Stenting of Nonacute Total Coronary Occlusions: Predictors of Late Angiographic Outcome

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Objectives. This study was designed to determine and assess factors predictive of the intermediate-term outcome of stenting of nonacute total coronary occlusions.

Background. Balloon angioplasty of recanalized coronary occlusions is associated with a combined restenosis/reocclusion rate of up to 65%. Adjunctive stenting holds the potential to reduce this rate significantly. However, variables affecting the late angiographic outcome of coronary stenting in the setting of a total occlusion have not been elucidated sufficiently.

Methods. Coronary stenting was performed in 143 consecutive patients with a nonacute total occlusion; 120 of these patients (84%), with a total of 121 occlusions, underwent repeat angiography within 6 months and comprised the study group. High pressure stent implantation aimed to cover the site of the occlusion as well as adjacent diameter stenoses ≥70% and all possibly induced dissections. Pertinent angiographic and procedural variables obtained at the time of the intervention were entered into a multivariate logistic regression analysis model to assess their influence on the angiographic outcome at follow-up.

Results. Mean preinterventional reference lumen diameter for the 121 vessels was 2.99 ± 0.53 mm (mean ± SD); occlusion length ranged from 4 to 44 mm (median of 7.7). After balloon angioplasty, dissections were found in 80% of patients. Lesions were covered with stents a median of 16 mm in length (range 8 to 53). The minimal lumen diameter (MLD) achieved after stenting was 2.89 ± 0.48 mm. After a median follow-up period of 4.5 months, mean MLD was assessed at 1.91 ± 0.90 mm, corresponding to a loss index of 0.34 ± 0.31. There were 27 vessels with a nonocclusive restenosis ≥50% and 8 with a reocclusion, for a combined restenosis/reocclusion rate of 29%. Factors found to adversely influence angiographic outcome were a post-stenting MLD ≤2.54 mm, a stented vessel segment length >16 mm, a balloon/vessel diameter ratio for final stent expansion ≤1.00 and the presence of a dissection after balloon angioplasty.

Conclusions. Compared with previous reports on stand-alone balloon angioplasty, stenting of nonacute total coronary occlusions lowers the 6-month restenosis/reocclusion rate to ~30%. The late procedural outcome is independently and statistically significantly influenced by the MLD after stenting, the length of the stented vessel segment, the balloon/vessel diameter ratio for final stent expansion and the incidence of dissections after balloon angioplasty.

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ful in 157 (67%). Of these 157 patients, 143 subsequently underwent stent implantation, with repeat angiography available in 120 (84%; 91 men, 29 women; mean age [±SD] 58 ± 10 years), who comprised the study group. A nonacute total coronary occlusion was defined as an occlusion at least 1 week old (assessed clinically or angiographically). Patients were either symptomatic (n = 89, median Canadian Cardiovascular Society functional class III) or had signs of myocardial ischemia (n = 31). There was a total of 121 occlusions, distributed by vessel as follows: right coronary artery, n = 57 (47%); left anterior descending coronary artery, n = 42 (35%); left circumflex coronary artery, n = 20 (16%); venous bypass graft, n = 2 (2%). In 58% of cases, the occluded vessel segment was proximal, in 42% it was mid or distal. Coronary flow distal to the occlusion was Thrombolysis in Myocardial Infarction (TIMI) flow grade 0 in 60 occlusions and TIMI flow grade 1 in 61. The median age of the occlusions was 8 weeks (range 1 week to 18 years).

Acute intervention. The patients were informed about the coronary interventional procedure and gave their written consent. All patients received 5,000 IU of heparin at the onset of the intervention. Once it became evident that the artery could be recanalized, another 5,000 to 10,000 IU of heparin was added. Balloon angioplasty before stent implantation was performed in 120 patients. Subsequently, stent implantation was performed at all lesion sites and was preceded in one patient by rotablation (Rotational Angioplasty System, Heart Technology, Inc.) and in four by excimer laser angioplasty (Vitesse C 1.4, Spectranetics). Subsequently, stent implantation was performed such that the site of the occlusion as well as the adjacent diameter stenoses ≥70% and all possibly induced dissections were completely covered. High pressure stent expansion (11 to 20 atm) was routinely performed without intravascular ultrasound control.

