Stenting After Optimal Lesion Debulking (SOLD) Registry

Angiographic and Clinical Outcome

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Background—Coronary stenting has reduced restenosis in focal de novo lesions, but its impact has been less pronounced in complex lesion subsets. Preliminary data suggest a role for plaque burden in promoting intimal hyperplasia after stent implantation. The aim of this study was to test the hypothesis that plaque removal with directional atherectomy before stent implantation may lower the intensity of late neointimal hyperplasia, reducing the incidence of in-stent restenosis.

Methods and Results—Seventy-one patients with 90 lesions underwent directional atherectomy before coronary stenting. Intravascular ultrasound–guided stenting was performed in 73 lesions (81%). Clinical success was achieved in 96% of patients. Procedural complications were as follows: emergency bypass surgery in 1 patient (1.4%), who died 2 weeks later; Q-wave myocardial infarction in 2 patients (2.8%); and non–Q-wave myocardial infarction in 8 patients (11.3%). None of the patients had stent thrombosis at follow-up. Angiographic follow-up was performed in 89% of eligible patients at 5.7±1.7 months. Loss index was 0.33 (95% CI, 0.26 to 0.40), and angiographic restenosis was 11% (95% CI, 5% to 20%). Clinical follow-up was performed in all patients at 18±3 months. Target lesion revascularization was 7% (95% CI, 3% to 14%).

Conclusions—Directional atherectomy followed by coronary stenting could be performed with good clinical success rate. Also, these data point to a possible reduction in angiographic restenosis and a significant reduction in the need for repeated coronary interventions. Therefore, a randomized clinical trial seems appropriate to test the validity of this approach. (Circulation. 1998;98:1604-1609.)

Key Words: stents ■ restenosis

Coronary stenting reduces restenosis in focal de novo lesions compared with balloon angioplasty.1,2 However, restenosis remains a problem in complex lesion subsets, such as long lesions in small or intermediate vessels, chronic total occlusions, ostial lesions, and bifurcational lesions.3,2 Suboptimal results in complex lesions may be partially due to the presence of a large plaque burden that may limit complete stent expansion and lead to longitudinal plaque redistribution, which may compromise adjacent coronary segments.8 In addition, preliminary intravascular ultrasound (IVUS) data suggest that a large plaque burden before stent implantation may promote neointimal hyperplasia, increasing the probability of in-stent restenosis.9 Currently, the most effective device to remove noncalcified plaque is directional coronary atherectomy (DCA),10,11 but even with optimal atherectomy, a restenosis rate of 31% has been reported.12 However, late lumen loss after DCA is the result primarily of late arterial constriction rather than neointimal hyperplasia.13

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We initiated a study to test the hypothesis that plaque removal with DCA before stent implantation may attenuate the degree of late lumen loss, reducing the incidence of stent restenosis.

Methods

Study Design and Patient Population

This pilot prospective registry was approved by our institution’s ethics committee. Between February 1996 and February 1997, 71 consecutive patients were recruited according to predetermined criteria: (1) clinical or functional evidence of ischemia; (2) no myocardial infarction (MI) within 48 hours; and (3) all the following: reference diameter ≥2.75 mm, diameter stenosis >70%, and lesion length <35 mm by visual estimate. Ostial and bifurcational lesions were considered for enrollment regardless of vessel size and lesion length. During the study period, slotted-tube stents were electively implanted without DCA in 356 patients (499 lesions). Reasons for excluding these patients were (1) left ventricular ejection fraction <35% (13 patients with 18 lesions) or (2) any of the following: reference diameter <2.75 mm (148 lesion), lesions >35 mm (5 lesions), lesions <10 mm and not in an ostial or a bifurcational location (126 lesion), moderate to severe fluoroscopic calciumifications (56 lesions), lesions at a bend of >45° (49 lesions), and thrombus at the lesion site (6 lesions). Other patients (91 lesions) were excluded because of operator decision or patient refusal to participate.

