Brief Rapid Communications

Background Incidence of Late Malapposition After Bare-Metal Stent Implantation

Vivek M. Shah, MS; Gary S. Mintz, MD; Sue Apple, DNSc; Neil J. Weissman, MD

Background—Late stent malapposition has been reported to be an abnormal finding after vascular brachytherapy and, possibly, implantation of drug-eluting stents. It can only be detected if intravascular ultrasound (IVUS) is performed at follow-up. However, the “background” frequency of late stent malapposition after bare-metal stent implantation is not known.

Methods and Results—We studied 206 patients with native artery lesions who had tubular-slotted bare-metal stent implantation and who had IVUS performed at index and after 6±3 months of follow-up. There were 9 patients (4.4%) with late malapposition, which is separation of at least 1 stent strut from the arterial wall intima that does not overlap a side-branch, with evidence of blood flow (speckling) behind the strut, and where the immediate postimplantation IVUS revealed complete apposition of the stent to the vessel wall. The location of late malapposition was the stent edge in 8 of 9 patients. The maximum area, length, volume, and arc of late malapposition measured 3.1±2.4 mm², 3.3±2.2 mm, 21±27 mm³, and 110±61 degrees, respectively. There was an increase in external elastic membrane (EEM) area (20.7±4.9 to 26.9±4.2 mm², P=0.0021) and plaque area (10.1±3.7 to 14.8±3.6 mm², P=0.0022); however, the increase in EEM was greater than the increase in plaque. The area of late malapposition correlated directly with the increase in EEM area (r=0.75, P=0.0025).

Conclusion—Late malapposition occurs in 4% to 5% of slotted-tube bare-metal stents, usually at stent edges. The main cause is positive remodeling out of proportion to the increase in peri-stent intimal hyperplasia. (Circulation. 2002;106:1753-1755.)

Key Words: stents ▪ remodeling ▪ restenosis

The major limitation of coronary stenting is in-stent restenosis, which is secondary to intimal hyperplasia and which tends to recur after conventional catheter-based interventions.1 The 2 approaches to preventing first-time and recurrent in-stent restenosis that have been proposed are brachytherapy and, more recently, drug-eluting stents. With the use of intravascular ultrasound (IVUS), a number of unusual findings have been reported after brachytherapy, including lack of healing of stent-edge dissections, black holes (echolucent neointimal tissue), and late stent malapposition, which is a separation of the stent struts from the intimal surface of the arterial wall that was not present after implantation.2 By providing a nidus for thrombus formation, there was concern that late malapposition contributed to the clinical complication of late thrombosis after brachytherapy.3 Brachytherapy and drug-eluting stents may have similar effects on stented lesions, including late malapposition.4 The frequency of late malapposition after brachytherapy or implantation of drug-eluting stents, however, must be compared with bare-metal stent implantation. For this reason, we sought to identify the “background” frequency of late malapposition after bare-metal stent implantation.

Methods

Patient Selection

From the Washington Hospital Center clinical and core IVUS laboratory databases, we identified 206 patients who underwent de novo bare-metal tubular-slotted stent placement into a native coronary artery (without adjunct brachytherapy) not in the setting of an acute myocardial infarction and who had high-quality IVUS imaging after implantation and at follow-up. Late stent malapposition was defined as separation of at least 1 stent strut from the arterial wall intima that was not overlapping a side-branch, with evidence of blood flow (speckling) behind the strut and where the immediate postimplantation IVUS revealed complete apposition of the stent to the vessel wall. Baseline and follow-up demographic and clinical data were obtained from hospital record chart review.

IVUS Imaging and Analysis

IVUS imaging was performed after intracoronary administration of 0.1 to 0.2 mg nitroglycerin using motorized transducer pullback and a commercially available scanner (SCIMED) consisting of either a 30 MHz rotating transducer within 3.2 Fr imaging sheath or a 40 MHz rotating transducer within a 2.6Fr imaging sheath. The imaging catheter was advanced approximately 10 mm beyond the stent into the distal vessel. The transducer was withdrawn at a speed of 0.5 mm/s back to the guiding catheter. All studies were recorded on 0.5-inch high-resolution super VHS videotape for subsequent analysis.

