Vessel Response After First- and Second-Generation Drug-Eluting Stent Detected by Optical Coherence Tomography

– Pathological Background and Clinical Importance –

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Although drug-eluting stents (DES) have dramatically decreased restenosis and target lesion revascularization rates, very late stent thrombosis has emerged as a new problem related to first-generation DES. Abnormal inflammatory vessel response to the polymer has been considered responsible for the development of stent thrombosis.¹ Pathological

examinations have revealed that in-stent neointima after implantation of a first-generation DES may contain inflammatory cells and fibrin. Recently, optical coherence tomography (OCT) has become widely available as a high resolution intracoronary imaging modality for detecting coronary plaque, providing the detailed morphological features related to unfavorable

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coronary events.²⁻⁴ Although intravascular ultrasound (IVUS) may still have the advantage over OCT of imaging the entire coronary vessel wall and detecting vessel remodeling,⁵ OCT has better resolution than IVUS and is therefore more suitable for detecting thin-cap fibroatheroma⁶⁻⁸ and in-stent neointima. Neointimal coverage,⁹ as well as in-stent neointimal tissue characterization,¹⁰ after DES can be clearly evaluated in vivo by OCT. Previously, Gonzalo et al classified the in-stent tissue pattern as homogeneous, heterogeneous or layered.¹⁰ It was, however, still uncertain if these differences in optical property reflected histological differences and clinical impact.

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In this issue of the Journal, Hiranuma et al¹¹ report their serial OCT imaging with pathological examination after implantation of first- and second-generation DES in a porcine coronary model. They compared the coronary vessel response at 1, 3 and 6 months after implantation, and found that the everolimus-eluting stent (EES) has more uniform neointimal coverage with less neointima and less persistent inflammation than the sirolimus-eluting stent (SES). In addition, they clearly demonstrated the relationship between neointimal tissue characterization by OCT and histological findings. They used mean signal intensity and attenuation to quantitatively and objectively assess tissue characterization and found that these indices related to vessel inflammation.

These results are interesting and may have clinical implications. However, they should be carefully interpreted. First of all, as the authors mentioned, stents were implanted in healthy coronary arteries of a porcine model rather than in diseased human coronary arteries. Therefore, the vessel response to each DES may be different in humans. In fact, neointimal proliferation after DES was more extensive in this porcine model than is found in clinical experience. Second, because truly “serial” pathological examination is impossible, the differences between 3 and 6 months may not reflect true “serial” changes in neointimal tissue. Despite these limitations, the findings from this study are important because they show the clinical implications of OCT-derived neointimal tissue characterization.

A recent study by Tada et al¹² suggested that the tissue characteristics of in-stent neointima may be related to mid-term results after paclitaxel-coated balloon (PCB) dilatation for in-stent restenosis (ISR). They found that the repeated ISR rate for lesions with a homogeneous pattern by OCT was significantly lower in the PCB group than in the balloon angioplasty alone group, but there was no significant difference between the 2 groups in the re-ISR rate for lesions with a heterogeneous or layered pattern. These results may be explained by differences in inflammation.

Another recent pathological examination of human in-stent neointimal tissue after first- or second-generation DES implantation revealed various degree of inflammation.¹³ Otsuka et al found that the inflammation score was low and fibrin deposition less frequent in lesions treated with EES than in those with SES or paclitaxel-eluting stent (PES). These results are concordant with those of the present study by Hiranuma et al.¹¹

Interestingly, despite the differences in inflammation, neo-atherosclerosis was similarly found in lesions treated with SES, PES and EES. Again, pathological examination does not provide serial changes of the same stented lesion. Therefore, these results should be confirmed clinically using serial, long-term

observation by OCT (Figure).

Very unusual and abnormal vascular structural changes, such as late incomplete stent apposition and multiple interstrut hollows, after SES implantation have been reported.^{1,14,15} These abnormal structural changes may also be caused by vessel inflammation after implantation of first-generation DES. It should also be investigated whether less inflammation after second-generation DES translates into absence or less frequent incidence of these abnormal structural changes at longer (>1 year) term angiographical or OCT follow-up (Figure).

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