DCA and Stent Implantation

DCA was performed by use of the Simpson AtheroCath (Devices for Vascular Interventions) as previously described.14 The goal was to

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achieve an angiographic residual diameter stenosis <20% by visual estimate.

Coronary stenting was performed with slotted-tube stents as previously described,\(^\text{15}\) with the aim of achieving near-zero residual diameter stenosis by visual estimate. Stents used were the following: Multilink (15 and 25 mm; Advanced Cardiovascular Systems, Inc) in 36 lesions (40%); Palmaz-Schatz (Johnson & Johnson Interventional Systems) in 28 lesions (31%); NIR (16, 19, 25, and 32 mm; SciMed, Inc) in 12 lesions (13%); BeStent (Medronic, Inc) in 8 lesions (9%); and AVE Micro-Stent (18, 24, and 39 mm; Arterial Vascular Engineering) to cover distal dissections after initial stent implantation in 6 lesions (7%).

**IVUS Imaging and Coronary Angiography**

IVUS imaging was performed with a 30-MHz transducer-tipped catheter (Ultracross 3.2, Boston Scientific Corp) as previously described.\(^\text{18}\) The plaque burden at the lesion site at baseline and after DCA was expressed as percent plaque area (%PA) calculated as follows: vessel cross-sectional area (CSA) minus lumen CSA divided by vessel CSA. Degree of stent expansion was expressed as percent stent expansion (minimal stent lumen CSA divided by vessel CSA. Degree of stent expansion was expressed as the ratio of minimal stent lumen CSA divided by average reference lumen CSA).

Computerized quantitative angiographic measurements were performed as previously described\(^\text{19}\) with the CMS system (version 3.0, MEDIS). Several angiographic indexes were calculated: short-term gain [postprocedure minimum lumen diameter (MLD) minus preprocedure MLD]; late loss (postprocedure MLD minus MLD at follow-up), and loss index (late loss divided by short-term gain). Angiographic restenosis was defined as ≥50% diameter stenosis at the treated site at follow-up. Lesions were classified according to the American College of Cardiology–American Heart Association classification.\(^\text{20}\)

**Postprocedure Management and Follow-Up**

All patients received aspirin (325 mg) once a day and ticlopidine (250 mg) twice daily for 2 weeks. Patients were asked to return for angiographic follow-up at 6 months. Clinical follow-up was performed through an interview or phone conversation. Clinical events were defined as previously described.\(^\text{19}\)

**Statistics and Data Management**

Statistical analysis was performed with StatView (StatView 4.51, Abacus Concepts Inc). Continuous variables were expressed as mean±SD and were compared by unpaired Student’s \(t\) test. Categorical variables were compared by \(\chi^2\) analysis. The relationship between 2 continuous variables was expressed by simple linear regression analysis. Differences were considered statistically significant at \(P<0.05\).

Patients who underwent IVUS interrogation after DCA and returned for angiographic follow-up were divided into 2 groups according to the residual %PA after DCA: lesions with residual %PA <0.60 and those with residual %PA ≥0.60. This cutoff %PA was based on previous IVUS observations.\(^\text{9}\)

Lesions that had angiographic follow-up in the study group (75 lesions in 62 patients) were matched with 75 lesions in 71 patients who underwent stenting without DCA and returned for angiographic follow-up. This control arm was selected from 356 patients (499 lesions) who underwent elective slotted-tube stent implantation without DCA and had an 80% angiographic follow-up rate. Matching was performed with respect to presence of diabetes, previous PTCA, vessel diameter, lesion length, lesion severity, and number and type of stents implanted.

**Results**

**Patients, Lesions, and Procedural Characteristics**

Clinical and angiographic characteristics are shown in Table 1. Nineteen lesions (21%) were located at large bifurcations (branch >2.5 mm). In these lesions, the side branch had ≥50% diameter stenosis and was treated by PTCA in 15 lesions and by DCA and stenting in 4 lesions.

