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Target lesion revascularisation of bioresorbable metal scaffolds: a case series study and literature review

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Introduction

Bioresorbable scaffolds (BRS) were introduced into clinical practice to overcome long-term limitations of drug-eluting stents (DES), but they were instead associated with a high rate of target lesion revascularisation (TLR) and thrombosis. Whereas scaffold discontinuity was the most frequent mechanism for polymeric BRS TLR[1], there are no studies on the causes of second-generation drug-eluting absorbable metal scaffold (MgBRS) TLR (Magmaris; Biotronik, Bülach, Switzerland). We sought to determine the optical coherence tomography (OCT) findings in patients who experienced an MgBRS TLR. Moreover, we performed a systematic review of the reported cases.

Methods

A retrospective screening was conducted to identify all the patients with an MgBRS TLR documented by OCT at six tertiary hospitals in Spain. Clinical data were anonymously collected with the approval of the local ethics committees. The patient selection process is shown in **Supplementary Appendix 1**. OCT and quantitative coronary angiography data were analysed offline in a core lab (BARCICORE-lab, Barcelona, Spain) using dedicated software (LightLab Imaging, Mountain View, CA, USA, and CAAS; Pie Medical Imaging, Maastricht, the Netherlands). A qualitative assessment of the entire OCT pullback was performed by two investigators (L. Ortega-Paz and S. Brugaletta) to determine the main OCT findings associated with TLR. These were predefined as scaffold discontinuity, malapposition, evagination, uncovered struts, neoatherosclerosis, restenosis without neoatherosclerosis, scaffold underexpansion/device collapse, edge dissection, or edge-related disease progression[1]. In case of disagreement, a third analyst (J. Gomez-Lara) was asked in order to reach a consensus. The complete OCT definitions are detailed in **Supplementary Appendix 2**.

CASE REPORTS FROM THE LITERATURE

Two independent reviewers (L. Ortega-Paz and S. Brugaletta) performed a systematic review of the literature applying the methodology detailed in **Supplementary Appendix 3** and **Supplementary Figure 1**.

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Results

Between December 2016 and October 2018, 100 patients received MgBRS at the participating institutions. No deaths were reported, and 12 cases of TLR (12%) were found **(Table 1)**. OCT data were available in all the TLR cases. The patients were mainly male (92%) with a median age of 56 (49-61) years. At the index procedure, all patients received one scaffold with a median diameter of 3.5 (3.0-3.5) mm and length of 20 (15-25) mm. In 10 out of 12 patients the device was implanted in an off-label scenario, mainly ST-segment elevation myocardial infarction (STEMI). Regarding the predilation, sizing, and post-dilation (PSP) technique, in one patient predilation was not performed; post-dilation was carried out in eight patients but in seven of them with a maximal balloon-to-scaffold ratio of 1:1. The complete patient and procedural characteristics are shown in **Supplementary Table 1**. There were no significant differences between the included and not included patients.

At the time of the TLR, six (50%) patients experienced an acute coronary syndrome (ACS), with one case of subacute definite scaffold thrombosis, due to abrupt interruption of dual antiplatelet treatment (DAPT), four days after the index procedure. The median occurrence of TLR was 164 days (IQR 63-242).

The main OCT findings were device underexpansion/collapse (n=7; 58%), scaffold discontinuity (n=4; 33%), and distal edge dissection (n=1; 9%) **(Figure 1, Supplementary Figure 2, Supplementary Figure 3, Moving image 1-Moving image 3)**. Two cases of underexpansion (#5 and #7 in **Table 1**) also had OCT data at the index PCI, showing a well apposed and expanded scaffold, therefore confirming the occurrence of a device collapse. No other baseline OCT data were available. The scaffold discontinuity phenomenon was identified at an earlier stage than underexpansion/collapse (70 days [32-111] vs 224 days [190-366]), p=0.022).

CASE REPORTS FROM THE LITERATURE

In the literature review, up to April 2019, we found six cases of MgBRS TLR with intravascular imaging assessment **(Supplementary Table 2)**[2-7]. The data relating to these cases are shown in **Supplementary Appendix 4**.

Discussion

The main findings of this case series study are the following. 1) The most frequent OCT findings were device underexpansion/collapse and scaffold discontinuity. 2) Scaffold discontinuity was found at an earlier stage than underexpansion/collapse. 3) The majority of the cases were off-label indications with a suboptimal PSP technique. 4) Only one case of scaffold thrombosis was observed.

In this retrospective analysis of patients treated with MgBRS who experienced TLR, the clinical characteristics and OCT

Table 1. Patient data at the index procedure, at the time of TLR and OCT analysis.

