The use of drug-eluting stents (DES) has markedly reduced the incidence of stent restenosis, but other types of stent failure such as late catch-up phenomenon and very late stent thrombosis have been documented as major concerns after DES implantation. Delayed arterial healing with incomplete endothelialization or persistent inflammatory process with hypersensitivity reactions are reported among the causes of intermediate or late stent failure after DES implantation. Furthermore, several studies have reported the progression of neatherosclerosis after implantation of DES and bare-metal stents (BMS), which might be related to poor outcomes, although greater incidence and shorter duration of neatherosclerosis progression were observed after DES implantation.

Meta-analysis and randomized trials have reported that 2nd-generation DES show increased long-term safety and effectiveness over 1st-generation DES, likely because of the thin-strut platform coated with biocompatible polymer used in manufacturing 2nd-generation DES. Specifically, histopathological examination has revealed lower levels of fibrin, inflammation, and thrombosis inside 2nd-generation DES, and intracoronary imaging data demonstrate greater uniformity and reduced neointimal proliferation, suggesting less persistent inflammation.

In this issue of the Journal, Dai et al. show angioscopic...
findings with more homogeneous coverage with white neointima and less thrombus after 2nd-generation DES than with 1st-generation DES, and comparable to BMS. This is the first multicenter study performing a comprehensive comparison of 2nd-generation DES against BMS and 1st-generation DES in terms of angioscopic findings.\(^8\) It is known that heterogeneous or incomplete neointimal coverage is a risk factor for thrombus formation,\(^9\) and the presence of yellow neointima inside stents is related to neoatherosclerosis progression.\(^11\) Neointimal proliferation in the early phase <1 year after BMS implantation is considered as stable, and complete neointimal coverage (ie, the stent strut and underlying atherosclerotic tissues) could be achieved. Compared with BMS, 1st-generation DES show a higher frequency of incomplete neointimal coverage, residual yellow plaque, and thrombus. The results of the CAS examination by Dai et al demonstrate that 2nd-generation DES are similar to 1st-generation DES regarding clinical effectiveness (ie, reducing restenosis), and to BMS regarding safety in patients with acute coronary syndrome or stable angina pectoris.\(^8\)

An optical coherence tomography (OCT) examination can provide qualitative and quantitative data in the form of high-resolution in-stent images with a high level of reproducibility, which may allow accurate assessment of neointimal proliferation and classification of the neointimal tissue. On the other hand, CAS, which allows direct visualization, enables identification of vulnerable neointimal tissue characteristics. Identification of in-stent yellow plaque is important for the prediction of very late stent failure,\(^12\) and the superiority of CAS to OCT in terms of detecting stent thrombosis has been demonstrated.\(^11\)

Interestingly, the CAS study by Dai et al showed that yellow plaque or thrombus inside stents was less frequent but not uncommon even with 2nd-generation DES,\(^8\) which is consistent with the results of a previous study\(^13\) (Figure 1). A pathological study documented neoatherosclerosis progression even after implantation of 2nd-generation DES, although with lower frequency, longer duration, and increased stability compared with 1st-generation DES.\(^7\) The relationship between the incidence of neoatherosclerosis and adverse clinical events remains unclear in patients receiving 2nd-generation DES, although pathological findings may explain the mechanism underlying this relationship. A recent prospective study showed that the frequency of late stent restenosis is lower in patients treated with 2nd-generation DES, but may gradually increase with time.\(^14\)

Lee et al identified various patient characteristics, but not stent type as independent predictors for neoatherosclerosis progression.\(^13\) Several factors other than stent type, including lesion morphology, underlying plaque characteristics, stent age, and various patient characteristics such as risk factors for cardiovascular disease, or use of specific medication, may influence the formation and nature of the in-stent neointimal tissue. In the current study, risk factors for cardiovascular disease, such as hypertension or levels of low-density lipoprotein cholesterol, were identified as independent predictors for the formation of yellow plaque or thrombus inside stents. These findings suggest that, if such risk factors are present, strict management and careful follow-up should be considered even in patients who receive 2nd-generation DES.

Although the CAS-based comparison performed by Dai et al has provided an overview of the efficacy and safety of 3 types of stent expected during the 1st year after stent implantation, long-term and serial observations are needed to confirm the clinical effectiveness and safety of 2nd-generation DES. In addition, further study is warranted to clarify the influence of neoatherosclerosis on the likelihood and severity of future adverse events related to 2nd-generation DES implantation (Figure 2).\(^15\)

References


