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"Full-plastic jacket" with everolimus-eluting Absorb bioresorbable vascular scaffolds: Clinical outcomes in the multicenter prospective RAI registry (ClinicalTrials.gov Identifier: NCT02298413)

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ABSTRACT

Objectives: The objective of this study was to investigate mid-term clinical outcomes of patients treated with 'full-plastic jacket' (FPJ) everolimus-eluting Absorb bioresorbable vascular scaffold (BRS) implantation.
Background: FPJ with BRS may represent an interesting option for patient with diffuse coronary artery disease (CAD), but data on the clinical impact of FPJ using the Absorb BRS are scant.
Methods: FPJ was defined as the implantation of >56 mm of overlapping BRS in at least one vessel. We compared outcomes of patients receiving Absorb FPJ vs. non-FPJ within the multicenter prospective RAI Registry.
Results: Out of 1505 consecutive patients enrolled in the RAI registry, 1384 were eligible for this analysis. Of these, 143 (10.3%) were treated with BRS FPJ. At a median follow-up of 649 days, no differences were observed between FPJ and non-FPJ groups in terms of the device-oriented composite endpoint (DoCE) (5.6% vs. 4.4%, p = 0.675) or the patient-related composite endpoint (PoCE) (20.9% vs. 15.9%, p = 0.149). Patients receiving FPJ had higher rates of target vessel repeat revascularization (TVR) (11.2% vs. 6.3%, p = 0.042). In the FPJ group, there was no cardiac death and only one (very late) stent thrombosis (ST) (0.7%).
Conclusions: Mid-term outcomes of a FPJ PCI strategy in the setting of diffuse CAD did not show a significant increase in composite device- and patient-related events, with rates of cardiac death and ST comparable to non-FPJ Absorb BRS implantation. However, these findings are hypothesis generating and requiring further validation.

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1. Introduction

The presence of diffuse coronary artery disease (CAD) is reported in over 20% of patients undergoing coronary angiography [1,2], and its treatment still represents an unsolved clinical issue. In this setting, optimal medical therapy is associated with grim prognosis [3] and coronary artery by-pass grafting (CAGB), although potentially representing the best therapeutic choice is not always feasible. The use of multiple drug-eluting stents (DES), the so-called "full-metal jacket" [4–7], is associated with poor outcome, because of the higher rates of repeat revascularization, stent thrombosis (ST) and in-stent restenosis [8,9]. Moreover, a full-metal jacket approach may preclude future surgical revascularization. In this regard, the introduction of bioresorbable scaffolds (BRS) may represent an interesting treatment option, in which a 'full-plastic jacket' (FPJ) is only temporary present [10]. Data on FPJ are largely limited to case reports and small single center studies [11–15], providing short-term outcomes only. Considering the increased rate of ST recently observed with the Absorb BRS device (Absorb BRS - Abbot Vascular, Santa Clara, CA, USA) [16], the manufacturer halted the commercialisation with effect from September 2017. Therefore, we investigated the safety of FPJ everolimus-eluting Absorb BRS within the prospective multicenter RAI registry (Registro Absorb Italiano, ClinicalTrials.gov Identifier: NCT02298413).

2. Materials and methods

2.1. Study population and data collection

The RAI registry [17–22] is an investigator-driven, multicenter, prospective registry, including all-comer patients successfully treated with 2nd generation everolimus-eluting Absorb BRS from March 2012 to January 2016 at 25 Italian sites. For the purpose of this analysis, patients treated with Absorb BRS due to in-stent restenosis or graft disease were excluded. Baseline clinical characteristics, angiographic data, clinical events during hospitalization and follow-up (obtained as outpatient visits or new hospitalizations) were prospectively collected into a web-based case report form (CRF). A dedicated clinical events committee (CEC) including clinical and interventional cardiologists not involved in the RAI Registry data collection was established for event adjudication. All adverse events (AE) were validated by checking the data collected in the web-based CRF. All participants were asked to keep documentation of clinical events. An independent Adjudication Committee systematically evaluated the detailed description of AE reported in the CRF and assessed source documents in case of uncertainty. Moreover, random source verification was performed for ≥5% of patients with examination of original documents [17]. Each local regulatory authority approved the study protocol, and the investigation was conducted according to the ethical guidelines of the Declaration of Helsinki. All patients provided informed consent for both the procedure and subsequent data collection and analysis using the approved informed consent form. The RAI Registry did not receive any form of economic support by the device manufacturer.