CASE	Time to failure (days)	INDEX PCI						TLR		OCT ANALYSIS		
		Baseline presentation	Target vessel	BRS size (mm)	Predilation (mm)	RVD (mm) (RVD/BRS)	Post-dilation (mm) @atm	Clinical presentation	$P2Y_{12}$ on top of ASA	Main finding	Neointimal pattern	Thrombus
1	6	NSTEMI (off-label)	LCX	3.0×20	2.5×15	2.23 (0.74)	No	STEMI (definite scaffold thrombosis)	None	Distal dissection	Homogeneous	Yes
2	8	NSTEMI (off-label)	RCA	3.5×15	2.5×10	2.58 (0.74)	No	NSTEMI	Ticagrelor	Discontinuity	Homogeneous	Yes
3	57	sCAD (on-label)	LAD	3.5×15	No	3.25 (0.93)	3.5×12; @16	sCAD	Clopidogrel	Discontinuity	Homogeneous	Yes
4	84	NSTEMI (off-label)	LAD	3.5×20	3.5×15	3.13 (0.89)	3.5×10; @20	UA	Ticagrelor	Discontinuity	Heterogeneous layered	Yes
5	85	NSTEMI (off-label)	LAD	3.5×25	3.5×15	2.95 (0.84)	No	NSTEMI	Clopidogrel	Collapse	Heterogeneous	No
6	139	STEMI (off-label)	LAD	3.0×20	2.5×15	2.86 (0.95)	3.0×15; @26	sCAD	Prasugrel	Discontinuity	Heterogeneous layered	Yes
7	190	STEMI (off-label)	RCA	3.5×20	2.5×10	3.49 (0.99)	3.5×15; @20	sCAD	Prasugrel	Collapse	Heterogeneous layered	No
8	203	UA (on-label)	RCA	3.0×15	3.0×10	2.82 (0.94)	3.5×10; @20	sCAD	Ticagrelor	Underexpansion/collapse	Heterogeneous layered	No
9	224	STEMI (off-label)	LAD	3.0×15	2.5×8	2.77 (0.92)	3.0×12; @18	UA	Ticagrelor	Underexpansion/collapse	Heterogeneous layered	No
10	248	NSTEMI (off-label)	LAD	3.5×15	2.5×10	3.16 (0.90)	No	NSTEMI	Ticagrelor	Underexpansion/collapse	Heterogeneous layered	No
11	366	STEMI (off-label)	LAD	3.5×25	2.5×15	2.23 (0.64)	3.5×15; @20	sCAD	Ticagrelor	Underexpansion/collapse	Heterogeneous layered	No
12	388	STEMI (off-label)	RCA	3.0×20	2.5×6	2.63 (0.87)	3.0×15; @18	sCAD	Ticagrelor	Underexpansion/collapse	Heterogeneous layered hyperplasia	No

ASA: aspirin; atm: atmospheres; BRS: bioresorbable scaffold; LAD: left anterior descending artery; LCX: left circumflex artery; NSTEMI: non-ST-segment elevation myocardial infarction; OCT: optical coherence tomography; RCA: right coronary artery; RVD: reference vessel diameter; sCAD: stable coronary artery disease; STEMI: ST-elevation myocardial infarction; TLR: target lesion revascularisation; UA: unstable angina

