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Are bioresorbable coronary scaffolds ready for a comeback?

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Take Home Messages

- Given the history with the first-generation BRS, large-scale randomised trials are required before the clinical community will adopt the next generation of devices.
- The evidence currently available is insufficient to justify the implantation of BRS outside of clinical trials.
- Given the efficacy and safety of current DES, even with reduced antiplatelet therapy, there is no urgent need to run this risk again, allowing for a robust resurgence of BRS technology.

Introduction:

In percutaneous coronary intervention (PCI), the concept of securing metal free angioplasty without leaving behind a permanent foreign body is highly attractive to patients and physicians and promises several advantages. However, target lesion failure and device thrombosis were important concerns with first-generation Bioresorbable scaffolds (BRS) leading to low rates of adoption in clinical practice (1-12). New iterations, incorporating improvements such as a smaller strut thickness have been proposed and evaluated in early investigations. However, it remains unclear whether these modifications are sufficient to achieve outcomes comparable to those of metallic drug-eluting stents (DES) while preserving the benefits of resorption (10-12).

What do we know so far?

There have been multiple trials to compare the efficacy of biodegradable scaffolds against drug eluting stents (1-12).

The portfolio of ABSORB trials, a multicentre, prospective, randomised control trial compared the Everolimus-eluting poly-L-lactic acid (PLLA)-based Absorb BRS (Abbott Vascular) with a contemporary cobalt-chromium Everolimus-eluting stent (CoCr-EES). Adverse ischaemic events, namely target lesion failure (TLF) and device thrombosis, were more common with this first-generation BRS; however, the period of excess risk ended at 3 years after the complete bio-resorption of the scaffold. Thereafter, event rates were similar or lower with BRS (1-3, 5).

Statistical analysis for definite or probable early, late, and very table stent thrombosis (ST) comparing bioresorbable scaffolds (BRS) and cobalt-chromium everolimus-eluting stents (CoCr-EES) are depicted in Table 1, Table 2 and Table 3 respectively (1-7).

ABSORB IV, that recruited 2604 patients of whom1296 patients were assigned to BRS, and 1308 patients were assigned to DES, included mandatory pre- and post-dilation, oversizing by ≤0.5 mm, and strict avoidance of small vessels (<2.25 mm reference diameter by quantitative

measurement). The trial demonstrated non- inferiority of BRS compared with CoCr-EES for TLF at one year (9). Nonetheless, 30-day and 1-year rates of device thrombosis and target lesion revascularisation trended higher with Everolimus-eluting poly-L-lactic acid (PLLA)-based Absorb BRS by Abbott Vascular (Absorb) with a contemporary cobalt-chromium Everolimus-eluting stent (CoCr-EES). (9).

In the FUTURE-II randomised trial (n=433), the Firesorb BRS demonstrated nearly identical 1-year angiographic in-segment late loss and tissue strut coverage by Optical coherence tomography (OCT) as the CoCr-EES, with 0.9% and 1.9% target lesion failure rates, respectively, with no scaffold thromboses (10).

Three randomised trials (FUTURE-II, XINSORB and NeoVas) with different polymeric BRS included fewer than 500 patients each with 1 or 3 years of follow-up. The respective BRS did not outperform the comparator DES (10-12). XINSORB was a multicentre randomized clinical trial, which showed XINSORB scaffolds showed similar efficacy and safety outcomes compared with the sirolimus-eluting stents (SES) up to the 3-year follow-up. The rates of target lesion failure (TLF) and device thrombosis were low and comparable between the two arms. (11).

The FUTURE-II trial is a randomized trial comparing a new, thin-strut bioresorbable scaffold - the FIRESORB -poly-L-lactic acid-based sirolimus-eluting vs. everolimus-eluting cobalt-chromium stent (EES). There was no difference was found in terms of target lesion failure between groups with very low rate of events (1.9% vs. 3.3%, p=0.37) and no definite probable device thromboses (10). In both FUTURE-II and NeoVas trials (10,12), in-device acute gain was significantly lower, and in-device late loss was significantly, (12) or numerically (10), higher with BRS than with DES.

Trial	BRS		CoCr-EES		Odds ratios (95% CI)
	Events (ST)	Total	Events (ST)	Total	
ABSORB II (1)	2	335	0	166	2.50 (0.12-52.3)
ABSORB Japan (2)	3	265	1	133	1.52 (0.16 - 14.7)
ABSORB China (3)	1	238	0	237	3.00 (0.12 - 74.0)
ABSORB-STEMI TROFI II (4)	1	95	0	96	3.06 (0.12 - 76.2)
ABSORB III (5)	14	1322	5	686	1.46 (0.52 - 4.06)
AIDA (6)	13	924	5	921	2.61 (0.93 - 7.36)
ABSORB IV (7)	8	1296	2	1308	4.05 (0.86 - 19.06)

Table 1: A table to show definite or probable early stent thrombosis (ST) compared to bioresorbable scaffolds (BRS) and cobalt-chromium everolimus-eluting stents (CoCr-EES).

