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CLINICAL RESEARCH **Interventional Cardiology**

Multiple Overlapping Drug-Eluting Stents to Treat Diffuse Disease of the Left Anterior Descending Coronary Artery

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OBJECTIVES We sought to determine the safety and efficacy of using multiple overlapping drug-eluting stents (DES) in patients with diffuse left anterior descending coronary artery (LAD) disease.

BACKGROUND Diffuse LAD disease represents a therapeutic challenge. Results after coronary artery bypass surgery are suboptimal, whereas the use of bare metal stents is limited by high rates of restenosis. The introduction of DES prompted treatment of long diffuse disease with multiple overlapping stents.

METHODS All consecutive patients with de novo diffuse LAD disease treated with more than 60-mm long DES from April 2002 to March 2004 were analyzed.

RESULTS The study population consisted of 66 patients. Thirty-nine patients were treated with sirolimus-eluting stents (SES), average length 84 ± 22 mm, and 27 patients with paclitaxel-eluting stents (PES), average length 74 ± 14 mm. The number of stents implanted per patient was 2.8 ± 0.7, whereas the mean total stent length for the LAD treatment was 80 ± 20 mm. Angiographic as well as procedural success was achieved in 95% of cases. Eleven (16.6%) patients had in-hospital non–Q-wave myocardial infarction (five SES and six PES), and one patient developed intraprocedural stent thrombosis. All patients had clinical follow-up, and 52 patients (79%) had an angiographic follow-up at six months. Hierarchical major adverse cardiac event rate was 15% (7.5% for SES and 7.5% for PES). No patients died, one patient had non–Q-wave myocardial infarction (non-index vessel), and 10 patients (15%) underwent target vessel revascularization.

CONCLUSIONS The implantation of multiple overlapping DES in patients with a diffusely diseased LAD is relatively safe and associated with good midterm clinical outcomes. (J Am Coll Cardiol 2005;45:1570–3) © 2005 by the American College of Cardiology Foundation

Diffuse coronary artery disease poses a significant therapeutic challenge. In 25% of these patients, coronary artery bypass grafting (CABG) cannot be safely performed, and the condition often is deemed inoperable (1). Furthermore, in many of these cases, complete revascularization and adequate myocardial perfusion cannot be achieved with CABG. Alternative revascularization procedures (2–4) often are undertaken, with suboptimal results.

The percutaneous implantation of bare-metal stents (BMS) is associated with high rates of restenosis (5–7). The use of drug-eluting stents (DES) has greatly attenuated the relationship between stent length and restenosis (8–10). The aim of the present study was to evaluate the safety and efficacy of using multiple overlapping DES to treat patients with diffuse left anterior descending coronary artery (LAD) disease.

METHODS

Patient population and procedures. Patients with diffuse de novo LAD disease undergoing implantation of minimum of 60-mm long sirolimus-eluting stents (SES) (Cypher, Cordis/Johnson & Johnson, Warren, New Jersey) or paclitaxel-eluting stents (PES) (Taxus, Boston Scientific, Natick, Massachusetts) between April 2002 and May 2004 composed the study population. Each patient signed an informed consent form. The implantation of DES was performed following the practice of fully covering the diseased segment. All patients had a combination of at least two overlapping stents (overlapping segment approximately 2 to 4 mm) in the LAD, with total stent length ≥60 mm. The reported stented length is based on the cumulative length of the adjacent stents. Heparin was administered at the beginning of the procedure at the dose of 100 IU/kg to achieve an activated clotting time >250 s. Glycoprotein (GP) IIb/IIIa inhibitors were administered at the discretion of the operator.

All patients received aspirin (at least 100 mg once daily) and clopidogrel 75 mg once daily or ticlopidine 250 mg twice daily at least three days before the procedure, with a loading dose of 300 mg of clopidogrel to patients not pretreated. Thienopyridines were continued for at least three months after the procedure.

Angiographic analysis. Cineangiograms were analyzed using a validated edge system (CMS, version 5.2, MEDIS, Leiden, the Netherlands). Angiographic success was defined

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Abbreviations and Acronyms

BMS = bare-metal stent
CABG = coronary artery bypass grafting
DES = drug-eluting stents
GP = glycoprotein
LAD = left anterior descending coronary artery
MACE = major adverse cardiac events
MI = myocardial infarction
PES = paclitaxel-eluting stents
SES = sirolimus-eluting stents
TIMI = Thrombolysis In Myocardial Infarction

as Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 and <30% residual diameter stenosis by visual assessment. Restenosis was defined as >50% diameter stenosis by qualitative coronary angiography within a previously stented segment. Angiography was scheduled at six months or earlier if clinically indicated.

