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EDITORIAL COMMENT

Bioresorbable Vascular Scaffold Technology Benefits From Healthy Skepticism*

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Current high-performance metallic drug-eluting stents (DES) represent the gold standard for the percutaneous treatment of obstructive coronary artery disease (CAD) (1). Notwithstanding this, the permanent nature of the metallic implants may elicit pathophysiological processes at the level of treated segments, and these processes have been found to be responsible for an accrual of adverse events over the long term (2).

Fully bioresorbable stents eluting antirestenotic drugs are drawing increasing interest; these platforms offer a transient arterial support until the elution process is completed and then self-degrade into inert breakdown products after a certain amount of time. In consideration of initial favorable conformity and safety reports (3), the everolimus-eluting bioresorbable vascular scaffold (BVS) (Absorb, Abbott Vascular, Santa Clara, California) has been the first of such devices to receive CE-mark approval.

New technologies with the potential of improvement of late outcomes are usually assessed against current established treatment to show at least noninferior early performance. In a recent meta-analysis of randomized trials, patients with simple to moderately complex CAD treated with BVS displayed a risk of device thrombosis at 1 year higher than that associated with everolimus-eluting stents, with most of the excess risk confined to the initial 30 days (4). Consistent findings have been observed in a number of registries including participants with relatively more complex CAD (5–7). In this regard, although the initial evidence regarding BVS paved the way for enthusiasm, more recent data tends to increase skepticism. The overall rates of scaffold thrombosis are higher than with contemporary metallic DES and may represent a worrisome premise for oncoming investigations of such platforms in higher-risk subsets (**Table 1**).

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With this in mind, in this issue of the *Journal*, Puricel et al. (8) present the results of a multicenter registry including ~1,300 patients treated with BVS. The declared objective was an in-depth analysis of incidence, predictors, and possible underlying mechanisms of scaffold thrombosis. In this series, definite/probable scaffold thrombosis occurred in 1.8% of patients within 30 days and in as high as 3.0% at 1 year, with acute coronary syndrome the most frequent clinical presentation. The treatment of ostial lesions, a reduced left ventricular systolic function, the final minimal lumen diameter, and the implementation of a specific protocol for BVS implantation were modifiers of thrombotic risk. Notwithstanding the limitations of retrospective data collection, incomplete outcomes, and multiple testing for adjusting imbalanced baseline features, the authors should be congratulated for their effort. The rates of BVS thrombosis described here are aligned with previous observations in comparable populations (**Figure 1**) and contribute to the body of evidence on this important topic in a timely fashion. Certainly, some points need careful discussion.

First, the reported association of higher risk of thrombosis by treating ostial lesions with BVS is

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TABLE 1 Ongoing Randomized Controlled Trials of Percutaneous Coronary Interventions With BVS*

Trial Name	Comparison	Population	Patients, N	Expected Completion Date	Primary Endpoints	Registration Number
ABSORB ISR	BVS vs. DCB	ISR	150	2016	9-month angiographic LLL	NCT02474485
ABSORB IV	BVS vs. EES	All-comers	3,000	2017	12-month angina recurrence; 12- to 60-month TLF†	NCT02173379
AIDA	BVS vs. EES	All-comers	2,690	2017	24-month TVF	NCT01858077
Angio-/OCT-guided BVS	Angio + BVS vs. OCT+BVS	Selected	414	2015	6-month neointimal coverage; malapposition rate	NCT02466282
BVS in STEMI	BVS vs. DES	STEMI	120	2016	12-month healing index‡	NCT02067091
COMPARE ABSORB	BVS vs. EES	All-comers	2,100	2018	12-month TLF	NCT02486068
ISAR RESORB	BVS vs. EES	Selected	230	2016	6- to 8-month %DS§	NCT02421016
OPreNBiS	NC balloon + BVS vs. BVS	Selected	50	2016	Apposition ratio‖	NCT02468960
PREVENT	BVS + OMT vs. OMT	Selected	1,900	2019	24-month CV death; nonfatal MI; unplanned hospitalization due to UA	NCT02316886
PROSPECT II – PROSPECT ABSORB	BVS + OMT vs. OMT	ACS	900	2018	24-month MACE related to nonculprit lesion	NCT02171065
RELEASE-BVS	BVS vs. CABG	All-comers	140	2017	12-month ischemia and LVEF¶	NCT02334826

Trial acronyms are detailed in the Online Appendix. *Only registered trials with source data verified within the last 6 months are included. †Landmark analysis. ‡OCT analysis. §angiographic surveillance. ‖≤1 h from procedure start. ¶magnetic resonance imaging.

