Bioresorbable Coronary Scaffold Technologies
What's New?

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KEYWORDS

• Bioresorbable scaffold • Vascular restoration therapy • Stent thrombosis • Dismantling

KEY POINTS

- Bioresorbable scaffolds (BRS) were designed to provide temporary mechanical support and early drug delivery followed by complete resorption.
- BRS may be identified as either polymeric (composed of polylactic acid or related compounds) or metallic (composed of magnesium alloy) according to the composition of the backbone.
- Different mechanical properties and biodegradation profile of both BRS type might affect different efficacy and safety outcomes.
- Further improvement in scaffold design and deployment technique might mitigate the proven early risk of failure enhancing the late benefit of complete resorption.

INTRODUCTION

The use of new-generation drug-eluting stents (DES) is recommended in almost every clinical and angiographic scenario in patients with coronary artery disease.[1] However, the permanent delivery of a metallic device is affected by several drawbacks, such as the persistent risks of neoatherosclerosis and very late stent thrombosis, the limitation of late lumen enlargement, the lack of reactive vasomotion in the stented vessel, the jailing of branches, and the exclusion from the possibility of future graft anastomosis especially in the midportion of the left anterior descending coronary artery.[2] Bioresorbable scaffolds (BRS) were designed to provide temporary mechanical support and to prevent neointimal proliferation by eluting immunosuppressive drugs. Moreover, the following complete bioresorption was supposed to be associated with restoration of vasomotion and endothelial function (vascular restoration therapy), luminal enlargement and plaque burden reduction, suitability for future possible treatment options (either percutaneous or surgical) and, most important, a decreased risk of lesion-related events when compared with permanent metallic DES.[3] According to the composition of the backbone, BRS may be identified as either polymeric BRS (pBRS, composed of polylactic acid or related compounds) or metallic (composed of a magnesium alloy).[4] Apart from the backbone, they typically consist of a biodegradable polymer matrix and an antiproliferative drug. This review aims to discuss the lights and shadows of the current available bioresorbable devices that have been evaluated in the management of patients with coronary artery disease. To date, 5 current generations of pBRS (Absorb BVS, DESolve,

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ART Pure, Fantom, and MeRes 100) and 1 absorbable metal scaffold (Magmaris) have received the "Conformité Européene" (CE) mark approval (Table 1).

