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Late Stent Recoil of the Bioabsorbable Everolimus-Eluting Coronary Stent and its Relationship With Plaque Morphology

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Objectives This study sought to evaluate late recoil of a novel bioabsorbable everolimus-eluting coronary stent (BVS), which is composed of a poly-L-lactic acid backbone, coated with a bioabsorbable polymer containing everolimus.

Background Little is known about the mechanical behavior of bioabsorbable polymer stents after deployment in diseased human coronary arteries.

Methods The study population consisted of 16 patients, who were treated with elective BVS implantation for single de novo native coronary artery lesions and were followed at 6 months. All patients underwent an intravascular ultrasound examination at post-procedure and follow-up. A total of 484 paired cross-sectional areas (CSAs) were acquired and analyzed. Late absolute stent recoil was defined as stent area at post-procedure (X) − stent area at follow-up (Y). Late percent stent recoil was defined as $(X - Y)/X \times 100$. In each CSA, plaque morphology was assessed qualitatively and classified as calcific, fibronecrotic, or fibrocellular plaque.

Results Late absolute and percent recoil of the BVS was 0.65 ± 1.71 mm^2 (95% confidence interval [CI]: 0.49 to 0.80 mm^2) and 7.60 ± 23.3% (95% CI: 5.52% to 9.68%). Calcified plaques resulted in significantly less late recoil (0.20 ± 1.54 mm^2 and 1.97 ± 22.2%) than fibronecrotic plaques (1.03 ± 2.12 mm^2 and 12.4 ± 28.0%, p = 0.001 and p = 0.001, respectively) or fibrocellular plaque (0.74 ± 1.48 mm^2 and 8.90 ± 19.8%, p = 0.001 and p = 0.001, respectively).

Conclusions The BVS shrank in size during the follow-up period. The lesion morphology of stented segments might affect the degree of late recoil of the BVS. (ABSORB Everolimus Eluting Coronary Stent System First in Man Clinical Investigation; NCT00300131) (J Am Coll Cardiol 2008;52:1616–20) © 2008 by the American College of Cardiology Foundation

Compared with metallic stents, bioabsorbable polymer stents could have a lower radial strength, resulting in more stent recoil after implantation, because polymers are more flexible than metals. The bioabsorbable everolimus-eluting coronary stent (BVS) (Abbott Vascular, Santa Clara, California) is composed of a high-molecular-weight poly-L-lactic acid (PLLA) backbone, coated with a matrix of bioabsorbable polymer and everolimus. All components of the BVS, except for 2 radio-opaque platinum markers on both ends of its surface, are expected to be fully metabolized and absorbed in the human body between 2 and 3 years (1,2). Although acute recoil of the BVS as assessed by quantitative coronary angiography (QCA) was slightly but not significantly higher than that of the everolimus-eluting metallic stent (2), little is known about late mechanical behavior of the BVS. In the present study, we evaluated late recoil of the BVS and assessed its relationship with lesion morphology of the stented segments.

Methods

Study population. Of the 30 patients included in the ABSORB (ABSORB Everolimus Eluting Coronary Stent System First in Man Clinical Investigation) trial, 16 were enrolled at the Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands. The trial has been described in detail previously (1,2). It was approved by the local ethics committee, and all patients gave written informed consent. In brief, patients were eligible for the study if they had single de novo native coronary artery lesions that could be covered with a single BVS. Patients were ineligible if they had evolving myocardial infarction, left main coronary

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artery stenosis, an ostial lesion, a bifurcation lesion, a totally occluded lesion, a lesion with moderate-to-heavy calcification, angiographically visible thrombus within the target lesion, or a left ventricular ejection fraction <30%.

Study procedure. Target lesions were electively treated with standard interventional techniques with mandatory pre-dilation and stent deployment at a pressure not exceeding the rated burst pressure (16 atm). Post-dilation with a balloon shorter than the implanted stent was allowed at operator discretion. Bailout stenting for edge dissection was permitted with metallic stents. At the end of the procedure, intravascular ultrasound (IVUS) procedures were performed with a 40-MHz IVUS catheter (Atlantis SR Pro, Boston Scientific Corporation, Natick, Massachusetts) with an automated pullback system at 0.5 mm/s. After IVUS examinations, no other stent-related procedures were added. All patients were planned to undergo both a coronary angiography and an IVUS examination 6 months after the initial procedure.

QCA and quantitative IVUS analysis. The QCA was performed with the CAAS II analysis system (Pie Medical BV, Maastricht, the Netherlands) by an independent observer blinded to the clinical and IVUS findings. The following QCA parameters were computed: minimal lumen diameter, reference vessel diameter, percent diameter stenosis, and lesion length. The accuracy of this method has been reported in detail previously (3).

