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EDITORIAL COMMENT

No Benefit of Different Drug or Design on Clinical Outcomes of First-Generation Polymeric Scaffolds

Does Resorption Time Play a Better Role?*

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The 40-year history of coronary angioplasty reminds us of how many new technologies were first embraced with enthusiasm and subsequently underwent a phase of fluctuating reputation. In fact, the accrual of clinical data through registries and randomized trials has many times deflated much of the early enthusiasm, with some new devices successfully surviving their respective "stress tests" and others either being replaced or disappearing. Bioresorbable scaffolds (BRS) are at a relatively early stage of their clinical development program where any new trial easily shifts the pendulum of physicians' perception toward undue enthusiasm or frustration. For example, the 1-year outcomes of ABSORB 3 (the regulatory study that led to approval of the everolimus-eluting bioresorbable vascular scaffold [BVS] [Abbott Vascular, Santa Clara, California] in the United States) were consistent with the hypothesis of BVS being noninferior to everolimus-eluting stent control subjects (1). Only 1 year later, the community was puzzled by the results of the ABSORB 2 trial, where angiographic and clinical outcomes of BVS at 3 years were worse than those of everolimus-eluting stents, and even vasomotion—a hallmark concept of the BRS credo—was not shown to be significantly improved (2).

Waiting for the next round of the BRS saga, some arguments put it in terms on which we can perhaps all agree: first, coronary scaffolds are not workhorse devices, and should be intended for use in carefully selected patients and lesions; second, correct scaffold implantation is a challenge, and meticulous implantation technique is required to optimize outcomes; and third and foremost, the fluctuating results of first-generation BVS should not detract from pursuing the development of new BVS iterations and alternative BRS systems, as the idea of a disappearing device remains intuitively attractive. To this extent, comparing procedural and clinical outcomes of different BRS is of utmost interest, as these comparisons may drive physicians toward more informed decisions in their practice, and companies toward better manufacturing strategies.

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In this issue of *JACC: Cardiovascular Interventions*, Wiebe et al. (3) enter the BRS debate in a timely manner by providing the community with a propensity-score matched comparison of the BVS and the novolimus-eluting bioresorbable coronary scaffold (BCS) (Elixir Medical Corporation, Sunnyvale, California), this latter being another type of BRS available in the European market since 2014. BVS and BCS share some similarities in that they are both made of poly-L-lactide and have approximately the same crossing profile and strut thickness, but also feature some differences. In fact, BCS have a higher number of peaks per hoop than BVS, a lower width in the circumferential direction, a slightly smaller footprint, and a higher radial strength (4). In addition, the 2 devices differ with respect to the drug eluted (novolimus for BCS and everolimus for BVS), the ability of BCS to "self-correct" its diameter to baseline dimensions and, perhaps more intriguingly, the resorption time (1 to 2 years for BCS and 3 to 4 years for BVS). Do any of these differences translate into a

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meaningful clinical advantage? The study of Wiebe et al. (3) showed no significant differences in target lesion failure (TLF) at 1 year between matched BCS and BVS. Indeed, because the study was retrospective and nonrandomized, its results can be considered only as good as the methods used to gather the data. In particular, considerations on how the propensity score was built and used for matching are crucial to drive a correct interpretation.

Propensity score matching is a statistical technique that mimics randomization by accounting for the confounding covariates that predict both receiving the intervention of interest and the outcome of the intervention. Therefore, in building a propensity score model, one should use single characteristics that distinguish the groups with regard to both exposure and outcome, as this is expected to increase the precision of the estimates (5). Particularly in small studies such as the one from Wiebe et al. (3), the inclusion of variables that are strongly related to the exposure (i.e., BCS or BVS) but only weakly related to the outcome (i.e., TLF) can lead to incremental bias. Consistently with this reasoning, the authors circumvented the general rule of including only baseline characteristics into their propensity score model, and perhaps legitimately included 2 procedure-related factors (pre-dilation and post-dilation) that are an essential part of the optimal implantation technique recommended by the BVS manufacturer as a way to achieve better clinical outcomes, together with adequate vessel sizing.

