REVIEW ARTICLE

Percutaneous Coronary Intervention with Bioresorbable Vascular Scaffolds

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Percutaneous coronary intervention (PCI) was the first revolution in interventional cardiology. Coronary stents solved the acute occlusion of the vessel, sealing dissections and preventing negative remodeling. Excessive intimal hyperplasia was reduced with drug-eluting stents (DES) mainly in diabetics, small vessels and long lesions. However, the mechanical effect of stent metal hinders the positive remodeling of the vessel wall, good endothelial function and vascular reactivity. Bioresorbable vascular scaffolds (BVS) provide good initial stability in the vascular structure and complete resorption of the material over time, resulting in better physiological adaptation of the artery. Recent studies show that these devices are safe. Despite some limitations in indication, evidence now offer unique options in the treatment of coronary artery disease (CAD) with the expansion of BVS use in daily practice, which is the reason for this review.

Introduction

Percutaneous coronary intervention (PCI) with balloon catheters showed good results in non-complex lesions. Yet, there was a risk of vessel dissections, acute occlusion, emergency surgical revascularization, negative vascular remodeling and restenosis.[1,2] The advent of bare-metal stent (BMS) reduced most of these events.[3-5] However, coronary flow altered by the stent mesh and platelet aggregation stimulation caused acute and subacute thrombosis.[4] Full anticoagulation with heparin and coumarin was used until the platelet aggregation was identified as the main cause of the problem and dual antiplatelet therapy (DAT) was established.[6] Reduction in strut thickness and greater

Keywords

Myocardial revascularization; Angioplasty; Angina pectoris.

flexibility allowed better conformation between the stents and the vascular wall, thus reducing poor apposition rates.

Intravascular ultrasound (IVUS) showed that the deployment of stents at higher pressures and coverage of the whole atherosclerotic plaque resulted in lower rates of acute events.[7] However, excessive intimal hyperplasia caused restenosis repeated revascularizations, particularly in high-risk subgroups (diabetes, small vessels and long lesions). DES promoted reduced restenosis[8] rates and expansion of indications for more complex CAD treatment such as long lesions, bifurcations, chronic occlusions, diabetic patients, restenosis and even left main coronary artery (LMCA).[8-12]

Regardless of the type of stent, permanence of the intravascular metal framework is definitive and with many negative aspects. Bioresorption of new devices allows the vascular wall to return to its primitive functions without jeopardizing the results compared with the latest generation of DES.[13] Greater understanding of the indications of this platform and the analysis of some technical and clinical aspects that are not yet clear have encouraged this review.

Drug-eluting stents (DES)

Follow-up of the first patients receiving DES showed minimal intimal proliferation and consequent reduction in restenosis, approaching the PCI results to those of the surgery.[8-10] In the first generation of DES, the metal and the need for the polymer to attach and protect the drug caused late poor stent apposition and exposure of non-endothelialized struts, causing late thrombosis.[11] In patients with multivessel disease, the combined rate of definite, probable and possible thrombosis was 9.4% in five years, with 32% of major acute cardiac events.[11] The disease showed exposed meshes and persistent inflammatory reaction. Vasomotion tests with

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acetylcholine showed abnormal vasoconstriction distal to the stent, suggesting abnormalities in the endothelial structure and function.[11]

The development of second-generation DES, of low profile, with greater radial strength, biocompatible and bioabsorbable polymers decreased endothelial inflammatory reaction. The use of Limus drugs (everolimus, biolimus and zotarolimus) which are eluted in the vessel within up to three months made PCI easier and safer in cases with growing complexities.[12] After absorption of the drug, the stent maintains the vessel radius, but the metal presence permanently affects vessel remodeling and healing, and hampers follow-up using non-invasive tests (cardiac computed tomography or magnetic resonance imaging). The metal may also compromise future treatment options with stenting or surgery. Moreover, although very late thrombosis rare, it can be a problem related to vessel metallization.[13,14]

Bioresorbable vascular scaffolds

In the process of BVS (bioabsorbable vascular scaffold) reabsorption, hydrolysis produces lactic acid, which enters the Kreb's cycle and is metabolized into carbon dioxide and water in two to three years. Vasoconstriction induced by methylergonovine maleate and vasodilation with nitroglycerin is observed in the treated segment.

