Towards a tailored approach in Percutaneous Coronary Interventions

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Chapter 8

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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Abstract

Background
The aim of this study was to evaluate the combination of a silicon carbide coated stent with the peri-procedural 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 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 or calcified. The involved vessel segment was stented. Silicon carbide coated stents were used in combination with peri-procedural abciximab administration. The main outcome measures were cardiac death, target vessel revascularisation, myocardial infarction and cerebrovascular accident.

Results
At 6 month follow-up, only four patients had a major adverse cardiac event (MACE). Three patients had undergone target vessel revascularisation (TVR) and one patient had suffered from a cerebrovascular accident. Sixteen patients underwent re-angiography six 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% MACE rate and a 7% TVR rate at 6 months in type b2/c lesions were recorded. Further investigation on the use of this specific treatment-combination is warranted.
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 with an improved clinical outcome.

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 up to 20%.¹ This unacceptably high thrombosis rate was reduced to approximately one percent in a more recently conducted analysis in which various efforts were combined 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 current anti-thrombotic techniques, passive stent coating (silicon carbide) and periprocedural abciximab. Both techniques are currently under investigation for their potential anti-restenosis and anti stent-thrombosis properties. Combining both modalities should enable the assessment of their potential synergistic effects. Silicon carbide coating provides the stent with an almost non-electropositive outer surface and abciximab appears to be the most effective anti-thrombotic drug used in daily clinical practice.³ ⁴ Therefore, it was hypothesized that the combination of the two treatment modalities could have a beneficial impact on sub-acute thrombosis and in-stent restenosis rates.

We evaluated this treatment strategy in patients with type B2/C lesions, as these patients have a major risk of developing peri-procedural 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 or c lesions. In the period from June 2001 to August 2001, 44 patients gave informed consent for clinical treatment and follow-up at the University Medical Centre 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) was used. No intra-vascular ultrasound guided optimal deployment methods were used in this study. All patients received abciximab as a bolus of 0.25 mg per kilogram of body weight, followed by 12-hour infusion of 0.125 microgram per kilogram per minute.

All patients had a follow-up either by re-angiography or interview after 6 months. Cardiac death, myocardial infarction, cerebrovascular events and target vessel revascularisation (TVR) were considered to be Major Adverse Cardiac Events (MACE).

Results

Table 1 shows the patient characteristics of the 44 patients in this clinical trial. The average age was 63 ± 2 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 pre-existent hypertension, hypercholesterolaemia and a positive family history rates were 31 %, 61 % and 61 % respectively. In our study group 30 % of patients had insulin-dependent diabetes. In the studygroup 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.

Table 2 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 lesions were located in the marginal obtuse branch. One patient had a lesion in the first diagonal branch and 3 had a lesion of a vein graft.

Quantitative Coronary Angiography showed a Minimal Lumen Diameter of 0.78 ± 0.08 mm. 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 lesion treated in this trial. All others were type c lesions. Further, of interest is the 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 after 6 months, three patients underwent target vessel revascularisation and one suffered a thrombotic cerebrovascular accident. Total MACE rate was 9 %. Target vessel revascularisation rate was 7 %. No major bleeding complications were observed. Sixteen patients underwent re-angi-
ography of 17 lesions. Two lesions showed > 50 % stenosis. One of these was totally occluded. After 6 months the average stenosis in lesions of the patients who underwent re-angiography was 15 % with a mld of 2.4 mm. The follow-up results are summarised in table 3.

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.) ± SD</td>
<td>63.4 ± 1.7</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>16</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>31</td>
</tr>
<tr>
<td>Hypercholesterolaemia (%)</td>
<td>61</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>30</td>
</tr>
<tr>
<td>Insulin dependent (%)</td>
<td>13</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>38</td>
</tr>
<tr>
<td>Positive family history (%)</td>
<td>61</td>
</tr>
<tr>
<td>Previous PTCA (%)</td>
<td>17</td>
</tr>
<tr>
<td>Previous CABG (%)</td>
<td>20</td>
</tr>
<tr>
<td>Previous Myocardial infarction (%)</td>
<td>30</td>
</tr>
<tr>
<td>Patients Using Bete-Blocker (%)</td>
<td>36</td>
</tr>
<tr>
<td>Ca-Antagonist (%)</td>
<td>31</td>
</tr>
<tr>
<td>Nitrates Oral (%)</td>
<td>15</td>
</tr>
<tr>
<td>Nitrates Intra-venous (%)</td>
<td>5</td>
</tr>
<tr>
<td>Anticoagulants Oral (%)</td>
<td>21</td>
</tr>
<tr>
<td>Lipid lowering Medication (%)</td>
<td>44</td>
</tr>
<tr>
<td>ACE inhibitors (%)</td>
<td>23</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>7</td>
</tr>
<tr>
<td>Thrombolitics (%)</td>
<td>4</td>
</tr>
</tbody>
</table>