Overview of Poly-L-Lactide Scaffold

The Absorb bioresorbable vascular scaffold (BVS; Abbott Vascular, Santa Clara, CA) was one of the first to enter this realm and the most thoroughly studied and widely used BRS. The device consists of a 150 μm polymer backbone of poly-L-lactide (PLLA) coated with poly-D,L-lactide (PDLLA), which contains and controls the release of everolimus with a similar pharmacokinetics to the newer generation metallic everolimus-eluting stents (EES).[5] Degradation occurs by stepwise hydrolysis in a progressive process with minimal inflammatory reaction. In the final stage, either PLLA or PDLLA particles degrade entirely to lactic acid, or small remnants that are phagocytized by macrophages.[2] Owing to the mechanical properties of their polymeric backbone, the struts have an increased thickness to reach an acceptable tensile strength and to decrease stiffness and the chance of deformation.[5] To date, Absorb BVS has been compared with newer generation EES in more than 10,000 patients from several randomized controlled trials (RCTs), covering a wide range of clinical and angiographic subsets.[3] The initial studies first showed late lumen enlargement as well as restoration of vasomotion and endothelial function at 2 years after the Absorb implantation.[2] In this initial, highly selected cohort of patients, excellent clinical performance with no events of very late stent thrombosis was confirmed.[6] Also, several registries have confirmed the feasibility of the Absorb implantation for the so-called off-label indications, as in acute coronary syndromes, bifurcations, saphenous vein grafts, chronic total occlusions, or long lesions.[7,8] However, additional data revealed that most promises associated with the advantage of resorption had been overestimated (Table 2). In a meta-analysis of 6 trials, the rates of target vessel failure (TVF), target lesion revascularization (TLR), myocardial infarction (MI), and death at 1 year were comparable for patients treated with the Absorb BVS and the Xience EES.[9] However, the risk of 1-year definite or probable scaffold thrombosis (ScT) was doubled for the Absorb BVS patients (odds ratio [OR], 3.11; 95% confidence interval [CI], 1.24–7.82; P = .02). Although the risk of TLR was much improved by applying a rigorous BVS-specific implantation protocol with routine before and after dilatation and avoiding small vessels in the following ABSORB IV and the COMPARE-ABSORB trial, the concerns about device thrombosis continued.[10,11] Moreover, the meta-analysis by Ali and colleagues[12] of 7 RCTs showed a higher risk of 2-year TVF in patients treated with the Absorb BVS (9.4% vs 7.4%; P = .0059). This difference was driven by increased rates of target vessel MI and ischemia-driven TLR. Also, the 2-year incidence of ScT was higher for the Absorb BVS than for the Xience stent (2.3% vs 0.7%; P<.001). Interestingly, a landmark analysis between 1 and 2 years confirmed higher rates of TVF (3.3% vs 1.9%; P = .0376) and device thrombosis (0.5% vs 0.0%; P<.001) in patients treated with the pBRS. These findings were strengthened by 2 recent analyses, one being a patient-data pooled analysis of 4 ABSORB trials, the other a meta-analysis of 7 RCTs comprehensive of higher risk subset of patients.[13,14] The results of these studies confirmed a significantly higher 3-year TVF, target vessel MI, and ischemia-driven TLR rates in the Absorb BVS group, with comparable cardiac mortality. Moreover, the risk of device thrombosis at 3 years was higher for BRS, at between 1 and 3 years. The key question of whether ABSORB BVS is able to reduce adverse events beyond complete device degradation was answered by the long-term clinical follow-up results of the ABSORB III trial with relatively simple coronary lesion.[15] At 5 years, the Absorb BVS showed equal performance in terms of TLF (17.5% vs 15.2%; P = .15) and there was no difference in ischemia-driven TLR (9.5% vs 8.0%; P = .27). However, the BRS-treated patients continued to show worse TV-MI (10.4% vs 7.5%; P = .04) and doubled ScT rates (2.5% vs 1.1%; P = .03). Importantly, there were time dependent effects in device-related events: Absorb BVS induced harm during the early time period (0–3 years) and showed similar outcomes in the subsequent 2 years with a downward trend in the annualized event rates. However, it must be considered that almost one-half of these patients continued dual antiplatelet therapy (DAPT) until 5 years. Disappointingly, other promises beyond the failed improvement of device-related events could not be confirmed. At longer follow-up, the results of several studies in patients with stable coronary disease, no sign of positive vessel remodeling, late luminal enlargement, or restoration of vasomotion was found between Absorb BVS and EES.[3,16] Further evidence is needed to fully understand and confirm these results. The Absorb technology is currently under refinement, and the next Falcon BVS generation is under preclinical testing. The new scaffold is expected to have thinner struts (<100 μm) and improved deliverability and acute performance.

Table 1
Technical characteristics of principal BRS currently available for clinical studies

Scaffold	Absorb GT1	DESolve Cx	Fantom	ART Pure	MeRes 100	Mirage	Magnitude	NeoVas	Magmaris
Manufacturer	Abbott Vascular	Elixir	Reva Medical	ART	Meril LifeSciences	Manli	Amaranth Medical	Lepu Medical	Biotronik
Design									
Strut material	PLLA	PLLA	Tyrosine polycarbonate	PDLLA	PLLA	PLLA	PLLA	PLLA	Mg
Strut thickness	156 μm	120 μm	125 μm	170 μm	100 μm	125 μm	98 μm	170 μm	150 μm
Eluted drug	Everolimus	Novolimus	Sirolimus	None	Sirolimus	Sirolimus	Sirolimus	Sirolimus	Sirolimus
Minimal resorption time	3 y	2 y	3 y	2 y	2 y	14 mo	N/A	2 y	1 y
Availability	CE mark, FDA approval, sales discontinued	CE mark	CE mark	CE mark	CE Mark	1 y RCT data vs Absorb available	FIM trial currently enrolling	1 y RCT data vs Xience available	CE mark

Abbreviations: CE, European Conformity; FDA, Food and Drug Administration; FIM, first in man; Mg, magnesium; PDLLA, poly-D,L-lactic acid; PLLA, poly-L-lactic acid; RCT, randomized clinical trial.