DCA was performed using a final GTO 7F cutter in 88 lesions (98%) and a 6F cutter in 2 lesions (2%) with 15±10 cuts per lesion. The final balloon-to-vessel ratio used for stent expansion was 1.16±0.15 with an inflation pressure of 17±4 atm.

**Angiographic and IVUS Analysis**

Preintervention, post-DCA, and poststenting angiographic and IVUS measurements are shown in Table 2. Twenty-eight lesions (31%) were in vessels <3 mm.

Preintervention and post-DCA IVUS was performed in 45 lesions. The %PA decreased from 79±7% to 49±13% after DCA (\(P<0.0001\)). Poststenting IVUS was performed in 73 lesions (81%). Figure 1 illustrates that DCA before stenting facilitated stent expansion (mean stent expansion, 97±16%). IVUS interrogation led to balloon upsizing and/or higher inflation pressure in 23 lesions (32%). In these lesions, mean balloon upsizing was 0.2±0.23 mm, and mean change in inflation pressure was 3.4±3.7 atm. This led to an increase in minimal lumen CSA from 7.32±1.23 to 8.62±1.23 mm\(^2\) (\(P<0.0001\)). This illustrates that IVUS imaging provides data that lead to further lumen enlargement even when DCA is used before stenting because of angiographic underestimation of true vessel size.

**Procedural Complications and Short-Term Outcome**

Coronary stents were successfully deployed in all patients, but 1 patient required prolonged balloon inflation for vessel...
Angiographic follow-up was performed in 62 of 70 eligible patients (89%). Figure 2 illustrates the angiographic measurements before intervention, after DCA, after stenting, and at follow-up. The loss index was 0.33 ± 0.33 (95% CI, 0.26 to 0.40) with angiographic restenosis in 8 of 75 lesions (11%) (95% CI, 5% to 20%). Three restenotic lesions (4%) were located at stent borders, and 5 (7%) were intrastent. Two intrastent restenoses occurred within a stent placed for a distal dissection when DCA was not performed, and the other 3 had suboptimal debulking after DCA (%PA >0.60). All restenotic lesions were focal. Two were treated conservatively, and 6 were treated with repeated balloon angioplasty (target lesion revascularization [TLR], the need for repeat intervention during 12-month follow-up period) 7%; 95% CI, 3% to 14%) with no further cardiac events. Long-term follow-up was performed at 18±3 months; no patients had MI, CABG, or death.

DCA Before Stenting Versus Stenting Alone: A Matched Comparison

A matched comparison was performed on 150 lesions treated with DCA plus stent (n=75) or stent alone (n=75). There was no difference between groups with respect to age (57±9 versus 59±9 years, P=0.20), sex (men, 92% versus 87%, P=0.41), prevalence of diabetes (13% versus 14%, P=0.84), or restenotic lesions (8% versus 8%, P=1.0). Similarly, there was no difference in number of stents per lesion (1.3±0.6 versus 1.4±0.7, P=0.35), balloon-to-vessel ratio (1.16±0.15 versus 1.14±0.12, P=0.15), and balloon inflation pressure (16.8±3.8 versus 17.3±3.0 atm, P=0.35). However, the DCA plus stent group had more lesions located at bifurcations (20% versus 7%, P=0.03), but there was no significant difference in frequency of chronic total occlusions (7% versus 13%, P=0.20) or ostial lesions (11% versus 4%, P=0.20). The immediate and late angiographic outcomes of matched lesions are shown in Table 3.

Relation Between Degree of Debulking Before Stenting and Loss Index at Follow-Up

This analysis was performed on lesions that underwent IVUS interrogation after DCA and had angiographic follow-up. The loss index was 0.28 ± 0.29 in lesions with post-DCA %PA <0.60 (n=45) compared with 0.52 ± 0.49 in lesions with post-DCA %PA >0.60 (n=7; P=0.067). The small number of lesions with large residual %PA resulted because the operator attempted to achieve a %PA <0.60 whenever possible. This difference in loss index led to a trend toward lower restenosis in lesions with low residual plaque burden.