Complete resorption promotes infiltration of functional muscle cells, return of vasomotor response, suggesting that normal endothelial structure be restored, and the possibility of reduction of late thrombosis. Clear reparative therapy of vascular function is observed, in which the restoration phases evolve immediately after implantation until complete resorption over time, with the possibility of final increment in luminal gain (Figure 1).[13-17]

Igaki Tamai was the first BVS implanted in humans. Built in poly-L-lactic acid (PLLA), it showed very favorable results with target lesion revascularization (TLR) of 16% in one year, 22% in five years and 38% in 10 years (Figure 2). The high profile and the fact that it is free of drug did not allow expansion of use, although the expected absorption has been observed in up to 36 months.[18] The BVS technology with magnesium did not present expressive results.[13,16]

BVS ABSORB (Vascular Abbot, Santa Clara, California) has a structure with a bigger profile than the latest generation of stents. This minor limitation may hinder access in more complex lesions

(Figure 3). Nevertheless, the device has radial force maintained, similar to metal stents associated with the antiproliferative agent everolimus observed in DES. This BVS has a PLLA polymer structure and is coated with poly-D, L-lactide polymer, which carries and elutes the drug.[19] Absorption of the polymer structure occurs by erosion of the mass, keeping the structure and the radial force even with enhanced absorption process.

The BVS everolimus elution rate (80% in 30 days) is similar to the latest generation DES permanent polymer used in the SPIRIT study; this produces safety and effectiveness results comparable to both techniques.[20]

ABSORB Cohort A was the first study of safety and viability. It evaluated 30 patients with stable and unstable angina, single-vessel non-complex de novo lesion in native coronary artery. ST segment elevation acute myocardial infarction (STEMI), ejection fraction (EF) < 30% and complex lesions were ruled out.[19]

Clinical outcomes in two years presented only one non ST segment elevation acute myocardial infarction (NSTEMI), and total absorption was observed during this period. At five years evolution in 27 patients, there were 3.4% of adverse cardiac events. There were no thrombosis reports, but late recoil in diameter related to the comparison with the historical series of drug-eluting stents with everolimus was higher for the BVS (6.9% vs. 4.3%).[19]

ABSORB B with 101 patients showed similar inclusion criteria with a maximum of two vessels treated, stratified into two groups (B1 = 56 and B2 = 45) for angiographic control at 6 and 24 months or at 12 and 36 months. No thrombosis was found. Three cases of NSTEMI, and seven TLR with ischemia.[21] The rate of adverse cardiac events was high (10%), although IVUS promisingly demonstrated late enlargement and restoration of the vasomotor function in cohorts A and B. Abizaid et al[22] evaluated, for one year, the first 512 BVS implanted, with cardiac death of 0.4%, TLR of 4.3% and thrombosis of 0.8%. The propensity score to compare BVS and the second-generation stent Xience V (everolimus) at 12 months presented superposition of results in mortality (0.3% vs. 0.6%), TLR (5.2% vs. 5.5%) and thrombosis (0.5% vs. 0.5%).[21]

Other studies comparing BVS and DES, with the latest generation everolimus, presented similar long-term results. The EVERBIO II[23] study randomized 240 patients in the real world and compared events and late luminal loss (LLL) using IVUS. LLL was similar in both groups with BVS (0.28 ± 0.39 mm) and

