Intravascular Ultrasound-Guided Percutaneous Transluminal Coronary Angioplasty With Provisional Spot Stenting for Treatment of Long Coronary Lesions

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OBJECTIVES

The purpose of this study was to evaluate the approach of intravascular ultrasound (IVUS)-guided percutaneous transluminal coronary angioplasty (PTCA) with spot stenting (SS) for the treatment of long coronary lesions.

BACKGROUND

Treating long coronary lesions with balloon angioplasty results in suboptimal short- and long-term outcomes. Full lesion coverage with traditional stenting (TS) has been associated with a high restenosis rate.

METHODS

We prospectively evaluated a consecutive series of 130 long lesions (>15 mm) in 101 patients treated with IVUS-guided PTCA and SS. The results were compared with those of TS in a matched group of patients. Coronary angioplasty was performed with a balloon to vessel ratio of 1:1, according to the IVUS media-to-media diameter of the vessel at the lesion site, to achieve prespecified IVUS criteria: lumen cross-sectional area (CSA) ≥5.5 mm² or ≥50% of the vessel CSA at the lesion site. The stents were implanted only in the vessel segment where the criteria were not met.

RESULTS

In the SS group, stents were implanted in 67 of 130 lesions, and the mean stent length was shorter than that of lesions in the matched TS group (10.4 ± 13 mm vs. 32.4 ± 13 mm, p < 0.005). The 30-day major adverse cardiac event (MACE) rate was similar (5%) for both groups. Angiographic restenosis was 25% with IVUS-guided SS, as compared with 39% in the TS group (p < 0.05). Follow-up MACE and target lesion revascularization rates were lower in the SS group than in the TS group (22% vs. 38% [p < 0.05] and 19% vs. 34% [p < 0.05], respectively).

CONCLUSIONS

Intravascular ultrasound-guided SS for the treatment of long coronary lesions is associated with good acute outcome. Angiographic restenosis and follow-up MACE rates were significantly lower than those with TS. (J Am Coll Cardiol 2001;38:1427–33) © 2001 by the American College of Cardiology

Treatment of long coronary lesions with plain balloon angioplasty has traditionally yielded poor immediate and long-term results (1,2). Coronary stents implanted in focal lesions in large vessels (≥3.0 mm) result in lower restenosis rates, as compared with balloon angioplasty (3,4). However, lesion length is an independent predictor of in-stent restenosis (5,6). Because improvements in stent implantation techniques and postprocedural pharmacologic management (7–9) have led to the broader application of coronary stenting in more complex lesions, the optimal approach for long lesions remains to be defined. Full lesion coverage with a stent from the proximal to distal normal segment has improved the immediate outcome, but has been associated with suboptimal long-term result (10,11). Stent length and the number of stents have been implicated as important predictive factors for restenosis in a number of studies (5,12–18). Pooled data from four clinical trials using a new-generation multicellular stent design stressed the importance of stent length, independent of postprocedural lumen gain, as a key predictor for in-stent restenosis (19).

In an effort to demonstrate the optimal intervention in long lesions, we introduced a new approach for the treatment of them. Intravascular ultrasound (IVUS)-guided percutaneous transluminal coronary angioplasty (PTCA) with spot stenting (SS) is a synergistic strategy employing PTCA, IVUS and stenting for the treatment of long lesions. This technique minimizes the need for stenting, with use of shorter stent lengths. Stents are only placed in the particular segments of a lesion where the luminal result does not meet prescribed IVUS criteria after balloon angioplasty.

METHODS

Study design and patient group. This prospective study was performed at Centro Cuore Columbus, Milan, Italy. All patients with angiographically significant coronary lesions referred for a coronary intervention were screened for inclusion. Patients with an acute myocardial infarction within the last 48 h were excluded. Any lesion with an angiographic length >15 mm and diameter stenosis >70%...
Intravascular ultrasound-guided PTCA with SS. Patients with long lesions (>15 mm) were initially treated with IVUS-guided PTCA and SS. A comparison was undertaken with a group of matched patients who were treated with a traditional stenting (TS) approach in which the lesion was fully covered from the proximal to distal normal segment. The two groups were matched in terms of clinical and angiographic variables. The matching process was performed as follows: all patients with stented lesions >15 mm with angiographic follow-up were screened for enrollment into the control group (TS). The first step in the process was to match for the reference vessel diameter and lesion length. All lesions within 0.05 mm of the reference vessel diameter of vessels in the SS group and within 2 mm of the lesion length were placed in the control group. Then, the left ventricular ejection fraction, which had to be within 0.05, was matched. The next step was to match for age, which had to be within ±2 years. Finally, there had to be an equal number of patients in each group with diabetes and unstable angina. To lower any possible bias, the first patient who satisfied the matching characteristics was entered from the initial group into the final TS group. This matching process resulted in a selection of 121 patients with 143 lesions in the TS group, to be compared with the SS group.

