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Bioresorbable vascular scaffold implantation for the treatment of coronary in-stent restenosis: Results from a multicenter Italian experience

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ABSTRACT

This multicenter experience sought to investigate the feasibility and safety of BVS for the treatment of ISR. From April 2012 to June 2014, a total of 315 patients (334 lesions) underwent PCI for ISR at the participating centers. Of those, 83 patients (90 lesions) received BVS.

Procedural success was achieved in all patients. At a median of 7 (IQR 3–18) months follow-up, MACCE rate was 12%, TLR 7.7%, while one (1.1%) definite BVS-in-stent thrombosis was reported.

The results of this multicenter experience suggest that BVS implantation for the treatment of coronary ISR is technically feasible and associated with favorable mid-term clinical results. These data could be considered hypothesis generating for a future randomized clinical trial.

1. Introduction

Drug-eluting stents (DES) have significantly reduced, but not eliminated, the rate of repeat revascularizations compared with bare-metal stents (BMS) [1]. However because of the widespread use of PCI, in-stent restenosis (ISR) still occurs [2,3]. Although several therapeutic options have been proposed, the optimal treatment for ISR still has to be identified [4].

The use of DES for the treatment of ISR have raised concerns about the risk of adding additional layers of stents into the arterial wall, thus predisposing patients to an increased risk of stent thrombosis (ST). [5].

Drug-eluting balloon (DEB) has been recently proposed as a valid alternative to current DES, thanks to the ability to elute the anti-proliferative drug without the long-term limitation of adding a further layer of struts. However DEB are limited by the shorter therapeutic window of the anti-proliferative drug, by a greater late lumen loss compared to new generation DES [6,7], and the frequent need for bail-out stenting due to the occurrence of flow limiting vessel dissection. Moreover as shown by the early results of the RIBS IV trial, the use of DEB is also associated with poorer clinical outcome when compared to EES for the treatment of DES ISR [8]. Based on this background, the bioresorbable vascular scaffold (BVS, ABSORB; Abbott Vascular, Santa Clara, CA, USA) could represent an attractive treatment option for ISR as it provides transient vessel scaffolding combined with drug delivery capability, avoiding the long-term limitations of permanent metallic stents. On the other hand the use of this new device in the complex ISR setting might be limited by the actual thickness (150 μm) of the BVS struts, particularly in case of implantation in small restenotic vessels. Furthermore the presence of the previously implanted metallic struts may partially attenuate the potential benefits associated to the BVS resorption.

As of today, there is an increasing amount of data demonstrating the performance of BVS for the treatment of complex coronary lesions [9]. However, very little is known about the feasibility and safety following the use of BVS for the treatment of ISR [10].

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This study sought to evaluate the feasibility, as well as early and mid-term results following BVS implantation for the treatment of ISR.

2. Methods

2.1. Study design and population

A collaborative, prospective cohort analysis was performed on all consecutive patients that underwent PCI with BVS 1.1 implantation for ISR between April 2012 and June 2014 in 6 Italian centers.

The study was conducted according to the Declaration of Helsinki, and written informed consent was obtained from all study patients.

The main characteristics of the BVS 1.1 were already described elsewhere [11].

In the analysis were included all consecutive patients with either DES or BMS ISR lesions (defined as a luminal diameter stenosis more than 50% within the stent or within 5 mm of the stent edges) occurring in a native coronary artery. The decision to treat the ISR lesion with a BVS rather than a new generation DES or a DEB was left to the operator's discretion in the presence of suitable anatomy (absence of tortuosity and/or severe calcification proximal to the target lesion), lesion (reference vessel diameter visually assessed at the target lesion site ≥2.3 mm and ≤3.7 mm without large thrombus burden in the target vessel) and clinical characteristics (absence of severe comorbidities known at the time of hospital admission, contraindications or high-likelihood of non-compliance to 12 months of dual antiplatelet therapy — DAT).

