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Use of multiple overlapping sirolimus-eluting stents for treatment of long coronary artery lesions: Results from a single-center registry in 318 consecutive patients

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Abstract

Drug-eluting stents (DES) are superior to bare metal stents in the prevention of restenosis and target lesion revascularization (TLR). This has led to a more aggressive use of DES in everyday interventional cardiology practice.

Methods: All consecutive patients who underwent coronary artery stenting with greater than 34 mm of overlapping, sirolimus-eluting stent (SES) were reviewed from a prospectively created database. A prespecified group of patients with greater than 60 mm of SES was also followed.

Results: 318 patients were followed up at a minimum of 6 months and a mean of 9 months. The mean target lesion stented length was over 55 mm. Use of IVUS was 19.8%. Forty patients (12.6%) suffered a peri-procedural CK-MB rise. The MACE rate at 9 months was 17% with 12.6% being periprocedural myocardial infarction (MI). Clinically driven TLR was 4.4% and cardiac death was 1.3%. There were 4 cases defined as late stent thrombosis. The independent predictors of periprocedural MI were the presence of a major side branch and longer target lesion stented length, with stable angina being a negative predictor. The independent predictors of in-stent restenosis were unstable angina and target lesion number per patient. There was a trend to increased MACE in the subgroup with longer than 60 mm of SES length.

Conclusion: The use of multiple, overlapping SES is safe and effective with an acceptably low follow up MACE rate. A significant peri-procedural CK-MB rise appears to be a risk of long segment stenting. Whether this translates to long-term sequelae needs further investigation.

Keywords: Drug eluting stents; Coronary artery; Overlapping; Sirolimus

1. Introduction

Drug-eluting stents (DES), and more specifically sirolimus-eluting stents (SES) have been shown to be superior to bare metal stents in the prevention of in-stent restenosis (ISR) and subsequent target lesion revascularization (TLR) in several randomized controlled trials [1–4]. This has led to a new era of more aggressive percutaneous intervention, with an increased use of DES that has been paralleled by the complexity of the lesions being treated [5–22]. Indeed, implantation of longer and multiple overlapping stents in diffusely diseased vessels, as well as total vessel reconstructions are frequently performed in daily clinical practice. Recently, however, concerns have been raised regarding the safety of DES use in off-label indications, especially with regard to the risk of late and very late stent thrombosis, often coinciding with the cessation of one or both antiplatelet agents [23–26].

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Our study was conducted with the aim to evaluate all patients who underwent long lesion stenting with SES since their introduction in our institution. Data were collected from a prospectively created database in which the specific target stented length, longer stented length subgroup and clinical follow-up were decided prior to data interpretation.

2. Methods

All patients who underwent stenting of long coronary lesions (defined as being a stented length ≥34 mm) with SES (Cypher™, Cordis/Johnson & Johnson, Warren, New Jersey, USA) from September 9th 2002 to December 28th 2005 were included. Other stents, including other DES in any vessel, were permitted as long as there was a total of ≥34 mm of adjacent overlapping SES. Chronic total occlusions (CTO), acute myocardial infarction-related lesions, in-stent restenosis (ISR) and saphenous vein graft (SVG) lesions were all included. Therefore, this was a true cohort of all comers with diffuse coronary artery disease. In addition, the presence of at least two or more overlapped SES was a criterion to select a high-risk patient subset. The reported stented length was the cumulative length of adjacent, overlapping stents. All patients were treated using standard angioplasty technique, the vast majority from a femoral approach. Peri-procedural anticoagulation (standard heparin, low-molecular weight heparin or bivalirudin), use of glycoprotein IIb/IIIa antagonists and choice of thienopyridine (clopidogrel or ticlopidine) was at the discretion of the operator. All patients were loaded with a thienopyridine at the time of the procedure (or prior to the procedure if this was possible) and treated with dual antiplatelet therapy for at least 6 months. The use of aspiration catheters, distal protection devices, debulking devices, pre- and post-dilatation and intravascular ultrasound (IVUS) were all at the discretion of the operator. Twelve lead electrocardiograms (ECG), creatine kinase (CK) and its muscle–brain isoform (CK-MB) were performed routinely in the peri-procedural period including the day after the procedure and any elevation was followed closely with 4–6 hourly CK/CK-MB levels to identify a peak. Patients were followed up at 6 and 12 months routinely, unless symptoms or events required earlier consultation. Repeat angiography was only performed for clinical indications. All follow-up data including symptoms, stress testing or perfusion imaging, repeat coronary angiography and any major adverse cardiac events (MACE) were recorded.

2.1. Clinical definitions

A non-Q-wave myocardial infarction (MI) was considered to have occurred when there was a peri-procedural rise in CK-MB isoform 3 times the upper limit of normal, without new pathological Q-waves. A Q-wave *MI* was defined as the afore mentioned elevation in serum CK-MB isoform with new pathologic Q waves. Successful stent placement was defined as achievement of Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow and a ≥30% reduction in the lumen diameter stenosis resulting in a final residual stenosis of <50% by visual estimation. TLR was defined as either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), due to in-stent restenosis or occlusion of the target lesion. In-stent restenosis was defined as a stenosis of 50% or more of the luminal diameter either within the stent or within 5 mm of either edge. A previously proposed classification of the angiographic pattern of ISR was utilized [27]. Stent thrombosis was classified as acute if it occurred within 24 h after the index procedure, subacute if it occurred between 1 and 30 days after and late if it occurred between 31 days and 1 year. Stent thrombosis was defined as a thrombosis within the stent or within 5 mm of either edge. All deaths were considered to be cardiac deaths unless an appropriate alternative explanation was possible. Any acute cardiac death was considered to be due to stent thrombosis unless the stent was proven to be patent at angiography or there was another proven cause, which excluded a stent thrombosis. Thus they were considered definite, probable or possible stent thrombosis in line with the Academic Research Council's (ARC) criteria [28].

2.2. Statistical methods

Data were recorded using a standard form and entered into an Excel™ spreadsheet (Microsoft Corporation, Richmond, VA), which was used to derive descriptive statistics. Data were transferred to an SPSS™ for Windows™ table (SPSS inc., Chicago, IL, USA). Continuous variables are presented as mean±standard deviation (SD) unless otherwise stated. Categorical variables are presented as a number (%). Continuous variables with a Gaussian distribution were compared with the unpaired Student's *t*-test, whilst those not in a Gaussian distribution were compared using a Wilcoxon Rank sum Test. Categorical variables were compared using the Chi-square test. Logistic regression analysis using SAS/STAT statistical software (SAS Institute Inc. Cary, NC, USA) was performed to assess for independent risk factors for peri-procedural MI and TLR.

3. Results

During a 3 year and 3 month period, 318 consecutive patients who were treated with ≥34 mm of continuous (at least one overlap) SES were entered into a prospectively collected database. All patients had been referred for coronary angiography with significant clinical symptoms of cardiac ischemia or infarction, an abnormal exercise stress test or nuclear isotope scan, or biochemical markers of myocardial damage. The patient demographics were typical for patients with significant coronary artery disease (Table 1). The majority of patients had stable angina pectoris