The contribution of “mechanical” problems to in-stent restenosis: An intravascular ultrasonographic analysis of 1090 consecutive in-stent restenosis lesions

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Objectives Serial intravascular ultrasonographic (IVUS) studies have shown that in-stent restenosis is the result of intimal hyperplasia (IH). However, routine preintervention IVUS imaging has suggested that many restenotic stents were inadequately deployed. The purpose of this IVUS study was to determine the incidence of mechanical problems contributing to in-stent restenosis (ISR).

Methods Between April 1994 and June 2000, 1090 patients with ISR were treated at the Washington Hospital Center. All underwent preintervention IVUS imaging. IVUS measurements included proximal and distal reference lumen areas and diameters; stent, minimum lumen, and IH (stent minus lumen) areas; and IH burden (IH/stent area).

Results In 49 ISR lesions (4.5%), there were morphologic findings that contributed to the restenosis. These were termed mechanical complications. Examples include (1) missing the lesion (e.g., an aorto-ostial stenosis), (2) stent “crush,” and (3) having the stent stripped off the balloon during the implantation procedure. Excluding mechanical complications, stent under-expansion was common. In 20% of the ISR cases the stents had a cross-sectional area (CSA) at the site of the lesion <80% of the average reference lumen area. Twenty percent of lesions had a minimum stent area <5.0 mm² and an additional 18% had a minimum stent area of 5.0 to 6.0 mm². Twenty-four percent of lesions had an IH burden <60%.

Conclusion Mechanical problems related to stent deployment procedures contribute to a significant minority of ISR lesions (approximately 25%). (Am Heart J 2001;142:970-4.)
The ultrasound catheter was advanced approximately 10 mm beyond the ISR lesion, and an imaging run was performed from beyond the target lesion to the aorto-ostial junction. Ultrasound studies were recorded on 0.5-inch high-resolution sVHS tape for offline analysis. Patients were studied after giving written, informed consent as part of ongoing protocols approved by the Institutional Review Board of the Washington Hospital Center.

**IVUS analysis**

Quantitative analysis was performed by computerized planimetry (Tape Measure, INDEC Systems). Measurements included proximal and distal reference lumen cross-sectional areas (CSA) and diameters; stent, minimum lumen, and IH (stent minus lumen) areas; and IH burden (IH/stent area). The reference segments were defined as the most normal-looking cross sections within 10 mm proximal and distal to the stented lesion but before any major side branch. When IH encompassed the catheter, the lumen was assumed to be the size of the image catheter. Validations of these measurements have been reported.\(^5\)\(^-\)\(^8\) In addition to the quantitative IVUS analysis, restenotic stents were assessed qualitatively to determine any unusual morphologic features that might have contributed to the ISR lesion. Unusual morphologic features include abnormal configuration of the stent strut architecture that might contribute to ISR. An unexpanded stent with a uniform circular and cylindric shape and an interstrut diameter ≤1 mm was assumed to be a stent “stripped” off the balloon during implantation. A crushed stent had an enlarged (greater than its unexpanded size), distorted, and grossly noncircular geometry, indicating that it had initially been expanded and then eccentrically and externally compressed. Edge restenosis was not considered to be an “unusual” morphologic characteristic unless there was also a “mechanical” complication associated with the edge restenosis.

**Statistical analysis**

Statistical analysis was performed with StatView 4.5 (Abacus Concepts, Berkeley, Calif). Quantitative data were presented as mean ± SD. Qualitative data were presented as frequencies.

**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>68%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>68%</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus</td>
<td>16%</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>70%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>81%</td>
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<tr>
<td>Smoking history</td>
<td>62%</td>
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</table>

**Results**

**Mechanical complications**

Preinterventional qualitative IVUS analysis of 1090 ISR lesions showed that in 49 ISR lesions (4.5%), there were morphologic findings that contributed to the restenosis. These were termed *mechanical complications*. Examples include (1) missing the lesion (eg, an aorto-ostial stenosis, n = 12 cases), (2) a “crushed” stent (n = 27), or (3) a stent getting stripped off the balloon (n = 10) during the implantation procedure (Figure 1).

**Quantitative IVUS analysis**

Excluding mechanical complications (see above), quantitative IVUS analysis of the remaining 1041 ISR lesions assessed the contribution of stent underexpansion to restenosis. Overall quantitative measurements are shown in Table II.

**Minimum stent area**

In 20% of the ISR cases, the stent area at the lesion site was <80% of the reference lumen area average. The minimum stent CSA in this group measured 7.1 ± 2.8 mm\(^2\). The frequency distribution of minimum stent CSA is shown in Figure 2. Sixty-five percent of ISR lesions had a minimum stent CSA <7.5 mm\(^2\), 38% had a minimum stent CSA <6.0 mm\(^2\), and 20% had a minimum...
stent CSA <5.0 mm². There were 229 (20%) ISR cases in which the stent CSA was >1.1 times the average reference lumen area.

**Intimal hyperplasia**

The IH CSA in this group measured 4.7 ± 2.1 mm². The frequency distribution is shown in Figure 2.

The IH burden (IH/stent CSA) in this group measured 66% ± 12%. The frequency distribution of the IH burden is shown in Figure 2. In 80% the IH burden was <75%, and in 24% it was <60%.

**Reference vessel size**

The mean reference lumen diameter was 2.8 ± 0.8 mm. In addition, 63% of ISR lesions were in vessels with a mean reference lumen diameter <3.0 mm, 45% in vessels with a mean reference lumen diameter <2.75 mm, 30% in vessels with a mean reference lumen diameter <2.5 mm, and 17% in vessels with a mean reference lumen diameter <2.25 mm.

