Journal of Cardiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Relationship between peri-strut low intensity areas and vascular healing response after everolimus-eluting bioresorbable scaffold implantation: An optical coherence tomography study

Takao Sato (MD)[a,b], John Jose (MD)[a], Mohamed El-Mawardy (MD)[a], Dmitriy S. Sulimov (MD)[a], Ralph Tölg (MD)[a], Gert Richardt (MD)[a], Mohamed Abdel-Wahab (MD, FESC)[a,*]

[a] Heart Center, Segeberger Kliniken GmbH, Academic Teaching Hospital of the Universities of Kiel, Lübeck and Hamburg, Bad Segeberg, Germany
[b] Cardiology, Tachikawa General Hospital, Nagaoka, Japan

ARTICLE INFO

Article history:
Received 4 May 2016
Received in revised form 23 June 2016
Accepted 28 June 2016
Available online xxx

Keywords:
Neointimal proliferation
Bioresorbable scaffold
Peri-strut low intensity areas

ABSTRACT

Background: Peri-strut low intensity areas (PLIA) surrounding metallic coronary stent struts on optical coherence tomography (OCT) images have been histologically related to delayed healing and inflammation, and have been associated with neointimal proliferation. The relationship between PLIA and vascular healing response after bioresorbable scaffold (BRS) implantation remains unclear.
Methods: This study includes 38 consecutive patients (50 scaffolds) evaluated using OCT 12 months after BRS implantation. Mean and percent neointimal area were quantified. A PLIA was defined as a peri-strut region with an homogenous lower intensity appearance than the surrounding tissue on OCT images without significant signal attenuation. Cross sections were scored as follows: score 0, no PLIA; score 1, <1 quadrant; score 2, ≥1 but <2 quadrants; score 3, ≥2 quadrants but <3 quadrants; and score 4, ≥3 quadrants. Scaffolds were divided into two groups (PLIA+ and PLIA−) based on the presence or absence of any PLIA in the scaffold segment.
Results: The frequency of any PLIA within the scaffold segment was 70.0%. The median PLIA score per scaffold was 0.51 (interquartile range 0–1.07). Using both scaffold- and frame-level analysis, a significant positive correlation was observed between PLIA score and both mean and percent neointimal area. Mean and percent neointimal area were significantly higher in the PLIA+ group than in the PLIA− group (1.95 ± 0.65 mm^2 vs. 1.51 ± 0.27 mm^2, $p < 0.01$ and 24.0 ± 7.0% vs. 17.4 ± 3.6%, $p < 0.01$, respectively).
Conclusion: The presence and extent of PLIA on OCT imaging after BRS implantation appears to be significantly associated with neointimal formation.

Introduction

Optical coherence tomography (OCT) is a high-resolution intravascular imaging tool useful in the systematic quantitative and qualitative evaluation of neointimal tissue following coronary interventions [1–3]. Varied morphological characteristics of neointimal tissue and their correlation with histological findings have been described in recent OCT studies [4,5]. "Peri-strut low intensity area" (PLIA), a frequently observed morphological finding in post stenting OCT imaging of neointima, is considered to represent fibrinogen and proteoglycans of the extracellular matrix as evidenced from pathological studies [6]. The relation between the presence of PLIA on OCT images and unfavorable vascular healing in humans treated with drug-eluting coronary stents (DES) and paclitaxel-coated stent implantation for the superficial femoral artery has been previously reported [7,8].

PLIA was found to be associated with peri-strut inflammation and neointimal proliferation, and hence considered to be a potential marker of abnormal neointimal healing. Recent reports have described that PLIA is also observed after everolimus-eluting bioresorbable scaffold (BRS; Abbott Vascular, Santa Clara, CA, USA) implantation [9,10].

* Corresponding author at: Heart Center, Segeberger Kliniken GmbH, Am Kurpark 1, 23795 Bad Segeberg, Germany. Fax: +49 4551 802 4805.
E-mail address: mohamed.abdel-wahab@segebergerkliniken.de (M. Abdel-Wahab).

http://dx.doi.org/10.1016/j.jjcc.2016.06.013
0914-5087/

BRS offers short-term vascular scaffolding and antiproliferative drug delivery capability while potentially avoiding some of the long-term limitations of metallic DES such as retarded endothelial growth over stent struts and impaired endothelial vasomotor response [11]. However, the relation between OCT-derived morphological findings as PLIA and vascular healing in patients after BRS implantation remains to be clarified. Therefore, in the present OCT imaging study, we investigated the prevalence of PLIA and its relation to neointimal proliferation after BRS implantation in patients with symptomatic coronary artery disease.

Methods

Study population

All patients treated with BRS at our institution are advised to undergo follow-up coronary angiography and OCT one year after intervention according to local institutional guidelines. The population of the current cross-sectional analysis includes 38 consecutive patients treated with 50 scaffolds between October 2012 and April 2014 who followed the institutional protocol (Fig. 1). Patients treated with overlapping scaffolds or with poor OCT image quality were not included in this analysis. Patients were prescribed oral aspirin (100 mg daily) lifelong and prasugrel (10 mg daily) for at least 6 months according to local institutional guidelines. Study outcomes were prevalence of PLIA, correlation of PLIA with neointimal area by OCT, and clinical outcomes at follow-up. Data collection was approved by the local ethics committee, and written informed consent for analysis of anonymized data was obtained from all patients.