Intravascular ultrasound-guided PTCA with SS. Patients with long lesions (>15 mm) were initially treated with PTCA. Baseline IVUS measurements were performed at the diseased segment of the artery. For the initial PTCA, the balloon size was selected according to the media-to-media diameter at the lesion site, so that the balloon to vessel ratio was 1:1. The lesion was predilated if it was severe enough to prevent pre-intervention IVUS evaluation. After the initial intervention, IVUS was performed. The procedure was complete if the treated segment satisfied either of the following two success criteria: 1) lumen cross-sectional area (CSA) ≥50% of the vessel at the lesion site, or 2) minimal lumen CSA ≥5.5 mm².

If any segment of the treated vessel did not meet either of these criteria, the operator could proceed with further balloon dilation or stenting. The stent length to be used had to be the shortest length necessary to cover only the segments of the lesion, in which the two aforementioned IVUS success criteria were not satisfied.

These success criteria did not take into account the presence of a dissection, as long as the true lumen CSA met the aforementioned IVUS criteria and angiographic Thrombolysis In Myocardial Infarction flow grade 3 was present. Intravascular ultrasound was performed at the end of the procedure to ensure achievement of the IVUS success criteria and to document the final lumen dimensions. Coronary stenting was performed using stents of slotted tubular or ring design. During the procedure, heparin was given to maintain an activated clotting time between 250 and 300 s. Patients were treated with aspirin, 325 mg/day, and ticlopidine, 250 mg twice daily, started at least on the day of the procedure.

**Angiographic analysis.** Coronary angiography was performed in a routine manner. Patients received intracoronary nitroglycerin (200 μg) before the initial and final angiograms to achieve maximal vasodilation. Vessel size and lesion length was visually estimated at the time of the procedure. Quantitative coronary angiography (QCA) was performed after the procedure, using a computer-based QCA-CMS system, version 4.0 (MEDIS Medical Imaging Systems Inc., Leiden, The Netherlands), with the dye-filled catheter as a reference. The reference vessel diameter, minimal lumen diameter, percent diameter stenosis and lesion length were measured at baseline and on the final angiogram. The interpolated reference diameter was considered as the reference segment diameter. Lesion length was defined as the distance from the proximal to distal segment of the lesion site. The lesions were characterized according to the modified American College of Cardiology/American Heart Association classification (20). Long lesions were defined as a single continuous narrowing >15 mm in length. Dissections were recorded and classified according to the National Heart, Lung and Blood Institute type (21).

**IVUS equipment and measurements.** Intravascular ultrasound imaging was performed using a 3.2-F Monorail system with a 30-MHz transducer-tipped catheter (Ultrasound 3.2, Boston Scientific Corp., Sunnyvale, California). All images were obtained with an automatic pullback system at 0.5 mm/s. The position of the catheter on fluoroscopy was used to correlate the angiographic and ultrasound images. Data were stored on 0.5-in. super VHS videotape. On-line quantitative measurements were performed during the procedure. The lesion site with the smallest lumen area was selected for measurement of each pass of the IVUS catheter. Side branches, calcium and perivascular structures were used for comparing IVUS runs. Reference lumen CSAs were measured proximal and distal to the treated segment in the closest, most normal appearing segments. The average reference lumen CSA was calculated as the mean value of the proximal and distal reference lumen CSAs.
Follow-up. Clinical follow-up was obtained approximately six months after the procedure and every six months afterward by telephone or direct patient interview. Angiographic follow-up was planned and encouraged for each patient.

Definitions. A major adverse cardiac event (MACE) was defined as any death, myocardial infarction or target lesion revascularization (TLR). Target lesion revascularization was defined as any repeat percutaneous intervention or coronary artery bypass graft surgery performed to treat the index lesion. A diagnosis of Q-wave myocardial infarction (QMI) was made when there was documentation of new pathologic Q waves on the ECG. A diagnosis of non-QMI was made when an elevation of CK greater than twice the normal value, with a positive CK-MB fraction, was documented without development of new pathologic Q waves. A diagnosis of ST elevation myocardial infarction (STEMI) was made when there was documentation of new pathologic Q waves on the ECG in conjunction with an elevation in creatine kinase (CK) greater than twice the normal value, with a positive CK-MB fraction.