All patients were pretreated with 100 mg of aspirin, which was continued until the repeat angiography procedure. Ticlopidine (250 mg twice daily) was added for 3 months. The first tablet was given after the arterial sheath had been removed, which usually took place 6 h after the procedure.

Follow-up. Repeat angiography was scheduled at ~6 months after the intervention and included a quantitative assessment of the patient’s angiographic status and, in cases of a percent diameter restenosis ≥50%, a repeat intervention. At that time, a clinical evaluation was obtained as well.

Angiographic measurements. Quantitative coronary angiography was performed by two experienced investigators (T.R., J.S.) using digital electronic calipers. The following variables were recorded at the time of the intervention and, if pertinent, at the time of repeat angiography: reference lumen diameter, minimal lumen diameter (MLD) and length of occlusion, all measured in the projection showing the smallest MLD. A dissection after balloon expansion was defined as an intraluminal filling defect or a deposit of contrast agent in the vessel wall.

Angiographic definitions. Acute gain = MLD after stenting minus MLD at baseline. Late loss = MLD after stenting minus MLD at follow-up. Loss index = late loss divided by acute gain.

Statistical analysis. Continuous variables are presented as mean value ± SD, if appropriate. In case of a non-Gaussian distribution, median and range are given. Nominal data were analyzed with the chi-square test. A multiple logistic regression analysis was performed to determine the chance of a restenosis (including reocclusion) within 6 months for a given set of covariates (13). For this analysis it is assumed that the logarithmic odds in favor of a restenosis/reocclusion can be expressed as a linear combination of n conditions Xᵢ with Xᵢ = 1, if the respective condition is fulfilled, and Xᵢ = 0, if it is not fulfilled:

\[ \log \text{Odds[Restenosis_Reocclusion]} = \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n \]

OR = \exp\left( \sum_{i=1}^{n} \beta_i - \sum_{m=1}^{m} \beta_m \right)

Thus, the regression coefficients \( \beta_i \) denote the relative weight of each condition’s contribution to the logarithmic odds. From these coefficients, a relative risk or odds ratio (OR)

may be calculated that gives the chance of a restenosis/reocclusion in the presence of n conditions fulfilled compared with m conditions fulfilled. Statistical significance was assumed at the 5% level.

Results

Stents. Palmaz-Schatz tubular slotted stents (Johnson & Johnson Interventional Systems) were implanted in 71 lesions (59%); the Microstent (Arterial Vascular Engineering, Inc.) was used for 38 lesions (31%) and Wiktor stents (Medtronic Inc.) for 6 lesions (5%). A combination of different stent types were deployed in the remaining six lesions (5%). The mean number of stents/lesion was 1.5 ± 0.8.

Acute angiographic results. Mean reference lumen diameter of the 121 occluded vessels at baseline was 2.99 ± 0.53 mm; in 67 vessels (55%), the reference vessel diameter was <3.0 mm. The median occlusion length was 7.7 mm (range 4 to 44 mm); stented segment length ranged from 8 to 53 mm (median 16) and exceeded the occlusion length by a mean of 9.6 ± 0.9 mm. Balloon angioplasty before stent implantation achieved an MLD of 1.58 ± 0.52 mm, which corresponded to a diameter stenosis of 46 ± 17%. The mean balloon/vessel diameter ratio for final stent expansion was 1.12 ± 0.17; maximal stent expansion pressure was 16.6 ± 1.6 atm. The
presence or absence of a dissection after balloon dilation could be determined in 118 patients and was observed in 94 (80%). After stenting, the MLD in the stented segment was significantly increased to 2.89 ± 0.48 mm (p < 0.001), corresponding to a diameter stenosis of 2 ± 17%.

