Pre–Drug-Eluting Stent Debulking of Bifurcated Coronary Lesions

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Objectives

The purpose of this study was to evaluate the efficacy of plaque debulking by directional coronary atherectomy (DCA) before drug-eluting stent (DES) implantation for bifurcated coronary lesions.

Background

The introduction of DES significantly reduces restenosis and repeated revascularization. However, percutaneous coronary intervention of bifurcated lesions using DES alone remains challenging regardless of whether simple or complex stenting is used.

Methods

Patients with bifurcated lesions were recruited in this prospective multicenter registry. Pre-DES plaque debulking by DCA was conducted. All patients were scheduled to undergo a 9-month coronary angiography. The primary end point was the 9-month binary angiographic restenosis rate. Secondary end points included procedure-related events and major adverse cardiac events (MACE) at 1 year.

Results

A total of 99 patients with bifurcated lesions were enrolled in this registry. Directional coronary atherectomy was performed successfully in all cases without any major procedure-related events. Simple stenting was achieved in all but 2 cases. No in-hospital MACE were observed. The 9-month binary restenosis rates in the main branch and side branch were 1.1% and 3.4%, respectively. Target lesion revascularization was performed in 2 patients (1 for the main branch and the other for the side branch). No deaths, no coronary artery bypass grafting, and no myocardial infarctions were reported in the patients within the first year.

Conclusions

Directional coronary atherectomy before DES implantation can possibly avoid complex stenting. This strategy may provide a good long-term outcome in patients with bifurcated lesions. (J Am Coll Cardiol 2007;50:1941–5) © 2007 by the American College of Cardiology Foundation

Percutaneous coronary intervention (PCI) of bifurcated lesions involving both the main and side branches remains complex and challenging in terms of technical demands and has a higher risk of restenosis regardless of the stenting strategy used (1). There are mainly 2 stenting strategies in bifurcated lesions: 1) stenting the main branch with balloon angioplasty of the side branch (simple stenting); and 2) stenting of both the main and the side branch (complex stenting) (2). Previous studies comparing simple versus complex stenting demonstrated comparable results between the 2 strategies (3–5). However, in clinical practice, a number of bifurcated lesions will ultimately require complex stenting (5), for example, if the side branch is of adequate size and heavily diseased with an atherosclerotic lesion extending from the main lesion into the proximal portion of the branch. Unfortunately, reported restenosis rates (range between 9.1% and 18.8% in the main branch and between 11.1% and 25.3% in the side branch) in complex stenting were unsatisfactory regardless of the implantation of the drug-eluting stent (DES) (6–8). The bifurcated lesion is therefore still considered one of the remaining problems in the DES era. To improve the treatment outcome, we used directional coronary atherectomy (DCA) mainly on the main branch before DES implantation for bifurcated lesions to avoid a significant lumen reduction on the side branch, which requires complex stenting.

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Methods

**Study design.** The PERFECT (PrE Rapamycin-eluting stent FlExi-CuT) registry, conducted at 17 Japanese centers, was a multicenter, prospective, nonrandomized study to evaluate the efficacy of pre-DES plaque modification by DCA for bifurcated coronary lesions. Suitable lesions for the PERFECT registry were selected by angiography, by intravascular ultrasound (IVUS), and by the clinical condition of the patient. Inclusion criteria included significant stenosis located in a distal left main trunk, ostium of the left anterior descending or left circumflex artery, or a major bifurcation located at the proximal left anterior descending or left circumflex; de novo lesion; suitable morphology for DCA catheter delivery (no severe calcification and acute proximal bending); and reference diameter in main branch > 2.5 mm by visual estimate. Exclusion criteria included a bypass graft, bending > 60°, restenotic lesion, thrombotic lesion, and acute myocardial infarction (within 2 weeks). Eligible patients were enrolled in this registry. The protocol was approved by ethics committees in each participating center, and all participants gave written informed consent.