2.2. Device and procedure

The Absorb BRS, a poly-L-lactide (PLLA) scaffold with an everolimus drug-eluting bioresorbable polymer coating, has been previously described elsewhere [23]. According to study protocol, the decision to implant a BRS rather than a metallic stent was left to the operator's discretion, in the absence of severe comorbidities with poor life expectancy. Planned or bail-out implantation for off-label indications (such as bifurcation with side-branch plain-old balloon angioplasty (POBA) or left main lesions, very-small vessel treatment and chronic total occlusion (CTO)) was allowed and left to operator's discretion, although compliance with the Absorb BRS instructions for use was recommended. The study protocol recommended: a) lesion preparation in order to obtain stent-like pre-dilation, b) careful BRS sizing, with recommended quantitative coronary analysis (QCA) or intravascular ultrasound (IVUS) guidance, c) scaffold implantation at a pressure not exceeding the burst pressure, and d) post-dilatation at high atmospheres with non-compliant balloon sized <0.5 mm than the scaffold size. In case of BRS overlap, marker-to-marker or scaffold-to-scaffold strategies were recommended. Dual antiplatelet therapy (DAPT) was started in all patients before or immediately after index procedure according to ESC guidelines, and included aspirin (100 mg/day) indefinitely in association with clopidogrel (75 mg/day) or prasugrel (10 mg/day) or ticagrelor (90 mg/twice a day) for a minimum of 12 months.

2.3. Definitions

FPJ was defined as the implantation of >56 mm of overlapping BRS in at least one vessel, as pre-specified by study protocol [17]. Clinical events were defined according to the Academic Research Consortium (ARC) Criteria and the American College of Cardiology/American Heart Association (ACC/AHA) cardiovascular endpoints data standards [24]. Related to myocardial infarction (MI), the 2010 addendum to historical definition by Vranckx et al. was used [25,26]. A device-oriented clinical endpoint (DoCE) was defined as the composite of cardiac death (CD), target-vessel related MI (TV-MI), and clinically driven target-lesion revascularization (ID-TLR). Furthermore, we evaluated a patient-related clinical endpoint (PoCE) defined as the composite of cardiac or non-cardiac death, Q-wave or non-Q-wave MI (including non-target territory) and any revascularization (including non-target and target vessels) [27]. All individual adverse events were also reported. Procedural success was defined as successful BRS implantation (final residual stenosis < 30% and post-procedural TIMI 3 flow) without any in-hospital adverse event.

2.4. Statistical analysis

Quantitative variables were summarized as mean ± standard deviation, while categorical ones with count and percentages in each category. Patient's quantitative characteristics were compared between overlap and non-overlap subgroups with unpaired Student's *t*-test or Mann–Whitney test, for categorical characteristics Chi-square or Fisher's exact test were used. Survival curves were estimated by the Kaplan–Meier method and compared using the log-rank test. All patients' characteristics statistically significant in the univariable analysis at the bilateral 5% level were included in a multivariable Cox proportional hazard regression model for the combined endpoints. The results of the analyses are reported as bilateral p-values and bilateral 95% confidence intervals (95% CI). Analyses were performed using R software (version 3.3.2).

3. Results

Of the total 1505 consecutive patients enrolled in the RAI Registry, 1384 all-comer patients with the novo coronary lesions treated with Absorb BRS were eligible for this analysis. Among these, 143 (10.3%) were treated with FPJ.

3.1. Baseline characteristics

The demographical and clinical characteristics of the FPJ and non-FPJ patients are shown in Table 1. Two thirds of the patients presented with an acute coronary syndrome. Patients receiving a FPJ had a lower left ventricular ejection fraction and a higher prevalence of hypertension and diabetes mellitus compared with the non-FPJ group. Angiographic and procedural characteristics of the total population and study groups are detailed in Table 1. Subjects in the FPJ group had more complex coronary anatomy as shown by the higher SYNTAX score, because of higher prevalence of multivessel disease, chronic total occlusions, calcifications, and longer lesions, thus requiring more BRS and overlaps per-patient. Consistently, the rate of incomplete revascularizations was higher in the FPJ group compared with controls. Intravascular imaging guidance was used more frequently in the FPJ group. More than 97% of patients underwent pre-dilatation (97% in FPJ group vs 98% in non-FPJ patients, $p = 0.1$), while post-dilation was performed in >96% of lesions in both groups (97% vs 99%, $p = 0.002$). Among FPJ patients, mean RVD was 2.90 ± 0.32 mm and mean implanted BVS diameter was 3.09 ± 0.28 mm, with a vessel-to-device ratio of 0.93 ± 0.14. Because of the small number of patients in which pre- and post-dilatation were not reported, no significant difference in implantation technique was found during the enrolment period. However, we cannot exclude a temporal evolution of the modalities of how to perform these techniques into practice (e.g. use of non-compliant balloons or use of high atmosphere). In the FPJ group, the left anterior descending artery (LAD) was the target vessel in 60.4%, while the right coronary artery (RCA) was treated in 27.4% of patients. As shown in Table 1, at discharge, patients with FPJ were more likely to receive a new P2Y12 inhibitor (ticagrelor or prasugrel) compared with the non-FPJ group. At 1-year follow up, approximately 1/3 of patients in both groups were still on dual antiplatelet therapy.

3.2. Clinical outcomes

More than 99% of patients had at least one available follow-up, with a median duration of 649 days (interquartile range, IQR 402-905.0); >600 patients had almost a 2-years follow-up. Adverse events are reported in Table 2. At the available follow-up, no differences were