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Impact of calcium on procedural and clinical outcomes in lesions treated with bioresorbable vascular scaffolds - A prospective BRS registry study

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ABSTRACT

Background: There is limited data on the impact of calcium (Ca) on acute procedural and clinical outcomes in patients with lesions treated with bioresorbable vascular scaffolds (BRS). We sought to evaluate the effect of calcium on procedural and clinical outcomes in a 'real world' population.
Methods: Clinical outcomes were compared between patients with at least 1 moderately or heavily calcified lesion (Ca) and patients with no/mild calcified lesions (non-Ca) enrolled in our institutional BRS registry.
Results: 455 patients (N) with 548 lesions (L) treated with 735 BRS were studied. Patients in the Ca group (N = 160, L = 200) had more complex (AHA B2/C lesion: 69.0% in Ca vs 14.9% in non-Ca, $p < 0.001$) and significantly longer lesions (27.80 ± 15.27 vs 19.48 ± 9.92 mm, $p < 0.001$). Overall device success rate was 99.1% with no significant differences between the groups. Despite more aggressive lesion preparation and postdilation compared to non Ca, acute lumen gain was significantly less in Ca lesions (1.50 ± 0.66 vs 1.62 ± 0.69 mm, $p = 0.040$) with lower final MLD (2.28 ± 0.41 vs 2.36 ± 0.43, $p = 0.046$). There were no significant differences in all-cause mortality, total definite scaffold thrombosis (ST), target lesion revascularization and myocardial infarction between the 2 groups. Late ST was more frequent in the Ca group compared to non Ca group (late ST: 2.1 vs 0%, $p = 0.02$).
Conclusions: Clinical outcomes after BRS implantation in calcified and non-calcified lesions were similar. A remarkable difference in timing of thrombosis was observed, with an increased rate of late thrombosis in calcified lesions.

1. Introduction

Bioresorbable scaffolds (BRS) have been developed as an alternative to metallic stents as the need for mechanical support for the treated vessel is temporary, and beyond the first few months there are potential disadvantages of a permanent metallic prosthesis. In earlier studies to demonstrate Absorb BRS feasibility and safety, severe calcification was an exclusion criterium [1–6]. Calcified lesions may be challenging and encountered in up to 35% of patients who undergo percutaneous coronary intervention (PCI) [7–8]. Lesion calcification has been associated with increased PCI complexity with worse procedural outcomes compared to non-calcified lesions [9]. Wire crossing, delivery of equipment during pre and post dilation and stent delivery may be more cumbersome. In calcific lesions, the effect of acute plaque recoil may affect stent expansion and is associated with adverse clinical and angiographic outcomes [10–11]. Currently there is still limited data on the impact of calcium (Ca) on acute procedural and clinical outcomes in patients with lesions treated with BRS. We sought to determine the impact of calcification on acute angiographic and 2 year clinical outcomes of a large cohort of patients treated solely with the Absorb Bioresorbable Vascular Scaffold (BVS) system (Abbott Vascular, Santa Clara, CA, USA).

2. Methods

This is an investigator-initiated, prospective, single-center, single-arm study evaluating performance of the Absorb BVS in lesions representative of daily clinical practice, including calcified lesions, total occlusions, long lesions and small vessels [12–13]. The study inclusion period was from September 2012 till January 2015. Inclusion criteria were patients presenting with STEMI [12], NSTEMI, stable/unstable angina, or silent ischemia caused by a de novo stenotic lesion in a native previously untreated coronary artery [13]. Procedural and long-term clinical outcomes were assessed. The primary endpoint was major adverse cardiac events, defined as a composite of cardiac death, myocardial infarction and target lesion revascularization.

Abbreviations: BRS, bioresorbable vascular scaffolds; Ca, calcium; DOCE, device oriented composite endpoints; MACE, major adverse cardiovascular events; MI, myocardial infarct; MLD, minimal lumen diameter; PCI, percutaneous coronary intervention; POCE, patient oriented composite endpoints; QCA, Quantitative Coronary Analysis; RVD, reference vessel diameter; ST, scaffold thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization.

