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Impact of Stent Overlap on Angiographic and Long-Term Clinical Outcome in Patients Undergoing Drug-Eluting Stent Implantation

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Objectives We compared the angiographic and long-term clinical outcomes of patients with and without overlap of drug-eluting stents (DES).

Background DES overlap has been associated with delayed healing and increased inflammation in experimental studies, but its impact on clinical outcome is not well established.

Methods We analyzed the angiographic and clinical outcomes of 1,012 patients treated with DES in the SIRTAX (Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization) trial according to the presence or absence of stent overlap and the number of stents per vessel: 134 (13.2%) patients with multiple DES in a vessel with overlap, 199 (19.7%) patients with multiple DES in a vessel without overlap, and 679 (67.1%) patients with 1 DES per vessel.

Results Angiographic follow-up at 8 months showed an increased late loss in DES overlap patients (0.33 ± 0.61 mm) compared with the other groups (0.18 ± 0.43 mm and 0.15 ± 0.38 mm, $p < 0.01$). The smallest minimal lumen diameter was located at the zone of stent overlap in 17 (68%) of 25 patients with stent overlap who underwent target lesion revascularization. Major adverse cardiac events were more common in patients with DES overlap (34 events, 25.4%) than in the other groups (42 events, 21.1% and 95 events, 14.0%) at 3 years ($p < 0.01$). Both the risk of target lesion revascularization (20.2% vs. 16.1% vs. 9.7%, $p < 0.01$) and the composite of death or myocardial infarction (17.2% vs. 14.1% vs. 9.1%, $p = 0.01$) were increased in patients with DES overlap compared with the other groups.

Conclusions DES overlap occurs in >10% of patients undergoing percutaneous coronary intervention in routine clinical practice and is associated with impaired angiographic and long-term clinical outcome, including death or myocardial infarction. (Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization; NCT00297661). (J Am Coll Cardiol 2010;55:1178–88) © 2010 by the American College of Cardiology Foundation

Stent overlap has been reported in as many as 30% of patients undergoing percutaneous coronary interventions owing to excessive lesion length, edge dissections, or incomplete stent coverage (1–3). Clinical outcome of patients with overlapping bare-metal stents (BMS) has been found to be inferior to that of patients treated with a single BMS, largely related to increased rates of target lesion revascularization (TLR) (4–7). The potent suppression of neointimal hyperplasia afforded by first-generation drug-eluting stents (DES) with a reduction in clinical and angiographic restenosis raised hopes of further improvement of results in patients with stent overlap (8–12). Yet, clinical outcomes of overlapping DES demonstrated conflicting results. A pooled analysis of studies assessing clinical outcomes of overlapping sirolimus-eluting stents (SES) showed similar rates of ischemic end points and repeat revascularization at both 30 days and 8 months compared with a single SES, and a significant reduction in the need for repeat revascu-

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larization compared with a BMS (13). Conversely, multiple overlapping paclitaxel-eluting stents (PES) were associated with improved efficacy but increased rates of periprocedural myonecrosis compared with overlapping BMS, presumably related to more frequent side branch compromise (14,15).

More recently, safety concerns surfaced with the use of first-generation DES during long-term follow-up, presumably related to delayed healing and impaired endothelialization (16). The latter phenomenon may be particularly pronounced at sites of DES overlap owing to increased drug and polymer concentrations. One experimental study specifically addressed the differential response of arterial healing at sites of DES overlap. Compared with nonoverlapping DES and BMS sites, overlapping DES segments showed more neutrophils, eosinophils, and fibrin deposition, suggesting impaired healing and increased inflammation (17). However, the impact of these findings on long-term clinical outcomes is not well established. The objective of the present study was to compare the angiographic and long-term clinical outcomes of patients with overlapping DES compared with those of patients with multiple DES with no overlap, or a single DES implanted in a vessel.

Methods

Patient population and intervention. The design of the SIRTAX (Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization) trial was previously reported (18). It was an observer-blind, randomized, controlled trial comparing the safety and efficacy of SES and PES in 1,012 patients undergoing percutaneous coronary interventions. Eligible patients had a history of stable angina or acute coronary syndrome and presented with at least 1 lesion with a stenosis ≥50% in a vessel with a reference vessel diameter between 2.25 and 4.0 mm suitable for stent implantation. There were no limitations on the number of treated lesions and vessels or lesion length. Before or at the time of the procedure, patients received at least 100 mg of aspirin, a loading dose of clopidogrel, and unfractionated heparin (70 to 100 U/kg body weight). After the procedure, all patients were prescribed lifelong aspirin therapy and clopidogrel for 12 months. All patients were requested at the time of randomization to undergo repeat angiography at 8 months. Subsequently, a research nurse contacted all patients and asked them at least once to schedule an appointment for repeat angiography. The study complied with the Declaration of Helsinki regarding investigations in humans and was approved by the research ethics committees at the University Hospitals of Bern and Zurich, Switzerland. All patients provided written informed consent.

Definition and end points. Stent overlap was defined as the presence of ≥2 stents within a single treated lesion and an overlapping stent zone of at least 1 mm, as determined by quantitative coronary angiography. Overlapping stent zones were identified based on the position of the stent balloon markers of the second stent relative to the first stent. Adverse events were assessed during the hospitalization, at 1, 6, and 9 months and at 1, 2, and 3 years. An independent clinical events committee unaware of the patient's treatment assignment adjudicated all end points. The prespecified primary end point was a composite of major adverse cardiac events (MACE), defined as cardiac death, myocardial infarction (MI), or ischemia-driven TLR at 9 months. Secondary end points included ischemia-driven TLR, target vessel revascularization, or target vessel failure at all scheduled follow-up visits. Definitions of ischemia-driven TLR, MI, and stent thrombosis were published previously (18).

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
MACE = major adverse cardiac events
MI = myocardial infarction
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TLR = target lesion revascularization

Quantitative coronary angiography. Coronary angiograms were digitally recorded at baseline, immediately after stent implantation, and at follow-up and were assessed at the angiographic core laboratory of the University of Bern. Digital angiograms were analyzed with the use of an automated edge-detection system (CAAS II, Pie Medical Imaging, Maastricht, the Netherlands). Quantitative measurements included the reference vessel diameter, the minimal lumen diameter, and percentage of diameter stenosis. Binary restenosis was defined as stenosis ≥50% in the target lesion at angiographic follow-up. All angiographic measurements of the target lesion were obtained within the stent and the areas 5 mm proximal and distal to the stent edge. All lesions of patients with stent overlap who underwent TLR at any time point up to 3 years were analyzed by quantitative coronary angiography to determine the zone of restenosis triggering the repeat revascularization and the site of minimal lumen diameter. The restenosis pattern was analyzed independently by 2 fellows in cardiology (L.R. and L.L.). In cases of disagreement, an external cardiologist who was not involved in the SIRTAX trial made the final decision.

Statistical analysis. For the purpose of the present study, we performed an analysis of clinical and angiographic outcomes stratified according to the presence or absence of stent overlap. Among patients without overlap, we specified 2 groups: the first group consisted of patients with multiple DES within a vessel but no overlap, and the second group consisted of the remaining patients who had a single DES implanted within a vessel.

Patient characteristics at baseline were compared among the 3 patient groups using chi-square tests for binary and maximum-likelihood linear regression models for continuous outcomes, which allowed the comparison of the 3 groups. In cases of multiple lesions in a patient, we restricted the analysis to the lesions that led to the final classification