To analyze and compare the IVUS data consistently, all IVUS examinations were retrospectively electrocardiogram (ECG)-gated with the validated Intelligate method, which automatically selects near end-diastolic frames from prerecorded non–ECG-gated IVUS data (4). The IVUS images of both post-procedure and follow-up studies were analyzed by side-by-side viewing, comparing for matched segments. Only the stented segments were analyzed and were identified by the first and the last cross section containing visible stent struts. The lumen, stent, and external elastic membrane contours were detected with the validated software (CURAD QCU Analysis Software, Curad B.V., Wijk bij Duurstede, the Netherlands), which allows semi-automated detection of the lumen–intima interface and the external elastic membrane in longitudinal reconstructed views of coronary vessels (5,6).

Late stent recoil assessment. Stent recoil was computed from measurements of IVUS cross-sectional areas (CSAs), obtained every 0.5 mm. Late absolute stent recoil was defined as stent area at post-procedure (X) − stent area at follow-up (Y). Late percent stent recoil was defined as $(X - Y)/X \times 100$.

Image-based plaque characterization. The IVUS appearance of the BVS struts is unique and differs from that of metallic stents. The polymer struts are visible as 2 parallel lines of echoes without acoustic shadowing (AS), due to the fact that the ultrasound is mainly backscattered at the interfaces (blood/polymer interface and polymer/tissue interface) of the struts with the surrounding environment. Therefore, plaque characterization of BVS implanted segments can be assessed without the image artifacts as seen in IVUS of metallic stents.

To investigate the possible relationship between the degree of late stent recoil and plaque morphology in stented segments, plaque characterization of BVS implanted segments was qualitatively assessed by IVUS appearance. All acquired CSAs were classified into 3 different plaque types: calcific, fibronecrotic, or fibrocellular plaque. Each plaque type was defined as follows (7–11): calcific plaque: highly echogenic areas having a density greater than that of the adventitia and causing AS, possibly combined with reverberations; fibronecrotic plaque: plaque components causing echolucent areas within the plaque combined with AS or plaque having AS without reverberations; and fibrocellular plaque: plaque components other than calcific and fibronecrotic plaques. In case several plaque types were identified in 1 CSA, the predominant plaque type was selected.

Abbreviations and Acronyms

AS = acoustic shadowing
BVS = bioabsorbable everolimus-eluting coronary stent
CI = confidence interval
CSA = cross-sectional area
ECG = electrocardiogram
IVUS = intravascular ultrasound
PLLA = poly-L-lactic acid
QCA = quantitative coronary angiography

Statistical analysis. Statistical analysis was performed with SAS software (SAS Institute Inc., Cary, North Carolina). Categorical variables were expressed as counts and percentages. Continuous variables were presented as mean values with SDs. The Student *t* test was performed for testing differences of late BVS recoil among 3 different plaque types of stented segments. To adjust for multiple observations/patient, with possible correlations of adjacent cross sections, the *t* statistic was divided by $C = (1 + [m - 1]\rho)$, where m is the number of observations/patient and ρ is the intracluster correlations (12). The intracluster correlation ρ is defined as: variance (between patients)/(variance [between patients] + variance [within patients]). A value of $p < 0.05$ was considered statistically significant.

Results

All patients were successfully treated and underwent follow-up coronary angiography and IVUS procedures at 6.0 ± 1.2 months. Only 1 patient received bailout stenting. A total of 484 paired (post-procedure and follow-up) CSAs were acquired. Baseline and follow-up results are shown in Table 1. According to the protocol, lesion complexity was relatively simple: no type C lesion, short lesion length (9.83 ± 4.02 mm), large reference vessel diameter (2.96 ± 0.48 mm), and mild degree of diameter stenosis (62 ± 13%). Late absolute stent recoil was 0.65 ± 1.71 mm^2 (95% confidence interval [CI]: 0.49 to 0.80 mm^2), and late percent stent recoil was 7.60 ± 23.3% (95% CI: 5.52% to 9.68%). All acquired CSAs were qualitatively assessable in terms of lesion morphology of stented segments. The fibrocellular,

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Table 1 Clinical, Lesion, and Procedural Characteristics