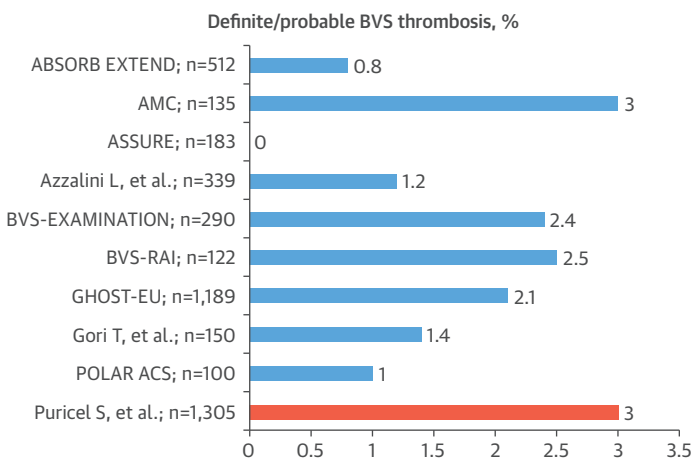
ACS = acute coronary syndrome; Angio = angiography; BVS = bioresorbable vascular scaffold; CABG = coronary artery bypass graft; CV = cardiovascular; DCB = drug-coated balloon; DES = drug-eluting stent(s); DS = diameter stenosis; EES = everolimus-eluting stent(s); ISR = in-stent restenosis; LLL = late lumen loss; LVEF = left ventricular ejection fraction; MACE = major adverse cardiac events; MI = myocardial infarction; NC = noncompliant; OCT = optical coherence tomography; OMT = optimal medical therapy; STEMI = ST-segment elevation myocardial infarction; TLF = target lesion failure; TVF = target vessel failure; UA = unstable angina.

consistent with a previous registry in which the 1-year rate of scaffold thrombosis was as high as 4.9% (9). Beyond the intrinsic challenge of aorto-ostial stenting—only partially resolved with metallic DES (10)—the attrition of the guiding catheter against BVS during implantation produces acute distortions of polymeric struts, which break more readily than those of metallic stents (11). The loss of structural BVS integrity with subsequent malapposition and anomalous bioresorption kinetics likely influences the healing of the stented segment and inherent thrombotic risk.

Second, cases in which a final minimal lumen diameter <2.50 mm post-BVS implantation was achieved displayed the highest risk of thrombosis. Similarly, in those randomized trials providing details of scaffold thromboses, more than one-half occurred in vessels <2.50 mm in diameter (12,13). This evidence, together with the instances of underexpansion/recoil described with BVS, raises concerns regarding the use of such a bulky device (150-μm of strut thickness) in small vessels (14).

Third, in the current analysis, the implementation of a dedicated protocol for BVS implantation (lesion selection, preparation, and proper post-dilation) led to a roughly 70% reduction in the risk of BVS thrombosis. The meticulous attention to procedural details should be the common denominator of all cases in which a stent is implanted in a coronary vessel. Interestingly, all randomized trials comparing BVS versus everolimus-eluting metallic stents have reported fairly high proportions of pre- and post-dilation in patients receiving BVS, superior to those reported in the metallic stent group (4). However, the analysis of aggregate data does not reveal that accurate lesion preparation prevents the 2-fold higher risk

FIGURE 1 Percentages of BVS Thrombosis in Published Registries With ≥100 Patients Included



Median follow-up, 12 months (interquartile range: 6 to 12 months; mean 9.6 ± 3.1 months). References and study acronyms are detailed in the Online Appendix.
BVS = bioresorbable vascular scaffold.

of thrombosis after BVS than that after metallic stent implementation (4). At the current stage, a more liberal use of intravascular imaging appears to be instrumental to anticipate, detect, and correct any possible technical shortcoming of current BVS technology and to further address whether the strut discontinuity in the absence of neointimal hyperplasia increases the thrombotic risk of this device (15,16).

Finally, the interplay among BVS, dual antiplatelet therapy (DAPT), and thrombotic risk seems less predictable than with newer-generation metallic DES (17). Indeed, besides some cases of early and late scaffold thromboses due to premature DAPT disruption or discontinuation, a number of very late thromboses in the present report occurred after a complete 12-month DAPT course (8). In line with this finding, recent evidence reported some cases of very late scaffold thrombosis despite chronic DAPT (16). Late and very late scaffold thromboses have been described as multifactorial in nature (16,18), and the optimal length of DAPT after BVS is still open to question. Indeed, guideline-writing authorities recommend 6-month DAPT in most patients receiving contemporary metallic DES, without mention of BVS (1). So far, an approach of ≥12-month DAPT duration for patients at low risk of bleeding seems reasonable until data from specific studies are available addressing the time at which the dissolution of the BVS is at advanced stages or nearly complete (16).

The body of evidence regarding the performance of BVS technology confers a certain sense of déjà vu, as with earlier DES, the concerns regarding a higher risk of adverse events became apparent with the availability of larger sample sizes and a broader clinical use. However, the awareness of intrinsic limitations of earlier-generation devices prompted continuous iterations, which led to contemporary high-performance DES with unprecedented safety and efficacy (19). This is certainly the future of BVS technology. Meanwhile, as the process of improvement of BVS technology goes on, the use of these devices should be guided by available evidence and follow procedural protocols specific to this technology. Confirmation of the expected late advantages of BVS will come from long-term follow-up data. However, this may take time, as the rapid pace of development of BVS technology outpaces the long-term data obtained with older products. Until then, cases of scaffold thrombosis will remain a matter of concern. The combination of optimism with healthy skepticism will certainly push forward the progress in BVS technology and revolutionize the field of percutaneous coronary interventions.

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APPENDIX For supplemental references and definitions for Figure 1 and Table 1, please see the online version of this article.