Commentary

Mechanisms of stent thrombosis: insights from optical coherence tomography

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Although the improvement of coronary stents and medical agents has reduced adverse cardiac events in patients undergoing percutaneous coronary intervention (PCI), stent thrombosis (ST) still remains one of fatal complications of stent therapy. However, the pathophysiology of ST has not been sufficiently established yet, and factors including comorbidities such as diabetes mellitus, stent design, and patients' response or adherence to antiplatelet therapy have had the association with ST occurrence (1,2). Recently, a large prospective registry study investigating the intravascular morphologies of coronary stents in patients suffering from ST was published (3). Using optical coherence tomography (OCT) that had higher resolution than intravascular ultrasound, the study demonstrated the underlying mechanisms of ST, helping to guide the ST treatment (3). In this article, ST-related factors focusing on coronary stents are discussed.

Stent malapposition and under-expansion

Stent malapposition is defined as separation of at least 1 stent strut from the intimal surface of the arterial wall that is not overlapping a side branch (4). Because these floating struts are associated with delayed healing after stent implantation, especially drug-eluting stent (DES), malapposed stents have been considered as a potential risk for the development of ST. However, clinical data about stent malapposition have been controversial. In intravascular ultrasound study investigating the long-term prognosis of late stent malapposition that was detected at 6 months after DES implantation, the stent malapposition was not associated with any major adverse cardiac events during a subsequent 10-month follow-up (4). A similar finding was observed in an OCT study, in which adverse cardiac events did not occur in patients with late stent malapposition during follow-up of mean 28 months after DES implantation (5). Contrary to these studies, cross-sectional OCT studies showed that the malapposition was a leading cause of early, late, or very late ST (3,6). These discrepancies were partly explained by the finding that stent malapposition could be spontaneously resolved over time (5,7). As a determinant for the resolution of stent malapposition, the distance between malapposed strut and vessel wall was proposed: the greater the distance, the more persistent the malapposition (8). In the study by Souteyrand *et al.*, the average maximal malapposition distance was 710 μm, indicating the severe malapposition (3).

Factors causing stent malapposition are multifactorial. During stent implantation, malapposition can occur for stent under-expansion, or appear for follow-up period due to positive vascular remodeling of stented lesion. In some cases presented with acute coronary syndrome, thrombus between struts and vascular wall may spontaneously dissolve, causing the malapposition. However, the important thing here is that inadequately expanded stent during PCI can be fully preventable using intravascular imaging modalities. Until recently, it has not been determined whether the routine usage of the imaging devices for PCI is beneficial or not. Nevertheless, the usefulness of intravascular imaging seems to be robust to achieve the optimal stent expansion, and to minimize large stent malapposition. Considering

the delayed healing of malapposed stents, the finding that stent malapposition and under-expansion were prominent mechanisms for early ST is not surprising.

Neoatherosclerosis

Emerging evidences have established that neoatherosclerosis, atherogenesis within neointima of implanted coronary stent, is one of mechanisms causing late stent failure. According to the pathologic study, neoatherosclerosis was not rare, and could have unstable features such as thin cap or rupture of neointimal tissue (9). In several OCT studies, neoatherosclerosis was more identified in patients presented with acute coronary syndrome than in those with stable restenotic lesion, resulting in more target lesion revascularizations (10,11). Thus, neoatherosclerotic lesion could be manifested with wide spectrum from stable coronary artery disease to acute myocardial infarction including late or very late ST (12). This feature was also confirmed in ST registries, in which ruptured neoatherosclerosis, as well as stent malapposition, was a frequent OCT finding in patients suffering from late or very late ST (3,6). Although the pathophysiology of neoatherosclerosis has remained unknown, several OCT studies suggested that specific factors such as stent type, stent age, patients' characteristics including current smoking, chronic kidney disease, usage of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockade, and the concentration of low-density lipoprotein cholesterol were associated with the presence of neoatherosclerosis at follow-up (13-15). Accordingly, the continued medical care for the inhibition of neoatherosclerosis may be warranted in patients receiving coronary stents.

Importantly, the OCT study from Souteyrand *et al.* revealed the underlying morphological abnormalities in most ST cases, introducing the possibility of patient-tailored therapy (3). For example, in ST resulting from malapposition, a simple balloon angioplasty may be sufficient to restore the coronary flow, and to attach malapposed struts to vascular wall. On the contrary, an additional stent implantation may be not beneficial without resolving the malapposition. In patients with neoatherosclerosis, a plain balloon angioplasty may be not appropriate to inhibit the future growth of neoatherosclerotic neointima. These individualized strategies, based on the mechanisms of ST occurrence, look reasonable, but it is not easy to prove the benefits of these approaches because the incidence of ST is quite low, requiring a large study population for screening. In the 2011 ACCF/AHA/SCAI guideline for PCI, the treatments of patients presented with ST were not established, thus emphasizing the importance of ST prevention that included ensuring compliance with dual antiplatelet therapy and adequate stent sizing and expansion (16). However, given the poor prognosis of ST, it is necessary to consider the specific treatment strategy based on intravascular imaging in patients undergoing ST.

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Footnote

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