Mechanisms of Residual Lumen Stenosis After High-Pressure Stent Implantation

A Quantitative Coronary Angiography and Intravascular Ultrasound Study

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Background—Intravascular ultrasound (IVUS) studies have demonstrated that stents are frequently suboptimally expanded despite the use of high pressures for deployment. The purpose of this study was to identify the mechanisms responsible for such residual lumen stenosis.

Methods and Results—Fifty-seven lesions from 50 patients treated with high-pressure (median±interquartile range, 14±2 atm) elective (44 de novo, 13 restenotic lesions) stenting were prospectively studied (29 Wiktor, Medtronic; 28 Palmaz-Schatz, Cordis Corp). Balloon subexpansion was calculated as the difference between maximal and minimal balloon cross-sectional areas at peak pressure measured by automatic edge detection; elastic recoil was calculated as the difference between minimal measured balloon size and IVUS-derived minimal lumen area within the stent. Angiographic residual diameter stenosis was 10±13% (reference diameter, 3.1±0.7 mm; balloon to artery ratio, 1.12±0.23) and IVUS-derived stent expansion was 80±28%. However, although balloon nominal size was 9.6±1.3 mm² and maximal balloon size measured inside the coronary lumen was 12.5±3.2 mm², final stent minimal lumen area was only 7.1±2.2 mm². Balloon subexpansion of 4.0±1.8 mm² (33%) and elastic recoil of 1.6±2.3 mm² (20%) (both P<0.0001) were the two mechanisms responsible for residual luminal stenosis. Wiktor stent and peak inflation pressure correlated with balloon subexpansion, whereas Wiktor stent, de novo lesion, and minimal lumen area at baseline correlated with elastic recoil.

Conclusions—Despite high-pressure deployment, lumen dimensions after stenting are only 57% of maximal achievable. Inadequate balloon expansion and elastic recoil are responsible for residual lumen stenosis, suggesting that plaque characteristics and stent resistance deserve further investigation. (Circulation. 1998;98:112-118.)

Key Words: stents ■ ultrasonics ■ revascularization ■ angioplasty ■ balloon

The final dimension of the vessel lumen has been shown to be crucial both for reducing the risk of subacute occlusion and for improving long-term patency after intracoronary stent implantation. IVUS has demonstrated that despite excellent angiographic results, the stented lumen may still be further enlarged with additional balloon inflations at high pressures. This observation has led to the routine use of high inflation pressures for stent deployment, although long-term data regarding the benefit of this strategy are sparse. Moreover, recent IVUS studies have demonstrated that even when routinely implanted using high pressures, stents frequently remain suboptimally expanded. The present study was therefore designed to elucidate the mechanisms responsible for residual lumen stenosis after high-pressure coronary stenting.

Methods

Patients

From May 1994 to January 1997, patients were enrolled prospectively if (1) ≥1 lesion was treated with a single elective Wiktor or Palmaz-Schatz stent implantation not preceded by any interventional device other than standard balloon predilation, and (2) IVUS examination was performed to assess the results of the procedure. Lesions with suboptimal angiographic or IVUS recordings were rejected. Thus, 57 coronary lesions (44 de novo; 13 restenotic; 29 Wiktor and 28 Palmaz-Schatz stents) from 50 patients (mean age, 59±14 years; 48 men, 2 women) constitute the basis of this study. At the time of intervention, 17 patients had stable angina, 29 had unstable angina, and 4 had postinfarction angina or inducible ischemia. The target vessel was the left anterior descending artery in 26 lesions, the right coronary artery in 20, the left circumflex in 10, and the left main in 1.

Written informed consent for intracoronary stenting and IVUS examination was obtained from all patients.

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Selected Abbreviations and Acronyms
B/A = balloon/artery
CSA = cross-sectional area
IVUS = intravascular ultrasound
MLA = minimal lumen cross-sectional area
MLD = minimal lumen diameter
QCA = quantitative coronary angiography

Procedure
All patients were premedicated with aspirin. Heparin was given as a bolus at the beginning of (10 000 to 15 000 IU IV) and during angioplasty (activated clotting time >300 seconds). After stenting, 46 patients received aspirin (150 to 360 mg/d) and ticlopidine (250 to 500 mg/d) and 4 received acenocoumarol.

