Recently, the incidence of restenosis after percutaneous coronary intervention has been greatly reduced by the widespread use of drug-eluting stents (DES). At the same time, however, safety concerns have been raised regarding the occurrence of late stent thrombosis (LST) after DES implantation. Although the mechanism of LST has not yet been fully explained, pathological data from a registry totaling 81 human autopsies of DES recipients revealed that the most powerful histological predictor of stent thrombosis was the degree of endothelial coverage, and that the best morphometric predictor of LST was the ratio of uncovered to total stent struts. Further, although the cases were collected before the DES era, a pathological analysis examining 13 cases with histological evidence of an acute occlusive or nonocclusive mural thrombus within a coronary stent in place ≥30 days showed that stenting across ostia of major arterial branches (5 cases) and exposure to radiation therapy (3 cases) were the most frequent pathological mechanisms of LST.

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Previous and recent angioscopic studies have shown that neointimal coverage (NIC) over bare metal stents (BMS) is usually completed within 6 months, but that NIC over DES is generally delayed. Recent reports using optical coherence tomography (OCT) assessment revealed that the incidence of complete NIC was less than 30% at 9–12 months after DES implantation. Accordingly, the lack or delay of NIC could be a possible explanation for the increased incidence of LST after DES implantation. DES at the site of side branches may be an especially high-risk combination for LST. In other words, stent struts placed across the ostia of the side-branch vessels could be typical candidates for LST, because of delayed NIC. However, few published data regarding NIC in such regions have been available until very recently.

Since 2011, several reports have demonstrated that variability among coronary stents in the strut coverage pattern assessed with OCT exists in the bifurcation. Kyono et al investigated 12,656 struts in 61 bifurcation segments (paclitaxel-eluting stent (PES): 16; sirolimus-eluting stent (SES): 14; zotarolimus-eluting stent (ZES): 23; BMS: 8) from 46 patients at 6 months after stent deployment. They found that PES had the highest prevalence of uncovered segments in the side-branch ostial region (PES 60.1, SES 17.0, ZES 13.2, BMS 12.3 (%), P<0.0001), whereas SES demonstrated the highest prevalence of uncovered segments opposite the ostial region (PES 3.3, SES 14.0, ZES 1.5, BMS 0.0 (%), P=0.0025). Her et al evaluated the degree of NIC crossing the side-branch vessel with OCT at 9.3 months after DES implantation. They found significant differences in the proportion of covered stents among the 3 DES types in 51 patients (62% of 356 struts, 20% of 165 struts, and 83% of 143 struts for SES, PES, and ZES, respectively; P<0.001). Further, the thickness of the neointimal hyperplasia in the SES group was significantly less than that with the ZES and BMS groups. In this issue of the journal, Liu et al used OCT to examine the frequency of NIC in segments with DES and PES placed across side branches. They report that SES and PES each had higher frequency of uncovered struts and thinner neointima than the struts with BMS. Further, they found that the frequency of uncovered struts for large side branches was greater than that for small ones for SES and PES, whereas there was no significant difference for BMS. To summarize these recent reports that have assessed NIC after stent implantation with OCT, the frequency of NIC in segments with DES across the side-branch ostia was less than that with BMS.

These reports have clinical importance because these give a support to the hypothesis that DES implantation at side branches is a high risk combination for LST. However, caution is needed before drawing this conclusion, because none of the studies have shown a direct association between the degree of NIC and the incidence of LST. The current foreign and Japanese guidelines recommend or suggest long-term use of dual antiplatelet therapies to prevent LST after DES implantation. However, there is no established evidence or recommendation regarding the type of patients or stents that should be treated with further long-term continuation of dual antiplatelet therapies. In this context, it is highly suggestive that Liu et al report a significantly increased incidence of absent or incomplete NIC over the struts across the side branches compared with that for the main vessels: 29.4% vs. 0.7% (P<0.001), 66.1% vs. 6.2% (P<0.001) and 58.6% vs. 4.0% (P<0.001) for BMS, SES, and PES, respectively, even though it was not emphasized enough by the authors. This observation by Liu et al suggests that the location of the implanted stent could be important information in the decision to continue or discontinue dual antiplatelet therapies in...
the clinical setting. In addition, differences in the stent platform or drug-release kinetics or the distribution of the DES should be of more concern in the near future because such difference could affect the incidence of thrombus formation over the stents and/or LST. Indeed, Hara et al reported that PES showed the highest incidence of thrombus formation compared with SES and BMS at 6 months after stent implantation. Accordingly, differences among DES in thrombus formation at the struts across side branches may be the next target for investigation. Anyway, the study by Liu et al provides us with important information about NIC at the stent struts across side branch ostia, although further investigations are needed to apply their observations to future clinical decision-making with regard to continuation of dual antiplatelet therapy and prevention of LST.

References