**Procedure and medication.** Percutaneous coronary intervention was performed through the femoral artery using an 8-F sheath introducer. All patients underwent the IVUS-guided DCA procedure in the main branch and in the side branch (when it was applicable) using a Flexicut (Abbott Vascular, Temecula, California) before implantation of a sirolimus-eluting stent (Cypher, Cordis Corp., Miami Lakes, Florida). The IVUS-guided DCA was performed according to a previous study (9). Balloon pressures were increased progressively from 10 to 30 psi to a maximum of 150 psi. Repeated debulking of the plaque using IVUS was performed according to the residual percent plaque plus the media cross-sectional area (PA). The target residual percent PA was < 60%. The DES was implanted after plaque debulking. The patients then underwent either single-crossover stenting or single noncrossover stenting (Fig. 1). Single-crossover stenting is a technique in which the Cypher stent is placed in the main branch covering the side branch. It was followed by: 1) kissing balloon technique (KBT); or 2) balloon angioplasty only for the side branch when necessary. In single noncrossover stenting, optimal debulking is performed in the ostial of the main branch. The Cypher stent is then placed just distal to the main branch ostium without covering the side branch. All patients were pre-treated with aspirin and ticlopidine. A 200-mg loading dose of ticlopidine before the index procedure was administered in patients who were not pre-treated. Ticlopidine combined with aspirin was continued after stenting. Administration of dual antiplatelet therapy was continued for 1 year.

**Quantitative coronary angiography and IVUS.** All angiographic and IVUS imaging was conducted immediately after administration of 200 μg of intracoronary nitroglycerin. Angiography was performed so that each lesion was viewed from at least 2 angles. Quantitative coronary angiography and IVUS were independently analyzed by a core laboratory (Cardiovascular Imaging Center, Toyohashi, Japan). Quantitative coronary angiography analysis was conducted using the Cardiovascular Measurement System (CMS-MEDIS, Medical Imaging Systems, Leiden, the Netherlands). Lesion length, reference diameter, minimal lumen diameter, and diameter stenosis were calculated. The analysis was performed in both the main and the side branch before and after procedures and at a 9-month follow-up. The IVUS was performed using a commercially available system (Boston Scientific, Natick, Massachusetts). The total vessel cross-sectional area and lumen cross-sectional area were calculated, and the difference between these 2 values was defined as the PA. The PA was then divided by the vessel cross-sectional area to obtain the percent PA.

**Patient follow-up.** In-hospital assessment was performed for all clinical outcomes, including hemorrhagic and vascular complications and routine ascertainment of creatine kinase (CK) and the CK-MB fraction before treatment and

![Figure 1 Stenting Strategies](image-url)

(A) Crossover stenting. The stent is placed in the main branch (MB) covering the side branch (SB) after directional coronary atherectomy (DCA) debulking. It was followed by kissing balloon technique (KBT) or balloon angioplasty (BA) for the SB when necessary. (B) Noncrossover stenting. Plaque debulking by DCA is performed in the MB. The stent is then placed in the MB ostium without covering the SB.
4 to 6 h and 24 h after procedure. After patient discharge, clinical follow-up examinations were conducted on an outpatient basis at least once per month for 1 year. Angiographic and IVUS follow-up examinations were conducted at 9 months regardless of symptoms. If target lesion revascularization (TLR) was performed before 9 months owing to the clinical condition of the patient, before-procedural angiography at that time was used for follow-up quantitative coronary angiography analysis of the patient.

**End points.** The primary angiographic end point was the 9-month binary angiographic restenosis rate, defined as ≥50% diameter stenosis. Secondary end points were procedure-related events and major adverse cardiac events (MACE) at 1 year. Procedure-related events included DCA procedural events (spasm, side branch occlusion, no flow, perforation) and in-hospital MACE (death, emergency coronary arterial bypass grafting/TLR, Q-wave myocardial infarction [QMI], complication at access site). All deaths were considered cardiac-related unless clearly attributable to a noncardiac cause. Documentation of new, pathological Q waves in 2 or more contiguous electrocardiogram leads associated with elevation of CK-MB was required for the diagnosis of QMI. Non–QMI was defined as the elevation of CK to more than twice the upper limit associated with any elevation of CK-MB without the appearance of Q waves.

**Statistical analysis.** Each participating center was prospectively required to record all patients’ data on case report forms. Data were forwarded to the core laboratory for data entry and analysis. Data that were missing, inconsistent, or both were obtained or clarified by direct communication by the core laboratory with the respective clinical center. Continuous variables were expressed as the mean ± SD. Variable categories were expressed as frequencies.