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2.1. Ethics

This is an observational study, performed according to the privacy policy of the Erasmus MC, and to the Erasmus MC regulations for the appropriate use of data in patient-oriented research, which are based on international regulations, including the declaration of Helsinki. Approval of the ethical board of the Erasmus MC was obtained. All patients undergoing clinical follow-up provided written informed consent for the PCI and to be contacted regularly during the follow-up period of the study.

2.2. Quantitative Coronary Analysis (QCA)

The angiographic analysis was performed by three independent investigators. Coronary angiograms were analyzed with the CAAS 5.10 QCA software (Pie Medical BV, Maastricht, the Netherlands). The QCA (Quantitative Coronary Analysis) measurements provided reference vessel diameter (RVD), percentage diameter stenosis and minimal lumen diameter (MLD). Acute gain was defined as post-procedural MLD minus pre-procedural MLD (in an occluded vessel MLD value was zero by default).

2.3. Angiographic assessment of lesion calcification

Lesion calcification was recognized as radio-opacities within the vessel wall at the treated lesion. Calcification was categorized as either none/mild or moderate if the radio-opacities were noted only during the cardiac cycle before contrast injection and further classified as either none/mild or moderate based on visual assessment. Severe calcification was defined as having multiple persisting (that are noted even without cardiac motion) opacifications of the coronary wall and visible in more than one projection, surrounding the complete lumen of the coronary artery at the site of the lesion as per SYNTAX definition (www.syntaxscore.com). Angiographic assessment of calcification was conducted independently by 2 cardiologists. In cases of disagreement, a third independent cardiologist reviewed the films and provided a final diagnosis.

2.4. Follow-up

Clinical demographic data of all patients were obtained from municipal civil registries. Follow-up information specific for hospitalization and cardiovascular events was obtained through questionnaires. If needed, medical records or discharge letters from other hospitals were requested. Events were adjudicated by an independent clinical events committee (CEC). All information concerning baseline characteristics and follow-up was gathered in a clinical data management system. Only patients who had given written consent for follow up were included in the clinical outcome assessments.

2.5. Definitions

The primary endpoint was major adverse cardiovascular events (MACE), defined as the composite endpoint of cardiac death, myocardial infarction (MI) and target lesion revascularization (TLR). The secondary endpoints were device oriented composite endpoints (DOCE: composite of cardiac death, target vessel myocardial infarct and clinically indicated target lesion revascularization) and patient oriented composite endpoints (POCE: composite of all-cause mortality, all-cause myocardial infarct and any revascularization). Deaths were considered cardiac unless a non-cardiac cause was definitely identified. TLR was described as any repeated revascularization of the target lesion. Target vessel revascularization (TVR) was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. Non-target vessel revascularization was described as any revascularization in a vessel other than the target lesion. Scaffold thrombosis (ST) and MI were classified according to the Academic Research Consortium (ARC) [14]. Clinical device success was defined as successful delivery and deployment of the first study scaffold/stent at the intended target lesion and successful withdrawal of the delivery system with attainment of final in-scaffold/stent residual stenosis of <30% as evaluated by QCA. Clinical procedure success was described as device success without major peri-procedural complications or in-hospital MACE (maximum of 7 days).

2.6. Statistical analysis

Categorical variables are reported as counts and percentages, continuous variables as mean ± standard deviation. The cumulative incidence of adverse events was estimated according to the Kaplan-Meier method. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. A cox regression was performed to investigate clinical outcomes at two years, with the binary variable calcification (yes/no). Adjusted cox regression were performed using fourteen patient and lesion factors (see Online Supplement Table 1) to account for baseline differences between patients with at least 1 moderately or heavily calcified lesion (Ca) and patients with no/mild calcified lesions (non-Ca). Statistical analyses were performed using SPSS, version 21 (IL, US). All statistical tests were two-sided and the p value of <0.05 was considered statistically significant.

