Restenosis of Coronary Bioresorbable Vascular Scaffolds

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Bioresorbable vascular scaffold (BVS) devices have represented an authentic conceptual revolution in interventional cardiology.1–6 Their particular design ensures perfect scaffolding for the vascular wall and has led to excellent immediate outcomes. Furthermore, they incorporate a drug with potent antiproliferative properties, which averts the development of restenosis.2–6 These 2 properties are also inherent to drug-eluting stents (DES) made of metal. Nonetheless, the attractiveness of BVS is that once their function has been achieved (vascular support and antiproliferative effect), both the scaffold and the polymer used to administer the drug completely disappear from the coronary wall.2–6 In contrast, with DES a metallic structure always remains in the vascular wall, and in those not containing a bioresorbable polymer, the permanent polymer covering the stent also persists.7,8 Several studies have conclusively confirmed that BVS completely disappear from the vascular wall over time, usually within a period of around 3 years.2,3 This implies that the artery will be released from the corset-like effect of a metallic mesh structure in its interior and can recover its physiologic functions.7,8 The vessel can respond once again to the stimuli generated by the coronary flow (shear stress), which may favor chronic phenomena of adaptive vascular remodeling and late lumen gain. Recovery of the physiologic vascular dynamics is also achieved, with restoration of acute vasodilatation or vasoconstriction responses to various stimuli and drugs.2,3 Some data have even indicated that regression of the underlying atheromatous plaque can occur in the treated region,2,3 and that implantation of BVS over vulnerable or complicated plaques may help to stabilize them.

Resorption also frees lateral branch vessels that have been “caged” by the scaffold. Moreover, the eventual disappearance of BVS structural elements that were improperly placed against the vessel wall (malapposition) due to an inadequate technique or unfavorable anatomy, and those that protrude excessively (in ostial lesions) may avoid the development of late complications.2–6 Finally, the nonmetallic structure of these scaffolds (with a platinum marker at each end) enables proper evaluation of the coronary anatomy by noninvasive techniques (eg, coronary computed tomography) because it does not produce radiologic artifacts, as occurs with metallic stents.2–6

There is some evidence that the permanent presence of foreign elements in the vessel wall may promote the development of adverse events during follow-up. Very late thrombosis causes the greatest concern, but late restenosis has also been described, sometimes caused by neatherosclerosis.7,8 BVS were designed in an attempt to circumvent all these limitations, associated with DES.

Numerous studies have reported excellent clinical results following BVS implantation.2–5 Observational studies and randomized studies performed in selected patients have both reported outcomes similar to those achieved with latest-generation DES.2–5 If the 1-year results obtained with these scaffolds are similar to those of the newest DES, it is tempting to speculate that the very long-term outcome may also be favorable for BVS-treated patients. We should remember, however, that the currently available scaffolds contain relatively thick support elements (156 μm) to ensure sufficient radial strength; therefore, they are inferior to the new generations of DES in terms of flexibility and navigability. This explains why their use has been constrained and cautious in patients with complex or calcified lesions. Furthermore, shaping and adaptation of current BVS to the vessel is very limited because of their plastic composition. Therefore, the diameters of these devices must be carefully chosen, as excessive expansion (or dilatation of the cells in the case of lateral branches) can cause fracture and disruption of the support elements.2,6 These problems rarely occur with DES, which allow for greater adaptation while maintaining their structural integrity within the limits required in clinical practice. These factors explain why the favorable initial results obtained with BVS (similar to those of the newest DES) are applicable to relatively straightforward lesions.2–5

As has always occurred in the history of interventional cardiology, every innovation is understandably accompanied by an initial phase of enthusiasm, which at some point becomes subdued by data that generate concern and reflection within the scientific community.1,9 One only has to recall the provocative editorial published not long ago in this same journal, predicting that we had achieved every interventional cardiologist’s dream: a 0% restenosis rate!10 However, reality soon returned us to a more cautious and humble scenario.1,7 Usually, the next phase of an innovation entails incorporation of additional technological advances, and the new devices are better used. The initial limitations are overcome and the innovation becomes consolidated, which
At this time, there is little information regarding the pathophysiological mechanisms implicated in the specific complications associated with BVS.

