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EDITORIAL COMMENT

Bioresorbable Scaffolds Versus Metallic Drug-Eluting Stents

Are We Getting Any Closer to a Paradigm Shift?*

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Since the first catheter-based coronary treatment in 1977, interventional cardiology has witnessed several practice-changing paradigm shifts. The transition from balloon angioplasty to bare-metal stents to drug-eluting stents (DES) substantially advanced the safety and efficacy of percutaneous coronary interventions (PCI) and improved patient outcomes (1). Bioresorbable vascular scaffolds (BVS) have emerged as a promising new link in this chain of major breakthroughs in intracoronary device technology. BVS provide temporary vessel support, retain the ability of antirestenotic drug elution, and dissolve within a well-defined time frame. Due to this principle function, BVS may provide therapeutic features that could extend well beyond current metallic DES by enabling positive vessel remodeling and late lumen gain (2), enhancing the process of long-term arterial healing (3), entailing plaque shielding properties (4), and restoring physiological vasomotion (5). In aggregate, these properties bear the potential to further advance clinical outcomes including the ability to reduce angina symptoms compared with metallic stents (6).

The conformability and superior flexibility of BVS allows for minimal changes of vessel geometry and along with the eventual absorption of the lumen-protruding struts attenuate the unfavorable hemodynamic changes that are typically imposed by rigid stents (7). Elimination of late-acquired malapposition (an established trigger of stent thrombosis) or edge-related vascular responses in the long term are additional theoretical benefits of BVS. On the other hand, strut thickness is larger compared with new-generation DES, which leads to suboptimal crossing profiles, limits the ability to treat complex (e.g., excessively tortuous or calcified) lesions or to implant overlapping BVS, and results in inferior immediate, post-procedural angiographic outcomes of device performance (6).

A variety of BVS is currently under investigation, and both polymer-based as well as metal (magnesium)-based BVS with drug-eluting properties have entered clinical investigations (8). The everolimus-eluting Absorb BVS is the most widely used and investigated device to date. The initial ABSORB Cohort A and B studies (ABSORB A and ABSORB B) demonstrated the feasibility of the BVS in highly selected patients with simple lesions (9). Real-world observations (10–13) and, more recently, randomized trials (3,6,14,15) have gone a step further by comparing the performance of the BVS with new-generation DES. Against this background, 1-year angiographic and clinical results of the ABSORB

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China trial are reported in this issue of the *Journal* (16). The trial, designed to enable regulatory approval of the device in China, randomized 480 patients with up to 2 de novo lesions in a 1:1 fashion to Absorb BVS or the metallic everolimus-eluting Xience stent platform. The study was able to show non-inferiority of the BVS versus Xience for the primary angiographic endpoint, in-segment late lumen loss at 12 months (0.19 ± 0.38 vs. 0.13 ± 0.37, p for

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noninferiority = 0.01). Of note, minimal lumen diameter was smaller (2.27 ± 0.03 mm vs. 2.50 ± 0.03 mm; $p < 0.001$), and % diameter stenosis was greater (18.5 ± 0.92% vs. 11.3 ± 0.76%; $p < 0.001$) for the BVS within the device, whereas in-segment measures did not differ. Clinical outcomes, including target-lesion failure and stent thrombosis, were similarly low between the 2 groups, although the study was not powered for any individual or composite clinical endpoint (16). The open-label design in contrast to the single-blind design of previous randomized trials of BVS versus DES (3,6,14,15) also needs to be taken into account.

The ABSORB China trial is a valuable contribution to the growing body of evidence comparing the angiographic and clinical performance of BVS versus the current standard-of-care for PCI, that is, new-generation DES (17). The findings are in line with recent randomized trials (3,6,14,15) indicating noninferiority of angiographic efficacy and comparably low mid-term rates of device-oriented as well as patient-oriented clinical events. The concordance of findings across different ethnicities corroborates their generalizability, and the consistency in a ST-segment elevation myocardial infarction cohort (3) extends the disease-specific indications of the device to patients with higher-risk clinical presentation. Notably, however, the findings remain applicable to relatively noncomplex anatomies because bifurcation and calcified lesions were underrepresented, and left main lesions and multivessel treatment were excluded from these trials.

With a handful of randomized comparisons of BVS versus metallic DES, including >1,800 patients, now available, our ability has grown to draw a more complete picture of this technology both in terms of mid-term angiographic efficacy as well as clinical performance. Because interpretation of findings is limited by the modest sample size of individual studies, a synthesis of the available evidence by performing a meta-analysis of 5 trials (ABSORB II [6]; ABSORB China [16]; ABSORB JAPAN [14]; EVERBIO II [Comparison of Everolimus- and Biolimus-Eluting Stents With Everolimus-Eluting Bioresorbable Vascular Scaffold Stents] [15]; and ABSORB STEMI-TROFI II [ABSORB STEMI: the TROFI II Study] [3] trials) focusing on angiographic and clinical endpoints that are comparable across the trials provides further insights. Statistical methods for this meta-analysis are presented in the Online Appendix. When addressing angiographic efficacy by using the primary endpoint of in-segment late lumen loss, BVS is associated with significantly greater late lumen loss than metallic DES (0.05 mm; 95% confidence interval [CI]: 0.01 to 0.09) (**Figure 1**). Risks of the device-oriented composite endpoint target lesion failure (odds ratio [OR]: 1.15; 95% CI: 0.71 to 1.85), the patient-oriented composite endpoint of death, myocardial infarction, or any revascularization (OR: 0.93; 95% CI: 0.67 to 1.30), and definite or probable stent thrombosis (OR: 1.86; 95% CI: 0.55 to 6.27) do not differ between BVS and metallic DES throughout the observed period of follow-up. Of note, there was no significant heterogeneity across trials for the analyzed outcomes.

Collectively, individual randomized trials have demonstrated noninferior angiographic efficacy results for the BVS compared with metallic DES (i.e., the Xience stent in all but 1 trial [15]); however, a significant difference of late lumen loss in favor of DES emerged in the present meta-analysis. This finding may need to be interpreted in light of the low reported rates of periprocedural intracoronary imaging in some of the trials (15,16). Given the importance of accurate size estimation and the limitations in terms of aggressive post-dilation techniques (due to the risk of polymeric stent disruption in case of excessive overexpansion), intracoronary imaging—in particular optical coherence tomography—to guide and optimize BVS implantation may assume a prominent role for improving post-procedural and presumably longer-term angiographic outcomes (18), although this requires confirmation in appropriately designed studies.

Whereas angiographic measures of device efficacy are essential, the clinical relevance of these differences needs to be placed in a broader perspective. The penetration of bioresorbable stents in routine interventional practice within the next years will be determined largely by their impact on patient outcomes. At present, both randomized and observational evidence (10–13) suggests comparable device efficacy and similarly low event rates, as confirmed also in the pooled analysis presented here. Although it becomes increasingly challenging for new intracoronary devices to achieve meaningful improvements against the current standard-of-care, clinical studies with larger and more complex populations and longer follow-up durations (extending to the time frame before, as well as after complete scaffold resorption) are critical to definitively establish at least the non-inferiority of the BVS (and of other BVS currently under development) versus the best available metallic DES. In this respect, long-term outcomes of ABSORB II, the ongoing ABSORB III (ABSORB III Randomized Controlled Trial; NCT01751906 and ABSORB IV trials (ABSORB IV Randomized Controlled Trial; NCT02173379) with 5,000 patients, and the