Trial	BRS		CoCr-EES		Odds ratios (95% CI)
	Events (ST)	Total	Events (ST)	Total	
ABSORB II (1)	1	335	0	166	1.49 (0.06 - 36.9)
ABSORB Japan (2)	1	265	1	133	0.50 (0.03 - 8.06)
ABSORB China (3)	0	238	0	237	
ABSORB-STEMI TROFI II (4)	0	95	0	96	
ABSORB III (5)	6	1322	0	686	6.78 (0.38 - 121)
AIDA (6)	8	924	1	921	8.03 (1.00 - 64.4)
ABSORB IV (7)	1	1296	2	1308	1.23 (0.53 - 2.84)

Table 2: A table to show definite or probable late stent thrombosis (ST) compared to bioresorbable scaffolds (BRS) and cobalt-chromium everolimus-eluting stents (CoCr-EES).

Trial	BRS		CoCr-EES		Odds ratios (95% CI)
	Events (ST)	Total	Events (ST)	Total	
ABSORB II (1)	6	335	0	166	6.57 (0.37 - 117)
ABSORB Japan (2)	5	265	0	133	5.64 (0.31 - 103)
ABSORB China (3)	1	238	0	237	3.00 (0.12 - 74.0)
ABSORB-STEMI TROFI II (4)	1	95	1	96	1.01 (0.06 - 16.4)
ABSORB III (5)	10	1322	0	686	11.0 (0.64 - 188)
AIDA (6)	10	924	2	921	5.03 (1.10 - 23.0)
ABSORB IV (7)	12	1296	10	1308	1.23 (0.53 - 2.84)

Table 3: A table to show definite or probable very late stent thrombosis (ST) compared to bioresorbable scaffolds (BRS) and cobalt-chromium everolimus-eluting stents (CoCr-EES).

Discussion:

The strut thickness of the Absorb (>150 µm) is almost twice that of drug eluting stents, resulting in greater luminal protrusion, more turbulent flow, delayed endothelialisation, and increased neointimal hyperplasia during follow-up compared with thinner-strut metallic DES (8-9).

Cumulative evidence suggests that the higher thrombogenicity observed with biodegradable scaffolds occurs due to suboptimal deployment techniques in combination with the bulky scaffold's strut design. The larger strut thickness of Absorb in the range of provides a larger platform profile in both the crimped and the expanded stage that induces local haemodynamic alterations prone to platelet activation (13). An optical coherence tomography study with simulation modelling showed low endothelial shear stress zones created between the strut surfaces of the Absorb BRS, which may predispose to acute thrombogenicity (14). These findings are further supposed by an animal *ex vivo* model study (15). Leesar et al have illustrated the fate of DES and BRS in Figure 1 (16).

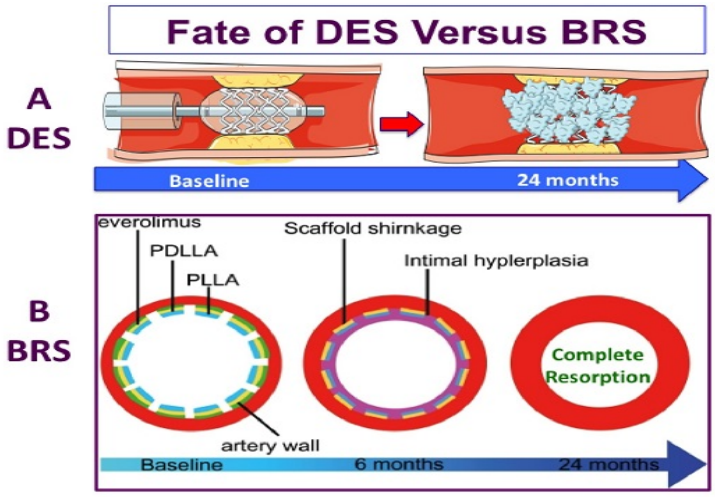

Figure 1: Fate of Drug eluting stent (DES) vs Bioresorbable scaffolds (BRS) (16)

The introduction of thinner-strut resorbable scaffolds with superior mechanical performance offers the potential for BRS technology (especially if implanted with intravascular imaging guidance) to achieve DES-like clinical outcomes within the first several years after implantation.

Conclusion:

Given the history with the first-generation BRS, large-scale randomised trials are required before the clinical community will adopt the next generation of devices. However, we predict that should such trials demonstrate even comparable early and late outcomes (let alone superiority), a mass migration away from permanent metallic cages (DES) to this more natural and holistic solution would occur. The development of thin-strut fully bioresorbable scaffolds implanted in appropriately selected lesions in a standardised fashion utilising PSP (preparing the lesion aggressively, sizing the scaffold correctly, and post-dilating at high pressure in all

cases) technique, and, ideally, with OCT imaging guidance, has set the stage for the resurgence of coronary BRS.

Disclosures:

No conflict of interest to disclose

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