Table 2
Randomized clinical trials comparing ABSORB BVS with DES

Study	ABSORB China	ABSORB II	ABSORB III	ABSORB IV	ABSORB Japan	AIDA	Compare ABSORB	EVERBIO II	TROFI II	ISAR-Absorb MI
BVS (n)	ABSORB (241)	ABSORB (335)	ABSORB (1322)	ABSORB (1300)	ABSORB (266)	ABSORB (924)	ABSORB (822)	ABSORB (78)	ABSORB (95)	ABSORB (173)
DES (n)	XIENCE (239)	XIENCE (166)	XIENCE (686)	XIENCE (1300)	XIENCE Prime (134)	XIENCE (921)	XIENCE (800)	Promus Element or Biomatrix Flex (160)	XIENCE (96)	EES (89)
Follow-up (years)	4	5	5	1	4	2	1	2	3	1
Primary end point	In-segment late loss at 1 y	Vasomotion and minimum lumen diameter at 3 y	TLF at 1 y	TLF at 30 d	TLF	TVF at 2 y	TLF at 1 y	Late lumen loss at 9 mo	Optical frequency domain imaging-derived healing score at 6 mo	1 y in-segment lumen loss
Clinical setting	Stable CAD	Stable CAD	Stable CAD	Stable CAD and ACS (including STEMI >72 h)	Stable CAD	Stable CAD and ACS (including STEMI and Cardiogenic Shock)	Stable CAD and ACS (including STEMI)	Stable CAD and ACS (including STEMI)	STEMI (no cardiogenic shock)	ACS (including STEMI)
Lesion characteristics	Up to 2 lesions De novo LL <28 mm	Up to 2 lesions De novo Overlapping allowed in lesions <48 mm	Up to 2 lesions De novo LL <28 mm	Up to 3 lesions De novo LL <24 mm	Up to 2 lesions De novo LL <28 mm	De novo LL <70 mm.	De novo Complex lesions (total occlusion, LL >28 mm, bifurcation with single stent strategy included)	No limits for lesion length, number of target lesions or vessels	No limits for lesion length, number of target lesions or vessels	De novo lesions in native vessels or coronary bypass grafts

