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EDITORIAL COMMENT

Bioresorbable Scaffold

Balancing Risks to Promissory Benefits?*

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The field of percutaneous coronary intervention has encountered several disruptive technologies from its inception when Andreas Gruentzig performed the first percutaneous transluminal coronary angioplasty in September 1977. Since that time, percutaneous revascularization has evolved into a safe, effective, and predictable procedure. Introduction of coronary stenting was a transformational development in this exciting journey of 40 years. Evolution in the stent materials and design from stainless steel to chromium cobalt and from bare-metal to third-generation drug-eluting stents, along with improvements in periprocedural pharmacotherapy, and insights from intravascular imaging with intravascular ultrasound and optical coherence tomography have resulted in better procedural and long-term outcomes. The current-generation metal stents with their small profiles are easy to deliver yet have excellent radial strength. The reported restenosis rates are in the single digits and annual risk of stent thrombosis (ST) is <1% (1).

Over the last 2 decades while working on improving the metallic stents, investigators envisioned an absorbable stent that would disappear overtime to leave the coronary artery without a permanent prosthesis. Proponents were rightfully enthusiastic, as such devices would have the potential benefits of restoring vasomotion and the ability to remodel as well as keep the option of future surgical or percutaneous revascularization even in extensively stented vessels. There are 4 approaches used for creating such scaffolds: the first using a semicrystalline poly-L-lactic acid scaffold (ABSORB Bioresorbable Vascular Scaffold [BVS], Abbott Vascular, Santa Clara, California; and DESolve, Elixir Medical Corporation, Milpitas, California), a second using a resorbable magnesium scaffold (Magmaris, Biotronik, Berlin, Germany), a third using a tyrosine-derived polycarbonate scaffold (REVA, Reva Medical, Inc., San Diego, California), and a fourth using salicylic acid (BTI stent, Bioabsorbable Therapeutic Inc., Menlo Park, California). Resorption properties of these stents are variable with proposed complete dissolution of scaffold between 1 and 3 years. All of the current generation absorbable scaffolds are impregnated with an antiproliferative limus family agent. To be clinically acceptable, the performance of these scaffolds has to match the current generation of metallic drug-eluting stents—a very high bar for an evolving technology. Currently, the ABSORB BVS is the most studied scaffold, with high-quality data from randomized controlled trials. These studies, with their methodological rigor and disciplined execution, together with careful reporting of the data have provided a wealth of valuable information.

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In this issue of *JACC: Cardiovascular Interventions*, Wiebe et al. (2) report 2-year data from the ISAR-ABSORB registry from Munich, Germany. In this study of 419 patients with an average age of 66 years, they report a disturbing 21.6% adverse event rate at 2 years with the use of the ABSORB BVS (6.3% death, 3.9% myocardial infarction, 3.8% ST, and 16% target lesion revascularization). The rate of definite or probable ST at 2 years was 4.2%. Importantly, there is

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1.3% definite ST reported between years 1 and 2. Of the 4 such patients (see Table 5 in Wiebe et al. [2]), only 1 was on dual antiplatelet therapy (DAPT), 1 patient had post-dilatation, and interestingly all 4 had 3.0-mm or 3.5-mm stents. These data are a very important addition to several recently reported series with 2-year follow up (Online Table 1). The current paper provides new insights using real-world, good-quality data with particular emphasis on patients with ST.

In the recent American College of Cardiology meeting, 2-year data from the ABSORB III randomized trial were presented by Dr. Stephen Ellis. The rate of the target lesion failure, the primary endpoint (a composite of cardiac death, target vessel myocardial infarction, or ischemia-driven target lesion revascularization), was 11% for the 1,322 patients in the ABSORB BVS group and 7.9% for the 686 patients who were randomized to XIENCE stent (Abbott Vascular) (hazard ratio: 1.42; 95% confidence interval: 1.04 to 1.94; $p = 0.03$). Definite or probable ST rate at 2 years was 1.9% with the ABSORB BVS versus 0.8% with the XIENCE stent. In the recently published randomized AIDA (Amsterdam Investigator-initiateD Absorb strategy all-comers) trial from the Netherlands, definite or probable device thrombosis occurred in 31 of the 924 patients in the scaffold group as compared with 8 of the 921 patients in the stent group. Two-year cumulative event rates were 3.5% versus 0.9% (hazard ratio: 3.87; 95% CI: 1.78 to 8.42; $p < 0.001$) (3).

Several post hoc analyses have been performed to understand the increased risk of ST after ABSORB BVS. Based on these data Abbott Vascular has emphasized specific measures that can potentially minimize risk of ST. The scaffold specific implantation technique known as pre-dilation, appropriate vessel sizing, and high-pressure post-dilation (PSP) has been proposed to minimize this risk. When patients in the ABSORB trials undergo adequate PSP technique of implantation (approximately 10% of all patients), the risk of ST and TVF was found to be comparable to the XIENCE stent (4). However, these data are derived from a post hoc analysis and need confirmation by a properly designed prospective, controlled study. It is worth noting that in the AIDA study, ST was observed regardless of implantation technique (2).

It is thought that larger strut thickness (150 μm) and cover index, intraluminal disintegration, inadequate opposition or combination of these factors may serve as a nidus for thrombus formation. Patients who are not taking DAPT may have increased risk; thus, prolonged DAPT may be necessary for these patients. Data for such recommendation are somewhat sparse. However, a consistent message of increased risk of ST up to 2 years provides a good rationale for continuation of DAPT for at least 2 years as recently reviewed (5).

With the new insights derived from longer follow-up, the Food and Drug Administration sent a letter to practitioners on March 18, 2017, informing them of the increased rate of major adverse cardiac events in patients receiving the ABSORB BVS and recommended that practitioners follow the approved indications in patient selection and best practices for implantation. Shortly after the presentation of the ABSORB III trial, Abbott Vascular, working jointly with the European Regulatory Agencies, sent an Urgent Field Safety Notice/Physician Advisory announcing restriction of the use of the ABSORB GT1 BVS to centers participating in registries.

U.S. cardiologists have demonstrated a cautious approach as evident from very low rates of BVS use. Considering the facts that there is no proven benefit, the theoretical advantages are promissory, and safety concerns raised by recent reports, the most prudent approach appears to be using the ABSORB BVS only within the context of research studies with careful follow-up and data collection. Adherence to the approved indications with meticulous attention to the scaffold specific implantation technique (PSP) is mandatory.

BVS remain a potentially disruptive technology, but it is clear from the data presented in this paper and other recent publications (Online Table 1) that further improvement is necessary. Perhaps thinner struts, newer design characteristics, appropriate patient selection, and standardized techniques of implantation may lead to better outcomes and improve the care of our patients (6).

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APPENDIX For an expanded references section and a supplemental table, please see the online version of this article.