3. Results

Baseline clinical characteristics are shown in Table 1A. A total of 548 lesions in 455 patients were studied of which 200 (36.5%) lesions in 160 patients (35.2%) were moderately or heavily calcified (Ca group) (Table 1A). Patients in the Ca group were older, with more hypertension, and kidney disease. In the calcified cohort, there were 1.24 lesions per patient. Lesion and QCA characteristics are as shown in Table 1B. The left anterior descending artery (n = 254, 46.4%) was the most commonly treated vessel in the study population. Lesions in the Ca group were more complex (AHA B2/C lesion: 69.0% in Ca vs 14.9% in non-Ca, p < 0.001) and significantly longer. Compared to non-Ca group, lesions in the Ca groups had smaller RVD and lower percentage diameter stenosis.

Procedural characteristics are as shown in Table 1C. Ca lesions were treated with more aggressive lesion preparation compared to non Ca as evidenced by the more significant use of predilation, rotational atherectomy and scoring balloon. The use of buddy wires was higher in Ca lesions compared to non Ca lesions. Fig. 1A illustrates the satisfactory expansion with minimal eccentricity on OCT of a calcified LAD treated with a BRS. Fig. 1B and C illustrates the acute and 2 year angiographic and IVUS result respectively after rotational atherectomy and lesion preparation followed by BRS implantation in a calcified coronary artery. A total of 735 scaffolds were implanted in the study population with more scaffolds per lesion for Ca lesions (1.58 vs 1.21). Scaffold diameter was similar in the two groups however scaffold length implanted was longer in the Ca group. Postdilation was more frequently used in the Ca group (Ca vs non Ca: 64.8% vs 42.1%, p < 0.001).

Procedural outcomes are shown in Table 2A. Post procedure, acute lumen gain was significantly less in Ca compared to non-Ca lesions (1.50 ± 0.66 vs 1.62 ± 0.69 mm, p = 0.040) with lower final MLD (2.28 ± 0.41 vs 2.36 ± 0.43, p = 0.046). RVD and percentage diameter stenosis were smaller in the Ca group compared to the non Ca group though the differences did not reach statistical significance. Procedural success was high for both patient groups (98.7 and 99.7%, p = 0.25). Overall device success rate and final TIMI 3 flow result were similar in the two groups.

We were able to obtain written consent for the follow up program in 395 patients (86.8%). Clinical outcomes were available in all (100%) of these patients (Table 2B). These patient had similar baseline and procedural characteristics as the total population. Kaplan-Meier curves for

Table 1A
Demographic characteristics of the study population.

	BRS (N = 455; L = 548)		
	Patients with at least 1 calcified lesion (N = 160/35.2%; L = 200/36.5%)	Patients with no calcified lesions (N = 295/64.8%; L = 348/63.5%)	
Age	62.12 ± 10.64	56.54 ± 10.25	<0.001
Male	122/160 (76.3)	220/295 (74.6)	0.734
Ex/active smoker	81/160 (50.7)	181/294(61.6)	0.064
Diabetes mellitus	31/160 (19.4)	40/295 (13.6)	0.107
Dyslipidemia	75/158 (47.5)	109/288 (37.8)	0.056
Hypertension	93/159 (58.5)	139/290 (47.9)	0.038
Family history	55/160 (34.4)	127/295 (43.1)	0.206
CVA/TIA	13/160(8.1)	16/295 (5.4)	0.260
Prior MI	26/160 (16.3)	27/295 (9.2)	0.032
Prior PCI	10/160 (6.3)	20/295 (6.8)	1.000
Prior CABG	1/160 (0.6)	0	0.352
Kidney disease	11/160 (6.9)	8/295 (2.7)	0.048
Heart failure	7/160 (4.4)	7/295 (2.4)	0.262
Clinical presentation			0.002
Stable angina	53/160 (33.1)	63/295 (21.4)	
Unstable angina	14/160 (8.8)	32/295 (10.8)	
STEMI	40/160 (25.0)	118/295 (40.0)	
NSTEMI	51/160 (31.9)	82/295 (27.8)	
CCF/others	2/160 (1.3)	0	
Disease involvement			0.060
SVD	97/160 (60.6)	210/295 (71.2)	
DVD	42/160 (26.3)	63/295 (21.4)	
LM/TVD	21/160 (13.1)	22/295 (7.4)	

Values are expressed in numbers (percentages) or mean ± standard deviation when appropriate.

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