## Results

**Patient and lesion characteristics.** Between August 2004 and October 2005, we screened 2,175 elective PCI patients. Of these, we enrolled 99 patients (99 lesions) who met the inclusion criteria of the registry. Baseline patient demographic and clinical data are shown in Table 1. Baseline lesion characteristics including Duke’s classification of bifurcated lesions (10) are summarized in Table 2. Sixty-three lesions (64%) were located in the left main trunk bifurcation, 15 were located in the ostial left anterior descending artery, and 3 were in the ostial left circumflex. Thus, 81 lesions (82%) were located around the left main trunk bifurcation.

**Acute results.** The DCA was performed using a FlexiCut size L in 98 lesions and a FlexiCut size M in 1 lesion. Plaque excision of the main branch was conducted in all lesions. In 3 lesions (3%) involving the left main trunk bifurcation, DCA was also performed for the ostial left circumflex artery (side branch). The total number of cuts was 18.2 ± 12.3, with a maximum cutting pressure of 59.4 ± 34.5 psi. No complications (spasm, side branch occlusion, no flow, or perforation) were observed during the plaque debulking. Successful stent delivery was achieved in all cases. Simple stenting was performed in 97 cases (crossover stent with KBT in 50, without any additional treatment in 26, with balloon angioplasty for side branch only in 6, and noncrossover stent in 15). Only 2 cases with left main trunk bifurcation (2%) required complex stenting (1 T-stent and 1 culotte stent) because of unsatisfactory results after stenting of the main branch. The mean stent size was 3.32 ± 0.26 mm, and the stent length was 21.9 ± 4.2 mm. Quantitative coronary angiography analysis for the main branch and side branch is shown in Table 3, and IVUS analysis of the main branch is shown in Table 4. After-DCA percent PA was 55.8 ± 14.3%, which means that DCA debulking in this study was not so aggressive.

The mean procedure time was 114.6 ± 42.1 min (41.1 ± 16.4 min mean fluoroscopy time). The average use of contrast medium was 338 ± 104 ml. During the procedure, intra-aortic balloon pumping was required in 11 patients (11%). Of those, elective intra-aortic balloon pumping was
Follow-up results. Angiographic follow-up was performed in 89 patients (90% follow-up rate) at a mean follow-up period of 259 ± 79 days. Follow-up quantitative coronary angiography results are shown in Table 3. Restenosis rates of the main and side branch were 1.1% (1 of 89) and 3.4% (3 of 89) respectively, and the total restenosis rate, the primary end point of this study, was 4.5% (4 of 89). One-year clinical follow-up was accomplished in 96 patients (97% of the entire cohort). No deaths, coronary arterial bypass grafting, or myocardial infarctions were reported in any patient.

Subanalysis of left main trunk bifurcation. This subgroup included 63 patients (53 men) with a mean age of 69 ± 11 years. Successful DCA and DES implantation (60 simple, 2 complex) was completed without any MACE. Angiographic follow-up was obtained in 55 patients, and the restenosis rate was 0% for both the main and the side branch. Clinical follow-up at 1 year was completed in 60 patients, and no clinical event, including TLR, was observed in any patient.

Drug-eluting stents significantly reduced restenosis rates compared with bare-metal stents in simple lesions. However, the issue of restenosis in complex anatomies such as bifurcated coronary lesions remained unclear. Directional coronary atherectomy was developed as a way of exciting coronary atheroma, possibly preventing plaque shift in bifurcated lesions. In the PERFECT registry, we can make the following conclusion: DCA before DES may lower the restenosis rate without increasing adverse events. Advantage of plaque debulking for bifurcated lesions. Previous studies compared the effectiveness of simple versus complex stenting in bifurcated lesions (3–5). The results of these studies indicated no significant differences between the 2 groups with regard to the primary end points defined in each study. Both strategies are effective in reducing the restenosis rate compared with bare-metal stent implantation; therefore, simple stenting is a favorable treatment strategy for stenting in bifurcated lesions. None of the previous studies showed that stenting in the side branch decreased the restenosis rate. However, complex stenting is often inevitable, especially in the case of a true bifurcated lesion with a massive plaque burden. In a study comparing complex stenting with a simple stenting technique (stent in the parent vessel plus balloon angioplasty of the side branch) conducted by Assali et al. (5), 9 of 25 patients (36%) in the simple stenting group underwent side branch “provisional” stenting because of unsatisfactory results. Colombo et al. (11) reported a high crossover rate (51.2%) in a randomized study to evaluate sirolimus-eluting stents implanted in coronary bifurcation lesions. A high crossover rate may be caused by plaque shift after the main branch stenting.