**Discussion**

We undertook this retrospective analysis to confirm our clinical suspicion that in a significant number of patients with ISR there was a mechanical problem with the stent.

**Mechanical complications**

We found that 4.5% of patients had mechanical “complications” and that, in a significant number of the rest of the patients, there was evidence of stent underexpansion.

Serial IVUS studies have shown that, once implanted, tubular slotted and multicellular stents recoil rarely or not at all.3,4,9-11 Thus any mechanical problem with the stent that is detected when a patient has ISR likely occurred during the initial implantation procedure. Stents are radiolucent, even second- and third-generation stents. Therefore mechanical “complications” (eg, stent crush or dislodgement of a stent from the delivery balloon) can easily go unrecognized, and certain lesions (especially aorto-ostial lesions) can be missed. Conversely, stents are intensely echoreflective and distorted stent geometry is easily detected. Although IVUS imaging will not prevent these complications, it does facilitate recognition and should lead to appropriate reparative measures.

**Stent underexpansion**

Stent underexpansion was the most common mechanical problem detected in the current study. Previous IVUS reports have indicated that the final stent CSA is an important predictor of ISR.12,13 The Multicenter Ultrasound Stenting in Coronaries (MUSIC) study used as one of the IVUS criteria for optimal stent expansion the in-stent minimal lumen area ≥80% of the average reference lumen area.14 Considering this criterion in our study, in 20% (206 lesions) of the ISR cases the in-stent minimal lumen area at the site of the lesion was <80% of the average reference lumen area. Besides that, in the cur-

**Table II. Quantitative IVUS analysis of 1041 ISR lesions**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (± standard deviation)</th>
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<tbody>
<tr>
<td>Stent length (mm)</td>
<td>24 ± 10</td>
</tr>
<tr>
<td>Proximal reference lumen CSA (mm²)</td>
<td>6.8 ± 2.8</td>
</tr>
<tr>
<td>Distal reference lumen CSA (mm²)</td>
<td>6.1 ± 3.1</td>
</tr>
<tr>
<td>Mean reference lumen CSA (mm²)</td>
<td>6.6 ± 2.9</td>
</tr>
<tr>
<td>Mean reference lumen diameter (mm)</td>
<td>2.8 ± 0.8</td>
</tr>
<tr>
<td>Minimum stent CSA (mm²)</td>
<td>7.1 ± 2.8</td>
</tr>
<tr>
<td>Minimum lumen CSA (mm²)</td>
<td>2.3 ± 1.1</td>
</tr>
<tr>
<td>IH CSA (mm²)</td>
<td>4.8 ± 2.1</td>
</tr>
<tr>
<td>IH burden (%)</td>
<td>67 ± 9</td>
</tr>
</tbody>
</table>

**Figure 2**

Frequency distribution of stent CSA, IH CSA, and IH burden in 1041 consecutive ISR lesions.
rent cohort 20% of lesions had a minimum stent CSA <5.0 mm². According to one previous report, patients with a final stent CSA <5.0 mm² had a restenosis potential of 46%. It is possible that these lesions were simply lesions in small vessels. A 5.0-mm² stent CSA would be equivalent to a 0% diameter stenosis in a 2.5-mm artery, and vessel size is known to be an important predictor of ISR. However, in the current study, 40% of lesions with a stent CSA <5.0 mm² were in vessels whose follow-up reference was >2.5 mm; reference vessel size is typically larger at the time of implantation than it is at follow-up. A similar relationship was noted for lesions with a stent CSA 5.0 to 6.0 mm² and equivalent reference vessel sizes.

This also applies to the analysis of reference vessel size in the current report. Although the mean reference lumen measured 2.8 mm, it was likely larger at the time of stent implantation. Therefore the current cohort does not simply represent small vessels. Additional stent expansion might have prevented restenosis in these patients. Although it has been suggested that aggressive stent implantation might exaggerate the neointimal response, this has not proved true. The Can Routine Ultrasound Influence Stent Expansion (CRUISE) Trial reported that IVUS guidance reduced ISR by optimizing final stent CSA and avoiding stent underexpansion; however, others have shown no benefit from IVUS guidance. The current study indicates that, even with current stent implantation techniques and modern angiographic imaging equipment, a significant number of stents are underexpanded. Conversely, because stents are intensely echoreflective, IVUS-guided stent implantation facilitates recognition of these “mechanical” problems at the time of stent implantation.

Limitations

This is a single-center retrospective analysis of patients referred with ISR, often for experimental protocols such as brachytherapy.

Both coiled and slotted tubular stents were included in this analysis; however, accurate identification of stent type by IVUS is difficult on follow-up examination.

Because many of these patients were enrolled in brachytherapy protocols, we cannot report the recurrence rate if an underexpanded stent is simply adequately expanded.

Because there is no control group, we cannot determine the frequency of stent underexpansion in patients without ISR.

We did not classify in-stent restenosis according to its pattern: focal, diffuse, proliferative, etc. Therefore we cannot determine whether mechanical complications or stent underexpansion is more common in one type compared with another.

We considered the IVUS quantitative analysis only at the time of the preinterventional procedure for treatment of the ISR, taking into account that the literature has already demonstrated that tubular slotted and multicellular stents recoil rarely or not at all.

Conclusion

Mechanical problems related to stent deployment procedures contribute to a significant minority of ISR lesions (approximately 25%). In most of these cases, a mechanical complication or stent underexpansion was not suspected angiographically and was only detected by IVUS imaging at the time of treatment of ISR.

References