Angiographic follow-up. Angiographic follow-up was obtained within a median of 4.5 months (range 1.9 to 13.0). The reference vessel diameter was determined at 3.00 ± 0.50 mm (p = 0.81 vs. baseline). Mean MLD was 1.91 ± 0.90 mm (Fig. 1), corresponding to a late loss of 0.98 ± 0.82 mm and a loss index of 0.34 ± 0.31. Mean diameter stenosis was 36 ± 29%. There were 27 vessels (22%) with a nonocclusive restenosis ≥50% and 8 (7%) with a reocclusion, corresponding to a combined restenosis/reocclusion rate of 29%. Pertinent angiographic, clinical and procedural variables for patients with and without a restenosis/reocclusion are presented in Table 1.

Table 1. Angiographic, Clinical and Procedural Variables for 120 Study Patients

<table>
<thead>
<tr>
<th></th>
<th>No Restenosis (86 lesions)</th>
<th>Restenosis/Reocclusion (35 lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline ref diam (mm)</td>
<td>2.96 ± 0.51</td>
<td>3.07 ± 0.57</td>
</tr>
<tr>
<td>Post-stenting MLD (mm)</td>
<td>2.94 ± 0.46</td>
<td>2.75 ± 0.51*</td>
</tr>
<tr>
<td>Post-stenting residual stenosis (%)</td>
<td>−1 ± 16</td>
<td>9 ± 17*</td>
</tr>
<tr>
<td>Stented segment length (mm)</td>
<td>19.1 ± 8.3</td>
<td>24.6 ± 10.7*</td>
</tr>
<tr>
<td>Clinical/procedural variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion age (mo)</td>
<td>2 (0.25–216)</td>
<td>2 (0.25–143)</td>
</tr>
<tr>
<td>Lesions in diabetic pts</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>PS stents</td>
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<td>19</td>
</tr>
<tr>
<td>AVE Microstents</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>Combined/other stents</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

*p < 0.05 versus no restenosis. Data presented are mean value ± SD, median (range) or number of lesions. AVE = arterial vascular engineering; MLD = minimal lumen diameter; PS = Palmaz-Schatz; pts = patients; ref diam = reference diameter.

Factors determining restenosis/reocclusion. Univariate analysis. Neither the patient’s age nor gender had a statistically significant impact on the occurrence of restenosis/reocclusion at follow-up. The distributions of stent types as presented in Table 1 for patients with and without restenosis/reocclusion were statistically not different (chi-square = 2.20, p = 0.33). Occlusion age between the two patient groups was also statistically not different (Table 1). There was no dependence of the restenosis/reocclusion rate on the reference vessel diameter at baseline (Fig. 2A). However, the prevalence of restenosis/reocclusion among patients with a post-stenting MLD ≤2.54 mm was, at 50%, more than twice as high as that for patients with a post-stenting MLD >2.54 mm (Fig. 2B).

Multivariate analysis. From the preceding univariate analysis the following conditions were derived and entered as predictors into the logistic regression model: 1) MLD after stenting dichotomized at ≤2.54 mm; 2) stented vessel segment length trichotomized into ≤16 mm, >16 to ≤26 mm and >26 mm; 3) balloon/vessel ratio dichotomized into ≤1.00, >1.00 to ≤1.25 and >1.25; and 4) the presence of a dissection after balloon dilation before stenting. The results are shown in Table 2 and can be interpreted as follows: Compared with patients with a post-stenting MLD >2.54 mm, patients with a post-stenting MLD ≤2.54 mm had a 9.25-fold risk of a restenosis/reocclusion; a stented vessel segment length >26 mm increased the risk by a factor of 6.53 compared with a stented vessel segment length ≤16 mm; patients in whom the balloon/vessel ratio for final stent expansion was ≤1.00 carried a 9.97-fold risk of restenosis/reocclusion compared with patients in whom this ratio was >1.25; and the presence of a dissection after balloon angioplasty increased the risk by a factor of 5.