TABLE 2. Quantitative Angiographic and IVUS Measurements

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention</th>
<th>Post-DCA</th>
<th>Poststenting</th>
</tr>
</thead>
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<tr>
<td>Angiographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Reference diameter, mm</td>
<td>3.27 ± 0.53</td>
<td>3.33 ± 0.51</td>
<td>3.49 ± 0.52</td>
</tr>
<tr>
<td>&lt;3.25 mm, n (%)</td>
<td>51 (57)</td>
<td>39 (43)</td>
<td></td>
</tr>
<tr>
<td>≥3.25 mm, n (%)</td>
<td>39 (43)</td>
<td>39 (43)</td>
<td></td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.87 ± 0.44</td>
<td>2.30 ± 0.58</td>
<td>3.47 ± 0.57</td>
</tr>
<tr>
<td>%DS</td>
<td>74 ± 13</td>
<td>31 ± 15</td>
<td>0.4 ± 10</td>
</tr>
<tr>
<td>Lesion length, mm</td>
<td>12.08 ± 6.31</td>
<td>. . . . .</td>
<td></td>
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<tr>
<td>≤10 mm, n (%)</td>
<td>35 (44)</td>
<td>45 (56)</td>
<td></td>
</tr>
<tr>
<td>&gt;10 mm, n (%)</td>
<td>27 (32)</td>
<td>10 (12)</td>
<td></td>
</tr>
<tr>
<td>Stent length, mm</td>
<td>. . . .</td>
<td>22 ± 13</td>
<td></td>
</tr>
<tr>
<td>Acute gain, mm</td>
<td>. . . .</td>
<td>2.61 ± 0.65</td>
<td></td>
</tr>
<tr>
<td>IVUS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>56</td>
<td>63</td>
<td>73</td>
</tr>
<tr>
<td>Minimum lumen CSA, mm²</td>
<td>2.83 ± 0.93</td>
<td>7.42 ± 2.14</td>
<td>8.63 ± 1.96</td>
</tr>
<tr>
<td>Vessel CSA, mm²</td>
<td>13.28 ± 3.86</td>
<td>14.91 ± 3.79</td>
<td>. . . . .</td>
</tr>
</tbody>
</table>

Figure 1. Frequency distribution of percent stent expansion.

Figure 2. Frequency distribution of angiographic MLD before intervention (Pre), after DCA, after stenting, and at follow-up (FU).
TABLE 3. Stenting After DCA Versus Stenting Alone

<table>
<thead>
<tr>
<th></th>
<th>DCA + Stent (n=75)</th>
<th>Stent (n=75)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
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<tr>
<td>RD, mm</td>
<td>3.26±0.53</td>
<td>3.26±0.40</td>
<td>0.92</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.85±0.44</td>
<td>0.85±0.36</td>
<td>0.96</td>
</tr>
<tr>
<td>DS, %</td>
<td>74±14</td>
<td>74±10</td>
<td>0.94</td>
</tr>
<tr>
<td>LL, mm</td>
<td>11.88±6.43</td>
<td>12.49±6.11</td>
<td>0.56</td>
</tr>
<tr>
<td>Postintervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RD, mm</td>
<td>3.49±0.53</td>
<td>3.30±0.44</td>
<td>0.015</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>3.48±0.60</td>
<td>3.15±0.43</td>
<td>0.0002</td>
</tr>
<tr>
<td>DS, %</td>
<td>0.3±10</td>
<td>4±11</td>
<td>0.037</td>
</tr>
<tr>
<td>Stent length, mm</td>
<td>21±10</td>
<td>22±11</td>
<td>0.56</td>
</tr>
<tr>
<td>Acute gain, mm</td>
<td>2.63±0.61</td>
<td>2.30±0.51</td>
<td>0.0004</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RD, mm</td>
<td>3.23±0.45</td>
<td>3.19±0.46</td>
<td>0.59</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.57±0.87</td>
<td>2.14±0.80</td>
<td>0.002</td>
</tr>
<tr>
<td>DS, %</td>
<td>21±23</td>
<td>35±21</td>
<td>0.0003</td>
</tr>
<tr>
<td>LL, mm</td>
<td>4.27±3.88</td>
<td>7.13±4.76</td>
<td>0.0001</td>
</tr>
<tr>
<td>Late loss, mm</td>
<td>0.91±0.94</td>
<td>1.02±0.75</td>
<td>0.44</td>
</tr>
<tr>
<td>Loss index</td>
<td>0.33±0.33</td>
<td>0.46±0.36</td>
<td>0.03</td>
</tr>
</tbody>
</table>