Statistical analysis. Statistical analysis was performed using the StatView statistical package (StatView version 5.0, Abacus Concepts Inc., Berkeley, California). Continuous, normally distributed data were expressed as the mean value ± SD. A comparison of continuous variables between the groups was performed by using the unpaired Student t test. Subgroup comparisons of categorical variables were performed by using the chi-square test. Differences were considered statistically significant at p < 0.05.

RESULTS

Patient characteristics. Patient characteristics for the two groups are shown in Table 1. There was no significant difference between the two groups in terms of baseline patient characteristics.

Angiographic and procedural variables. The angiographic and procedural characteristics of the two groups are shown in Table 2. There were no significant differences between the SS and TS groups in terms of treated vessel, lesion location, lesion type and presence of calcium or total occlusions. Complex lesions (type B2 or C) comprised the majority of the lesions in both groups. Of the 130 lesions treated with SS, 67 (52 patients) required stenting, because they did not meet the IVUS criteria for IVUS-guided balloon angioplasty. The final balloon size, balloon/artery ratio and maximal inflation pressure were similar between the two groups (p = NS). The mean stent length was significantly shorter in the SS group (10.4 ± 13 mm vs. 32.4 ± 13 mm, p < 0.005). Calculation of the average stent length for the SS group included all of the lesions, on an intention-to-treat basis (n = 130). This average includes only the lesions in the SS group that did receive a stent (n = 67). Data are presented as the mean (%) of lesions or the mean value ± SD.

The QCA measurements before and after the intervention are shown in Table 3. At baseline, the only significant differences between the SS and TS groups were shown in Table 2. There were no significant differences between the SS and TS groups in terms of treated vessel, lesion location, lesion type and presence of calcium or total occlusions. Complex lesions (type B2 or C) comprised the majority of the lesions in both groups. Of the 130 lesions treated with SS, 67 (52 patients) required stenting, because they did not meet the IVUS criteria for IVUS-guided balloon angioplasty.

The final balloon size, balloon/artery ratio and maximal inflation pressure were similar between the two groups (p = NS). The mean stent length was significantly shorter in the SS group (10.4 ± 13 mm vs. 32.4 ± 13 mm, p < 0.005). Calculation of the average stent length for the SS group included all of the lesions, on an intention-to-treat basis (n = 130). However, only 67 lesions in this group actually required a stent. The calculated mean stent length for this subgroup of patients with 67 lesions is 20.2 ± 12 mm; the median stent length was 16 mm. When comparing this subgroup of 67 lesions with those of the patients in the TS group, there was still a significant difference in stent length (p < 0.005).

Glycoprotein IIb/IIIa inhibitors were used in three patients in the SS group and in 11 patients in the TS group. A typical example of a long lesion treated with the SS approach is shown in Figure 1.

QCA analysis. The QCA measurements before and after the intervention are shown in Table 3. At baseline, the only significant differences between the SS and TS groups were...
the minimal lumen diameter and percent diameter stenosis, representing unfavorable lesion characteristics for the SS group. There was a trend toward a greater acute gain in the TS group as compared with the SS group (p < 0.06). The stent length to lesion length ratio was significantly higher in the TS group (0.79 ± 0.4 vs. 1.3 ± 0.5, respectively; p < 0.0001).

Procedural outcome and clinical events. Procedural outcome and 30-day events are shown in Table 4. There was no significant difference between the two groups in terms of procedural complications. Cumulative 30-day MACE (death, coronary artery bypass graft surgery, QMI and non-QMI) occurred in five patients (5%) in the SS group and in six patients (5%) in the TS group. Residual angiographic dissections were left untreated in 51 lesions (39%) in the SS group and in 12 lesions (8%) in the TS group (p < 0.0001). Most of the untreated dissections (82%) were type B in both groups. There was no significant difference in the rate of procedural complications between the lesions with residual dissection and those without dissection, including acute and subacute thrombosis (0 [0%] vs. 2 [0.9%] and 1 [1.6%] vs. 1 [0.4%], respectively).

