict clinical outcomes represents a new opportunity to improve the understanding and prevention of ACS or SCD.

**Disclosures**

The authors declare no conflict of interest.

**References**