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Difference of Neointimal Formational Pattern and Incidence of Thrombus Formation Among 3 Kinds of Stents

An Angioscopic Study

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Objectives The purpose of this study is to compare the neointimal formational pattern and incidence of thrombus formation among sirolimus-eluting (SES), paclitaxel-eluting (PES), and bare-metal stents (BMS) with coronary angioscopy.

Background Neointimal formation and incidence of mural thrombus are different with the type of stent.

Methods One hundred successive patients who received 43 SES, 40 PES, or 32 BMS implantation underwent 6-month follow-up coronary angioscopy. We evaluated angioscopic parameters, including minimum and maximum neointimal grade; presence and number of red mural thrombus; neointimal grade around thrombus; and heterogeneity score, which is defined by subtracting minimum from maximum grade within 1 stent by classifying angioscopic neointimal coverage grades into 4 categories. We compared these parameters among 3 kinds of stent groups.

Results Heterogeneity scores of SES, PES, and BMS were 0.79 $\pm$ 0.60, 1.27 $\pm$ 0.75, and 1.03 $\pm$ 0.82, respectively ($p = 0.011$). The PES showed the highest incidence of angioscopic red mural thrombus (50% in PES, 12% in SES, and 3% in BMS, $p < 0.001$), and the number of thrombus observed within 1 stent in the PES group tended to be larger than those in the SES and BMS groups.

Conclusions At 6 months after stent implantation, PES showed the most heterogeneous neointimal formation and the highest incidence of thrombus formation compared with SES and BMS. (J Am Coll Cardiol Intv 2010;3:215–20) © 2010 by the American College of Cardiology Foundation

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Strong evidence of benefits with first-generation drug-eluting stent (DES) compared with bare-metal stent (BMS) both for on- and off-label indications have led to the use of DES in the majority of percutaneous coronary interventions (1,2). However, the risk of stent thrombosis after DES implantation remains a serious concern. One of the possible mechanisms for an increased risk of stent thrombosis in DES is delayed arterial healing and high incidence of mural thrombus, which have been revealed by several postmortem pathological studies and real-time imaging studies such as optical coherence tomography or coronary angioscopy (3–5). Moreover, neointimal formation is different with the type of DES (6,7).

The purpose of this study is to compare the neointimal coverage pattern and incidence of thrombus formation among sirolimus-eluting stent (SES), paclitaxel-eluting stent (PES), and cobalt alloy BMS with coronary angioscopy.

Methods

Patients. The study patients consisted of 100 successive patients who underwent single type stent implantation for de novo lesions, with SES (Cypher, Cordis, Miami Lakes, Florida), PES (Taxus Express2, Boston Scientific, Natick, Massachusetts), or BMS (Vision, Abbott, Saint-Laurent, Canada; and Driver, Medtronic, Santa Rosa, California). They all accepted 6-month angiographic follow-up with angioscopic assessment of the stent. We compared patient and lesion characteristics, late lumen loss with quantitative coronary angiography, and coronary angioscopic parameters among these 3 kinds of stent groups. Major adverse cardiac events (cardiac death, nonfatal myocardial infarction, or target vessel revascularization) were also assessed at 1 year after coronary angioscopy.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
DES = drug-eluting stent(s)
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)

All SES were implanted between September 2006 and May 2007, because SES was the only DES available in Japan during the period, and all PES were implanted between June 2007 and December 2007 in the same manner. The PES was approved for clinical use from May 2007 in Japan and became available in June 2007 at our institution. The decision to use either a BMS or DES was at the discretion of the attending physician, on the basis of the relative advantages and disadvantages of each type of stent (8). We defined late lumen loss as the difference between the minimum lumen diameter immediately after stenting and that at 6-month angiographic follow-up with quantitative coronary angiography with QAngio XA (Medis Medical Imaging Systems, Leiden, the Netherlands).

The ethics committee at Osaka Rosai Hospital approved this study, and written informed consent was obtained from all patients before catheterization.

Antiplatelet regimen. All patients received 100 mg aspirin during the follow-up period. Ticlopidine (200 mg) was given additionally as a dual antiplatelet regimen for at least 3 months after stent implantation in the SES group, for at least 6 months in the PES group, and for at least 2 weeks in the BMS group. The drug was changed to cilostazol (200 mg) if side effects were present. Dual antiplatelet therapy was ceased at attending physician's discretion.

Angioscopic technique and analysis. Angioscopy (Fiber Catheter, Fiber Tech, Chiba, Japan) was performed after follow-up coronary angiography after intravenous administration of 5,000 U heparin. The optical fiber was manually pulled back from the distal part of the stent to the proximal part under careful angioscopic and angiographic guidance to evaluate as many parts of stents as possible. Angioscopic images were recorded on digital video discs for subsequent analysis.

We classified neointimal coverage grade into 4 categories. Grade 0 represents stent struts without endothelialization showing glistening metallic luster similar to that immediately after stent implantation. Grade 1 represents stent struts with very thin neointimal coverage and visible metallic color but without metallic luster. Grade 2 represents stent struts without metallic color but not fully embedded in neointima. Grade 3 represents invisible stent struts with full neointimal coverage (Fig. 1). The best-covered segment was defined as the maximum grade, the worst-covered was the minimum grade, and heterogeneity score was defined by subtracting the minimum from maximum grade within 1 stent.

We also evaluated the incidence and number of red mural thrombus and neointimal coverage grade around thrombus. Red mural thrombus was defined as an isolated coalescent red superficial or protruding mass that could not be flushed out by dextran solution injection. Overlapping stent area was excluded from evaluations of this study. Two independent observers who were unaware of the clinical information analyzed the images.

Statistical analysis. Statistical analysis was performed with SPSS for Windows, version 11.0 (SPSS, Inc., Chicago, Illinois). We assumed that the data were approximately normally distributed. Continuous and ordinal variables were presented as mean ± SD. We employed analysis of variance for the evaluation of continuous variables and Kruskal-Wallis test for the evaluation of ordinal variables. Post hoc multiple comparisons were additionally performed for assessing neointimal coverage grade and heterogeneity score with Tukey's test or Games-Howell test after Levene's test for equality of variance, because a nonparametric multiple comparison test was not available with the statistical soft-