A look at drug eluting stents with optical coherence tomography

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This editorial refers to ‘Neointimal coverage of sirolimus-eluting stents at 6-month follow-up: evaluated by optical coherence tomography’† by D. Matsumoto et al., on page 961

In the last year, following several publications in peer reviewed journals and presentations during the 2006 European Society of Cardiology congress,† concerns have been raised about a possible increase in the incidence of death and myocardial infarction in patients treated with drug eluting stents (DESs) due to the occurrence of stent thrombosis. The incidence of stent thrombosis in the bare metal stent (BMS) era has become low after the introduction of dual antiplatelet therapy.‡ Stent thrombosis in this setting is associated with persistent dissection, stent length, and final diameter. § With paclitaxel and sirolimus-eluting stents, premature discontinuation of thienopyridine therapy has become the most important risk factor for stent thrombosis.¶ In event-free patients 6 months after stent implantation, there was still an increase in death and/or myocardial infarction at 24 months follow-up in patients treated with DES without long-term thienopyridine therapy compared with DES with thienopyridine therapy. † This impact on outcome of clopidogrel was not observed in patients who received a BMS.

What could be the cause of this long-term increased thrombogenicity of DES? Two small Japanese studies using angioscopy¶¶ showed incomplete coverage of sirolimus-eluting stents of 20–87% of the stents and this was associated with the presence of strut-related thrombus material. Furthermore, an intravascular ultrasound (IVUS) study in patients with sirolimus-eluting stents found no or almost absent neointimal coverage in ~75% of the stents. †† However, the resolution of IVUS is too limited to accurately discern thin neointima. Therefore, Matsumoto et al. †² have used optical coherence tomography (OCT) together with IVUS and have reported their findings. OCT is an imaging modality based on the back reflection of infrared light where IVUS is based on the back reflection of ultrasound. †³

The catheter is small (0.017 in.) and image acquisition is fast. The axial resolution of OCT is superb (10–20 μm) compared with the axial resolution of IVUS (100–150 μm). However, there are two major limitations of this technique: (1) the penetration depth of OCT is only 1.25–2 mm and (2) the need for saline flushes for optimal imaging. A major effort has been taken to validate the ability of OCT to characterize plaque. The discrimination of a thin cap by OCT is excellent and it may even be possible that OCT is able to discern areas with macrophages and foam cells. This makes OCT the ideal tool to clarify the findings obtained with IVUS in the study of neointimal coverage of stents.

In the study of Matsumoto et al., †² 36 patients in whom a sirolimus-eluting stent was implanted were studied 6 months after stent implantation with angiography, IVUS, and OCT. Ticlopidine was discontinued 3 months after stent implantation. Using IVUS, no or almost no neointimal layer could be found. When looking with OCT at every separate stent strut, 91% of the struts were well apposed to the vessel wall and covered with neointima, 7% of the struts were well apposed without neointimal coverage, and 1% were malapposed to the vessel wall without neointimal coverage. In about 64% of the covered struts, the thickness of the neointimal layer was too thin to be discerned with IVUS. Therefore, it can be concluded that IVUS severely underestimates the neointimal coverage of DES. Nevertheless, these OCT data show convincingly that only 16% of all stents were completely covered. Therefore, in a majority of stents, a part of the stent remains susceptible for thrombosis. For not yet clarified reasons, the incidence of stent thrombosis is far lower than what you could potentially expect given the high percentage of uncovered stent struts. Although in this study no thrombus-related clinical events were reported, thrombus formation was found in several sirolimus-eluting stents. One thrombus was located at the site of a stent fracture and two were adjacent to malapposed struts without neointimal coverage. This study in 36 patients is too small to define the patient or lesion characteristics associated with absent neointimal coverage. The fact that highest incidence was found in overlapping sirolimus-eluting stent struts and the lowest incidence was found in restenosed BMS lesions, does give a direction for future studies.

Matsumoto et al. †² have performed an elegant analysis of the very important issue of neointimal coverage long-term

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after implantation of the current generation DESs. Their findings establish that OCT is the preferred technique to study neointimal coverage after stent implantation. Although large scale clinical trials will remain the cornerstone of further developments in (drug-eluting) coronary stenting, ‘neointimal coverage confirmed by OCT’ seems a perfect surrogate or intermediary endpoint to study the next generations of intracoronary stents.

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References