Mandatory PSP	No	No	No	Yes	No	No	Yes	No	No	No
Mandatory Use of Intravascular Imaging	No	No	No	No	Yes (IVUS or OCT)	No	No	OCT in first 30 willing patients	Follow-up only	No
TVF RR/HR [95% CI]	1.00 [0.51–1.94] *P* = .99	2.11 [1.00–4.44] *P* = .0425	1.41 [1.10–1.81] *P* = .006	1.35 [0.93–1.97] *P* = .11	1.15 [0.48–2.72] *P* = .75	1.12 [0.85–1.48] *P* = .43	1.33 [0.88–2.02] *P* = .17	*P* = .12	*P* = .465	1.04 [0.39–2.78]
Ischemia-driven TLR RR/HR [95% CI]	1.66 [0.61–4.49] *P* = .31	1.65 [0.46–5.92] *P* = .56	1.23 [0.85–1.79] *P* = .27	2.28 [0.99–5.25] *P* = .0457	1.17 [0.31–4.46] *P* = 1.00	1.17 [0.86–1.68] *P* = .31	0.89 [0.48–1.62] *P* = .69	*P* = .23	*P* = .678	0.84 [0.27–2.57]
Cardiac death RR/HR [95% CI]	0.33 [0.03–3.17] *P* = .37	0.50 [0.10–2.43] *P* = .56	1.17 [0.51–2.69] *P* = .71	N/A	N/A	0.78 [0.42–1.44] *P* = .43	4.87 [0.57–41.7] *P* = .11	*P* = .55	N/A	1.02 [0.19–5.58]
TV MI RR/HR [95% CI]	2.99 [0.61–14.65] *P* = .28	5.70 [1.36–23.87] *P* = .0061	1.47 [1.02–2.11] *P* = .03	1.23 [0.84–1.81] *P* = .29	1.51 [0.41–5.47] *P* = .76	1.60 [1.01–2.53] *P* = .04	1.96 [1.10–3.51] *P* = .0204	*P* = .11	*P* = .327	0.51 [0.03–8.20]
Device thrombosis probable/definitive RR/HR [95% CI]	N/A *P* = .50	N/A *P* = .0331	3.12 [1.21–8 –05] *P* = .01	4.05 [0.86–19.06] *P* = .06	1.02 [0.19–5.47] *P* = 1.00	3.87 [1.78–8.42] *P*<.001	3.31 [1.22–9.98] *P* = .0123	N/A	*P* = .55	0.51 [0.07–3.62]

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; CI, confidence interval; Co-Cr, cobalt-chrome; HR, hazard ratio; IVUS, intravascular ultrasound; LL, lesion length; OCT, optical coherence tomography; PSP, predilatation, sizing, post-dilatation; RR, risk ratio; STEMI, ST-elevation myocardial infarction; TLF, composite of cardiac death, target-vessel myocardial infarction, ischemia-driven target vessel revascularization (TLR).

Apart from the leading first-generation Absorb BVS technology, several pBRS devices are under clinical and preclinical investigation (see **Table 1**). These devices include, but are not limited to, DESolve (Elixir Medical, Sunnyvale, CA), Fantom (REVA Medical, San Diego, CA), ART Pure (ART, Paris, France), MeRes100 (Meril Life Sciences, Gujarat, India), Mirage (Manli Cardiology, Singapore), NeoVas (Lepu Medical Technology, Beijing, China), Renuvia (Boston Scientific, Marlborough, MA), Aptitude and Magnitude (Amaranth Medical, Mountain View, CA), Xinsorb (HuaAn Biotechnology, Hangzhou, China), Firesorb (MicroPort, Shanghai, China), Unity (QualiMed, Winsen, Germany), and Falcon (Abbott Vascular, Chicago, IL).

The DESolve scaffold is a novolimus-eluting BRS that received CE mark approval in May 2014. The first generation had 150-μm strut thickness, and the currently available second generation, DESolve Cx PLUS, has 120-μm struts. The DESolve scaffolds differ from the ABSORB stents owing to an intrinsic self-correcting deployment property that should decrease strut malapposition, a relative elasticity that provides a wide range of expansions without risk of strut fracture, and an early degradation and resorption profile.[17] However, this self-correcting feature is able to generate only small radial forces, so that it improves stent positioning with no relevant impact on the vessel wall.[17] Randomized clinical data on the comparison with other BRSs or metallic DES are not available to date.

The Fantom scaffold is a sirolimus-eluting BRS made principally from an iodinated polycarbonate copolymer of tyrosine analogues (desaminotyrosine) and biocompatible hydroxyesters which received CE mark approval in 2017. Despite a strut thickness of 125 μm, the design and structural properties of the polymer afford radial strength comparable to contemporary metallic DES, with low rates of recoil, allowing rapid inflation during deployment.[18] However, limited comparison data are available on clinical outcomes after Fantom scaffold implantation.

