How to Treat Recurrences of In-Stent Restenosis?

Koh Arakawa and Fumitaka Ohsuzu

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Percutaneous coronary intervention (PCI) is widely performed for patients with ischemic heart disease. Restenosis is one of the pivotal problems of PCI. Drug-eluting stents (DES) dramatically reduce the restenosis rate after initial stent implantation, and it would seem that this problem has been resolved, but it is not yet completely resolved. Therefore, restenosis following PCI, even in an era of DES, is still a major target to overcome. The other problem is thrombosis. After stenting, dual antiplatelet therapy for several months reduces the frequency of subacute thrombosis. After discontinuation of antiplatelet therapy, late thrombosis frequently occurs in patients with DES implantation compared to those with bare-metal stent (BMS) implantation. Though, the deployment of DES is the gold standard treatment for preventing in-stent restenosis (ISR).

Once ISR has occurred, strategies to treat ISR remain problematic.

The most popular therapy for ISR after deployment of BMS is repeat PCI with balloon or cutting balloon which results in subsequent high recurrence rates (20-80% of restenosis rate depending on the restenosis pattern) (1, 2), and intracoronary radiation therapy (IRT) affording the best results (17-32% of restenosis rate) (3) at 6 months follow-up. In the long-term follow-up, recurrence rate and adverse cardiac events increased beyond the first 6 months in IRT for ISR, and these numbers have doubled in 3 years (4). Recently the challenges of DES implantation for ISR have been reported. Airoldi et al reported that the deployment of sirolimus-eluting stent is associated with a 57% reduction in binary restenosis compared with the cutting balloon treatment (5). Numerous prospective, multicenter randomized studies were performed to evaluate the efficacy of two types of DES (sirolimus- and paclitaxel-eluting stents) for the treatment of patients with ISR comparing with that of IRT. These studies demonstrated that the treatment of ISR with DES is superior in clinical and angiographic outcome than that of IRT; target lesion revascularization (TLR) was required for 19.2% in IRT, and for 8.5% in the sirolimus-eluting stent group, the rate of binary angiographic restenosis was 31.2% for IRT and 14.5% for the paclitaxel-eluting stent group (6, 7). Though, the reported rates of target vessel revascularization after DES for the treatment of ISR are still at 10%.

Furthermore, the treatment for repeat recurrent in-stent restenosis in patients who failed radiation therapy for previous ISR is also a problem. Waksman et al (8) studied 51 patients, who failed a previous brachytherapy following ISR after bare-metal stent deployment, with repeat IRT compared with repeat PCI. The repeat IRT group had lower rates of TLR than those of the repeat PCI group (23.5% versus 54.6%) and of major adverse cardiac events (29.4% vs 61.3%). They recommended considering the repeat IRT for this problematic patient subset as a therapeutic option.

Regarding DES deployment for this problematic patient subgroup, an interesting study was reported by Chu et al (9). They enrolled 88 patients who were present with recurrence after DES implantation for the treatment of ISR, and treated them with DES or PCI with repeat IRT. The immediate outcomes were excellent with both treatment strategies. But at the long-term follow-up (10 months), the results showed a lower tendency of target vessel revascularization (TVR) and a higher survival rate in PCI with the repeat IRT group. Therefore, the repeat IRT may have some benefit for this problematic patient subgroup with repeat recurrence after IRT.

In the DES era, repeat recurrence following DES implantation will also remain troublesome, even if the frequency is low. Reported risk factors for angiographic restenosis after DES deployment were small vessel size and use of a paclitaxel-eluting stent, and the traditional risk factor of diabetes mellitus was controversial (10). The restenosis rate following retreatment (about 60% of them were DES in DES group and the rest were balloon angioplasty) was 17.8% when the restenosis pattern was focal, but when the restenosis pattern was diffuse, the restenosis rate was up to 51.1% (11). The optimal PCI for restenosis is not conclusive at present. It will be necessary to wait for future studies to determine the best strategy, DES in DES, IRT, or coronary bypass grafting.

Department of Medicine, Division of Cardiology, National Defense Medical College
Correspondence to Dr. Koh Arakawa, karakawa@ndmc.ac.jp

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The case of Lan et al of this Journal had frequent recurrences of restenoses within a short time and was refractory to repeat PCI including DES (12). The authors could not disclose the reason why so many recurrences occurred following PCI. But this case report points to the necessity to consider the treatment strategies for ISR. In the special situation that IRT is not yet available in our country, we must choose the best treatment for each patient with repeat ISR among the limited strategies. That is, 1) how many times of PCI should be allowed for the treatment of ISR from the standpoint of the medical and economical views (for a patient to undergo repeat PCI with DES more than 2 or 3 times, the total cost is equal to CABG), and 2) when to choose the coronary artery bypass grafting surgery, at the second recurrence, third recurrence, or later? We do not have any answer to date.

A repeat coronary bypass grafting surgery may be associated with a high mortality rate, but fortunately, she has not undergone previous coronary artery bypass grafting. It is obvious that we should not exclusively depend on repeat PCI, and we should not hesitate to choose coronary bypass grafting for patients with repeat recurrences of restenosis as a therapeutic option, especially for the patient who has not undergone coronary artery bypass grafting surgery.

References


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