### Table 3 QCA Analysis of the Main and Side Branch

<table>
<thead>
<tr>
<th></th>
<th>Main Branch</th>
<th>Side Branch</th>
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</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>16.0 ± 8.4</td>
<td>7.1 ± 6.9</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>3.28 ± 0.47</td>
<td>2.60 ± 0.74</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.33 ± 0.37</td>
<td>1.71 ± 0.67</td>
</tr>
<tr>
<td>DS (%)</td>
<td>59.6 ± 9.4</td>
<td>34.5 ± 16.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Before (n = 99)</th>
<th>After (n = 99)</th>
<th>Follow-up (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD (mm)</td>
<td>3.76 ± 0.46</td>
<td>3.76 ± 0.46</td>
<td>3.36 ± 0.44</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>3.43 ± 0.65</td>
<td>2.14 ± 0.64</td>
<td>2.90 ± 0.65</td>
</tr>
<tr>
<td>DS (%)</td>
<td>9.1 ± 11.6</td>
<td>21.4 ± 14.6</td>
<td>13.8 ± 13.7</td>
</tr>
<tr>
<td>Late loss (mm)</td>
<td>0.52 ± 0.53</td>
<td>0.15 ± 0.44</td>
<td>0.56 ± 0.32</td>
</tr>
<tr>
<td>Loss index</td>
<td>0.24 ± 0.25</td>
<td>0.10 ± 0.36</td>
<td>0.24 ± 0.25</td>
</tr>
</tbody>
</table>

### Table 4 IVUS Analysis of the Main Branch

<table>
<thead>
<tr>
<th></th>
<th>Pre-DCA (n = 99)</th>
<th>Post-DCA (n = 99)</th>
<th>Final (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen CSA (mm²)</td>
<td>2.46 ± 1.17</td>
<td>6.50 ± 2.33</td>
<td>9.31 ± 3.28</td>
</tr>
<tr>
<td>Vessel CSA (mm²)</td>
<td>14.85 ± 4.20</td>
<td>15.56 ± 3.47</td>
<td>17.99 ± 4.69</td>
</tr>
<tr>
<td>PA (%)</td>
<td>82.3 ± 7.2</td>
<td>55.8 ± 14.3</td>
<td>46.3 ± 8.0</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or mean ± SD. DS = diameter stenosis; MLD = minimum lumen diameter; QCA = quantitative coronary angiography; RVD = reference vessel diameter.
previous study investigating the clinical and angiographic results of DCA followed by stent implantation versus a series of matched lesions treated with stent implantation alone for ostial left anterior descending artery showed that a significant reduction in ostial left circumflex artery occurred in patients treated with stenting alone, whereas DCA stent expansion was effective in avoiding a significant lumen reduction in the left circumflex artery (12). Thus, plaque shift and complex stenting can be minimized by the use of DCA debulking. In our registry, only 2 patients (2%) underwent provisional stenting in the side branch, which may have contributed to the low restenosis rate. Thus, plaque debulking before DES implantation in bifurcated lesions possibly offers an optimal treatment outcome, especially in bifurcated lesions that are expected to require stent implantation in the side branch. PCI of left main trunk bifurcation lesions, even with a DES, remains challenging (11). Compared with nondistal left main trunk lesions, a previous study showed a high in-stent restenosis rate of 13% (13). In the PERFECT registry, a 0% restenosis rate of left main trunk bifurcated lesions was achieved by the use of DCA debulking before DES implantation. Despite the lack of strong scientific evidence supporting the advantage of plaque debulking in bifurcated lesions, these results strongly suggest that it is preferable to combine DCA and DES when the anatomical setting is appropriate to achieve a good long-term outcome.

**Study limitations.** The main limitation is the characteristics of the lesions involved in the PERFECT registry, which included lesions with a larger reference vessel diameter and without severe calcification that are suitable for DCA. In addition, DCA involves specific procedural techniques such as the precise evaluation of plaque distribution by IVUS and the appropriate control of athero-catheters. Thus, longer procedural and fluoroscopy times are required, as well as in-depth training of operators. Furthermore, the study was performed in a nonrandomized manner. Although this was a multicenter registry, only 99 patients were included. Therefore, a prospective randomized trial is required to demonstrate the efficacy of pre-DES debulking by DCA for bifurcated lesions.

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**REFERENCES**