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EDITORIAL COMMENT

Bioresorbable Vascular Scaffold Thrombosis

Solutions to the Problem?*

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This year marks the 40th anniversary of the first percutaneous coronary intervention (PCI), performed by Andreas Gruentzig. Since that time there has been an ongoing panorama of technological breakthroughs that have improved the safety and efficacy of PCI. These range from simple balloon angioplasty to directional, rotational, and laser atherectomy to bare-metal stents to vascular brachytherapy and to drug-eluting stents (DES). Each new technology has had to prove itself compared with the accepted standards of the time. The most recent "holy grail" of PCI has been to develop a fully bioresorbable DES that would treat the plaque without leaving a permanent foreign metal body in the coronary artery. And so, as with previous technologies, this concept must be compared with the current generations of metal DES for safety and efficacy.

Although a variety of bioresorbable vascular scaffolds (BVS) are currently in development, the most clinical data and experience have been with the Absorb stent (Abbott Vascular, Santa Clara, California). This stent consists of a semicrystalline poly-L-lactic scaffold that elutes everolimus into the vessel wall with loss of mechanical support in 6 months and full resorption within 3 years (1). The ABSORB II trial analysis at 1 year set the mark for noninferiority of the Absorb stent compared with conventional second-generation permanent polymer everolimus-eluting stents (EES) (2). As a result, the Absorb stent was quickly adopted in Europe. The larger ABSORB III trial follow-up at 1 year reaffirmed the noninferiority of the bioabsorbable platform (3) and led to Food and Drug Administration approval of the Absorb BVS GT1 in the United States.

However, this initial exuberance was met most recently with darkening concerns about the Absorb stent as more long-term follow-up data were reported. The 3-year follow-up of the ABSORB II study with straightforward noncomplex stenoses reported higher rates of late stent thrombosis (ST) and repeat PCI with the Absorb BVS (4). Two-year data from the ABSORB III trial, presented by Dr. Stephen Ellis at the 2017 American College of Cardiology meeting, reported a 1.9% incidence of definite or probable ST with the Absorb BVS compared with 0.9% with the XIENCE EES (Abbott Vascular) (5). As a result, the Food and Drug Administration sent a letter informing interventional cardiologists of these increased event rates and urged compliance with the listed indications for the Absorb BVS and to use proper technique. In addition, the European Regulatory Agency in conjunction with Abbott Vascular decided to restrict the use of the Absorb GT1 BVS only to centers that participated in outcomes registries in Europe.

Another blow to the Absorb stent occurred in June 2017, with the publication of a meta-analysis of 7 randomized trials involving 5,583 patients (6). This study found no significant differences in mortality between the groups but did report a significant increase in ST in the BVS group (2.4%) compared with the metal EES group (0.7%). Included in this meta-analysis was AIDA (Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial), which reported an almost 4-fold increase in the risk for ST with BVS compared with metal EES (7).

Amid all this turmoil, the study by Ellis et al. (8) in this issue of *JACC: Cardiovascular Interventions* sheds

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light on the clinical, angiographic, and procedural correlates of acute, subacute, and late Absorb BVS scaffold thrombosis.

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The investigators identified and verified independent correlates of device thrombosis from an analysis of multicenter trials and registries. This included high-quality randomized clinical trials and registries enrolling at least 200 Absorb BVS patients with clinical follow-up in >95% to 12 months and procedural quantitative coronary angiography available either via the study directly or with willingness to send images to the Cleveland Clinic Core Angiographic Laboratory for blinded review.

Among 8,463 consecutively treated patients, 105 (1.24%) were identified with scaffold thrombosis within 1 year of implantation. They were matched 2:1 with control subjects selected randomly from nonthrombosis patients. Data-restricted multiple logistic analysis was used to identify significant independent covariates of the outcome.

The investigators reported that early (within 1 month) scaffold thrombosis occurred in 69 patients and that late (1- to 12-month) scaffold thrombosis occurred in 36 patients. Modeling found significant correlations of scaffold thrombosis to be final minimal luminal diameter <1.85 mm (odds ratio [OR]: 3.1; $p = 0.004$), off dual-antiplatelet therapy (DAPT) status (OR: 3.1 to 3.5; $p = 0.006$ to 0.053), no postdilatation with balloon/scaffold ratio >1.1:1 (OR: 2.3; $p = 0.022$), and reference vessel diameter <2.40 mm (OR: 2.1; $p = 0.036$).

Ellis et al. (8) conclude that suboptimal vessel sizing, procedural technique, angiographic outcomes, and DAPT discontinuation appear to be the principal determinants of Absorb BVS scaffold thrombosis risk through 12 months after implantation. These conclusions are applicable to the "real world." They reaffirm the PSP concept (prepare the lesion, size appropriately, and post-dilate) to improve apposition and long-term results. Ongoing studies and trials are under way to provide more data on outcomes with the PSP technique.

But what is one to do as a practicing interventional cardiologist in the real world? First, the data with the first-generation BVS and ST are very sobering. Ideally speaking, an individual and institution's use of the current Absorb BVS should be as part of a randomized multicenter trial with meticulous PSP technique. As long as the Food and Drug Administration approval is still in effect, the clinical use of Absorb outside a randomized trial should be done only after a good deal of thoughtful reflection given to the individual patient. The listed indications, contraindications, and anatomic factors for the Absorb GT1 BVS should be followed, in addition to the valuable guidelines provided by Ellis et al. (8). The use of meticulous PSP techniques is imperative.

Consideration should also be given to the duration of DAPT with BVS. The default should be at least a 12-month uninterrupted DAPT regimen, with the option for an extended regimen in selected patients with multiple BVS implanted and at low bleeding risk (9). One could even argue for a 3-year duration of DAPT for patients at low bleeding risk.

A good candidate for BVS may be a younger patient with early coronary disease and significant risk factors, such as diabetes, strong family history, and hypercholesterolemia, which would predispose them to experience repeated proliferative events. Such a strategy of early BVS use may keep future revascularization options open rather than dealing with a "railroad track" of multiple metal stents. If the Absorb GT1 BVS is used in nontrial clinical practice, the patient should sign informed consent and be part of a registry such as the National Cardiovascular Data Registry CathPCI Registry. An extra institutional effort should be made to keep in touch with the patient and track long-term outcomes.

In conclusion, one must put into perspective that the Absorb BVS is a first-generation bioresorbable scaffold that is significantly evolving in technique. Long-term findings from the ABSORB III, ABSORB IV, and other studies will be crucial. The development of second- and third-generation BVS with thinner struts may eventually further improve safety and efficacy, much like the evolution of second- and third-generation metal DES. In the meantime, the solid analysis by Ellis et al. (8) provides "solutions" in the here and now to help deal with the "problem" of bioresorbable scaffold thrombosis.

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