Coronary angiography was performed through the femoral approach (8F catheters). Several angiographic projections of the segment of interest were obtained before intervention. The target lesion was predilated and stented by use of standard techniques. Balloon catheters (noncompliant and semicompliant) were selected among several manufacturers and sized according to angiographic vessel size. Balloons shorter than 20 mm were not used. Selection of type, length, and size of the stent was left to the individual operator, and the maximal inflation pressure (≥12 atm). If a residual stenosis persisted, additional balloon inflations were allowed, with larger balloons used if necessary. Balloons were filled with a 1:1 saline–contrast medium solution and were filmed during every inflation at maximum pressure. Special attention was given to purge the balloon and to allow sufficient time to achieve complete expansion during each inflation. Intra-coronary nitroglycerin (200 μg) was administered before every set of angiograms and IVUS pullbacks.

Quantitative Coronary Angiography
Paired, identical, orthogonal views before and after stenting were chosen for QCA with the use of the Coronary Measurement System (versions 2.1 and 3.0, MEDIS Medical Imaging Systems).11 End-diastolic frames were selected for analysis, and the contrast-filled guiding catheters were used as the scaling device. A single catheter of each model used in the study was measured ex vivo filled with contrast on a 1-cm grid.12 Calibration factors were derived from these measurements for each catheter model and then used for in vivo analyses. MLDs and reference lumen diameters at baseline and after stenting were measured, as well as minimal, mean, and maximal balloon diameters at peak pressure. All balloon measurements were taken within balloon shoulders, and minimal balloon diameter was measured within stent boundaries. Diameters were averaged from paired angiograms and IVUS pullbacks. There were no differences in the average measurements obtained from each angiographic view. Interobserver and intraobserver (>3 months apart) variabilities (10 randomly selected angiograms) of minimal balloon diameters were ±0.19 mm (±6%) and ±0.17 mm (±4%), corresponding to ±0.9 mm2 (±13%) and ±1.1 mm2 (±9%) of balloon minimal CSA, respectively. Rintraclass values of interobserver and intraobserver reproducibilities were 0.72 and 0.95, respectively.

Intravascular Ultrasound
IVUS examination was performed using 30 MHz catheters (3.5F Sonication or 2.9 to 3.2F CVIS, Boston Scientific Corp). The transducer was advanced distal to the target segment and then withdrawn manually or mechanically. A second pullback was then performed, and contrast was injected through the guiding catheter at the most relevant sites to improve lumen delineation. The complete study was recorded on 0.5-in Super VHS videotape for off-line analysis. Images of the MLA within the stent were digitized for measurement. Proximal and distal (only distal for ostial lesions) reference segments, within 10 mm of the stent borders, were also digitized. Care was taken to choose sites with the least disease within the reference segment. Lumen area was defined as the area within the leading edge of intimal and/or stent struts echoes. Analysis of IVUS recordings was performed without knowledge of the QCA results.

In 35 lesions (19 Wiktor, 16 Palmaz-Schatz), IVUS examination was also performed at baseline. From the image showing the smallest lumen, the following morphometric variables were measured13: MLA, plaque area, plaque eccentricity, arc of calcium (none, 0°, or >0°), and normalized plaque echogenicity (ratio between gray-scale values of plaque and adventitia).

Derived Parameters
Balloon nominal CSA was derived from the nominal diameter provided by the manufacturer. In vivo balloon subexpansion was calculated as maximal minus minimal QCA-measured balloon CSA. IVUS-derived elastic recoil was calculated as balloon minimal CSA minus IVUS MLA, whereas QCA-derived elastic recoil was computed as balloon minimal diameter minus MLD after stenting.14 Relative (%) values of subexpansion and recoil were obtained with absolute values normalized by the first term of their subtraction definition. Acute luminal gain was calculated as final MLA (derived from IVUS) minus minimal lumen CSA at baseline (derived from QCA). Maximal achievable gain was calculated as maximal measured balloon size in vivo minus minimal lumen CSA at baseline. Stent expansion was defined as the ratio between MLA within the stent and the average lumen CSA of proximal and distal references. Stent symmetry was defined as major/minor lumen diameters within the stent (measured by IVUS).

Statistical Analysis
Results are expressed as median±interquartile amplitude. Reproducibility and agreement were analyzed by Bland-Altman analysis15 and intraclass correlation coefficients (Rintraclass).16 Univariate analyses were performed with Spearman’s correlation coefficient and paired t tests. Variable selection for the multiple linear regression models of balloon subexpansion and elastic recoil was performed by use of forward stepwise selection among the most relevant procedural and angiographic variables. The additive value of IVUS morphometric variables on these initial models was then screened by use of a global “chunk test” in the sample of 35 lesions with baseline IVUS examination; if this global test was significant, a second stepwise regression procedure was performed to select most relevant IVUS variables related to the effect. A 2-tailed P value <0.05 was considered significant.