The ART BRS is made from a PDLLA amorphous polymer and received CE mark approval in May 2015. Notably, the device is free from antiproliferative drugs, which might be associated with early endothelial coverage. Moreover, it showed rapid degradation time, which might lead to a decreased risk of late device thrombosis. Nevertheless, this concept should be confirmed in further studies.[5]

The main feature of the Mirage BRS is its helicoidal structure, which allows enhanced flexibility and low crossing profile. The radial strength of the device is comparable to metallic stents. In addition, a better embedding into the vessel wall has been suggested for its monofiber circular struts than other BRS; this should cause less peristrut shear stress and disturbance in the coronary blood flow, but no comparison data have been presented yet.[5]

The MeRes100 BRS has a hybrid cell design (closed cells at the edges and open cells along the length), which allows optimal vessel wall conformability and high radial strength. The couplets of triaxial platinum radiopaque markers may facilitate the device positioning. Twelve-months randomized angiographic results showed comparable late luminal loss to Absorb BVS; however, no more clinical data are available.[19]

The Renuvia BRS uses a Synergy DES delivery system, which may allow for good deliverability and trackability of the device; it has thinner struts and increased overexpansion capability compared with Absorb BVS. However, given the discouraging results from Abbott's Absorb clinical trial program, the clinical development of this device has been stopped.[20]

Amaranth has introduced 3 different bioresorbable stents in the past decade: FORTITUDE, APTITUDE, and MAGNITUDE. The latest has a strut thickness of 98 μm with preserved radial strength and overexpansion capabilities. Interestingly, at the interim 9-month results of the first-in-man trial, no ScT was found. Nevertheless, larger clinical studies would be needed to confirm these findings.[20]

The NeoVas is a novel sirolimus-eluting PLLA-based BRS with acceptable in-scaffold late loss and a high percentage of scaffold strut coverage at 6 months without ScT cases. In the first reported randomized study it was noninferior to cobalt chrome EES with comparable in-segment late loss, clinical efficacy and safety outcomes, including recurrent angina.[20] However, longer term follow-up and larger trials are needed to determine the true impact of this device.

OVERVIEW OF MAGNESIUM SCAFFOLDS

The Magmaris (BIOTRONIK AG, Bülach, Switzerland) BRS, formerly known as DREAMS 2G, is the first sirolimus-eluting, biocorrodible metallic BRS with a bioresorbable PLLA coating. It gained CE mark approval in June 2016. It is the successor to the uncoated AMS and the paclitaxel-eluting DREAMS platforms.[21] Compared with previous generation devices, it was conceived to achieve sufficient radial support as well as the possibility of some expansion reserve, and a 12-month scaffolding time followed by resorption. Magnesium alloy resorption is a

process starting at the backbone surface: the alloy reacts with water to create magnesium hydroxide that is slowly converted to an amorphous calcium phosphate phase, which is absorbed by the body. It has been speculated that the electronegative charge of magnesium during the degradation process might result in antithrombotic and antiarrhythmic properties.[21] The preclinical studies supported the safety profile of the Magmaris scaffold with a higher expansion capacity without scaffold fracture, advanced healing, and lower acute thrombogenicity compared with the pBRS, with the absence of excessive lumen loss up to 2 years.[22] The BIOSOLVE II and III RCTs demonstrated encouraging acute and long-term clinical outcomes in type A/B lesions in patients affected by stable or unstable angina. They showed a 6.8% 3-year TLF rate similar to outcomes of the Absorb BVS and the Xience DES.[23] Remarkably, no definite or probably stent thrombosis was reported at 3 years, which is in marked contrast with the 3-year ST rate of 2.4% with Absorb BVS.[13] Moreover, a serial optical coherence tomography observational substudy demonstrated at 6-month follow-up an excellent vessel healing consisting in reduction of incomplete scaffold apposition, dissections, intraluminal mass, and jailed side branch.[24] Further safety data continue to be collected in worldwide registries, including patients with ACS. The preliminary midterm outcomes showed low TV-MI, ischemia-driven TLR, or ScT rates.[25] Thus, so far, magnesium-based scaffolds fulfill the main assumptions of vascular restoration therapy: support, resorption, and restoration. However, no RCT results are available and, learning from the undesirable experience gained with the Absorb BVS, Magmaris implantation has been restricted to patients with a long life expectancy and no contraindications to DAPT, and to de novo lesions with high likelihood to regain vasomotion and no complex anatomy. Moreover, meticulous vessel preparation and image-guided implantation are highly recommended to optimize the deployment. Conversely, in a recent report the second-generation drug-eluting bioresorbable Magmaris was associated with lower angiography efficacy (ie, higher late lumen loss) and a higher rate of TLR without thrombotic safety concerns at 1 year.[26] The next-generation magnesium scaffold DREAMS 3-G with thinner struts (ranging from 99 microns for the 2.5 mm scaffold to 147 microns for the 4.0 mm scaffold), a longer targeted scaffolding time of at least 3 months, improved radial strength, and superior deliverability owing to a better crossing profile, has been recently released.[21] It will be under evaluation in large-scale clinical trials, including randomized studies, where its efficacy will be compared against metallic DES to confirm further advancements in performance in terms of safety and efficacy.