Patient demographic data (n = 16 patients)	
Age, yrs	60.9 ± 8.6
Male	11 (69%)
Hypertension	10 (63%)
Hypercholesterolemia	12 (75%)
Diabetes	1 (6%)
Current smoking	4 (25%)
Prior myocardial infarction	2 (13%)
Lesion characteristics (n = 16 lesions)	
Treated vessel	
Right coronary artery	4 (25%)
Left anterior descending	5 (31%)
Left circumflex artery	7 (44%)
ACC/AHA lesion type	
Type A	0 (0%)
Type B1	8 (50%)
Type B2	8 (50%)
Type C	0 (0%)
Procedural characteristics	
Pre-dilation before stenting	16 (100%)
Post-dilation	12 (75%)
Maximal pressure during entire procedure, atm	16.1 ± 0.89
Stent/artery ratio	0.98 ± 0.16
Clinical success	16 (100%)
QCA results	
Pre-procedure	
Lesion length, mm	9.83 ± 4.02
Reference vessel diameter, mm	2.96 ± 0.48
Minimal lumen diameter, mm	1.09 ± 0.31
Diameter stenosis, %	62 ± 13
Post-procedure	
Minimal lumen diameter, mm	2.45 ± 0.33
Diameter stenosis, %	19 ± 8
Acute gain, mm	1.36 ± 0.46
Follow-up	
Minimal lumen diameter, mm	2.00 ± 0.27
Diameter stenosis, %	29 ± 14
Late loss, mm	0.45 ± 0.39
IVUS results (n = 484 CSAs)	
Post-procedure	
Stent area, mm^2	6.94 ± 1.47
Follow-up	
Stent area, mm^2	6.29 ± 1.70
Lumen area, mm^2	5.83 ± 1.51
Neointimal area, mm^2	0.47 ± 0.58
Late absolute stent recoil, mm^2	0.65 ± 1.71
Late percent stent recoil, %	7.60 ± 23.3

Values are mean ± SD or n (%).
ACC/AHA = American College of Cardiology/American Heart Association; CSA = cross-sectional area; IVUS = intravascular ultrasound; QCA = quantitative coronary angiography.

fibronecrotic, and calcific group consisted of 204, 126, and 154 CSAs, respectively. The relationship between late stent recoil and lesion morphology is shown in Figure 1. Late absolute and percent stent recoil were significantly less in calcified lesions (0.20 ± 1.54 mm^2 and 1.97 ± 22.2%, respectively) than in fibrofatty lesions (0.74 ± 1.48 mm^2 and 8.90 ± 19.8%, p = 0.001 and p = 0.001, respectively) or in fibronecrotic lesions (1.03 ± 2.12 mm^2 and 12.4 ± 28.0%, p = 0.001 and p = 0.001, respectively). Although there was a trend toward more recoil in fibronecrotic lesions than in fibrocellular lesions, no significant differences in late absolute and percent stent recoil were observed between these 2 lesion types (p = 0.18 and p = 0.1, respectively).

Discussion

The present study indicated that the BVS shrank in size during the follow-up period. This observation was at variance with the observed 6 months' late recoil of the Igaki-Tamai stent, which was the first polymeric stent examined in diseased human coronary arteries (13). Although the Igaki-Tamai stent was composed of the same material (PLLA) as the BVS, it became larger in size (0.71 mm^2 at 6 months according to IVUS analysis). This discrepancy could have been caused by the differences in study protocols and/or baseline characteristics of the target lesions between 2 studies. However, the main reason might be associated with differences in stent design. Because the Igaki-Tamai stent was self-expandable, whereas the BVS was balloon-expandable, the Igaki-Tamai stent tends to expand gradually in time until it reaches fully unconstrained dimensions.

The current results also differed from reported late recoil of metallic stents as assessed by IVUS. The Palmaz-Schatz stent exhibited only a little recoil (0.1 mm^2 and 0.6%) at 4 months (14). Late recoil of the XIENCE V everolimus-eluting stent (Abbott Vascular), which is a metallic stent coated with the same antiproliferative drug as in the BVS, was computed as 0.02 mm^2 and 0.3% at 6 months (1,15). These changes are in the range of reproducibility measurements. However, it is obvious that the vessel scaffolding properties of the BVS have not been maintained for a long period compared with metallic stents, even if the BVS shows a good radial strength, similar to metallic stents, immediately after deployment (2). This might be due to differences in material components between both stent types. Because polymers are more flexible than metals, there is a potential that polymer stents are affected by the elastic properties of the arterial wall more directly and have been compressed steadily. In addition, because the BVS is designed to be gradually metabolized, the polymer backbone will lose its structural integrity over time, which could diminish its radial strength and lead the stent to shrink. However, no clear image of such a degradation process of the BVS was documented, even when using a 40-MHz IVUS catheter, probably due to an insufficient resolution of IVUS to clarify this phenomenon.