Before even generating the propensity score, the authors excluded a proportion of patients with BVS belonging to the early part of the learning curve at their institution, where post-dilation was initially uncommon (24%) as was the use of intravascular imaging (9%) (6). Apparently, BCS capitalized on the procedural missteps initially made with BVS, because no evidence of a learning curve effect was noted. In the final matched cohorts (including all 106 patients treated with BCS and 212 matched patients treated with BVS in a 1:2 ratio), post-dilation rates were as high as 87% and 84% in the BCS and BVS groups, respectively (3). These numbers are notably higher than those reported in the BVS groups of ABSORB 2 (61%) and ABSORB 3 (66%) (1,2). Yet, post-dilation can be a double-edged sword if performed with balloons that are too large compared with the nominal size of the scaffold, due to risk of device fracture. Indeed, the authors found the maximum diameter of the balloon used for post-dilation to be a significant independent predictor of TLF. This finding acts as a useful reminder for the interventional community that balloons for post-dilating polymeric scaffolds should be noncompliant and no more than 0.5 mm above the nominal scaffold size (7). It is also of interest that intravascular imaging was more commonly used in the study when implanting BCS (52%) compared with BVS (36%; $p < 0.001$), which remains a possible residual confounder in the study even after propensity score matching, despite both rates being laudably higher than in the ABSORB 3 trial (11%).

In aggregate, the results of the study by Wiebe et al. (3) apply to a population of relatively selected patients and lesions, and reflect contemporary procedural standards. At 1 year, the Kaplan-Meier estimates of TLF were as low as 4.7% and 4.5% in the BCS and BVS groups, respectively. These findings are reassuring in terms of the antirestenotic efficacy of both BRS in the period where scaffolding functions are necessary, and are in line with the 1-year results of a recent BVS meta-analysis (8). Scaffold thrombosis was 2.0% in the BVS group and 1.0% in the BCS group, but only 5 thrombotic events were counted in total, which precludes from making any safety considerations from these findings. Clearly, if differences between the 2 devices exist, these will be more likely to emerge after 1 year, when the BCS rapidly loses its mass while the BVS stays longer. The relatively long durability of BVS in the vessel wall has been advocated as one of the reasons for the disappointing results of the ABSORB 2 trial in which the absolute risk difference in TLF compared with EES was 1.8% at 1 year, 2.2% between 1 and 2 years, and 1.5% between 2 and 3 years (2). Whether a more rapid mass loss such as that of BCS or other upcoming BRS in the pipeline may be associated with superior clinical outcomes is a question for randomized studies versus BVS and, ideally, versus drug-eluting stents, with a follow-up plan of at least 5 years.

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REFERENCES

1. Ellis SG, Kereiakes DJ, Metzger DC, et al. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. N Engl J Med 2015;373:1905–15.

2. Serruys PW, Chevalier B, Sotomi Y, et al. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial. Lancet 2016;388:2479–91.

3. Wiebe J, Dörr O, Ilstad H, et al. Everolimus- versus novolimus-eluting bioresorbable scaffolds for the

treatment of coronary artery disease: a matched comparison. J Am Coll Cardiol Intv 2017;10:477–85.

4. Ormiston JA, Webber B, Ubod B, Darremont O, Webster MW. An independent bench comparison of two bioresorbable drug-eluting coronary scaffolds (Absorb and DESolve) with a durable metallic drug-eluting stent (ML8/Xpedition). EuroIntervention 2015;11:60–7.

5. Brookhart MA, Schneeweiss S, Rothman KJ, Glynn RJ, Avorn J, Sturmer T. Variable selection for propensity score models. Am J Epidemiol 2006;163:1149–56.

6. Wiebe J, Liebetrau C, Dorr O, et al. Impact of the learning curve on procedural results and acute outcome after percutaneous coronary interventions with everolimus-eluting bioresorbable scaffolds in an all-comers population. Cardiovasc Revasc Med 2015;16:455–60.

7. Tamburino C, Latib A, van Geuns RJ, et al. Contemporary practice and technical aspects in coronary intervention with bioresorbable scaffolds: a European perspective. EuroIntervention 2015;11:45–52.

8. Stone GW, Gao R, Kimura T, et al. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. Lancet 2016;387:1277–89.

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