The developments in tomographic imaging and in particular Optical Tomography, or OCT, have provided new insights into the dynamic processes occurring within the vessel wall. OCT can be used to examine the coronary structures in vivo, to detect plaque progression and regression, and to monitor the effects of various interventional techniques. OCT provides high-resolution images of the coronary walls and can be used to identify components of plaque such as lipid core, fibrous cap, and calcification. These features are crucial in understanding the mechanisms of plaque rupture and thrombosis, which are the main causes of adverse outcomes after stent implantation.

OCT has been shown to be highly effective in guiding stent deployment and in assessing the quality of the stent strut apposition. OCT imaging can help to identify residual stenosis, dissections, and neointimal hyperplasia, which are important factors in the late stent failure. OCT has also been used to evaluate the impact of various drug-eluting stents on the neointimal response and to assess the efficacy of new stent designs.

OCT has several advantages over other imaging modalities such as angiography and intravascular ultrasound (IVUS). OCT provides higher spatial resolution and can visualize the vessel wall in real-time, allowing for dynamic assessment of the vessel wall changes. In contrast, IVUS provides lower spatial resolution and requires the use of a catheter. OCT also provides higher contrast resolution and can distinguish between different tissue types, which is important for assessing the composition of the plaque.

The use of OCT in clinical practice is still evolving, and further research is needed to fully understand the role of OCT in the management of patients with coronary artery disease. However, the potential of OCT to provide detailed information about the coronary anatomy and to guide interventional procedures makes it an attractive imaging modality.

In conclusion, OCT is a valuable imaging modality in the assessment of coronary artery disease and the evaluation of interventional procedures. Further research is needed to fully understand the clinical value of OCT and to optimize its use in clinical practice.

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**CLINICAL VARIABLES ASSOCIATED WITH BVS**

**VASCULAR PROBLEMS ASSOCIATED WITH BVS**

**DIAGNOSTIC TECHNIQUES USED WITH BVS**

**VASCULAR SCAFFOLDS**
Mechanisms Implicated in Restenosis of Bioresorbable Vascular Scaffold Systems

1. Excessive neointimal proliferation

2. Neoatherosclerosis
   - Stable (gradual development)
   - Complicated (capsule rupture with associated thrombosis)

3. Underexpansion of the scaffold with preserved structure

4. Target vessel too small (< 2 mm) (strut overcrowding)

5. Scaffold structural changes
   - Acute:
     - Due to damage during implantation or inappropriate overexpansion (BVS fracture)
     - Due to insufficient relative radial strength: acute collapse (acute recoil)
   - Late: due to programmed resorption
     - Within the wall (due to a loss of structural support)
       - Maintaining their configuration and position
     - With displacement, disruption or late collapse (late recoil). Loss of alignment or circularity.
     - With disrupted elements within the lumen (outside the wall) (poor apposition)
     - Maintaining their configuration
     - Changing their spatial configuration. Loss of alignment or circularity

6. “Delayed” scaffold resorption. Very late persistence (> 3-4 y) of BVS structural elements

7. Resistance to antiproliferative drug

8. Adjacent segment not covered by the scaffold
   - Disease progression (plaques having a different composition) at the initially untreated edges (5 mm adjacent to the BVS)
   - Progression of the adjacent atherosclerotic plaque, which was treated, but went uncovered by the scaffold (geographical miss)
   - Overlapping failure (gap) between 2 scaffolds

9. Excessive overlapping of adjacent scaffolds (long lesions)

BVS, bioresorbable vascular scaffold.