IVUS and QCA Assessment of Final MLA
Agreement between IVUS and QCA in the assessment of MLA within the stent was −0.04±1.8 mm2 (Wiktor, −0.20±1.72 mm2; Palmaz-Schatz, 0.11±1.96 mm2; P=0.5). Rintraclass values also demonstrated poor agreement (0.42) between techniques (Wiktor, 0.36; Palmaz-Schatz, 0.48).

Results
Procedural Results
Procedural, angiographic, and IVUS data at baseline and after stenting are shown in Table 1. No subacute occlusions occurred in the first 2 weeks after the procedure.

Balloon nominal CSA was 9.6±1.3 mm2 (Wiktor, 9.6±1.4; Palmaz-Schatz, 9.6±2.2 mm2; P=0.8), and maximal balloon dimension measured inside the coronary lumen was 12.5±3.2 mm2 (Wiktor, 13.0±3.5; Palmaz-Schatz, 11.4±3.1 mm2; P=0.08); however, final stent MLA was only 7.1±2.2 mm2, 74% and 57% of these values, respectively. At the end of the procedure, only 55% (6.1±3.0 mm2) of
maximal achievable acute luminal gain (11.0±3.5 mm²) was obtained (P<0.0001; Figure 1).

Balloon Subexpansion

Measurements of the reference segment and balloon size are shown in Figure 2. Although in vivo measured mean balloon CSA was similar to nominal size, the size of the balloon was not uniform on its entire length. The balloon maximal CSA was substantially larger than its minimal CSA (12.5±3.2 versus 8.1±2.3 mm²; P<0.0001); therefore, values of absolute and relative balloon subexpansion were 4.0±1.8 mm² (Wiktor, 4.4±1.8; Palmaz-Schatz, 3.5±1.7 mm²; P=0.1) and 33±12% (Wiktor, 34±10%; Palmaz-Schatz, 31±11%; P=0.4), respectively. Compared with nominal balloon size, minimal balloon CSA was 12% smaller (mean difference, 1.1 mm²; 95% CI, 0.7 to 1.4 mm²; P<0.001) and maximal CSA was 30% larger (mean difference, 3.1 mm²; 95% CI, 2.5 to 3.6 mm²; P<0.001), yielding a B/A ratio of 1.30±0.3 at the sites of maximal balloon CSA.

Elastic Recoil

As shown in Table 2, the final lumen within the stent was smaller than the minimum balloon size (P<0.0001 both for QCA-derived diameter and IVUS-derived CSA differences); thus, values of acute recoil were 0.4±0.5 mm (12±16%) and 1.6±2.3 mm² (20±25%) as assessed by QCA-MLD and IVUS-MLA, respectively.

Factors Related to Balloon Subexpansion and Elastic Recoil

Increased absolute balloon subexpansion and absolute elastic recoil were found in Wiktor stents in multiple regression analysis (Table 3). As shown, peak balloon pressure directly correlated with balloon subexpansion, whereas elastic recoil was higher in de novo than in restenotic lesions. Baseline IVUS variables added no predictive value in the assessment of balloon subexpansion, whereas preintervention MLA inversely correlated with elastic recoil. When the multivariate models were rerun to assess factors related to relative values of subexpansion and recoil, the association between stent type and balloon subexpansion became nonsignificant (β=-0.2, P=0.2); predictors of elastic recoil remained unchanged (stent type, β=-0.2, P=0.06; type of lesion, β=-0.3, P=0.03).

Discussion

It is generally believed that supranominal inflation pressures should completely expand an angioplasty balloon catheter...
and that hoop resistance of stents should virtually avoid the vessel elastic recoil that follows balloon deflation.\textsuperscript{17,18} Accordingly, final vessel lumen size after stenting should closely match the size of the balloon used for deployment. However, the present study shows that lumen size after stenting reaches only 74% of the balloon nominal size and 57% of its inflated maximal in vivo size. The 10% angiographic residual diameter stenosis noted in the present study is lower than in previously reported randomized trials\textsuperscript{19,20} and is consistent with previous studies that used high-pressure inflations for stent deployment.\textsuperscript{1} Despite the routine use of slightly oversized balloons and high inflation pressures, balloon subexpansion and elastic recoil do occur and constitute 2 major sources of residual stenosis. The identification of these 2 mechanisms may help to develop strategies to improve stent deployment and, consequently, long-term results.