Clinical follow-up. Clinical follow-up was performed by either telephone contact or office visit. All patients were evaluated for the occurrence of major cardiac events (MACE), a composite end point comprising death, myocardial infarction (MI), and target vessel revascularization. A diagnosis of non–Q-wave MI was made when there was an increase of creatine kinase two times the upper limit of normal accompanied by increased values of creatine kinase-myocardial band. Diagnosis of Q-wave MI was made when development of new abnormal Q waves, not present in baseline electrocardiogram, also occurred. Intraprocedural stent thrombosis was defined as an angiographically confirmed intraluminal filling defect within the stent resulting in TIMI anterograde flow grade 0 or 1 that occurred during the procedure. Postprocedural stent thrombosis was defined as any of the following between the end of the procedure and the end of follow-up: angiographic documentation of stent occlusion, unexplained sudden death when the stent was not known to be patent, or MI or urgent target lesion revascularization occurring in the territory of the LAD. Target vessel revascularization was defined as revascularization driven by significant luminal narrowing (>50%) within the stent or within the 5-mm borders proximal and distal to the stent.

Statistical analysis. Discrete variables are presented as percentages and continuous variables as mean values ± SD. The Student paired *t* test was used to identify changes over time in the same patients, whereas the Kaplan-Meier method was used to analyze the occurrence of the composite end point of MACE during follow-up.

Table 1. Baseline Clinical and Procedural Characteristics (n = 66)

Age, yrs	62 ± 9.6
Men, n (%)	61 (92)
LVEF, %	50 ± 11.5
Hypercholesterolemia, n (%)	52 (79)
Hypertension, n (%)	46 (70)
Diabetes mellitus, n (%)	19 (29)
Previous MI, n (%)	30 (45)
Previous PCI, n (%)	18 (27)
Previous CABG, n (%)	8 (12)
Angina type, n (%)	
Silent ischemia	27 (41)
Stable	20 (30)
Unstable	19 (29)
>1 vessel treated, n (%)	51 (77)
Concomitant bifurcation treatment on the side branch, n (%)	35 (53)
Balloon angioplasty, n	13
DES, n	22
Glycoprotein IIb/IIIa inhibitors, n (%)	31 (47)
Reference vessel diameter, mm	2.53 ± 0.6
Mean diameter of DES stent, mm	2.8 ± 0.7
Mean length of lesion, mm	64 ± 18
Mean length of DES per lesion, mm	80 ± 20
Mean number of DES per lesion, mm	2.8 ± 0.7

CABG = coronary artery bypass grafting; DES = drug-eluting stents; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Table 2. Quantitative Coronary Angiographic Analysis at Baseline, After Procedure, and at Six-Month Angiographic Follow-Up (n = 52)

	Baseline	After Procedure	Six-Month Follow-up
RVD, mm	2.43 ± 0.6	2.86 ± 0.48	2.88 ± 0.56
MLD, mm	0.76 ± 0.5	2.54 ± 0.5	2.22 ± 0.86
Percent diameter stenosis	68.5 ± 19.3	11.4 ± 7.8	24.2 ± 22.8
Late lumen loss, mm			0.44 ± 0.77
Restenosis rate			19.6%

MLD = minimal luminal diameter; RVD = reference vessel diameter.

RESULTS

Immediate results. Baseline clinical and procedural characteristics are presented in Table 1. Diabetes mellitus was present in 19 patients (29%), and 19 (29%) had unstable angina. Ten patients had an ejection fraction ≤40%, and coronary bypass surgery had been performed previously in eight (12%). Chronic total occlusions were present in 13 (20%) patients. The lesion length per vessel was 64 ± 18 mm and reference vessel diameter was 2.53 ± 0.6 mm.

Thirty-nine patients were treated with SES (average length, 84 ± 22 mm) and 27 patients with PES (average length, 74 ± 14 mm). Angiographic success was achieved in 95% of the patients treated. Three patients had TIMI flow grade 2 at the end of the procedure. Directional atherectomy was performed in five patients, rotational atherectomy in one patient, and cutting balloon in seven patients. The number of stents implanted per lesion was 2.8 ± 0.7 (range, 2 to 4 stents), and the diameter of the stents was 2.8 ± 0.7 mm. Thirty-five patients (53%) received bifurcation treatment of diagonal branches: balloon angioplasty of the side branch was performed in 13 patients, and DES implantation was performed in the remaining patients (SES in 15 patients and PES in 7 patients). Glycoprotein IIb/IIIa