Application of Drug Eluting Stents to Clinical Practice in Japan
– Are We Going in the Right Direction? –

Jiro Aoki, MD, PhD

Interventional cardiologists started to use drug-eluting stent (DES) in daily practice in 2002 in Europe and 2003 in the United States. In Japan, DES were finally introduced in 2004. DES was developed to overcome in-stent restenosis (ISR), which has long been considered the main complication limiting the long-term efficacy of coronary stenting. When the initial clinical trials of the first DES reported zero-level rates of restenosis, we expected that we would overcome this powerful enemy and open the doors to a world without restenosis. After that, DES vs bare-metal stents (BMS) randomized pivotal trials showed that DES significantly reduced the ISR rate compared with BMS. As a result, the share of DES rapidly expanded and they have been used in more complex patients and lesions. However, a small number of patients with ISR after DES treatment still exists. DES cannot completely cut the Gordian knot of ISR. In September 2006, a new enemy, the so-called late stent thrombosis, emerged to overshadow the use of DES, and the long-term safety after DES implantation was called into question, especially after discontinuation of dual antiplatelet therapy. In addition, the COURAGE trial in April 2007 showed that percutaneous coronary intervention (PCI) with optimal medical therapy was not superior to optimal medical therapy alone in patients with stable coronary artery disease (CAD). After this new evidence, DES use declined in Europe and United States (Figure).

The current study also investigated the prevalence of DES in all PCI procedures. DES were used in approximately 80% of all stented cases in AP patients and one-third of all stented cases in acute myocardial infarction (AMI) patients. Interestingly, the proportion did not change from 2005 to 2007. DES use quickly spread and the proportion reached a plateau in the next year. In Europe and United States, the proportion of DES use decreased after the issue of late stent thrombosis. However, the proportion of DES in Japan did not decrease. In Japan, many hospitals perform PCI, although the number of PCIs might be underestimated compared with the actual number. The SYNTAX trial, the first large randomized comparison of DES and BMS was published at March 2009 and the result might affect the PCI to CABG ratio in Japan. In any case, after the introduction of DES, coronary interventions increased and conservative therapies decreased. Treatment options in Japan go in the opposite direction of the COURAGE trial, which supports the optimal medical therapies. Medical insurance for the whole nation might support physicians in preferring invasive therapies to conventional therapies.

Other important finding from the present study was the...
penetration of DES use in AMI patients. Despite AMI being an off-label use of DES, one-third of patients were treated with DES in all stented cases. Although the Horizons trial showed the efficacy and safety of DES in AMI patients, the use of DES should be carefully judged by a more individualized approach in emergency cases, because it is difficult to obtain patients’ baseline characteristics, such as compliance with dual antiplatelet drugs and the surgical plan, in such cases. The current study provides the proportion of DES use in AMI only, not ST elevation myocardial infarction (STEMI) and NSTEMI. The situation for these is different and it would be interesting to know the proportion of DES usage among STEMI patients in Japan.

Are we going in the right or wrong direction? Is the current proportion of treatment (DES, BMS, CABG, or conservative therapies) for CAD appropriate? Although overall in-hospital mortality in both AMI and AP patients decreased from 2004 to 2007, both cardiologists and cardiovascular surgeons should consider the cost-effectiveness of the current approach under the current strict national healthcare budget and the long-term outcomes after the current treatment options for CAD in order to establish the consensus guideline and the CAD treatment scheme in our country.

References