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EDITORIAL COMMENT

The Dilemma of Selecting Patients for Bioresorbable Vascular Scaffolds in Our Daily Routine

Neither Too Much Nor Too Little!*

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Despite the striking improvements achieved with second-generation drug-eluting stents (DES), long-term (>1 year) device-oriented composite endpoints (DOCEs), including cardiac death, target-lesion myocardial infarction, and clinically driven target lesion revascularization still occur at a frequency of 2% to 3% per year, which partially offsets the very long term benefits of percutaneous coronary revascularization. Thus, bioresorbable vascular scaffolds (BRSs) have been recently proposed as an alternative to these permanent prostheses because they might provide the mechanical properties and drug-elution capability of metal DES for the first months after percutaneous coronary intervention (PCI) and then completely resorb, eliminating the late vessel "caging" and all the inconvenience related to it.

The first of these devices to become available for daily practice was the ABSORB scaffold (Abbott Vascular, Irvine, California), which combines a fully biodegradable poly-L-lactic acid backbone with the same antiproliferative agent (everolimus) and delivery system used in the second-generation metal Xience DES (Abbott Vascular). Due to intrinsic properties related to its design and composition, the deployment of this BRS might require some caveats, with special attention needed for proper vessel sizing, lesion preparation, and device post-dilation.

The initial *in human* trials of this device (ABSORB cohort A and cohort B) (1,2) have demonstrated, in very select, low-complexity patients, sustained efficacy of the ABSORB during 5 years of follow-up, based on multimodality imaging (3) as well as the presence of unique new findings such as restoration of nitrate-induced vasomotion (4) and vessel enlargement (positive remodeling) in the treated segment after 2 to 5 years of scaffold deployment (3,5), which prompted the adoption of this technology in clinical practice and introduced a new concept of percutaneous vessel "restoration" (5).

In the past 12 months, 6 randomized trials, ABSORB II (ABSORB II Randomized Controlled Trial) (6), EVERBIO II (Comparison of Everolimus- and Biolimus-Eluting Stents With Everolimus-Eluting Bioresorbable Vascular Scaffold Stents II) trial (7), ABSORB Japan (8), TROFI II (ABSORB STEMI: the TROFI II trial) (9), ABSORB-III (ABSORB III Randomized Controlled Trial) (10), and ABSORB China (11), were published comparing the ABSORB with current-generation metal DES. On the positive side, they all demonstrated, in low- to moderate-complexity populations, the noninferior efficacy of the BRS up to the midterm follow-up. Conversely, this technology very often resulted in higher rates of failure to deliver the device to the lesion site and inferior acute angiographic performance (less acute gain, higher in-device residual stenosis). Although none of these studies were powered to compare the occurrence of device thrombosis, most of them showed a numerically, not statistically, higher incidence of device

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thrombosis among patients treated with the ABSORB. Furthermore, in the largest of these trials (ABSORB-III), treatment of small vessels (≤2.25 mm) was associated with a higher occurrence of target-lesion failure and device thrombosis.

Although randomized trials provide the highest quality scientific data, their inclusion/exclusion criteria frequently limit the applicability of their results to the broader population of our daily practice. Published earlier this year by Capodanno et al. (12), the GHOST-EU (Gauging coronary Healing with biOresorbable Scaffolding plaTforms in EUrope) (12) registry was of great importance for this purpose. Conducted at 10 experienced European centers, this study enrolled 1,189 patients treated with the ABSORB in a variety of complex clinical and anatomic conditions, usually excluded or understated in the published randomized trials, such as multivessel disease (40.9%), ST-segment elevation myocardial infarction (STEMI) (16.1%), renal insufficiency (14.9%), severe left ventricular dysfunction (3.3%), bifurcations (26.7%), chronic total occlusions (7.8%), ostial lesions (6.1%), and left main coronary artery disease (1.2%). Notably, despite the cumbersome profile of the population, the ABSORB had a very good overall performance, with low rates of 6-month target-lesion failure (4.4%), cardiac death (1.0%), target-vessel myocardial infarction (2.0%), and ischemia-driven target-lesion revascularization (2.5%). Diabetes mellitus was the only independent predictor of target-lesion failure (hazard ratio: 2.41, 95% confidence interval: 1.28 to 4.53; p = 0.006). Conversely, the rate of 6-month definite/probable device thrombosis was considered high (2.1%) and brought the attention to the safety of this novel technology when applied to the "all-comers" scenario. Of note, 16 of 23 thrombosis cases occurred within 30 days. However, the lack of a comparison arm versus contemporary metal DES precluded a proper assessment of the role of the ABSORB in daily PCI practice.