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Qualitative analysis was performed by reviewing all 206 follow-up IVUS tapes to identify cases of malapposition. Next, index (immediately after stenting) tapes were reviewed side-by-side to exclude cases where malapposition was present at the time of implantation. This review included independent review of baseline and follow-up IVUS studies by the 2 senior authors (G.S.M. and N.J.W.).

Quantitative IVUS analysis was performed using computerized planimetry (Tape Measure, Indec Systems). Quantitative measurements of late malapposition sections included external elastic membrane (EEM), stent, plaque and media, intrastent lumen (subtended by the boundary that includes the intrastent neointima and the malapposed stent), effective lumen (subtended by the boundary that includes the intrastent and peri-stent intima outside the malapposed stent), and intrastent intimal hyperplasia cross-sectional areas (in mm²). IVUS images were measured every 1 mm. Lengths (in mm) and volumes (in mm³) of late malapposition were calculated using motorized transducer pullback and Simpson’s rule. The angle of malapposition was measured using an electronic protractor centered on the lumen. The measurements are shown in Figure 1.

Statistics
Statistical analysis was performed using StatView 5.0. Quantitative data are presented as mean±SD and compared using Student’s t test and correlation coefficients.

<table>
<thead>
<tr>
<th>Post-Stenting</th>
<th>Follow-Up</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM CSA, mm²</td>
<td>20.7±4.9</td>
<td>26.9±4.2</td>
</tr>
<tr>
<td>Stent CSA, mm²</td>
<td>10.6±1.5</td>
<td>10.7±1.6</td>
</tr>
<tr>
<td>P&amp;M CSA, mm²</td>
<td>10.1±3.7</td>
<td>14.8±3.6</td>
</tr>
<tr>
<td>Intra-stent lumen CSA, mm²</td>
<td>10.6±1.5</td>
<td>7.9±2.0</td>
</tr>
<tr>
<td>IH CSA, mm²</td>
<td>3.0±1.5</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. CSA indicates cross-sectional area; P&M, plaque plus media; and IH, intima hyperplasia.

Results
Of the 206 patients who met the inclusion criteria, malapposition was identified at follow-up in 10 patients. Review of the index IVUS study showed that 1 patient had malapposition after stent implantation. Therefore, the criteria for late malapposition were fulfilled in 9 patients (4.4%). Mean duration from implantation to follow-up was 6±3 months (range 2.5 to 9.2 months). All patients were male (ages 57±13 years). Cardiac risk factors included hypercholesterolemia in 7, diabetes in 2, and current smoking in 2. All but 1 patient presented initially with stable angina or a positive stress test, and 1 patient had rest angina.

The location of stent-vessel wall malapposition was almost exclusively at the edges of the stent; 5 were at the proximal edge, 3 at the distal edge of the stent, and 1 within the body of the stent. An example is shown in Figure 2.

The Table shows index and follow-up IVUS measurements. In these 9 patients within the length of malapposed stent, there was an increase in EEM and plaque and media areas, but no change in stent area. The effective lumen increased because of the late malapposition; however, the intrastent lumen decreased because of intrastent intimal hyperplasia (Figure 1). Intrastent neointima occurred only where the stent was in contact with the vessel wall; areas of malapposed stents were free of intrastent neointima (Figure 1). The increase in EEM area (6.2±4.2 mm², range 0.4 to 13.4 mm²) was larger than the increase in plaque and media area (4.7±3.2 mm², range 0 to 9.1 mm²). The maximum area, length, volume, and arc of late malapposition measured 3.1±2.4 mm², 3.3±2.2 mm, 21±27 mm³, and 110±61 degrees, respectively. The area of late malapposition correlated directly with the increase in EEM area (r=0.75, P=0.0205). The

Figure 1. Area measurements of the late malapposition lesions are illustrated in a single cross-section that is replicated: (a) late malapposition, (b) intimal hyperplasia, (c) plaque and media outside the stent, (d) intrastent lumen, (e) stent, (f) effective lumen, and (g) external elastic membrane. Note that the intimal hyperplasia is not located on the surface of the malapposed struts.

