Original articles

Treatment synergy of silicon carbide-coated stenting and abciximab for complex coronary artery lesions: clinical results of a single-center study

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Abciximab; Coronary artery disease; Stents; Thrombosis, intravascular.

Background. **The aim of this study was to evaluate the combination of a silicon carbide-coated stent with the periprocedural use of abciximab in patients with type B2/C lesions. The study was a prospective cohort study and was conducted at the University Medical Center of Groningen.**

Methods. **Elective percutaneous transluminal coronary angioplasty was performed in a total of 44 patients. All had lesions with type B2/C characteristics and most were relatively small, tortuous and calcified. The involved vessel segment was stented. Silicon carbide-coated stents were used in combination with periprocedural abciximab. The main outcome measures were cardiac death, target vessel revascularization, myocardial infarction, and cerebrovascular accident.**

Results. **At 6 months of follow-up, only 4 patients had a major adverse cardiac event. Three patients had undergone target vessel revascularization and 1 patient had suffered from a cerebrovascular accident. Sixteen patients underwent re-angiography 6 months after the initial procedure. The average stenosis at 6 months was 15% with a minimal lumen diameter of 2.4 mm.**

Conclusions. **A 9% major adverse cardiac event rate and a 7% target vessel revascularization rate at 6 months in type B2/C lesions were recorded. Further investigation on the use of this specific treatment combination is warranted.**

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Introduction

Coronary stenting has dramatically changed interventional cardiology over the years. Initially, stenting was introduced for complicated procedures. From this perspective, bail-out stenting provided a solid rescue-tool for flow-obstructing dissection. Subsequently, more complex lesions could be treated and the clinical outcome was improved even for these lesions.

Subacute thrombosis has been a major limitation of stenting since its introduction in 1986. In pioneering studies, the rate of subacute stent thrombosis was reported to be as high as 20%[1]. This unacceptably high thrombosis rate was reduced to approximately 1% in a more recently conducted analysis in which various efforts were combined in an attempt to cope with this limitation[2]. In addition to the acute effects of platelet adherence and aggregation, the interaction of the stent with circulatory thrombogenic compounds may contribute to late cardiac events and restenosis.

The electropositive charge on the outer surface of the stent may activate platelets. Activation of platelets at this bare interface is an important factor in the process of in-stent restenosis.

In order to minimize the probability of stent thrombosis, we used two currently available antithrombotic techniques: passive stent coating (silicon carbide) and periprocedural abciximab. Combining both modalities should enable the assessment of their potential synergistic effects. Both techniques are currently under investigation for their potential anti-restenosis and anti-stent-thrombosis properties. Silicon carbide coating provides the stent with an almost non-electropositive outer surface and abciximab appears to be the most effective antithrombotic drug available to date[3,4]. Therefore, it was hypothesized that the combination of the two treatment modalities could have a beneficial impact on the rates of subacute thrombosis and in-stent restenosis. We evaluated this treatment strategy in patients with type B2/C le-

sions, as these patients have a higher risk of developing periprocedural thrombosis and restenosis. In the present pilot study, we evaluated the use of silicon carbide-coated stents associated with an optimal periprocedural drug regimen in daily clinical practice.

Methods

All patients underwent elective angioplasty of complex type B2/C lesions. From June to August 2001, 44 patients gave their informed consent for clinical treatment and follow-up at the University Medical Center of Groningen, The Netherlands. This study was approved by the institutional review board and complied with the declaration of Helsinki.

A silicon carbide coated-slotted tube stent (Rithron, Biotronik, Nijmegen, The Netherlands) was used. No intravascular ultrasound-guided optimal deployment methods were used in this study. All patients received abciximab as a bolus of 0.25 mg/kg of body weight, followed by a 12-hour infusion of 0.125 μg/kg/min.

All patients were either resubmitted to angiography or interviewed after 6 months. Cardiac death, myocardial infarction, cerebrovascular events and target vessel revascularization were considered to be major adverse cardiac events (MACE).

Results

Table I shows the characteristics of the 44 patients included in this clinical trial. The average age was 63.4 ± 1.7 years. Two patients presented with an acute coronary event and 42 underwent elective angioplasty of complex type B2/C lesions because of angina pectoris NYHA class III. The rates of preexisting hypertension, hypercholesterolemia and a positive family history were 31, 61 and 61% respectively. In our study group 30% of patients had diabetes mellitus; 6 of these patients had insulin-dependent diabetes. In the study group, 38% were self-declared smokers at the time of intervention.

The rates for previous percutaneous transluminal coronary angioplasty, coronary artery bypass grafting and myocardial infarction were 17, 20 and 30% respectively.

Twenty-one percent of patients were on oral anticoagulants and 44% on lipid-lowering treatment. Two patients received thrombolytics 48 hours prior to intervention.

Table II shows the characteristics of all the 51 lesions that were treated in this trial. Twenty-five lesions were located in the left anterior descending coronary artery, 14 in the right coronary artery, 6 in the circumflex artery, and 2 in the obtuse marginal branch. One patient had a lesion in the first diagonal branch and 3 had a lesion of a vein graft.

Quantitative coronary angiography was performed yielding a mean stenosis of 71 ± 2.6%. The minimal lumen diameter was 0.78 ± 0.08 mm. The average lesion length was 10.6 ± 2.5 mm. The lesions were relatively short, but very calcified and tortuous. Type B2 lesions constituted 86% of all the lesions treated in this trial. All others were type C lesions. Further, of interest is the

Table I. Patient characteristics.

