EDITORIAL COMMENT

Scaffold Resorption Process Is Not the Achilles' Heel of the Absorb BVS

But What Then?*

Laura S.M. Kerkmeijer, MD, Joanna J. Wykrzykowska, MD, PhD

Bioresorbable scaffolds were developed to restore vasomotion; allow for adaptive shear stress, luminal enlargement, and vessel wall remodeling; and most importantly, improve long-term clinical outcomes after complete resorption compared with metallic drug-eluting stents. However, the AIDA (Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial) trial and a meta-analysis of the ABSORB trials demonstrated that the Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular, Santa Clara, California) increases the risk of target vessel myocardial infarction and device thrombosis compared with the Xience everolimus-eluting stent (EES) (Abbott Vascular) during the time of scaffold resorption (1,2).

The cause of this device failure is not yet fully understood. It is thought that the underlying mechanism of very late scaffold thrombosis is mostly scaffold discontinuity (3), which suggests an unfavorable resorption-related process. Although the Absorb BVS is no longer commercially available, detailed knowledge on the in vivo interaction between the vessel wall and scaffold is of the utmost importance for further development of this technology.

In this issue of *JACC: Basic to Translational Science*, Cheng et al. (4) evaluated the vascular healing response of the Absorb BVS up to 4 years compared with the XIENCE EES in 11 familial hypercholesterolemic swine using serial multimodality imaging and histology. At 3 years, still 7% of struts appeared as preserved boxes by optical coherence tomography (OCT), and at 4 years, all struts were no longer discernible. The 4-year late lumen loss was less pronounced in the Absorb BVS than in the Xience EES $(1.14 \pm 0.37$ mm vs. 2.09 ± 0.12 mm; p = 0.006). This difference in luminal dimension was confirmed by intravascular ultrasound assessment of the absolute change of lumen area within 4 years $(0.21 \pm 0.95$ mm^2 vs. -2.37 ± 1.25 mm^2; p = 0.026). For both devices, the average total plaque area increases over time (BVS at baseline: 5.82 ± 2.41 mm^2, at 4 years: 12.47 ± 5.95 mm^2; EES at baseline: 4.39 ± 1.54 mm^2, at 4 years: 14.63 ± 1.70 mm^2). In addition, histology showed evidence of neoatherosclerosis in both devices starting at 2 years. The vessel response to the Absorb BVS and Xience EES was similar, with comparable injury scores, neointimal inflammation, and growth.

So far, the bioresorption process of the Absorb BVS has been directly investigated only in normal swine and has been indirectly investigated in clinical studies. Therefore, the present study is unique and provides knowledge of the resorption process in hypercholesterolemia plaques. Cheng et al. (4) confirm that the resorption process of the Absorb BVS takes between 3 and 4 years. Although the study did not include serial observations, the results suggest that positive vessel wall remodeling and late lumen enlargement is possible in Absorb BVS-treated lesions. The study is of great importance because it shows that the long-term vascular healing in the

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Absorb BVS is comparable to the Xience EES, and both devices are not immune to the progress of atherosclerosis.

Cheng et al. (4) characterized for the first time the vascular healing process of BVS in swine with familiar hypercholesterolemia. However, the lesions created in the pigs do not represent the majority of lesions seen in clinical practices. The diameter stenosis at baseline was low (12.05 ± 8.89% vs. 9.05 ± 7.06%), and it is most likely that these lesions consisted of homogenous soft plaques. All struts were found to be apposed at baseline and were completely embedded and incorporated with neointima during follow-up. Hence, no adverse events occurred in these swine models.

Therefore, it seems that when the struts are well embedded and encapsulated early, scaffold dismantling is a benign process. In cases in which struts are not covered by neointima, discontinuity allows protrusion of part of the scaffold into the lumen, brings thrombogenic proteoglycan into contact with blood, and could potentially cause scaffold thrombosis. In homogenous soft lesions, as in the swine models, full embedment and incorporation of struts is easily accomplished. However, when lesions become more complicated, such as those seen in the real-life clinical population, apposition, embedment, and early encapsulation of struts become an issue (2,3).

Accurate deployment and embedment of the struts of the Absorb BVS is more difficult to obtain in significant heterogenic lesions because of the low radial strength. Underdeployment and malapposition are major risk factors of scaffold thrombosis (5). There were hopes that the introduction of a specific implantation technique, so-called PSP (pre-dilatation, sizing, and post-dilatation), would diminish the risk of scaffold thrombosis. However, the COMPARE-ABSORB (ABSORB Bioresorbable Scaffold vs. Xience Metallic Stent for Prevention of Restenosis Following Percutaneous Coronary Intervention in Patients at High Risk of Restenosis) trial showed us that even when we apply routinely pre- and post-dilatation according to the PSP criteria, the concern for scaffold thrombosis remains (Pieter Smits, unpublished data, September 25, 2018).

Moreover, even though we manage to obtain well-apposed struts by using intravascular imaging, intraluminal scaffold dismantling is still seen during follow-up (6). Encapsulation of thick struts with a mature neointimal layer appears to be an issue as well. It is also plausible that even good apposition at baseline would not prevent the occurrence of acquired malapposition, as large plaque burden continues to exert an inner force on the progressively weaker resorbing device. Therefore, one can hypothesize that thinner struts and better mechanical properties are the key factors for improvement of this device, rather than changing the nature of the scaffold dismantling process. To allow for assessment of novel devices with more favorable mechanical properties, we will certainly need preclinical models that better mimic the complexity of human patients. However, the ultimate test of the device will still need to take place in the context of a well-designed, randomized, real-clinical-practice trial, with long-term follow-up performed and completed before commercialization will take place.

ADDRESS FOR CORRESPONDENCE: Dr. Joanna J. Wykrzykowska, Department of Clinical and Experimental Cardiology, Amsterdam Cardiovascular Sciences, Medical Center, University of Amsterdam Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. E-mail: j.j.wykrzykowska@amsterdamumc.nl.

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