Late Stent Failure in Clinical Trials

Although the early failure of drug-eluting stents (DES) is mainly associated with procedural factors, the mechanism for late DES failure has not been fully clarified. However, neoatherosclerosis or progression of atherosclerosis in the stented segment has been regarded as a major mechanism of late DES failure. Long-term follow-up of large clinical head-to-head trials has recently shown that the Endeavor zotarolimus-eluting stent (ZES-E) has a similar outcome to the Cypher sirolimus-eluting stent (SES-C) at 5 years, although the ZES-E has a larger late loss and thus a larger target lesion revascularization (TLR) rate within 1 year. Judging by the long-term follow-up results from clinical trials of each DES, the ZES-E has a low incidence of late TLR events after 1 year, although both the first-generation DES and one of the newest DES Xience everolimus-eluting stents (EES-X) have a steep increase in late events after 1 year up to 5 years (Figure).

Neoatherosclerosis as a Cause of Late Stent Failure

Late DES failure presents as stent thrombosis or restenosis, and some studies using intracoronary imaging have shown that both are associated with atherosclerosis and thrombus formation. Therefore, the higher frequency of late events with the SES-C than with the ZES-E suggests faster progression of atherosclerosis in SES-C than in ZES-E. It has been reported that implantation of SES-C makes the lesion more yellow in appearance at 1-year angiographic follow-up, suggesting that SES-C accelerates the progression of atherosclerosis. This phenomenon has never been observed after bare metal stent (BMS) implantation, which usually makes the lesion white, even when implanted in ruptured yellow plaque. Segments with ZES-E implantation usually become white at 1-year follow-up, similar to BMS, because of the formation of thick, white neointima.
over the stent. The prevalence of yellow plaque with ZES-E has been reported as 58% at 4 months and 13% at 8 months. Therefore, lesion color at 1 year, as a marker of atherosclerosis progression, may be a factor associated with the future event of DES failure. SES-C accelerates the progression of ath erosclerosis and ZES-E, like BMS, resets the atherosclerosis by sealing and shielding it under the stent by a thick, fibrous nonatherosclerotic neointima. It takes a longer time for the occurrence of very late stent thrombosis after BMS implantation than after DES implantation.

Evaluation of Neoatherosclerosis by Coronary Imaging

It is therefore important for coronary imaging to be able to evaluate the extent of atherosclerosis in segments with stent implantation. Angioscopy gives full-color real-time images of the luminal vessel wall, whereas intravascular ultrasound (IVUS) and optical coherence tomography (OCT) give reproduced images of vessel wall using sound or light. Angioscopic images could be translated by the accumulated information of macroscopic pathology, whereas IVUS and OCT images require pathological validation for their interpretation and definition. A major limitation of IVUS and OCT is that each tissue is characterized according to methodology specific definitions. For example, we know what red or white thrombus looks like and can detect them on angioscopic images; however, in OCT images, red or white thrombus is judged by separate definitions. Another problem for imaging is that the tissues are not pure (eg, a mixture of necrotic core, fibrous tissue, calcium, and thrombus). Furthermore, the composition of a thrombus changes during the process of organization. However, the most important thing is the purpose of each imaging technique, which is not to get closer to pathology. If the purpose is to predict future ACS events, we should evaluate the value of imaging by how well it can predict the event regardless of what the image means pathologically.

In this issue of the Journal, Inoue et al examine 26 coronary segments by angioscopy and OCT at 10 months after the implantation of SES-C to evaluate neoatherosclerosis. They divided the segments into white or yellow by angioscopy, and divided the yellow segments into 3 groups according to the OCT findings: high-attenuation tissue covering struts, high-attenuation tissue underneath struts, and low-attenuation and low-intensity tissue covering struts. They regarded the high-attenuation tissue covering struts as neoatherosclerosis and found that macrophage-like appearance was most frequently detected in this group among the 3 groups. On the other hand, they reported that the detection of thrombus appeared to be better by angioscopy than by OCT (ie, some red thrombus detected by angioscopy did not fulfill the OCT criteria for red thrombus). They found thrombus only on the yellow area, which, consistent with previous reports, suggests that a thrombogenic lesion is well characterized by yellow appearance. From the angioscopic viewpoint, yellow and high-attenuation tissue covering struts would be atherosclerotic neointima formed after stent implantation; yellow and high-attenuation tissue underneath struts would be atherosclerotic tissue of the original vessel wall but might form after stent implantation; and yellow and low-attenuation+low-intensity tissue covering struts may also be atherosclerotic neointima of lower vulnerability. Angioscopically, the grade of yellow color of plaques is associated with their vulnerability.

The most important thing is not if this OCT classification well matches pathologic findings but if it can well predict the outcome. If the in-stent yellow plaques have different outcomes according to this OCT classification, this classification has great meaning. Although Inoue et al showed that it had good correlation with the presence of macrophage-like appearance, it does not necessarily mean a worse outcome. Yellow plaque of high-attenuation tissue underneath struts may also cause the next event by its disruption.

This OCT classification is just the beginning of the authors’ investigation and we are looking forward to seeing their next report showing a significant association between clinical outcome and this classification.

References