Legend Table 1:
SD = Standard Deviation
PTCA = Percutaneous Transluminal Coronary Angioplasty
CABG = Coronary Artery Bypass Grafting
ACE = Angiotensin Converting Enzyme
Table 2. Lesion characteristics

<table>
<thead>
<tr>
<th>Nr of Lesions</th>
<th>51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions in</td>
<td></td>
</tr>
<tr>
<td>LAD (n)</td>
<td>25</td>
</tr>
<tr>
<td>1ST Diagonal (n)</td>
<td>1</td>
</tr>
<tr>
<td>CX (n)</td>
<td>6</td>
</tr>
<tr>
<td>OM1 (n)</td>
<td>2</td>
</tr>
<tr>
<td>RCA (n)</td>
<td>14</td>
</tr>
<tr>
<td>Vene Graft (n)</td>
<td>3</td>
</tr>
</tbody>
</table>

Localisation
- Ostial (n) 2
- Proximal (n) 16
- Mid (n) 26
- Distal (n) 3
- Bifurcation (n) 4

QCA
- % Stenosis +/- SD 71 2.6
- MLD (mm) +/- SD 0.78 0.08
- Lesion Length (mm) +/- SD 10.6 2.5
- Reference Diameter (mm) +/- SD 2.2 0.2

Lesion type
- B2 (%) 86
- C (%) 14

Legend Table 2:
LAD = Left Anterior Descending Coronary Artery
CX = Left Circumflex Coronary Artery
OM1 = Obtuse Marginal Coronary Artery
RCA = Right Coronary Artery
QCA = Quantitative Coronary Angiography
SD = Standard Deviation
MLD = Minimal Lumen Diameter
Table 3. Follow up after 6 months

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value 1</th>
<th>Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-Angiography (n)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>QCA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stenosis +/- SD</td>
<td>15</td>
<td>4.2</td>
</tr>
<tr>
<td>MLD (mm) +/- SD</td>
<td>2.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Lesion Length (mm) +/- SD</td>
<td>3.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Reference Diameter (mm) +/- SD</td>
<td>2.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

MACE (n) in 45 patients 4
Cardiac Death (n) 0
TVR (n) 3
Myocardial infarction (n) 0
CVA (n) 1

Legend Table 3:
QCA = Quantitative Coronary Angiography
SD = Standard Deviation
MLD = Minimal Lumen Diameter
MACE = Major Adverse Cardiac Events
TVR = Target Vessel Revascularization
CVA = Cerebrovascular Accident

Discussion

It has been shown that type B₂/C lesions are related to an increased risk for developing Major Adverse Cardiac Events and in-stent restenosis. Kastrati et al reported a 17 % MACE rate after 6 months in 1999. The authors used uncoated stents and a more traditional regimen of anti-thrombotic drugs, which did not include the administration of an IIb/IIIa antagonist. As the high rates for a positive family history, smoking, hypercholesterolaemia and a previous myocardial infarction contribute to the conception that our study group was characterised by a pre-existent 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% TVR rate at 6 months follow-up in this study suggest a probable synergistic action of the silicon carbide coating with peri-procedural 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 vary from 5.8% MACE for a sic-c coated stents compared to 15.3 % MACE at 6 months for conventional stents (p<0.05) to non-significant differences in MACE and stenosis percentages at 4.7 months and 81 weeks. However, these studies did not use a IIb/IIIa receptor antagonist in their peri-procedural drug regimen.

The added value of abciximab has been confirmed in many studies using a wide variety of study populations and lesion-types. 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 towards surgery for high grade or complex lesions. 10,11 However, it should be emphasized that these studies were implemented according to traditional pharmacological regimens, non-coated stent designs 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 appear to be a feasible alternative. However further research on this issue may elucidate the impact 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 with bare metal stents or one with abciximab 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.

Conclusions
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.

Acknowledgments
The stents (Rithron) that were used in this trial were provided bij Biotronik.
References


