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SCIENTIFIC EDITORIAL

Bioresorbable vascular scaffolds: Time to absorb past lessons or fade away?

Stents coronaires biorésorbables : absorber les leçons du passé ou disparaître ?

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Background

Bioresorbable vascular scaffolds (BVS), announced as the fourth revolution in interventional cardiology, have for many years been the source of several rounds of expectations, but also disappointments. This technology was introduced more than two decades ago, with the seductive idea of providing transient mechanical support and drug delivery, while avoiding the adverse events associated with permanent metallic stents such as late stent thrombosis, restenosis and neoatherosclerosis. The premise of the BVS was that after complete resorption of the scaffold, there would be full restoration of cyclic pulsatility and physiological vasomotion, adaptive vascular remodelling capability, plaque regression, preservation of future revascularization options — by either repeat percutaneous coronary intervention or coronary artery bypass graft surgery — and, finally, removal of the trigger for late adverse events, as with permanent metallic stents [1]. The use of BVS could also allow subsequent assessment with non-invasive imaging, such as coronary computed tomography.

Abbreviations: BVS, bioresorbable vascular scaffold; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; MACE, major adverse cardiac events; PLLA, poly-L-lactic acid; ST, scaffold thrombosis; PSP, Prepare the lesion, Size adequately, Post-dilate.

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The Absorb™ BVS experience

Among BVS, the poly-L-lactic acid (PLLA) everolimus-eluting Absorb™ BVS (Abbott Vascular, Santa Clara, CA, USA) quickly became the leading technology, supported by preclinical and clinical data. In 2008, Ormiston et al. [2] published their first experience with the Absorb™ BVS, demonstrating great feasibility, with high procedural success and decent safety and efficacy at 1-year follow-up (3.3% rate of major adverse cardiac events [MACE], with no scaffold thrombosis [ST]), confirmed at 2-year and 5-year follow-up, with a positive signal on vasomotion restoration [3,4]. The enthusiasm associated with the preliminary studies and investigator-initiated studies was mitigated by the 3-year results of the ABSORB II trial [5], in which the Absorb™ BVS failed to meet its coprimary endpoint of superior vasomotor reactivity and non-inferior late luminal loss compared with the cobalt-chromium everolimus-eluting stent. In addition, there were worrisome significantly higher rates of target vessel-related myocardial infarction and very late ST associated with the Absorb™ BVS. These deceptive results were further confirmed by the Amsterdam Investigator-Initiated Absorb Strategy All-Comers (AIDA) [6] and ABSORB III trial results, demonstrating that the Absorb™ BVS was associated with higher rates of target lesion failure compared with the latest generation of drug-eluting stents (DES), driven by an increased risk of target vessel-related myocardial infarction and higher ST [7]. Subsequently, the manufacturer called a halt to sales as of 14 September 2017. The increased rates of ST with the Absorb™ BVS raised the question of whether it is caused by the scaffold design, patient or lesion selection, implantation technique, dual antiplatelet therapy (DAPT) issues or a combination of these factors.

Improving implantation technique, lesion selection and DAPT duration

One of the explanations for the disappointing results associated with the Absorb™ BVS might be implantation technique. Since its European approval in 2011, investigators and manufacturers have increasingly recognized the importance of adequate lesion preparation, appropriate vessel sizing and post-dilation performance (the so-called PSP [Prepare the lesion, Size adequately, Post-dilate] technique) to allow device success. Indeed, in a large-scale analysis from the major ABSORB studies, after multivariable adjustment for baseline patient and lesion characteristics, vessel sizing and operator technique were strongly associated with BVS-related outcomes during a 3-year follow-up [8].

In addition, the use of intravascular imaging (mainly optical coherence tomography) might be helpful to optimize BVS implantation, and might improve the clinical outcome associated with implantation of these devices [9]. Therefore, BVS users should have a low threshold for the use of imaging before and after BVS implantation, to optimize scaffold sizing and apposition. Nevertheless, whether implantation technique optimization will translate into better clinical outcomes in randomized controlled trials has yet to be demonstrated, and additional information will be addressed by the ongoing ABSORB IV trial, in which the PSP technique has already been recommended.

Lesion and patient selection might also be important. Indeed, reference vessel diameter has been proven to be associated with altered outcomes. In the ABSORB III trial, Absorb™ BVS implantation in vessels < 2.25 mm had a significantly higher rate of ST, which led to its use being restricted to de novo vessels with a reference vessel diameter > 2.5 mm and < 3.75 mm [10]. The use of such a scaffold in ostial lesions, calcified lesions, bifurcation lesions, in-stent restenosis and chronic total occlusions has also been evaluated in registries, but their results were controversial, and no definite conclusion can be drawn about these lesion types. Anyway, patients with limited life expectancy and those who cannot take long-term DAPT or have planned surgery might not benefit from BVS implantation, as the theoretical benefit of BVS should occur when the device is resorbed (i.e. 2—3 years after implantation). Potential preferred applications could theoretically include younger patients, long lesions to avoid full metal jacket and acute coronary syndromes, as the wider strut of a BVS may be associated with better thrombus entrapment, reduced distal embolization and reduced malapposition at longer-term follow-up [10,11].

DAPT duration has also been discussed with regard to these increased ST rates. However, only registries have evaluated the incidence of ST depending on DAPT duration, and demonstrated that the incidence of ST was low while on DAPT, but potentially higher when DAPT was terminated before 18 months [12]. This provides a rationale for considering a longer duration of DAPT therapy. More potent $P2Y_{12}$ inhibitors in patients receiving a BVS may also be advocated, at least in those at low bleeding risk, as advised in the most recent European Society of Cardiology focused update on DAPT [13].

Improving scaffold design, and new devices

The design considerations potentially involved in higher ST rates include strut thickness and BVS composition. One barrier to the development of BVS is the challenge to equal the excellent outcomes of the latest-generation DES. Indeed, it seems difficult to expect better performances from BVS compared with DES in the initial period, particularly because the characteristics that allow for bioresorption require scaffold struts to be substantially thicker and wider than the current DES platform, in order to maintain an adequate radial strength, as bioresorbable polymers, such as PLLA, have low tensile and radial strength compared with metallic alloys. Thicker struts have been demonstrated to increase the risk of ST [14] and restenosis [15]. Indeed, as areas of recirculation are created behind thick struts, deposition of fibrin/platelets and thrombi in the microenvironment around the struts is promoted [16]. Moreover, the crossing profile for the Absorb™ BVS is higher than that of the latest-generation DES, making it less deliverable, and resulting in a lower procedural success rate. Therefore, companies developing BVS have started to work on next-generation BVS with thinner struts. However, thinner struts may have the chal-

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