Because the extent of stent recoil is the result of the balance between the elastic recoil and radial strength of the stent, along with the elastic properties of the arterial wall, it can be affected by the plaque characteristics of the stented segments. The elastic property of the arterial wall is determined by atherosclerotic plaque constituents. Previous studies revealed the following: 1) calcific plaques had stiffer mechanical properties than other types of plaques and thus

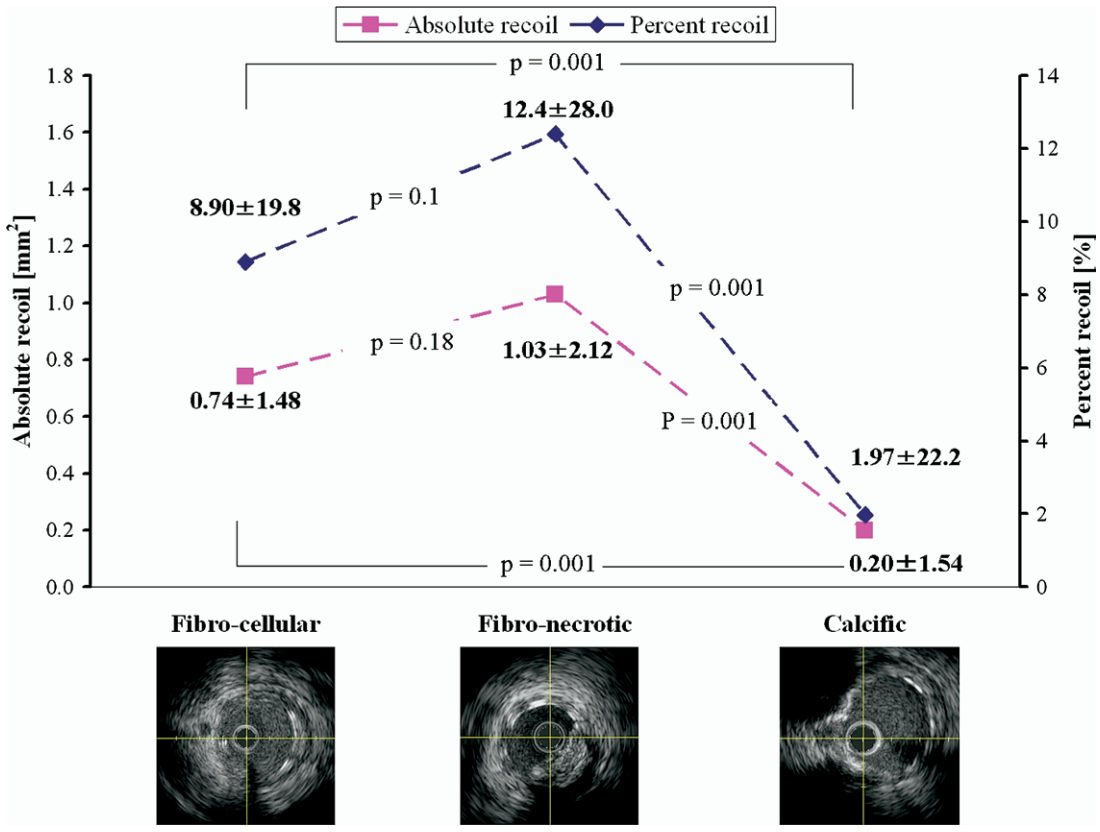

Figure 1 **Correlation Between Late Recoil of the BVS and the Lesion Morphology of the Stented Segments**

Representative intravascular ultrasound images of fibrocellular, fibronecrotic, or calcific plaque are shown at the **bottom of the figure**. BVS = bioabsorbable everolimus-eluting coronary stent.

exhibited less elasticity; and 2) fibrofatty or fibronecrotic plaques had more elasticity than calcific plaques, but no significant difference was observed between these 2 plaque types (10,11). In concurrence with these statements, the present study demonstrated that calcified plaques resulted in significantly less late recoil than the other plaque types and that fibrocellular or fibronecrotic plaques induced more late recoil than calcified plaques, although no significant differences in late recoil were observed between these 2 plaque types (Fig. 1). These findings suggest that an IVUS examination of the target lesion before stenting could be useful to predict the extent of stent recoil in case of BVS implantation.

Study limitations. Limitations are the small number of enrolled patients and that the clinical implication of the BVS shrinkage remains unclear. Target lesions were relatively simple, and late recoil of the BVS might increase in more complex lesions. Further investigations are warranted to determine the recoil properties of the BVS at the time of its complete degradation.

Conclusions

A certain degree of late stent recoil was observed 6 months after BVS implantation, indicating that the BVS shrank in size during the follow-up period. The lesion morphology of stented segments might affect the extent of late recoil of the BVS.

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Key Words: bioabsorbable ■ coronary artery disease ■ recoil ■ stents.