RD indicates reference diameter; DS, diameter stances; and LL, lesion length.

(4%) compared with lesions with large residual plaque burden (29%; P=0.08).

Discussion

Rationale for Debulking Before Stent Implantation

Restenosis after implantation of slotted-tube stents is due mainly to neointimal proliferation.18 The degree of neointimal hyperplasia after stenting is proportional to the degree of initial vessel wall stretch.19 The stretching force needed to expand the vessel is proportionate to the vessel wall resistance manifested by the absolute amount and consistency of the plaque. Therefore, it is logical that the maximal stretching force will need to be applied when the plaque is most severe to achieve adequate lumen gain. Theoretically, this effect may lead to a greater propensity for neointimal hyperplasia at the original plaque site. In fact, preliminary data in animal models support this concept.20 In humans, observational IVUS data2 indicate that a larger plaque burden leads to a higher rate of late lumen loss after stenting. In addition, observational angiographic data2 indicate that in-stent restenosis tends to occur at the original lesion site (where the plaque burden is largest). From these observations, we hypothesized that removal of the atherosclerotic plaque with DCA before stenting may attenuate late lumen loss, reducing the incidence of stent restenosis.

Is the Combination of DCA and Stenting Safe?

In this study, major adverse cardiac events (death, CABG, or Q-wave MI) in the first 30 days occurred in 3 patients (4.2%), similar to what has been reported in trials with a “simpler” approach in more favorable lesions. For example, in the STRESS trial,1 major adverse cardiac events at 30 days occurred in 4.9% of patients (Q-wave MI, 2.9%; CABG, 2%). Non–Q-wave MI in our study occurred in 8 patients (11.3%), similar to what was reported in the BOAT trial.12 Elevation of the serum CK-MB isoform level is not uncommon after otherwise successful coronary interventions. However, its impact on long-term outcome is the subject of ongoing investigations. Cutlip et al12 reported an analysis of 3387 patients treated in the BOAT, STARS, and STRATAS trials. In this analysis, no association was found between cardiac enzyme elevation and mortality at a 1-year follow-up. On the other hand, Simoons et al23 reported an analysis of 4762 patients from the CAPTURE, EPIC, and EPILOG trials. In this analysis, the authors found an association between the degree of CK-MB rise and mortality at the 6-month follow-up.

Furthermore, a subanalysis of the EPIC trial suggested that the use of abciximab reduces the incidence of non–Q-wave MI in patients undergoing DCA from 15% in the placebo arm to 5% in the abciximab arm.24 No conclusions could be drawn from the present study with regard to the effect of abciximab on the incidence of MI because it was not used in this cohort. However, most patients who developed MI in our study underwent aggressive debulking for several lesions in the same procedure. Therefore, perhaps the use of abciximab may be of benefit when aggressive debulking is anticipated.

Does Plaque Removal Before stenting Lead to a Reduction in Restenosis? A Matched Comparison to Stenting Alone

As shown in Table 3, the higher short-term lumen gain achieved in the DCA plus stent group compared with the stent alone group led to similar (not higher) late lumen loss. This led to a significantly lower loss index in the DCA plus stent group. This suggests that when atherosclerotic plaque is removed before stenting, a larger lumen could be obtained without being penalized with the same proportion of late lumen loss that would be expected when stenting without atherecomy. Figure 3 illustrates that for every given amount of short-term gain, there is less late lumen loss when DCA is used before stent implantation. However, the correlation coefficient between short-term gain and late loss, albeit statistically significant, is weak in the stent group (r=0.22, P=0.01) and only moderate in the DCA plus stent group (r=0.39, P=0.005). This may limit the strength of conclusions made with respect to the relationship between these 2 curves. Furthermore, the regression lines converge and intersect at a high level of lumen gain. This may suggest that in vessels in which large short-term lumen gain can be achieved with stenting alone, such as large vessels, the addition of DCA might be of less benefit. Alternatively, perhaps more plaque removal in these lesions might have maintained the favorable balance between short-term gain and late loss.