2.2. Procedures

ISR lesions were classified according to Mehran's classification [12]. The BVS were implanted after mandatory pre-dilatation at a pressure not exceeding the rated-burst pressure of 16 atm, while the use of scoring balloon was left at operator's decision. BVS implantation was performed in order to cover 2 mm of non-diseased tissue on either side of the target lesion. Post-dilatation with non-compliant balloon (with a maximum diameter 0.5 mm higher than the BVS diameter) and intra-coronary imaging with optical coherence tomography (OCT, Ilumien Optis, St. Jude Medical, St. Paul, MN, USA) and/or intravascular ultrasound (IVUS) pre- and post-BVS implantation, were not mandatory. The BVS overlap strategy ("marker-to-marker" or "marker over marker") was left to the operator's discretion as well as arterial access (radial or femoral), and peri-procedural anti-thrombotics (i.e., glycoprotein IIb/IIIa inhibitors and heparin or bivalirudin).

All patients were required to receive more than 75 mg of aspirin daily lifelong in association with clopidogrel (75 mg/daily) or ticagrelor (90 mg bid) or prasugrel (10 mg/daily) for a minimum of 12 months.

2.3. Patients follow-up

Clinical data were collected by hospital visit or telephone contact at 30-day intervals. Angiographic follow-up was not scheduled but performed only in case of symptom recurrence and/or non-invasive demonstration of inducible myocardial ischemia. Clinical events were defined according to the Academic Research Consortium definitions [13].

2.4. Study end-points

Any clinical events have been adjudicated by 3 physicians not involved in patient's management.

The primary endpoints of the study were: *procedural success* defined as the successful delivery and deployment of the BVS at the target lesion with less than 30% final residual stenosis by quantitative coronary angiography (QCA) without in-hospital major adverse cardiac and/or cerebro-vascular events (MACCE) defined as a composite of cardiac death, Q-wave myocardial infarction (MI), stroke, or any repeat target lesion revascularization (TLR).

Furthermore, we evaluated the mid-term occurrence of MACCE; *TLR* defined as any ischemia-driven repeat revascularization due to restenosis (diameter stenosis ≥50%) within the scaffold or in the 5 mm distal or proximal markers; target vessel revascularization (TVR) defined as any revascularization performed on the treated vessel; and *BVS-in-stent thrombosis* defined according to the Academic Research Consortium definitions [13].

2.5. Angiographic analysis

Quantitative coronary angiographic (QCA) analysis was performed offline by an expert analyst using automated edge-detection algorithms. In each lesion, the coronary segment including the stent and 5-mm proximal and distal to the stent edge were analyzed at baseline and at follow-up. The following QCA parameters were measured: reference vessel diameter (RVD), minimal lumen diameter (MLD) and percent diameter stenosis (%DS), acute percent recoil (%SD) defined as the difference between the mean diameter of the stent delivery balloon (or if used, mean diameter of postdilatation balloon) at the highest pressure and the mean lumen diameter of the stented segment after balloon deflation, expressed as percentage. Binary restenosis was defined as stenosis >50% of the luminal diameter in the target lesion [14].

3. Statistical analysis

This feasibility study was designed to provide preliminary observations and generate hypotheses for future studies. The sample size was not defined on the basis of an endpoint hypothesis but rather to provide some information about device efficacy and safety. QCA results are presented as paired matched angiographic views after procedure and at follow-up. Continuous variables were expressed as mean ± SD. Comparisons of clinical, angiographic, or procedure-related characteristics of patients were performed by means of Student-t test or Wilcoxon rank-sum test (continuous variables), or chi-square (Categorical) and on the basis of the distribution according to the lesion types (focal or diffuse and de novo or recurrent). All analyses were conducted using SPSS software (IL, USA) version 16.0 for Windows. The p values were considered significant if < 0.05.