MECHANISM OF FAILURE

Owing to the disappointing above-mentioned outcomes, the currently clinically available BRS were given a class III indication for clinical use outside of studies in current European Society of Cardiology guidelines.[1] Careful considerations should be given to the possible mechanism of such results, because the available BRS have different mechanical properties, footprints, and thicknesses, as well as a unique biodegradation profile. Reasonably, it can be speculated that the failure of pBRS, especially of the leading first-generation Absorb BVS, was caused by a combination of faulty device design and a far from optimal implantation technique.[27] As a matter of fact, differently from metal alloys that are used for permanent implants, BRS materials have insufficient ductility and limited elongation to break, which limit scaffold expansion during deployment, along with low tensile strength and stiffness, which require the struts to be thick to prevent recoil during vessel remodeling. Other disadvantages include lower crossing profiles owing to greater strut thickness, limited biocompatibility of PLLA, and an extensive and heterogeneous time until degradation.[2,4] Therefore, several mechanisms have been acknowledged to be involved in BRS failure (**Fig. 1**).

Device Related

First, bulkier struts can promote the formation of platelet aggregates owing to their protrusion into the lumen and interruption of the laminar blood flow, inducing flow disturbances and amplifying endothelial shear stress, especially in cases of suboptimal implantation. Additionally, the limited mechanical properties of the scaffold have been associated with a lower acute minimal lumen diameter, which results in a greater risk of recoil compared with metallic EES, along with greater late luminal loss and decreased mean lumen area.[3,4] Mentioned features, associated with a greater neointimal hyperplasia, led to greater coronary artery lumen narrowing and consequent device failure.[27] Also, specifically for BRS technologies, as a result of the bioresorption process, the loss of integrity of the scaffold backbone led to prolapse of the scaffold remnants into the vessel lumen, possibly affecting the coronary blood flow, especially in case of delayed endothelization owing to wider struts and polymer coverage. However, it remains unknown the level