Angiographic and clinical follow-up. Six-month angiographic and clinical follow-up data are presented in Table 4. Clinical follow-up data were obtained for all patients in both groups. The angiographic follow-up rate at six months was 84% in the SS group.

Figure 1. An example of intravascular ultrasound (IVUS)-guided spot stenting (SS). (A) Preprocedural angiogram and IVUS images of a long lesion in the intermediate branch. The IVUS catheter could not cross the distal part of the lesion. (B) After balloon angioplasty. Angiogram and IVUS image after dilation with a 3.5 × 20 mm balloon. Intravascular ultrasound revealed a dissection and suboptimal dilation at the lesion site (74% residual stenosis).
DISCUSSION

IVUS-guided PTCA with SS. The approach of IVUS-guided PTCA for the treatment of coronary lesions has shown promising results. In the CLinical Outcomes with Ultrasound Trial pilot trial (22), IVUS guidance was used to optimize PTCA results. Larger balloon sizes were required in 73% of lesions, despite an optimal angiographic result. This oversized balloon in PTCA resulted in significantly larger final minimal lumen diameters, without increased rates of significant dissections or ischemic complications. In our study, despite the use of stents in only about half of the lesions treated, the average acute gain achieved was 1.94 ± 0.77 mm. This is comparable to the acute gain achieved in the stent arms of the BElgian NEtherlands STENT (BE-NESTENT) trial and the STent REStenosis Study—1.40 ± 0.44 mm and 1.72 ± 0.46 mm, respectively (3,4).

The Washington Hospital Center compiled a prospective registry of IVUS-guided balloon angioplasties utilizing balloons sized according to the media-to-media diameter, as determined by IVUS (23). The one-year TLR rate was 8% in the PTCA group, as compared with 16% in the stent group (p = 0.01). In approximately half of the patients treated with IVUS-guided PTCA, stent implantation could be avoided without increasing acute complications or late adverse outcomes.

In the randomized Strategy for Intracoronary ultrasound-guided PTCA and Stenting trial (24), a total of 269 patients with focal lesions were randomized to IVUS-guided provi-

Table 3. Quantitative Angiographic Measurements

<table>
<thead>
<tr>
<th></th>
<th>SS Group (n = 130)</th>
<th>TS Group (n = 143)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference artery diameter (mm)</td>
<td>2.95 ± 0.48</td>
<td>2.98 ± 0.48</td>
<td>0.39</td>
</tr>
<tr>
<td>Minimal lumen diameter (mm)</td>
<td>0.75 ± 0.43</td>
<td>0.88 ± 0.40</td>
<td>0.01</td>
</tr>
<tr>
<td>Stenosis (%)</td>
<td>75 ± 14</td>
<td>71 ± 11</td>
<td>0.01</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>26.5 ± 9.8</td>
<td>25.0 ± 8.7</td>
<td>0.17</td>
</tr>
<tr>
<td>After procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference artery diameter (mm)</td>
<td>3.12 ± 0.50</td>
<td>3.19 ± 0.50</td>
<td>0.26</td>
</tr>
<tr>
<td>Minimal lumen diameter (mm)</td>
<td>2.70 ± 0.66</td>
<td>2.99 ± 0.48</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stenosis (%)</td>
<td>14.2 ± 16</td>
<td>5.8 ± 11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Early gain (mm)</td>
<td>1.94 ± 0.77</td>
<td>2.09 ± 0.59</td>
<td>0.06</td>
</tr>
<tr>
<td>Stent length/lesion length ratio</td>
<td>0.79 ± 0.40*</td>
<td>1.3 ± 0.46</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*This mean value includes only the stented lesions from the SS group (n = 67). Data are presented as the mean value ± SD.

SS = spot stenting; TS = traditional stenting.