### Table 2. Values of Final Lumen Dimensions After Stenting and Absolute and Relative Values of Acute Elastic Recoil as Assessed by QCA and IVUS

<table>
<thead>
<tr>
<th>Measured parameters</th>
<th>Total</th>
<th>Wiktor</th>
<th>Palmaz-Schatz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon minimum diameter, mm</td>
<td>3.2±0.4</td>
<td>3.3±0.4</td>
<td>3.1±0.5*</td>
</tr>
<tr>
<td>Balloon minimum CSA, mm$^2$</td>
<td>8.1±2.2</td>
<td>8.4±2.3</td>
<td>7.7±2.6</td>
</tr>
<tr>
<td>Stent MLD by QCA, mm</td>
<td>2.9±0.6$\Dagger$</td>
<td>2.9±0.6</td>
<td>2.8±0.6</td>
</tr>
<tr>
<td>Stent MLA by IVUS, mm$^2$</td>
<td>7.1±2.2$|$</td>
<td>6.9±1.8</td>
<td>7.3±2.9</td>
</tr>
</tbody>
</table>

Elastic recoil

| Absolute by QCA, mm | 0.4±0.5 | 0.5±0.5 | 0.3±0.5 |
| Relative by QCA, % | 12±16 | 14±15 | 9±14 |
| Absolute by IVUS, mm | 1.6±2.2 | 2.2±2.1 | 1.1±1.8$\ddagger$ |
| Relative by IVUS, % | 20±25 | 26±23 | 15±22$\ddagger$ |

\textsuperscript{*}P<0.1; $\Dagger$P<0.06; $\|$P<0.05 for Palmaz-Schatz versus Wiktor-stent group comparison; \textsuperscript{$\Dagger$}P<0.0001 versus balloon minimum diameter; and \textsuperscript{$\|$}P<0.0001 versus balloon minimum CSA.

### Table 3. Univariate and Multivariate Predictors of Balloon Subexpansion and Elastic Recoil

<table>
<thead>
<tr>
<th>Univariate Predictors</th>
<th>Univariate</th>
<th>Multivariate</th>
<th>Elastic recoil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural and QCA (n=57)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wiktor (0)/Palmaz-Schatz (1)</td>
<td>0.1</td>
<td>-0.4</td>
<td>0.01</td>
</tr>
<tr>
<td>de novo/restenotic</td>
<td>0.9</td>
<td>0.0009</td>
<td>-0.3</td>
</tr>
<tr>
<td>B/A ratio</td>
<td>0.3</td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Peak balloon pressure</td>
<td>0.8</td>
<td>0.4</td>
<td>0.009</td>
</tr>
<tr>
<td>MLD</td>
<td>0.4</td>
<td></td>
<td>0.9</td>
</tr>
<tr>
<td>IVUS (n=35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All variables</td>
<td>0.4</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>MLA</td>
<td>0.5</td>
<td>0.2</td>
<td>-0.3</td>
</tr>
<tr>
<td>Plaque area</td>
<td>0.8</td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Plaque eccentricity</td>
<td>0.2</td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Plaque echogenicity</td>
<td>0.8</td>
<td></td>
<td>0.9</td>
</tr>
<tr>
<td>Extent of calcium</td>
<td>0.3</td>
<td>0.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Angiographic and procedural variables selected on whole sample group of 57 coronary lesions. The potential additive value of IVUS variables was tested in the group of 35 lesions with baseline IVUS examination.

### Balloon-Vessel Interaction During Stent Deployment

The dimensions of an inflated balloon in vivo, which have been extensively studied for standard balloon angioplasty, represent a complex interaction of balloon diameter, balloon material, inflation pressure, and vessel compliance.\textsuperscript{21,22} Of these factors, size selection seems crucial because randomized trials\textsuperscript{23} have demonstrated that procedural complications may increase when B/A ratios >1.1 are used. Similarly, several cases of coronary perforation during high-pressure stent implantation have been reported due to oversized balloons.\textsuperscript{1,18,24} Our study demonstrates that even adequately sized balloons achieve supranominal dimensions at certain points during high-pressure stent implantation, leading to potentially hazardous vessel stretch of the artery. It also demonstrates that supranominal pressures are frequently not enough to offset the high vessel impedance of the diseased artery.
An interference of stent architecture with balloon expansion constitutes another potential source of subexpansion. However, it has been reported that Palmaz-Schatz stents expand by almost 90% of peak size below 5 atm.25 Beyond this point, it is believed that no significant increase in pressure is needed in vitro to achieve full expansion of the balloon-stent assembly compared with the balloon alone. Because strain hardening of 316L stainless steel during stent expansion is negligible (Cordis Corp, unpublished data, 1997), stent size should parallel the size of the balloon without imposing relevant resistance. Whether stents behave similarly during in vivo high-pressure implantation remains to be ascertained.