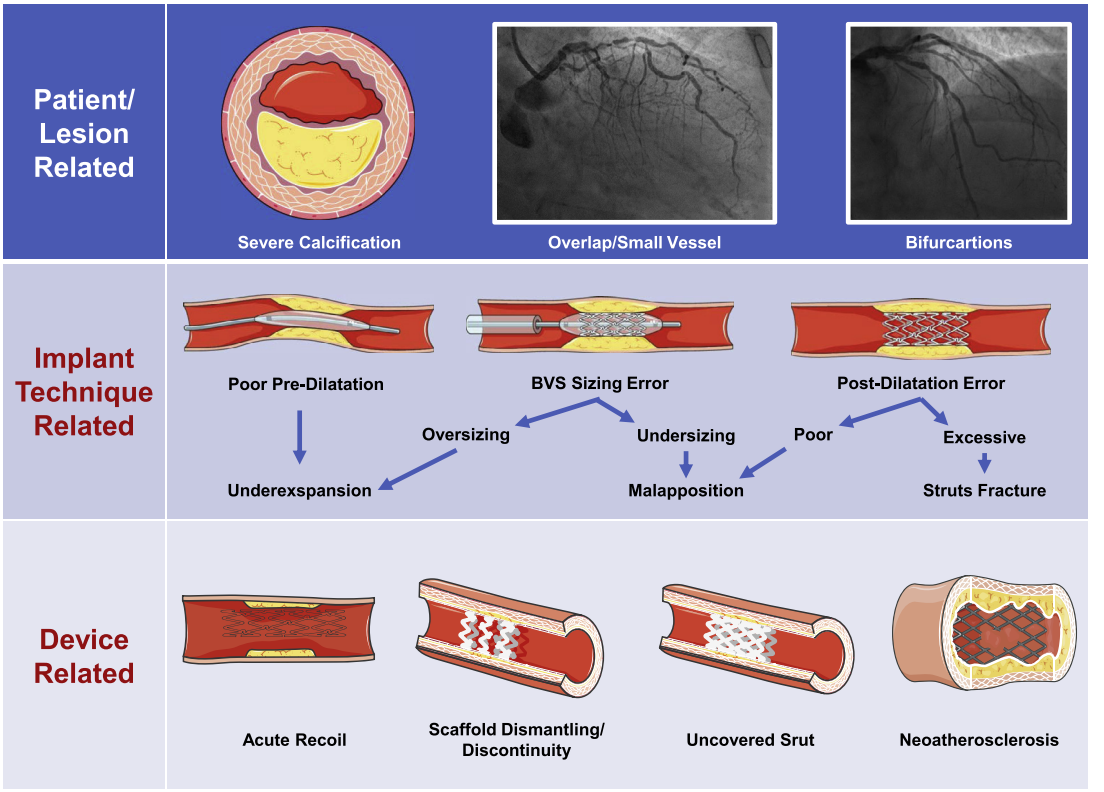

Fig. 1. Possible mechanism of BRS failure leading to clinical adverse events.

of thickness and maturity of the intimal layer required for the BRS structure to avoid losing mechanical integrity during bioresorption.[28] The finding of evagination and peristrut contrast staining in first-generation BRS is also linked to inflammatory reaction during polymer degrading process.[29] Last, the relatively long resorption, an excessively thin neointimal layer, and the endothelial dysfunction possibly accelerated by PLLA might allow the development of neoatherosclerosis.[3]

Implant Technique Related

As first reported by Puricel and associates, greater thrombogenicity might be associated with a suboptimal deployment technique. As a matter of fact, the thicker struts and larger footprint of pBRS require dedicated implantation protocol (prepare the lesion, size adequately, postdilate) to achieve the complete expansion of the backbone, avoiding malapposition.[30] A recent subanalysis of the available ABSORB RCTs showed that accurate adjustment of the scaffold and optimal postdilation correlate with a lower risk of TLF, whereas aggressive predilatation correlates with a lower risk of ST.[31] Therefore, suboptimal implantation with incomplete lesion coverage, underexpansion, and malapposition would require a longer duration of DAPT to compensate for the much longer healing time and the higher risk of ScT.[32]

Patient or Lesion Related

Recent studies have identified several clinical scenarios associated with a greater risk of TLF than in use of DES. Owing to the pBRS design and possible failure of the recommended implantation protocol, the treatment of aorto-ostial lesions, bifurcations, small (reference vessel diameter of <2.40 mm) or calcified vessel is still discouraged.[5]

There have been limited reports of scaffold failure after metallic BRS implantation, some of them discovered in asymptomatic patients during planned staged procedures. Moreover, owing to the lack of systematic intracoronary imaging at the baseline procedure, it cannot be excluded the operator role rather than a scaffold failure. To date, the identified mechanisms of TLF included early focal recoil and collapse with scaffold dismantling and neointimal hyperplasia.[33]