Table 4. Early and Late Outcomes

<table>
<thead>
<tr>
<th></th>
<th>SS Group (101 pts, 130 lesions)</th>
<th>TS Group (121 pts, 143 lesions)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated dissection</td>
<td>51 (39%)</td>
<td>12 (8.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Type A</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Type B</td>
<td>42</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Type C</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Acute thrombosis</td>
<td>0 (0%)</td>
<td>2 (1.4%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Subacute thrombosis</td>
<td>1 (0.8%)</td>
<td>1 (0.7%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Procedural non-QMI</td>
<td>2 (2%)</td>
<td>3 (2.5%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Procedural QMI</td>
<td>2 (2%)</td>
<td>3 (2.5%)</td>
<td>0.94</td>
</tr>
<tr>
<td>CABG</td>
<td>1 (1%)</td>
<td>1 (0.8%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.99</td>
</tr>
<tr>
<td>30-day MACE</td>
<td>5 (5%)</td>
<td>6 (5%)</td>
<td>0.99</td>
</tr>
<tr>
<td>6-month MACE</td>
<td>22 (22%)</td>
<td>46 (38%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Restenosis</td>
<td>27 (25%)</td>
<td>55 (39%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TLR</td>
<td>25 (19%)</td>
<td>48 (34%)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data are presented as the number (%) of patients or lesions. MACE = major adverse cardiac event; pts = patients; QMI = Q-wave myocardial infarction; TLR = target lesion revascularization; Other abbreviations as in Table 1.
sional stenting or standard angiographic guidance. Stenting was performed in ~50% of lesions in both groups. Intravascular ultrasound-guided provisional stenting improved the two-year clinical results.

On the basis of these concepts, we modified the IVUS-guided PTCA approach to include the SS technique for the treatment of long lesions. The shortest possible stent length was used to optimize the results, but only in the segments of a long lesion where the lumen dimensions did not meet prespecified IVUS criteria. The rationale behind this approach is avoidance of full-lesion stent coverage of long segments, for which restenosis rates are expected to be high (12–16). Stent length may exacerbate neointimal hyperplasia.

An unsatisfactory angiographic result, which would normally lead to additional stenting, when evaluated by IVUS, may be considered as acceptable. This decision is based on true lumen evaluation rather than angiographic silhouette assessment.

How does this approach translate into an operational strategy? First, determine whether the lesion needs SS, which may be a laborious and time-consuming approach and should be used only if necessary. We empirically stated that this approach should be used in lesions >15 mm and, generally, when the vessel size is not >3.5 mm in size. This statement is based on the fact that implanting long stents in vessels with a large angiographic reference vessel size (>3.5 mm) is usually associated with more acceptable restenosis rates (17).

Second, if the lesion needs SS, the first step is to perform IVUS to determine the optimal balloon size needed to perform angioplasty. Intravascular ultrasound is necessary because these lesions are frequently located in a vessel with diffuse disease. This situation leads to an underestimation of the true vessel size when angiography is used to make the assessment. Dilation of a lesion with an undersized balloon may lead to a suboptimal result.

Procedural safety. The rate of major procedural complications in this study does not differ significantly from the complication rates reported with TS in focal lesions in the BENESTENT II trial (25). The cumulative incidence of acute and subacute thromboses in the SS group was 0.8%, and should be used only if necessary. We empirically stated that this approach should be used in lesions >15 mm and, generally, when the vessel size is not >3.5 mm in size. This statement is based on the fact that implanting long stents in vessels with a large angiographic reference vessel size (>3.5 mm) is usually associated with more acceptable restenosis rates (17).

Six-month follow-up outcome. Considering that the lesions treated with the IVUS-guided SS approach had a mean vessel diameter of 2.95 mm and a mean length of 26.5 mm, an angiographic restenosis rate of 25%, a TLR rate of 19% and a six-month follow-up MACE rate of 22% represent a considerable improvement in outcome, as compared with the rates reported on the treatment of long lesions (10–16).

Implications for management of dissections after coronary interventions. Traditionally, dissections after PTCA have been considered a marker of acute closure or stent thrombosis (26). However, inducing dissections is an integral part of lumen enlargement with PTCA, and not all dissections should be judged to be equal (27). In this study, final residual angiographic dissections were left untreated in 39% of lesions treated with the SS approach (82% type B). If the IVUS measurement of the true lumen at the dissection area was >50% of the vessel CSA, the dissection was considered as acceptable. If this target was not met, a stent was implanted at the site of the dissection. Subgroup analysis of the vessels with untreated dissections in this study demonstrated no difference in the incidence of adverse events, including short- and long-term outcomes.

Study limitations. The major limitation of this study is that it was not a randomized trial. Even if it was accurate, the matching process may have led to a selection bias. In addition, we cannot determine the contribution of IVUS, versus the use of provisional and short stents, to the improved outcome.

Conclusions. Intravascular ultrasound-guided balloon angioplasty with SS permits safe treatment of long lesions. Long-term outcomes, including angiographic restenosis and follow-up MACE, are superior to the outcomes achieved in the matched group of patients treated with TS and to those in historical control subjects treated with balloon angioplasty alone or TS.

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