Figure 1
Bioresorbable coronary scaffold anatomopathology. Restoration of normal vascular structure after BVS implant observed by optical microscopy in three distinct phases. BVS: bioresorbable vascular scaffold..
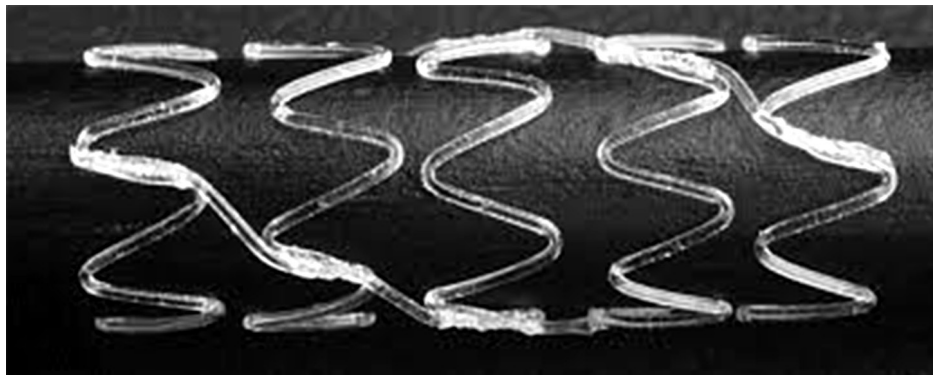
Figure 2
Igaki-Tamai bioresorbable vascular scaffold. Platform structure of the first Igaki-Tamai BVS. BVS: bioresorbable vascular scaffold.
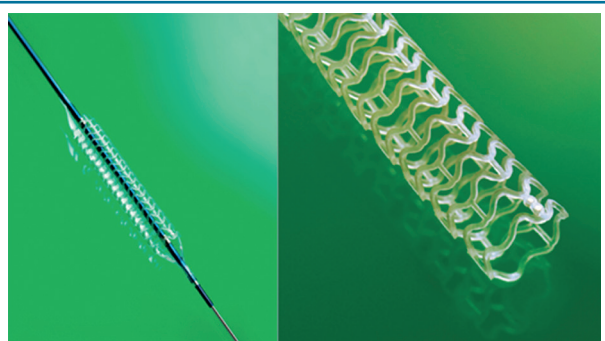
Figure 3
Bioresorbable vascular scaffold. ABSORB-type BVS platform structure. BVS: bioresorbable vascular scaffold.

DES (0.25 ± 0.36 mm) (p = 0.30). There was a possible thrombosis in the BVS group. Clinical outcomes were also similar (27% vs. 26%; p = 0.83) as well as those related to the stent (12% vs. 9%; p = 0.6).[23]

Literature data and the availability of this device with small sizes allow safe anatomical indication for young patients with long non-calcified lesions involving large epicardial vessels.

Small studies and individual experiences expand this variety of options to more complex patients. A great Italian registry with the use of BVS in arteries of moderate to high complexity showed cardiac death of 1%, TLR of 4.4% and thrombosis of 1.7% in six months.[24] The maximum BVS (ABSORB) length available is 28 mm. However, the use of more than one BVS to longer lesions is stimulated since an appropriate overlap of 1 mm is provided between the two devices. In the absence of technical difficulties, such as large load of calcium, vessel diameter tortuosity and limitations, treatment of long lesions constitutes one of the great advantages in its use.

The bifurcation test model showed the possibility of using BVS with a good safety margin. Although the level of evidence of its use is still low, there is a tendency to

use BVS in the main branch whenever access to the side branch is not necessary. The use of classical techniques of access to the lateral branch must be individualized, with the possibility of using a balloon catheter, DES, or even another BVS, provided that the lateral branch is of a good caliper, generally above 2.0 mm, according to the first reports.[25,26]

Cases of STEMI present good hospital and medium-term results with strong recommendation for prior aspiration of coronary thrombus. The nature of the platform may be an advantage in preventing distal embolization. Initial results show no increase in the rates of thrombosis compared to BVS used in non-acute cases.[27-29] Use in very calcified lesions should be preceded by a preparation of the lesion with pre-dilatation semicomplacent balloon-type devices or rotational atherectomy to reduce residual lesion before implantation. The use of IVUS is recommended in these cases. Regarding chronic occlusion, the technique is possible since it follows the rules for calcification and it is certain that access to true lumen has been reached.