OCT examination

OCT imaging of target vessels with implanted BRS was acquired by using the C7-XR OCT imaging system (Lightlab Imaging, Inc., St. Jude Medical, St. Paul, MN, USA). OCT images were generated at 100 frames/s, while the catheter was pulled back at 20 mm/s and a contrast medium continuously flushed through the guiding catheter at a rate of 4–5 ml/s for 3–4 s. Images were continuously acquired and stored digitally for subsequent analysis. It was left to operator's discretion whether OCT was used at the initial percutaneous coronary intervention (PCI).

OCT measurements

OCT measurements were performed with proprietary software for offline analysis (Lightlab Imaging, Inc.). All OCT images were analyzed by personnel who remained blinded to both patient and procedural information. For quantitative measurements, cross-sectional OCT images were analyzed at 1-mm intervals. Cross-sections with side branches were excluded from this analysis.

When compared with metallic stents, BRS present important differences on OCT imaging in view of their optically translucent polymeric struts. These struts appear as a black central core framed by light scattering borders that do not shadow the vessel wall and hence complete imaging of the strut thickness is possible. Quantitative measurements at follow-up (lumen area, scaffold area, black central core) were measured in accordance with previous studies [12,13]. Neointimal area was defined as [scaffold area − (lumen area + black central core)] if all struts were apposed, while it was calculated as [(scaffold area + incomplete strut apposition area + malapposed strut with surrounding tissues) − (lumen area + strut area)] in case of malapposed struts [12]. Percent neointimal area was defined as neointimal area × 100/scaffold area. Additionally, the thickness of the coverage was measured between the endoluminal side of the strut core and the boundary of the lumen drawing the line of measurement. The threshold for coverage was defined as 30 μm [14,15]. The percent of uncovered scaffold struts was calculated by dividing the total number of uncovered scaffold struts by the total number of BRS struts and multiplying the value by 100.

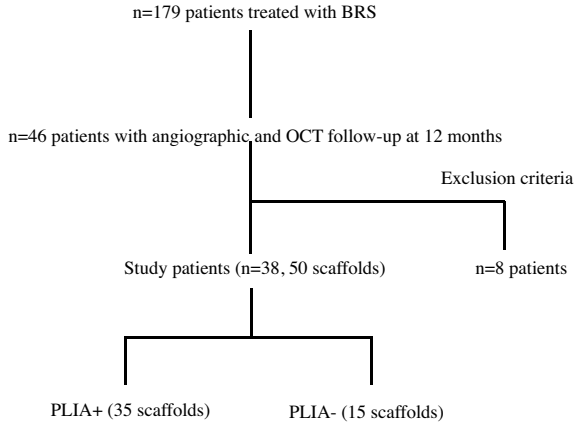

Fig. 1. Study flowchart. BRS, bioresorbable scaffold; OCT, optical coherence tomography; PLIA, peri-strut low intensity area.

PLIA definition

For the qualitative analysis, PLIA was assessed as previously described [7]. PLIA was defined as a region around scaffolds with a homogenous lower intensity appearance than the surrounding tissue area on OCT images without significant signal attenuation behind the area (Fig. 2). If the region with lower intensity had no higher intensity area behind it, we excluded the region from the category of PLIA because of possible difficulties in differentiation from regions with signal attenuation.

PLIA per frame was semiquantitatively scored as follows based on the extent of PLIA occupying the number of quadrants: score 0, no PLIA; score 1, <1 quadrant; score 2, ≥1 but <2 quadrants; score 3, ≥2 quadrants but <3 quadrants; and score 4, ≥3 quadrants [16]. The severity of PLIA per frame on cross-sectional OCT images at 1-mm intervals within the BRS was evaluated, and the PLIA score per scaffold was averaged, using the PLIA score per frame. Additionally, all scaffolds were divided into two groups according to the presence or absence of any PLIA (PLIA+ group and PLIA− group).

Quantitative coronary angiography

For each patient, baseline quantitative coronary angiography (QCA) was performed and the following QCA parameters were computed: lesion length, reference vessel diameter, and minimum lumen diameter (MLD).

Clinical follow-up

The incidence of non-fatal myocardial infarction, scaffold thrombosis, and target lesion revascularization (TLR) were evaluated at follow up. TLR was defined as any re-intervention (surgical or percutaneous) to treat in-scaffold restenosis of the analysis segment.

Statistical analysis

All statistical analyses were performed using IBM SPSS version 22 (IBM Japan Corp., Tokyo, Japan). Continuous data with a normal distribution are presented as mean ± SD and categorical

Please cite this article in press as: Sato T, et al. Relationship between peri-strut low intensity areas and vascular healing response after everolimus-eluting bioresorbable scaffold implantation: An optical coherence tomography study. J Cardiol (2016), http://dx.doi.org/10.1016/j.jjcc.2016.06.013