4. Results

From April 2012 to June 2014 a total of 315 patients underwent PCI for ISR (334 lesions). Among these 232 (73.6%) patients (244 lesions) received DES and/or DEB while 83 (26.3%) patients (90 lesions) underwent BVS implantation. Among the ISR lesions treated with BVS, the majority were DES-ISR (55, 61%). More than half (57, 63%) of the

Table 1
Baseline patient characteristics.

	Overall	De novo ISR	Recurrent ISR	P Value	Focal ISR	Diffuse ISR	P Value	DES ISR	BMS ISR	P Value
Number of patients	83									
Number of lesions	90	57	33		32	58		54	36	
Age (years)	65.2 ± 10.0	66.2 ± 10.1	66.3 ± 10.8	0.2	66.9 ± 11.2	63.2 ± 13.2	0.2	63.1 ± 10.8	66.6 ± 14.7	0.2
Male gender	70 (84.3)	48 (84.2)	28 (84.8)	0.9	27 (84.4)	49 (84.5)	0.8	46 (85.2)	30 (83.3)	0.9
Body mass index (kg/m^2)	27.5 ± 4.4	27.0 ± 4.3	27.2 ± 4.6	0.4	26.8 ± 6.1	25.7 ± 7.7	0.3	26.9 ± 6.6	24.9 ± 7.8	0.2
Hypertension	62 (74.7)	42 (73.7)	25 (75.7)	0.9	23 (71.9)	44 (75.9)	0.7	41 (75.9)	26 (72.2)	0.7
Hypercholesterolemia	56 (67.5)	40 (70.2)	23 (69.7)	0.8	20 (62.5)	43 (74.1)	0.2	40 (74.1)	23 (63.9)	0.3
Diabetes	28 (33.7)	18 (31.6)	12 (36.4)	0.5	12 (37.5)	18 (31.0)	0.5	19 (35.2)	11 (30.6)	0.6
IDDM	11 (13.3)	9 (15.8)	2 (6.1)	0.2	5 (15.6)	6 (10.3)	0.5	7 (12.9)	4 (11.1)	0.8
Smoking history	34 (40.9)	26 (45.6)	10 (30.3)	0.2	9 (28.1)	27 (46.6)	0.09	25 (46.3)	11 (30.6)	0.1
Previous myocardial infarction	51 (61.4)	36 (63.2)	18 (54.5)	0.4	21 (65.6)	33 (56.9)	0.4	33 (61.1)	21 (58.3)	0.8
Previous bypass surgery	6 (7.2)	3 (5.3)	4 (12.1)	0.4	3 (9.4)	4 (6.9)	0.6	5 (9.3)	2 (5.6)	0.5
Peripheral artery disease	8 (9.6)	5 (8.8)	4 (12.1)	0.9	3 (9.4)	6 (10.3)	0.8	6 (11.1)	3 (83.3)	0.6
Chronic kidney disease (eGFR <60 ml/min)	11 (13.2)	8 (14.0)	3 (9.1)	0.6	5 (15.6)	6 (10.3)	0.4	8 (14.8)	3 (83.3)	0.4
Clinical presentation										
UA	18 (21.7)	9 (15.8)	11 (33.3)	0.2	6 (18.8)	14 (24.1)	0.6	14 (25.9)	6 (16.7)	0.3
NSTEMI	16 (19.3)	10 (17.5)	6 (18.2)	0.8	4 (12.5)	12 (20.7)	0.3	11 (20.4)	5 (13.9)	0.4
STEMI	5 (6.0)	4 (7.0)	1 (3.0)	0.5	0	5 (8.6)	0.9	3 (5.6)	2 (5.6)	1
Stable CAD	44 (53.0)	34 (59.6)	15 (45.5)	0.3	22 (68.8)	27 (46.6)	0.4	26 (48.1)	23 (63.9)	0.1
Ejection fraction	48.3 ± 9.4	49.6 ± 10.3	49.2 ± 7.6	0.3	48.5 ± 9.6	46.7 ± 12.8	0.2	46.3 ± 11.1	48.9 ± 12.7	0.3