Treatment of in-stent restenosis (hyperplasia) or the presence of neoatherosclerosis lesions seems quite promising. Although the positive remodeling defect does not occur, in-stent drug release for a period of time can prevent new restenosis. The fact that there is no future overlap suggests that the BVS should be used to cover the entire stent area rather than only the restenotic area. Left main coronary artery lesions are still an evidence based on case reports only.[30]

Expanded use of BVS still depends on data based on evidence and daily practice. Detailed study of clinical indication and anatomical parameters is very useful. Visual assessment and quantitative analysis of the coronary artery allow understanding the type of injury, calcifications, length and vessel diameter, making the approach tactic easier and allowing a suitable choice of material. The use of IVUS and optical coherence tomography (OCT) is recommended to optimize the procedure with regard to good strut apposition, coverage of the entire lesion, to avoid damage to the platform and dissections on edges.[31] BVS does not present the same stiffness as the metal stent; therefore, after the placement, the implant should be set with gradual elevation of the balloon pressure to prevent rupture of the structure and impairment of results.

Regarding the DAT after implantation of BVS, some authors recommend its use for a period of one year but this is not consensus. In acute syndromes and complex cases, DAT is recommended as established for DES. The use for a period of six months appears to be quite safe. Because the device has an increased profile until the reabsorption mechanism is initiated, the use of latest generation antiplatelet agents, such as prasugrel and ticagrelor, has become daily practice.[13]

BVS, when recommended in these protocols, have additional advantages, which are related to the disappearance of the platform in the vessel over time (Chart 1).

Discussion

BVS provide mechanical support in the early stages of angioplasty without the disadvantage of metal structure remaining in the coronary artery. Disappearance of the support allows smaller inflammatory reaction, recovery of vasomotor properties, endothelial function and adaptive shear force. The vessel may expand as if it were the adaptation of the initial phase of atheroma where there is lumen expansion and expansion of the vessel itself in relation to the plaque area (Glagov phenomenon).[32]

There are many BVS devices used in medical practice, but because the ABSORB was the first device approved and tested in various scenarios, it has become the focus of this review. Initial studies demonstrated the safety of this human BVS platform in human beings, with high implant success rate, low thrombosis and TLR. Comparison of BVS with latest generation DES confirm that there is no inferiority for BVS concerning clinical criteria or late luminal loss.

De novo lesions in epicardial vessels of caliber compatible with the availability of BVS are the main indication, with emphasis on the possibility of using in long lesions, avoiding the complete vessel metallization. Expansion of the variety of indications such as calcifications, tortuosity, bifurcations, restenosis, AMI and LMCA lesions are still seen individually and require further evidence. DAT follows the recommendation of DES with respect to time of use. However, there is consensus of specialists for the use of ticagrelor or prasugrel to be established as a routine to increase safety in the prevention of late thrombosis (30 days to 1 year) and very late thrombosis (more than one year).[13,33] The possibility of, in the medium term, to maintain the use of aspirin only, without the risk of late thrombosis, makes BVS very attractive. In areas of friction, with some curvature, the possibility of strut fracture due to metal wear over time is eliminated.

Chart 1
Additional advantages of BVS

- Smaller inflammatory reaction

- Easy monitoring with computed tomography or magnetic resonance imaging

- Possibility of new successive interventions (percutaneous or surgical)

- Reestablishment of vasomotion

- Possibility of positive remodeling (Glagov)

- Lateral branches are not incarcerated by metal structures

- Elimination of the risk of delayed fracture of structures

BVS: bioresorbable vascular scaffold.

The learning curve for BVS implantation is not an additional challenge, but careful preparation of the lesion and careful device deployment increases the possibility of success. Major BVS limitations are related to the higher material profile, making it difficult to approach very calcified lesions, with large tortuosity, bifurcations with thin lateral branches and distal lesions.

In the clinical follow-up, absence of the metal improves accuracy while viewing the vessel treated using non-invasive methods such as computed tomography angiography and magnetic resonance imaging. In cases of BVS restenosis, the possibility of a new revascularization using PCI or surgery becomes feasible, even if the need for a new device or graft implant is at the site where the BVS was positioned.

In conclusion, there is a large number of options for indications of BVS. However, the safest and best established indications for these devices are in younger patients, long proximal lesions, in straighter segments, good caliper vessels and with good possibility in the treatment of vulnerable high-risk plaques.

Economic factors and lack of robust evidence are still limiting. The development of BVS with smaller profile can now be seen as the near future. Only major cost-effective clinical trials can reveal the true role of BVS, supporting or not its wide use in the treatment of coronary artery disease.

Author contributions

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Study Association

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