To further illustrate the results of the multivariate logistic regression analysis, consider a patient in whom the risk factors are the presence of a dissection after balloon angioplasty and a stented vessel segment length >16 but ≤26 mm. Compared with a patient without a dissection and a stented vessel segment length ≤16 mm, this patient’s relative risk to develop...
Restenosis, or even reocclusion, within 6 months has been the major drawback of an initially successful coronary intervention aimed at reestablishing coronary flow. For a total coronary occlusion, the combined restenosis/reocclusion rate after recanalization and adjunctive balloon dilation has been reported to be as high as 65% (14). The present study of 120 patients with a total coronary occlusion at least 1 week old revealed that coronary stenting performed in addition to balloon angioplasty was associated with comparatively low 6-month restenosis and reocclusion rates of only 22% and 7%, respectively. Four variables were found to have an independent, statistically significant influence on the likelihood of a restenosis/reocclusion: 1) the presence of a dissection after balloon angioplasty; 2) the size of the post-stenting MLD; 3) the length of the stented vessel segment; and 4) the balloon/vessel diameter ratio for final stent expansion.

**Discussion**

**Main findings.** Restenosis, or even reocclusion, within 6 months has been the major drawback of an initially successful coronary intervention aimed at reestablishing coronary flow. For a total coronary occlusion, the combined restenosis/reocclusion rate after recanalization and adjunctive balloon dilation has been reported to be as high as 65% (14). The present study of 120 patients with a total coronary occlusion at least 1 week old revealed that coronary stenting performed in addition to balloon angioplasty was associated with comparatively low 6-month restenosis and reocclusion rates of only 22% and 7%, respectively. Four variables were found to have an independent, statistically significant influence on the likelihood of a restenosis/reocclusion: 1) the presence of a dissection after balloon angioplasty; 2) the size of the post-stenting MLD; 3) the length of the stented vessel segment; and 4) the balloon/vessel diameter ratio for final stent expansion.

**Dissection after balloon angioplasty.** This complication occurred in 80% of the 118 patients in whom it could be confidently assessed. Among the 34 patients with restenosis/reocclusion, a dissection was observed in 32 (94%). Consequently, as shown by the logistic regression analysis, patients in whom dissection occurs during balloon dilation bear an increased risk of a restenosis/reocclusion at follow-up, which is five times higher than that of patients without this complication.

This finding is in concordance with a recent study by Goldberg et al.,(10) who found that “only the presence of a procedure-related moderate to severe dissection was associated with higher follow-up percent diameter stenosis and clinical events.” The mechanism by which a dissection favors the development of a restenosis is still unclear. The high rate of dissection after balloon angioplasty of an occluded vessel found in the present study is probably a consequence of a significant plaque burden at the lesion site. The exertion of radial force in this situation might create deep vessel wall
injury in some patients, with an extensive destruction of the endothelium and deeper layers of the wall; this in turn could enhance an inflammatory response and intimal hyperplasia. However, that two-thirds of the patients with a dissection experienced no restenosis suggests that only minor vessel injury occurred after balloon angioplasty.

**Post-stenting MLD.** The post-stenting MLD exhibited a cutoff value of 2.54 mm with regard to the presence of restenosis/reocclusion at follow-up. When the MLD was ≤2.54 mm, the restenosis/reocclusion rate was at 50% significantly higher than for patients with an MLD >2.54 mm in whom the restenosis/reocclusion rate varied around 20%. The logistic regression analysis consequently assigned the condition of a post-stenting MLD ≤2.54 mm an ∼9-fold increased risk of restenosis/reocclusion relative to the condition of a post-stenting MLD >2.54 mm.

The association of the post-stenting MLD with the risk of restenosis/reocclusion is known from studies on stenting for nonocclusive coronary lesions (15,16). To our knowledge, the present study is the first to demonstrate this interdependence for coronary occlusions. Our finding is in contrast to a previous study(10) in which no relation between the MLD and the risk of restenosis was found. This discrepancy might be due to the lower number of patients in that study, particularly those with a small MLD.