With respect to angiographic and clinical outcomes, the DCA plus stent group had a restenosis rate of 11% compared with 21% in the stent alone group (P=0.07). This led to significantly lower target lesion revascularization in the DCA plus stent group (7% versus 19%, P=0.03) despite the inclusion of more bifurcational lesions. A case example of...
combined DCA and stenting in a bifurcation lesion is shown in Figure 4. Other investigators have also reported low clinical and/or angiographic restenosis rates with DCA and stenting in different patient cohorts.25,26

It is difficult to perform a meaningful comparison with randomized trials testing the efficacy of stents alone because these trials have traditionally included patients with short lesions and excluded patients with total occlusions, restenotic, ostial, and bifurcational lesions. Instead, it may be more meaningful to compare the present study with other retrospective series with heterogeneous patient populations. In vessels <3.25 mm, Mehran et al3 reported a TLR rate of 22% after stenting lesions 10 to 15 mm long and 28% in lesions >15 mm. However, TLR was 14% in lesions <10 mm in vessels >3.25 mm. Kornowsky et al27 reported on the clinical outcome of patients who had stent implantation in 3.25-mm vessels. In that study, TLR varied according to whether lesions were de novo or restenotic (14% versus 23%, respectively). However, it should be noted that when TLR is based on clinical follow-up, the true incidence of significant luminal renarrowing may be underestimated because of silent ischemia, atypical symptoms, or administration of medical therapy instead of repeated intervention.

In summary, DCA before stenting in the present study led to a TLR rate of 7%. This is at least 50% lower than TLR after stenting alone in the control arm in our study and in the above retrospective series.

How Much Debunking Is Needed to Lower the Incidence of Restenosis After Coronary Stenting?

In the present study, reducing %PA to <0.60 after DCA led to a trend toward a reduction in angiographic restenosis. Interestingly, if another threshold %PA, such as 0.50, was empirically chosen to dichotomize the study population, 2 groups could be identified: lesions with %PA <0.50 (n = 28) and lesions with %PA >0.50 (n = 24). According to this categorization, loss index was 0.25±0.30 versus 0.40±0.35 (P=0.10) and restenosis rate was 4% versus 13% (P=0.23), respectively. This suggests that more aggressive debunking may lead to further reduction in loss index and restenosis, but the relative benefit narrows beyond a threshold residual %PA of 0.50.

Study Limitations and Clinical Implications

This study has several limitations. First, the number of patients is relatively small; therefore, wide CIs exist for both restenosis and target lesion revascularization rates. Second, the matching process may lead to selection bias. Finally, because IVUS was used to guide stenting in most patients, it is unclear whether angiographic guidance alone would have resulted in a similar outcome.

Combined DCA and stenting may lead to increased procedural time and costs. Thus, for this approach to be justified, short-term safety and improvement in long-term outcome need to be established to offset the initial increase in procedural complexity and cost. Because treatment of focal nonbifurcating de novo lesions is safe and effective with stenting alone,2 the combined approach may be best applied for lesions in which stenting alone has a high restenosis rate, such as long lesions in small or intermediate vessels, aorto-ostial lesions, bifurcational lesions, and chronic total occlusions.

Conclusions

DCA followed by coronary stenting could be performed with good clinical success. Also, these encouraging data point to a possible reduction in angiographic restenosis and a significant reduction in the need for repeated coronary interventions. Therefore, a randomized clinical trial appears appropriate for testing the validity of this approach.
References

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