Age (years)	63.4 ± 1.7
Females (%)	16
Hypertension (%)	31
Hypercholesterolemia (%)	61
Diabetes (%)	30
Insulin-dependent (%)	13
Smokers (%)	38
Positive family history (%)	61
Previous PTCA (%)	17
Previous CABG (%)	20
Previous myocardial infarction (%)	30
Patients using (%)	70
Beta-blockers	36
Calcium antagonists	31
Oral nitrates	15
Intravenous nitrates	5
Oral anticoagulants	21
Lipid-lowering drugs	44
ACE-inhibitors	23
Diuretics	7
Thrombolytics	4

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty.

Table II. Lesion characteristics.

No. lesions	51
LAD	25
First diagonal	1
CX	6
OM1	2
RCA	14
Vein graft	3
Localization	
Ostial	2
Proximal	16
Mid	26
Distal	3
Bifurcation	4
Quantitative coronary angiography	
Stenosis (%)	71 ± 2.6
Minimal lumen diameter (mm)	0.78 ± 0.08
Lesion length (mm)	10.6 ± 2.5
Reference diameter (mm)	2.2 ± 0.2
Total stent length (mm)	15.9 ± 7.5
Final lumen diameter (mm)	2.7 ± 0.51
Lesion type (%)	
B2	86
C	14

CX = left circumflex coronary artery; LAD = left anterior descending coronary artery; OM1 = obtuse marginal coronary artery; RCA = right coronary artery.

extremely small vessel reference diameter in the present study. However, in the clinic where the study was performed these are fairly normal values for patients with type B2/C lesions.

All patients were submitted to clinical follow-up after 6 months. Four patients had a MACE within 6 months, 3 patients underwent target vessel revascularization and one had a thrombotic cerebrovascular accident. The total MACE rate was 9%. The target vessel revascularization rate was 7%. No major bleeding complications were observed. Sixteen patients with a total of 17 lesions underwent re-angiography. Two lesions showed > 50% stenosis. One of these was totally occluded. After 6 months the average stenosis in the lesions of the patients who underwent re-angiography was 15% with a minimal lumen diameter of 2.4 mm. The follow-up results are summarized in table III.

Discussion

It has been shown that type B2/C lesions are related to an increased risk of MACE and in-stent restenosis[5]. Kastrati et al.[5] reported a 17% MACE rate after 6 months in 1999. The authors used uncoated stents and a more traditional regimen of antithrombotic drugs, which did not include the administration of IIb/IIIa antagonists. Since the high rates for a positive family history, smoking, hypercholesterolemia and a previous myocardial infarction contribute to the feeling that a group of patients such as ours would be characterized by a preexistent high-risk profile with the concomitant presence of severe lesions, it may be less likely that these variables form a plausible explanation for the difference in outcome. From this perspective, the 9% MACE rate and the 7% target vessel revascularization rate at 6 months of follow-up in this study suggest a probable synergistic action of the silicon carbide coating with periprocedural abciximab when compared to a standard, less aggressive, therapeutic approach.

Only a few randomized controlled clinical trials concerning the use of silicon carbide-coated stents have been published. The results range from the 5.8% MACE rate for silicon carbide-coated stents to the 15.3% MACE rate at 6 months for conventional stents ($p < 0.05$)[6] to non-significant differences in MACE stenosis percentages at 4.7 months[7] and 81 weeks[8]. However, these studies did not include IIb/IIIa receptor antagonists in their periprocedural drug regimen.

The added value of abciximab has been confirmed in many studies using a wide variety of study populations and lesion types[4,9]. Yet, the debate on the cost-effectiveness for its implementation continues. The data from this study fit the overall clinical experience with abciximab at Dutch high-volume angioplasty centers and may support the hypothesis that abciximab, in combination with a coated stent, is justified and beneficial in patients with complex coronary lesions. Prior studies comparing bypass surgery and stenting in high-grade versus simple lesions, showed a tendency toward surgery for high-grade or complex lesions[10,11]. However, it should be emphasized that these studies were implemented with the use of traditional pharmacological regimens and non-coated stents and stenting techniques. Considering the fact that repeated thrombosis and stenosis, especially in complex lesions, may require alternative treatment strategies such as drug-eluting stents, brachytherapy or bypass surgery, the proposed regimen could be a feasible alternative. However, further research on this issue may elucidate the impact of such an approach on daily clinical practice.

Study limitations. Since this study was designed as a pilot trial for the assessment of silicon carbide-coated stents in patients with complex lesions, the number of patients in the present study, and especially the number of patients with an angiographic follow-up, is small. Furthermore, the institution's ethical committee did not allow a study design that incorporated a control group treated either with bare metal stents or one with abiciximab alone within the framework of a pilot study. To further investigate the full potential of the proposed treatment combination, larger multicenter studies would be necessary. This was beyond the scope of this study.

In conclusion, the findings of our study suggest that the use of a silicon carbide-coated stent in combination with abciximab is a treatment option that deserves consideration when treating complex calcified and tortuous coronary lesions. However, larger studies must be conducted to further elucidate the value of silicon carbide-coated stents.

Table III. Follow-up after 6 months.

Re-angiography (n=)	16
Quantitative coronary angiography	
Stenosis (%)	15 ± 4.2
Minimal lumen diameter (mm)	2.4 ± 0.3
Lesion length (mm)	3.1 ± 0.7
Reference diameter (mm)	2.8 ± 0.2
MACE in 44 patients (n=)	4
Cardiac death	0
Target vessel revascularization	3
Myocardial infarction	0
Cerebrovascular accident	1

MACE = major adverse cardiac events.

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