BIORESORBABLE SCAFFOLDS PERSPECTIVES

Collectively, too many of the prophecies on pBRS technology remain unfulfilled and the available evidence on metallic BRS is currently limited to small observational studies. The Class IIIC recommendation in the latest European guidelines seems to be reasonable, because the current generation of BRS are not ready for clinical use outside of well-designed studies and should not be preferred over the current generation of DES in everyday clinical practice so far.[1,4] Nevertheless, all ongoing studies should be thoroughly monitored to understand the impact and possible mechanism of adverse events to guide the newer generation of scaffold improvements.[4] Regarding new studies, the preclinical testing should include mechanical and biocompatibility testing, and bench and in vivo examinations in animal models should evaluate luminal dimensions during degradation, acute and chronic inflammation, drug concentration, change in tissue composition, and the essential features of degradation products. Importantly, the duration of follow-up should be sufficient to capture all relevant biological processes pertaining to stent safety. The clinical pre–CE-mark phase should include initial human feasibility studies with BRS based on intravascular imaging evaluation and angiographic follow-up (small sized, selected patients) and a subsequent randomized trial based on surrogate endpoints (medium sized, comparator device). The post–CE-mark phase should include a large-scale, clinical, randomized trial with long-term follow-up and should be powered to confirm superiority over the comparator.[4] The design of newer devices is aimed to producing thinner and more biocompatible struts, with a smaller crossing profile and a more optimized degradation profile to allow rapid and full neointimal coverage before biodegradation without inflammation, and all this by maintaining or even improving the radial force. Apart from device developments, a rigorous dedicated protocol implantation seems to be fundamental to achieve optimal results of BRS implantation, even if recent study suggest that even optimal postprocedural results by predilatation, sizing, and postdilatation may not guarantee freedom from undesirable dismantling.[30] Furthermore, proper lesion selection is crucial and the use of BRS is strongly discouraged in heavily calcified vessels and coronary arteries with an reference vessel diameter of less than 2.5 mm, and excessive scaffold overlap should be avoided and a device-to-device technique should be applied yet.[4] Moreover, operators should be strongly encouraged to use intracoronary imaging for lesion assessment during implantation and follow-up. Finally, because prolonged DAPT may limit the risk of ScT, BRS should not be recommended in patients who cannot tolerate prolonged DAPT or who require treatment with oral anticoagulants.[32]

SUMMARY

Despite some expected benefits of BRS, none of the available data have confirmed the advantage of the first-generation BRS over the metallic DES. Thus, the current generations of BRS, especially the Absorb BVS, should not be preferred to conventional DES in everyday clinical practice. To not leave behind the desirable vascular restoration therapy concept, the next generations of BRS should aim not only to improve the acute performance of the device but, above all, to improve long-term safety. Such developments might be achieved both by device improvement, but also with a proper technique of implantation, intravascular imaging guidance, as well as careful patient and lesion selection. Accordingly, new-generation devices have been developed with thinner struts, greater radial force and vessel wall coverage, less recoil and shorter resorption time with a lesser degree of inflammation secondary to polymer resorption. Reasonable long-term safety/efficacy evaluations are now recommended to establish comparable mid-term clinical outcomes and clear clinical advantages after complete resorption compared with currently available metallic DES.

CLINICS CARE POINTS

- Despite advanced iterations in metallic DES, there remains a 2% to 3% per year incidence of device-related adverse events, regardless of stent type.
- The BRS aims to provide early drug delivery and mechanical support similar to metallic DES followed by complete resorption.
- Available long-term evidence focused on the Absorb BVS showing higher adverse events compared with everolimus-eluting DES, with a substantial reduction of the BRS-relative hazard after 3-year follow-up (complete resorption time).
- Careful considerations should be given on the possible mechanism of such unsatisfactory results because the available BRS have different mechanical properties, footprint and thickness and a unique biodegradation profile.
- An improved scaffold design and deployment technique to mitigate early BRS risk may

enhance the late benefit of complete resorption.

DISCLOSURE

G. Masiero, G. Rodinò, and G. Tarantini declared no conflicts regarding this publication.

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