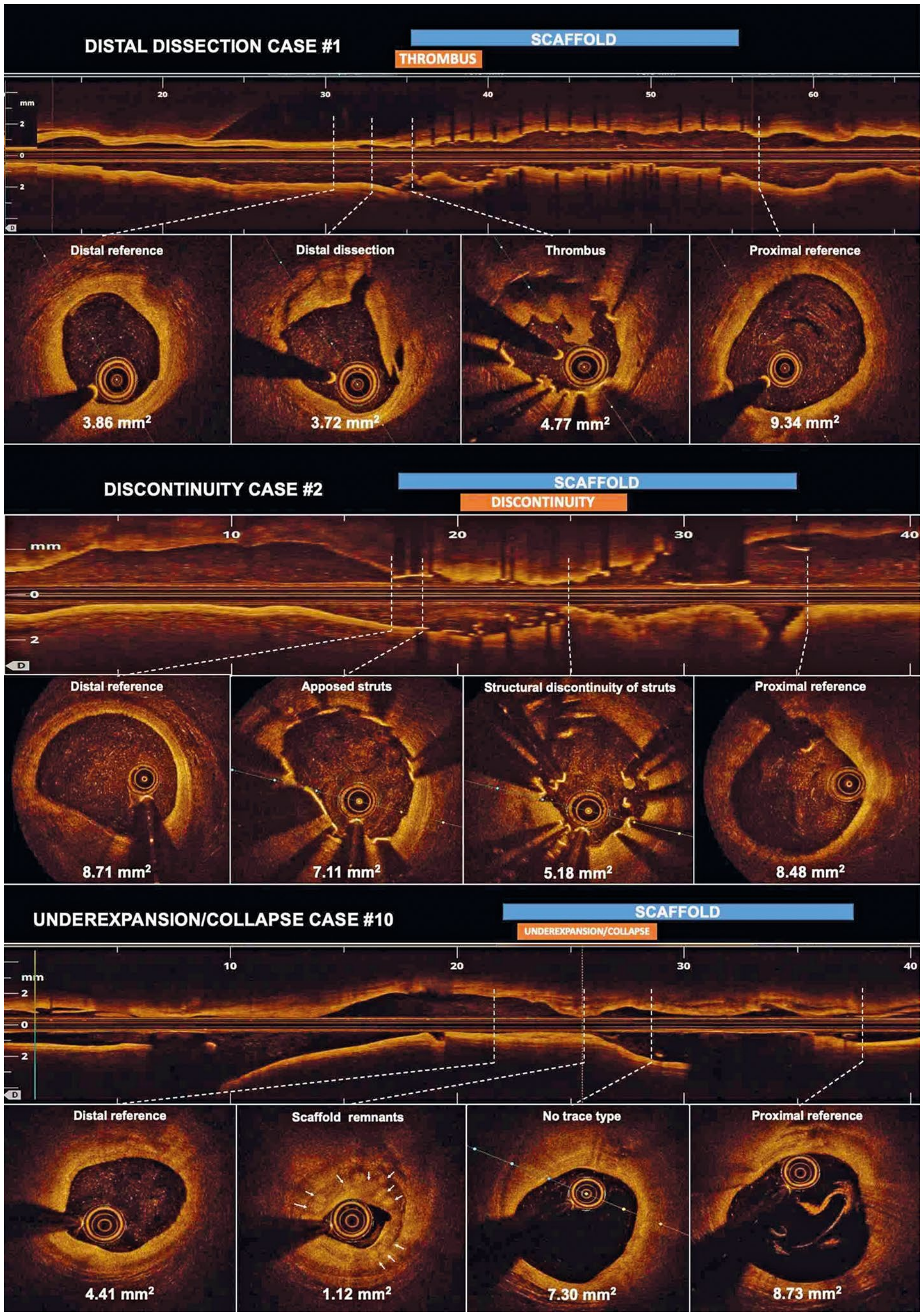

Figure 1. *Second-generation drug-eluting absorbable metal scaffold target lesion revascularisation OCT findings. Minimum lumen area is shown per each cross-section. In case #2, predilation was performed before OCT assessment. Therefore, it cannot be ruled out that the scaffold structure was iatrogenically altered. A three-dimensional reconstruction of case #2 is shown in Supplementary Figure 3.*

findings resembled very closely those of the cases reported in the literature. Although both populations are very selected, the TLRs analysed may be related either to scaffold use in an off-label scenario or to a suboptimal PSP implantation technique[8,9]. Nevertheless, a recent study showed that the procedural characteristics do not impact on the MgBRS healing process[10]. It is worth mentioning that in first-in-man studies MgBRS were used in a very selected population, including only simple lesions and excluding ACS patients[9]. Notably, the off-label implantation in STEMI patients may be related to the high TLR rate because of the difficulties of accurate device sizing and worse clinical outcomes.

Of note is that, irrespective of adverse OCT findings, only one patient had definite scaffold thrombosis, in the context of early DAPT interruption, which is in line with previous studies showing a lower acute MgBRS thrombogenicity as compared to polymeric BRS[11].

Eventually, prolongation of the scaffolding time and increasing the radial force could reduce the incidence of scaffold discontinuity or device collapse during follow-up. These hypotheses need to be confirmed in larger studies and should be taken into consideration for further improvements in the technology.

Limitations

This study has limitations that should be acknowledged. First, this is a retrospective study without a control group. However, to date, this is the largest cohort of MgBRS TLR analysed at a core lab facility. Second, only two cases had baseline and TLR OCT data. Third, for the assessment of MgBRS, the use of intravascular ultrasound (IVUS) and virtual histology may be better than OCT[9], although the spatial resolution of OCT is higher than that of IVUS. Fourth, as the magnesium scaffold shadow disappears by six months, the struts can be ambiguously identified, making the discrimination of the OCT findings challenging. Fifth, the OCT definitions applied were derived from polymeric BRS studies. However, currently there are no standardised definitions for MgBRS failure assessment.

Conclusion

In patients who experienced an MgBRS TLR, the most frequent OCT finding was device underexpansion/collapse followed by scaffold discontinuity.

Impact on daily practice

The most common OCT findings in patients who experienced an MgBRS TLR were device underexpansion/collapse and scaffold discontinuity. The discontinuity cases occurred at an earlier stage compared to device underexpansion/collapse. However, a scaffold thrombosis conditioning a myocardial infarction was unusual. All these data should be considered for the clinical decision-making process and further improvements in the technology.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Patient selection criteria.

Supplementary Appendix 2. Optical coherence tomography definitions.

Supplementary Appendix 3. Systematic literature review methodology.

Supplementary Appendix 4. Systematic literature review results.

Supplementary Figure 1. Search strategy flow chart.

Supplementary Figure 2. Second-generation drug-eluting absorbable metal scaffold target lesion revascularisation OCT findings.

Supplementary Figure 3. OCT three-dimensional reconstruction of the scaffold discontinuity case number two.

Supplementary Table 1. Patient and procedural characteristics.

Supplementary Table 2. Case reports of magnesium-based bioresorbable scaffold TLR found in the systematic literature review.

Moving image 1. Distal dissection case #1.

Moving image 2. Discontinuity case #2.

Moving image 3. Underexpansion case #10.

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