**Length of stented vessel segment.** Because of the discrete lengths of commercially available stents, stented vessel segment length is a discrete rather than a continuous variable. In ~60% of our patients, stented vessel segment length was ≤16 mm. In patients in whom the stented vessel segment length exceeded 16 mm, the relative risk of restenosis/reocclusion was significantly increased over that of patients in whom stented vessel segment length was ≤16 mm: by a factor of 4.6 if the total stented length was maximally 26 mm, and by a factor of 6.5 if total stented vessel length exceeded 26 mm.

The higher restenosis/reocclusion rates associated with increasing stented vessel segment lengths are most likely related to the increased amount of plaque present in longer occlusions. In contrast to short lesions, placing and expanding stents to completely cover a long lesion obviously increases the likelihood of tearing the vessel wall at any single stented site or may even result in multiple tears along the lesion. With wall injury being the major source for neointimal hyperplasia and subsequent restenosis, the increasing restenosis/reocclusion rate with longer stented vessel segment lengths appears plausible.

**Balloon/vessel diameter ratio for final stent expansion.** The last variable found to exert an independent, statistically significant influence on the likelihood of restenosis/reocclusion was the balloon/vessel diameter ratio for final stent expansion. The restenosis/reocclusion rate was lowest (i.e., 12%) for the 31 patients in whom the balloon diameter chosen for final stent expansion was >25% larger than the reference vessel diameter at baseline (balloon/vessel ratio >1.25). Compared with these patients, the chance of restenosis/reocclusion increased by a factor of nearly 10 if the balloon diameter was less than (or maximally equal to) the reference vessel diameter (balloon/vessel ratio ≤1.00); the risk was still increased by a factor of ~6.5 for intermediate balloon/vessel ratios (>1.00 but maximally 1.25).

This finding shows that not only does the absolute value of the post-stenting MLD influence the 6-month outcome of stenting of a reopened coronary occlusion, but the relative variable of the balloon/vessel diameter ratio has a comparably strong influence. Regardless of the reference vessel diameter or the MLD achieved with stenting, the higher the amount of overexpansion of the vessel the lower will be the restenosis/reocclusion rate and vice versa.

**Clinical relevance.** This study shows that nonacute total occlusions should be stented once they are recanalized. Stenting, as opposed to stand-alone balloon angioplasty, apparently limits the restenosis/reocclusion rate to the order of 30%. Previous studies support this finding (10–12). The MLD and the balloon/vessel ratio for final stent expansion were shown to be decisive variables affecting the restenosis rate. The findings of the present study relating to these variables suggest that the MLD after stenting should be at least 2.5 mm and that the balloon diameter for stent expansion should exceed the vessel reference diameter by 25%. However, overexpansion of the vessel harbors the risk of severe dissection or vessel rupture (17,18). To prevent either complication, two aspects need to be considered: 1) The length of the balloon used for stent expansion must not exceed the length of the stented vessel segment. 2) In case of a calcified or hard (i.e., highly resistant to balloon expansion) lesion, debulking by means of atherectomy might be useful before stent implantation.

The stented vessel segment length in the present study reflects the occlusion length plus the extension of adjacent stenotic vessel segments. Whether focal stenting (of the occluded segment only) would have resulted in a reduced restenosis/reocclusion rate for longer lesions is not known. In a previous study (19) we showed that the success rate of recanalization of chronic total occlusions by means of the laser wire is inversely related to the occlusion length. Thus, the upper limit of the lesion length and the lower limit of the vessel diameter that warrant an attempt at recanalization and stenting need to be clarified.

**Limitations of the study.** This study had a retrospective design. Computerized quantitative coronary angiography was not available, and angiographic measurements were obtained using hand-held digital calipers. However, both techniques have been shown to compare favorably (20).

**Conclusions.** The present study showed that stenting of nonacute total coronary occlusions in a consecutive series of patients is associated with a combined restenosis/reocclusion rate of ~30%. To our knowledge, this is the first study to clearly identify four factors that independently influence the restenosis/reocclusion rate in this setting: 1) the incidence of dissections after balloon angioplasty, 2) the MLD after stenting, 3) the length of the stented vessel segment, and 4) the balloon/vessel diameter ratio for final stent expansion. The clinical significance of these factors needs to be established in a future prospective study.
References