Bioresorbable vascular scaffold: promises and the fallen child-as-king?

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THE BIORESORBABLE VASCULAR SCAFFOLDS ‘BVS’
The main limitation of percutaneous coronary intervention compared to open-heart surgery is the insertion of a foreign body (usually a stent) inside the coronary artery. This is associated with foreign body inflammation that triggers restenosis, neointimal hyperplasia and late-occurring scaffold thrombosis. As such, BVS were considered as a possible solution as early as the late 60s by Dotter with preclinical work, and then with the first human study by Higaki and Tamai in the late 90s. In these two preliminary experiments, device materials had weak radial strength and came with the risk of scaffold thrombosis. However, BVS were considered as a possible alternative to the current gold standard, stent technology, since their clinical introduction in 2004. The first promise was easily held: although its deliverability remains slightly below the current DES standard, BVS can be implanted in virtually all types of lesions. However, very accurate sizing with qualitative comparative analysis or intravascular ultrasound imaging (or optical coherence tomography (OCT)) is necessary to minimise malapposition, or the rupture of the scaffold backbone. We also learnt that edge dissections could originate from the manufacturing process of the scaffold (laser cutting without polishing).

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BVS IS EFFICIENT
This promise remains a topic of debate. The very first clinical trial results with direct comparison between BVS and DES were available at TCT 2014 (over 10 years from first clinical implant), with the presentation of the EverBio-2 and ABSORB-II.5 Key findings were as follows: no difference between devices on clinical end points with a reduced cumulative duration of secondary angina
pectoris with BVS in ABSORB-II; but an increased in-segment late-lumen loss—a surrogate marker of efficacy—with BVS in EverBio-2. The ABSORB III trial subsequently confirmed these results. Nevertheless, the power of these studies taken individually remains insufficient to conclude about individual clinical end points, especially device thrombosis. Furthermore, the study designs with generous thresholds chosen for non-inferiority have favoured BVS (such as a wide δ margin of 4.5% in ABSORB III).

SCT AND THE FALLEN (CHILD-AS-) KING

A firestorm arose in early 2014 from the observational GHOST-EU registry,\(^6\)\(^7\) which showed an increased rate of ScT in unselected patients, with an incidence of >2% at 6 months. These results were confirmed by other studies. Intravascular imaging studies at time of ScT identified similar causative factors: scaffold maleexpansion, dissection, malaposition and insufficient antplatelet therapy.\(^8\) Subsequently it was shown that, careful patient and lesion selection with a dedicated implantation technique significantly reduces the risk of ScT as demonstrated by Puricel et al.\(^9\) Nevertheless and as already experienced by Dotter or Higaki and Tamai, BVS thrombogenicity remains higher than with DES. This was nicely illustrated by Joner\(^10\) using an arteriovenousous shunt model, this group demonstrated how accentuated fibrin deposition forms in the vicinity of the struts with the formation of a ‘chronic thrombus’. This demonstration breaks the myth of capping. Indeed, in light of these results, it is reasonable to think that the capping visible at OCT does not represent healing but an organised ‘chronic’ thrombus. Furthermore, from late SCT, we learnt some further points: (A) BVS is associated with peristrut low intensity areas when studies with OCT analyses are performed after 3 months. This may indicate parietal oedema induced by chronic inflammation or polymer degradation itself (via the Krebs cycle). This is associated with strut discontinuities, sagging, recoil and occasionally complete collapse of the scaffold within the coronary lumen.\(^11\) (B) Obstructive neointimal hyperplasia might be found in BVS. (C) The duration for complete degradation remains unknown, particularly in diseased segments but takes more than initially considered, possibly 3–4 years. (D) Positive remodelling of the artery is not necessarily positive for the patient, since it may be associated with coronary aneurysm and ScT.

BVS AND CLINICAL EVIDENCE

From the DES saga, we should yet remember that stent (or scaffold) thrombosis has little impact on clinical outcome.\(^12\) Therefore, it is time to turn back to clinical evidence. Accordingly and in this edition of the journal, Farag et al.\(^13\) present a meta-analysis of the first trials on BVS. This is the fifth meta-analysis on this subject.\(^14\)–\(^17\) This meta-analysis differs from the first four analyses by separating analysis of the six randomised controlled trials from analysis of six clinical registries. The authors should be congratulated for their work. Using powerful statistical tools, they show convincing results that are close to previous meta-analyses with a significantly increased risk of myocardial infarction and ScT rates with BVS. This new meta-analysis also demonstrates that these differences seen in RCTs, disappeared in registries. This is a new finding and may provide some reassurance to patients receiving BVS. The reasons of the apparent discrepancy are beyond the scope of the current analysis. However, there are some plausible explanations: one possibility advanced by the authors could be the use of a dedicated implantation technique in the registry arm (2× more intravascular imaging use, higher postdilation balloon size and pressure in registries compared to RCT). But such interpretation is open to possible biases and type 2 errors. Finally, what these studies omit to underscore is that the typical patient with BVS is on average 6 years younger than the typical DES patient; with a higher proportion of men, less diabetes, less acute coronary syndromes and less treated lesions.

REFERENCES


