Angioscopy applies fiber-optic technology to directly visualize the luminal surface of the arteries and is able to characterize plaque composition on the basis of luminal appearance. In native coronary plaques, the grade of yellow color as defined by angioscopy is correlated with fibrous cap thickness.\(^1\) According to a previous pathological and clinical review,\(^2\) the following major criteria are necessary for the detection of vulnerable plaque: 1) active inflammation with extensive macrophage accumulation; 2) thin fibrous cap with a large lipid core (thin-cap fibroatheroma: TCFA); 3) endothelial denudation with superficial platelet aggregation; 4) fissured/injured plaque; and 5) severe stenosis. The minor criteria for the detection of vulnerable plaque include the following: 6) superficial calcified nodules; 7) yellow color (on angioscopy); 8) intraplaque hemorrhage; 9) endothelial dysfunction; and 10) expansive (positive) remodeling.\(^2\) Therefore, angioscopy can partly identify the features of vulnerable plaques e.g. 4) fissured/injured plaque, 5) severe stenosis and 7) yellow color (on angioscopy).

Many clinical studies have investigated the pathogenesis of vulnerable plaques in native coronary plaques using angioscopy.\(^3\)\(^-\)\(^5\) However, there have been few clinical studies that have elucidated the pathogenesis of neointimal proliferation after coronary stent implantation using angioscopy. In this issue of the journal, Sato et al. have reported that the minimum neointimal coverage grade was significantly greater and yellow color grade was significantly lower in patients with diabetes mellitus (DM) receiving a first generation drug-eluting stent (DES) than in patients without DM.\(^6\) However, these results did not suggest that the lesion implanted by the first generation DES was better covered and more stable. The results of this study merit attention. The lower yellow grade of the lesions after DES implantation in patients with DM does not imply that the lesions were desirable, because interpretation of the color differs between native coronary plaques and lesions after stent implantation. Greater thickness of neointimal proliferation is an adverse phenomenon in the context of stent implantation. Tanaka et al. previously demonstrated that neointimal coverage and neointimal thickness were greater in patients with DM than in patients without DM after DES implantation.\(^6\) The results reported by Sato et al. were concordant with these previous results.\(^6\)

From the pathological standpoint, increased smooth muscle cell proliferation in patients with DM results from the effects of platelet-derived growth factor (PDGF) and insulin-like growth factor that stimulate excess extracellular matrix production and cell growth.\(^8\)\(^,\)\(^9\) PDGF is known to be the main contributor to the intimal thickening induced by balloon catheter injury, one of several forms of arterial injury.\(^9\)

It has been shown that vascular matrix accumulates proteins modified by advanced glycosylation end-products (AGEs), and time-dependent glucose-induced deposition of AGEs on matrix proteins may promote monocyte infiltration into the sub-endothelium.\(^9\) Therefore, vascular responses after vascular injury might differ between patients with DM and those without DM, particularly after coronary stent implantation. Angioscopy can visualize only the luminal surface, whereas pathological degeneration after DES implantation is more complicated. Inoue et al. reported the relationship between neointimal color detected by angioscopy and thickness and patterns of neointimal prolifera-
tion evaluated by optical coherence tomography (OCT) after DES implantation.\textsuperscript{10} Low-intensity neointimal proliferation detected by OCT showed as a yellow color, whereas high-intensity homogenous neointimal proliferation showed as a white color by angioscopy.\textsuperscript{10} However, the color of the thickened low-intensity neointimal proliferation has not been fully clarified. As shown in Fig. 1, the color of neointimal proliferation after stent implantation is determined according to a two-by-two matrix, whereas that of native plaques is determined only by the thickness of the fibrous cap.\textsuperscript{1} In this issue of the journal, Sato et al. have raised an important issue about the color after DES implantation in patients with DM.\textsuperscript{6}

Regarding second generation DES, the authors demonstrated that vascular responses after DES implantation were similar in patients with DM and in patients without DM.\textsuperscript{6} This result reinforced previous optical coherence tomography studies.\textsuperscript{11-13} On the other hand, Komatsu et al. reported an intriguing study showing that the degree of neointimal proliferation was associated with insulin resistance evaluated by the homeostasis model assessment of insulin resistance (HOMA–IR) index, even after second generation DES implantation.\textsuperscript{14} Studies including many patients and dividing them into sub-groups by their background will be required to elucidate the features of vascular response after second generation DES implantation.

**Disclosure Statement**

I have no financial or other relations that could lead to conflict of interest.

**References**