In this issue of *JACC: Cardiovascular Interventions*, Tamburino et al. (13) revisited the GHOST-EU database and throughout a very sophisticated and elegant statistical analysis, matched the population of their "real-world" registry to patients also enrolled in the contemporary XIENCE V USA registry. After the adjustment, no difference was observed regarding 1-year DOCEs (DOCEs, 5.8% for the ABSORB vs. 7.6% for the metal everolimus-eluting stent; p = 0.12), ischemia-driven target lesion revascularization (4.6% for the BRS vs. 3.5% for the metal DES; p = 0.22) and definite/probable device thrombosis (1.8% for the ABSORB vs. 1.1% for Xience; p = 0.23). Of note, the use of the ABSORB resulted in fewer cardiac deaths (0.7% vs. 1.9%; p = 0.03) and a trend toward fewer myocardial infarctions (2.4% vs. 4.0%; p = 0.07).

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However, the interpretation of these data goes beyond the comparison of 1-year outcomes between the cohorts. When analyzing population and lesions characteristics before propensity-score matching, some of the operators' thoughts regarding patient/lesion selection become apparent. For treatment with the BRS, patients were usually younger (long-term potential benefits of the technology?) and less likely to have a restenotic or ostial lesion (mechanical properties of the ABSORB such as less radial force?). Conversely, there was a preference for these devices in acute coronary syndrome, including STEMI (passivation of vulnerable plaques?). Also, there are still some important issues to be addressed in the future by the authors, such as the comparison of procedural length and costs, rates of device and procedure success, and differences in vessel sizing and lesion preparation between the 2 groups as well as the role of intravascular imaging guidance in acute and long-term outcomes.

Establishing limits is one of the most important yet challenging steps in raising a child. The first generation of this technology, largely represented by the ABSORB, is leaving its infancy. Therefore, Tamburino et al. and all GHOST-EU co-investigators should be congratulated for their initiative to expand the indications and point out the "shoulds and coulds" of these devices. Although it is fair to note that no statistical adjustment is capable of completely eliminating the possible bias related to the lack of randomization, the present results are reassuring in that, in experienced hands, the ABSORB may be used in a more liberal way, without compromising the midterm results of PCI. Nonetheless, because most of the thrombosis cases experienced with the current generation of these devices were clustered within the first few weeks after PCI, patient/lesion selection and device implantation technique might play an important role in their genesis. Therefore, caution is advised when using the ABSORB BRS in small (≤2.25 mm) or very large (>4.0 mm) vessels, in very tortuous/calcified coronary anatomies, in acute coronary syndrome patients (especially STEMI), in ostial lesions, in bifurcation and/or left main lesions, and when overlapping is required. Also, mainly in the beginning of the learning curve, more liberal use of intravascular imaging (intravascular ultrasound or optical coherence tomography) should be encouraged, and there may be a role for a more potent

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antiplatelet regimen, with the new antiplatelet agents (ticagrelor and prasugrel) combined with aspirin, at least in patients at low risk of bleeding.

In the future, as part of the "maturing" process, we should expect the introduction of new generations of the BRS, incorporating some highly anticipated features, such as low strut thickness/crossing profile, better tolerability of overexpansion, radiopacity, and self-correction/self-apposition mechanisms. The technology development in combination with adequate PCI technique might result in a paradigm shift in percutaneous coronary revascularization, with a wider incorporation of these devices in our daily practice.

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