Figure. Optical coherence tomography (OCT) images in patients with restenosis of bioresorbable vascular scaffold (BVS) devices. A: Substantial underexpansion of a BVS. The neointimal growth has a bright and relatively homogeneous appearance. B: Severe neointimal proliferation, but showing clear areas of attenuation (+) in a properly expanded BVS. C: Proliferation having a heterogeneous appearance, with very bright intima near the lumen and broad areas of attenuation that partially obscure the structural elements of a morphologically elliptical BVS. D: BVS disruption, seen as an absence of continuity and circularity of the structural elements, with moderate associated neointimal growth. E and F: Restenosis of a BVS caused by heterogeneous tissue, with areas of attenuation (+) showing well-delimited borders (E). The BVS had been implanted to treat restenosis of a metallic stent. The structural elements of the BVS are visualized as “black boxes” with no shadowing, whereas the struts of the metallic stent are seen as very bright focal areas with posterior shadowing. *: guidewire artifact.
acteristics of 17 patients with BVS restenosis. The results are of considerable interest because of the meticulous analyses carried out and the scant information available on this uncommon complication. The series was derived from a total population of 330 patients who underwent BVS implantation (398 BVS to treat 380 lesions), rigorously followed up for 19 ± 10 months. The use of coronary computed tomography angiography in all patients during follow-up, and OCT analysis in all those who developed stenosis, lends particular value to the study. Eighteen BVS with restenosis were detected in 17 patients, yielding a restenosis incidence of 5.4%. Computed tomography showed low-density, noncalcified tissue as the cause of the new lesion. The mean time to the development of restenosis was 9.4 months. The most common morphology was a focal pattern (12 patients, 67%) that usually affected the proximal edge of the scaffold (9 patients, 75%). Among the 9 patients with compromise of the edge, 3 also showed a lesion within the BVS, and in the remaining 6, the lesion was located immediately outside the scaffold. When these focal restenoses affected the interior of the scaffold, the tissue had a heterogeneous or layered appearance. However, in 6 patients (33%), restenosis showed a diffuse morphol-

y. In these cases, OCT depicted a lipid pattern or layered pattern, associated with microcalcifications and microvessels, all features indicative of neatherosclerosis. Of interest, available OCT images taken immediately after scaffold implantation in 10 patients enabled comparison with those obtained at the time of restenosis. In one-third of these patients, postprocedural OCT showed significant underexpansion of the BVS, which may have favored later development of restenosis. Furthermore, serial studies showed that late lumen loss was never a consequence of collapse of the BVS structure or elastic recoil. In addition, it is relevant that in patients with focal restenosis at the scaffold edge, postprocedural OCT showed significant lipid plaques in that position. Also of note, in 5 of the 18 BVS restenoses, certain elements were seen to be completely overlapped, indicating that major disruption of the scaffold had occurred in the late phase of degradation. In fact, in 3 cases of BVS disruption during follow-up, immediate postprocedural OCT showed correctly expanded struts without overlapping. Finally, the authors found that early restenoses (<6 months) tended to be more focal, affected the BVS edges, and showed tissue with a homogeneous appearance. In contrast, late stenoses had a more diffuse angiographic pattern and showed heterogeneous tissue, often with clear features of neatherosclerosis.

Retreatment involved DES implantation in all patients, except in 4 with restenosis at the proximal edge just outside the scaffold, who underwent implantation of another BVS. In this study, restenoses were documented at a time when the BVS structure was still in existence. New studies are needed to characterize the very late restenosis patterns, once the scaffold has completely disappeared.

CONCLUSIONS

It seems reasonable that optimized implantation of BVS can improve their safety and effectiveness, and the systematic use of intravascular imaging techniques can aid in this regard. However, we should humbly recognize that we were fully aware of these technical and methodological considerations when we began using these devices some years ago. Finally, the currently available data indicate that the appropriate duration and type of antiplatelet therapy used following BVS implantation should be reconsidered. New generations of BVS (with significant improvements in the classic polyolactic acid scaffold or with biocorrosive magnesium scaffolds) will soon be available for generalized clinical use, and are expected to overcome many of the limitations of the current scaffolds. Nonetheless, rigorous critical evaluations of the results obtained with the new scaffolds should always follow the dictum that governs the development of interventional cardiology: Treatment for our patients should not and cannot be based on simple expectations, no matter how attractive they may be.

CONFLICTS OF INTEREST

None declared.

REFERENCES