Greater balloon subexpansion was observed for Wiktor than for Palmaz-Schatz stents in the present study. However, because maximal achieved balloon size was also larger for Wiktor stents, we believe such a difference in subexpansion could be due in part to greater compliance of the balloons used for Wiktor stent deployment. This hypothesis is supported by the observation of similar values of relative balloon subexpansion in both stent types, a parameter that corrects for differences in maximal balloon size within the coronary lumen.

**Elastic Recoil During Stent Implantation**

Acute elastic recoil designates the immediate reduction in vessel lumen that occurs after balloon deflation14 and accounts for a 50% loss in acute lumen gain during standard balloon angioplasty.26,27 The present study demonstrates that stents do not abolish recoil, because 20% of CSA was lost as a result of this phenomenon. This result is in agreement with recent observations in studies that used IVUS to assess final lumen CSA28 and with preliminary results from studies using an IVUS imaging wire.29 Angiographically measured recoil was 12%, which is consistent with previously reported values for Wiktor30–32 and Palmaz-Schatz stents.33–35

Due to their low yield point (close to 0.1 atm), balloon-expandable stents are plastically deformed during deployment and compression.36,37 However, greater force is needed in vivo to compress than to expand the stent due to the favorable effects of vessel impaction, friction, and longitudinal constraint.37 Pressures >0.8 and 0.5 atm are necessary to focally compress Wiktor and Palmaz-Schatz stents, respectively, in vitro.38,39 The observation of 1.6 mm² (20%) of lumen recoil therefore demonstrates that elastic vessel hoop stress is above these values. Differences in vessel compliance probably account for the greater recoil observed in de novo than in restenotic lesions. Nevertheless, plaque protrusion through the stent struts also needs to be considered as a mechanism of lumen recoil, as demonstrated by IVUS40 and angiography examinations.41 Due to their smaller metallic surface, this mechanism may be responsible for the greater vessel recoil observed in coil stents in the present and in previous studies.42

**Study Limitations**

The overall reproducibility of QCA measurements of balloon minimal diameter was ±0.19 mm, slightly above the repeatability of QCA determination of lumen diameter.43 Furthermore, the calculation of balloon CSA from diameters implies the assumption of a circular shape of balloon cross sections. Although these are potential sources of error, derivation of balloon CSA from QCA diameters has been validated by densitometric analyses,14 even when highly radiopaque stents were attached to the inflated balloon.44 Future studies using smaller IVUS devices that are capable of imaging the artery through the inflated balloon should, however, improve in vivo measurements of expanded balloons.29,45

Lesions were predilated before stenting to allow the introduction of the device; it cannot be excluded that some noncontrolled factors, such as balloon type, size, or inflation pressure, might have influenced balloon subexpansion or elastic recoil.

Because baseline IVUS data were unavailable in a subset of patients, this study cannot correctly address how important plaque characteristics are as determinants of subexpansion and recoil; however, in the subset of lesions available, these factors seem less important than other procedural variables.

**Clinical Implications**

Serial IVUS studies have demonstrated that stent restenosis is related to neointimal hyperplasia because chronic vessel remodeling is negligible.46 Until adjuvant therapies aimed at reducing hyperplasia prove to be efficacious, obtaining the lowest residual lumen stenosis is the only available method to reduce restenosis of intracoronary stents and improve long-term outcome.3,5 The present study identifies that despite high-pressure deployment, only 55% of achievable acute lumen gain is finally obtained. Assessment of vessel size by IVUS examinations improves balloon-vessel matching and may help to reduce residual lumen stenosis after stenting, as demonstrated in standard PTCA procedures.37 Baseline IVUS examination may also enable identification of plaque characteristics related to subexpansion and recoil48 and hence, definition of tailored deployment techniques. Debubling before stenting modifies vessel impedance and seems to be another tempting strategy to increase luminal gain.49,50 Finally, the observation of an important loss of acute luminal gain due to immediate elastic recoil emphasizes the need for further research on stent design to maximize hoop strength and minimize tissue prolapse.

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**References**


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