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EDITORIAL COMMENT

Bioresorbable Vascular Scaffolds in Routine Clinical Practice

Should We Wait Longer?*

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The practice of cardiovascular medicine is rapidly evolving, with an increasing number of new pharmaceutical agents and medical devices being evaluated for clinical safety and efficacy. Recommendations for good clinical practice are on the basis of the results derived from quality studies. Data from prospective randomized clinical trials establish the highest level of scientific evidence and remain the gold standard for comparing safety and efficacy among different therapies. Randomized trials eliminate the differences between treatment groups and provide unbiased estimates of outcomes in the trial populations. However, the outcomes of randomized trials often take time, and the trials commonly enroll highly selected population groups from specific study centers. Hence, registry data have gained increasing importance in the past few years in providing information, especially with regard to safety. Registry data provide insight into real-world practice and information on clinical situations that may not have been assessed in randomized studies. Outcomes are quick and may be hypothesis generating for testing in randomized studies. Notwithstanding the inherent limitations of registry data (the presence of confounding factors that are difficult to adjust, a tendency for selection bias, and being unsuited for deriving relationships between treatments and outcomes), knowledge from registry studies does contribute to better understanding of device-oriented patient outcomes, as in the present study.

The long-term presence of a metal platform inside a coronary artery is undesirable. Late stent failure is still a concern, even with second-generation metallic drug-eluting stents (1,2). The current goal of treating obstructive coronary artery disease has moved beyond the relief of ischemia. The physiological restoration of the vessel wall to its normal vasomotor state can be achieved by eliminating the caged effect imposed by a metallic drug-eluting stent. The development of bioresorbable vascular scaffolds (BVS) precisely addresses this issue, and scaffolds of the current generation are expected to fully resolve after 2 years of implantation.

The vast majority of data on BVS come from studies using the Absorb BVS (Abbott Vascular, Santa Clara, California). After an initial evaluation in the ABSORB clinical trial (Cohorts A and B) with encouraging results, many registry studies and a few randomized controlled trials were conducted. Clinical outcomes from the large amount of registry data have shown acceptable rates of target lesion failure. The GHOST-EU (Gauging coronary Healing with biOresorbable Scaffolding plaTforms in EUrope) registry analyzed 1,189 subjects and reported a cumulative incidence of target lesion failure of 4.4% and a scaffold thrombosis rate of 2.1% at 6 months (3). The rates of ischemia-driven major adverse cardiac events and target vessel failure were 4.3% and 4.9%, respectively, at 1 year in 512 patients enrolled in the ABSORB EXTEND study (4). The cumulative rate of scaffold thrombosis was 0.8% at 1 year.

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In this issue of *JACC: Cardiovascular Interventions*, Felix et al. (5) report medium- to long-term clinical

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outcomes with the ABSORB BVS in 244 subjects. This was a prospective, single-arm, single-center registry study in patients with lesions that are reflective of routine clinical practice (38% type B2/C, 21% bifurcation, and 42% calcified lesions). The primary outcome was major adverse cardiac events, defined as a composite of cardiac death, myocardial infarction, and target lesion revascularization. In the per-treatment population group, the investigators report major adverse cardiac event rates of 5.1% at 12 months and 6.8% at 18 months. The investigators conclude that BVS implantation in subjects seen in daily practice was associated with an acceptable rate of adverse events in the long term. In the study, the clinical device and procedural success rates were high, with no cases of early or very late scaffold thrombosis. In contrast to other registries, the clinical outcomes for this study were reported at 18 months, which reassures us of the medium-term performance of BVS. Although the investigators should be commended for the extended follow-up of this real-world population beyond 1 year, there are a few issues that need to be considered.

The intention-to-treat design is preferred for complete analysis rather than per-treatment analysis. Of the 249 subjects allocated to the intervention in the study, delivery failure was reported in 5 (2%), and data were analyzed only in subjects who had BVS successfully implanted. It is a recognized fact that 1 of the major limitations of BVS is related to the mechanical properties of the scaffold. The increased strut thickness limits deliverability, and the higher crossing profile hampers its use in difficult anatomic settings. The investigators mention but do not elaborate on the reasons for the failure of scaffold delivery in each of those unsuccessful cases. With an accrual of experience, there is no question that operators are able to select appropriate subjects for BVS implantation on the basis of coronary anatomy.

A quarter of the recruited participants had scaffold underexpansion on the basis of quantitative coronary analysis, with a trend toward an increased rate of major adverse cardiac events in this subset. Scaffold underexpansion is a known important risk factor for scaffold thrombosis and restenosis. This can be addressed if an intravascular imaging modality is more commonly adopted. Intravascular ultrasound and optical coherence tomography were used in 39% of the patients. Routine high-pressure balloon post-dilation is also recommended, unless intracoronary imaging confirms full expansion and apposition. In the study, balloon post-dilation was performed in only 53.3% of the cases. In the narrated cases of scaffold thrombosis, underexpansion and malapposition were frequently observed, which further emphasizes the importance of optimal implantation technique for immediate procedural and long-term clinical success (6,7). The rate of overall scaffold thrombosis was 2.7% at 18 months, with a definite scaffold thrombosis rate of 1.9%. Although the rates are similar to those observed in other BVS trials, they are still higher compared with second-generation metallic drug-eluting stents. With the universal adoption of optimal implantation techniques and enhanced scaffold design, it remains to be seen whether scaffold thrombosis rates will be further reduced. The study by Felix et al. (5) also included lesions with moderate to severe calcification in 42% of the patient population. Although the long-term benefits of vasomotion restoration and positive remodeling are unclear in this group of patients, the limited use of debulking strategies (rotational atherectomy in 3.1% and scoring balloon in 2.7%) to optimize the immediate post-procedural gain is of concern.

So far, a meta-analysis of major randomized trials has shown no significant difference in 1-year clinical outcomes between BVS and second-generation cobalt-chromium everolimus-eluting stents (8). However, the 2-year follow-up results of ABSORB II, presented at Transcatheter Cardiovascular Therapeutics 2015, revealed a higher rate of target lesion failure in the BVS group (7.0%) than the group with cobalt-chromium everolimus-eluting stents (3.0%) ($p = 0.07$). Although this study was not adequately powered for clinical endpoints, they are indicators of concern. The unique properties of BVS are not expected to be obvious until 3 to 5 years after implantation. The reported follow-up period of 18 months in this registry might be insufficient to address the potential plausible advantages of BVS. Certainly, the reported cases of late scaffold malapposition and very late scaffold thrombosis have also raised a small red flag regarding the long-term safety of this novel technology (9,10). The long-term clinical outcomes from ongoing large scale randomized trials (ABSORB IV) is much anticipated.

This study has added more evidence to our current wealth of knowledge regarding the safety and efficacy of BVS. However, it is still unclear whether BVS should be used routinely in clinical practice, in anticipation of their potential promising long-term advantages. Perhaps there is a need to wait a bit longer for the final verdict to be known.

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