Figure 2. Poststent and follow-up IVUS images (every 2.5 mm) are shown to illustrate a case of marked late malapposition (white arrows).
intrastent neointimal area correlated inversely with the area of late malapposition \(r=0.53, P=0.14\) and directly with an increase in EEM area \(r=0.63, P=0.071\); a larger area of late malapposition was associated with less intrastent neointima.

**Discussion**

In this retrospective analysis of 206 patients undergoing bare-metal stent implantation in de novo native coronary vessels, we identified 9 cases (4.4%) of late stent malapposition. The mechanism was an increase in EEM that was greater than the increase in plaque plus media, i.e., positive remodeling. In most of the current cases, late malapposition was focused and located just at the stent edges; only in 1 case was late malapposition extensive.

**Mechanisms of Late Malapposition**

There are 4 potential mechanisms of late malapposition after implantation of tubular slotted stents, which are malapposition that is not recognized at the time of implantation and only detected at follow-up; a decrease in plaque with or without any change in EEM; chronic stent recoil in the absence of any change in vessel wall dimensions; and an increase in EEM that either occurs in the absence of an increase in plaque or that is greater than the increase in plaque. In the current analysis, unrecognized malapposition after implantation was present in only 1 of 10 patients, and none of the patients had a decrease in plaque. Reasons for a decrease in plaque could include clot lysis, plaque regression, or apoptosis; in the current analysis, we excluded patients with an evolving myocardial infarction. Previous serial IVUS studies\(^5,6\) (as well as the current data) have virtually excluded the presence of chronic stent recoil after tubular-slotted stent implantation. In the current analysis, an increase in EEM (positive remodeling) was the explanation for all of the cases of late malapposition. In effect, the vessel grew and the vessel wall pulled away from the stent.

Using serial IVUS, a number of investigators have reported positive remodeling and an increase in peri-stent plaque after bare-metal stent implantation, presumably reflecting peri-stent intimal hyperplasia.\(^7,8\) It is not known whether the increase in EEM is in response to peri-stent intimal hyperplasia or whether an increase in peri-stent tissue mass occurs secondary to positive remodeling, but in these 2 reports, the increase in EEM equaled the increase in peri-stent plaque. An increase in EEM greater than the increase in plaque leading to an increase in lumen dimensions has been reported in 10% of nonstent interventions and in early atherosclerosis.\(^9,10\) Animal studies in porcine coronary arteries have shown that neointimal hyperplasia occurs on both the inner and outer surfaces of the stent.\(^11\) In 1 IVUS report, peri-stent intimal hyperplasia correlated directly with the amount of intrastent neointima,\(^7\) whereas another report suggested that positive remodeling lesions had less intrastent neointima,\(^8\) similar to the present study. No serial IVUS reports mentioned late malapposition, however, and late malapposition cannot be detected angiographically.

Positive remodeling without an increase in intimal hyperplasia has been noted after brachytherapy, especially in de novo stenting with adjunct catheter-based radiation and after “hot-ends” \(^32\)P-emitting stent implantation.\(^2,12\) This has resulted in late malapposition in some patients.\(^3,13\) The present study indicates that late malapposition can occur after bare-metal stenting in the absence of radiation. Late malapposition was associated with minimal adjacent intrastent neointima. Intimal hyperplasia occurred only in zones of complete stent-vessel wall apposition.

Of note, none of the patients in the current report had untoward clinical events, i.e., late thrombosis or late total occlusion. The association between late malapposition and late thrombosis will be difficult to prove. Patients with late thrombosis are rarely studied using IVUS, and the presence of thrombus would most likely obscure late malapposition.

**Limitations**

This is a retrospective analysis from a single center. The number of patients with late malapposition was small. The current findings only apply to tubular-slotted stents; progressive expansion of self-expanding stents should obliterate any space between the stent and the expanding vessel wall. The current findings do not apply to restenting of in-stent restenosis lesions. Finally, the current report could not relate plaque composition to late malapposition; pre-intervention IVUS was not consistently performed.

Because the diagnosis of thrombus by IVUS is presumptive, it is not possible to absolutely exclude thrombus dissolution as a cause of late malapposition in all patients.

**Conclusions**

Late malapposition occurs in 4% to 5% of slotted-tube bare-metal stents, usually at stent edges. The main cause is an increase in EEM (positive remodeling) out of proportion to the increase in peri-stent intimal hyperplasia.

**References**

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