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Optical coherence tomography assessment of incidence, morphological characteristics, and spontaneous healing course of edge dissections following percutaneous coronary intervention with stent implantation in patients with non-ST segment elevation myocardial infarction

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ABSTRACT

Background: Stenting-induced edge dissections (ED) can be assessed in detail by optical coherence tomography (OCT). This study sought to investigate the incidence, morphological characteristics, and spontaneous healing course of OCT-identified EDs following drug-eluting stent (DES) implantation in a non-ST segment elevation myocardial infarction (NSTEMI) patient-population.

Methods: Acute vessel wall injury at the 5-mm stent adjacent distal and proximal reference segments was assessed by post-procedure OCT and intravascular ultrasound (IVUS) in n = 97 NSTEMI-patients (n = 97 lesions). Six months OCT follow-up was available in 82 patients (including 35 untreated post-procedure EDs).

Results: The overall incidence of post-procedure OCT-detected ED was 38 per 97 patients (39.2%), and 47 per 182 stent edges (25.8%). None of the EDs were angiographically visualizable, while 10 (21.3%) were visible on concomitant IVUS-analysis. Morphologically, there was a significant difference in plaque type present at ED-edges vs. non-ED-edges when assessed with OCT; (1) lipid-rich and calcified plaques: 80.9% vs. 57.0%, (2) fibrous plaques: 17.0% vs. 26.7%, and (3) normal coronary vessels: 2.1% vs. 16.3%, $p < 0.01$. Plaqueburden, assessed by IVUS, was substantially larger at ED-containing borders: 54.5 ± 10.0% vs. 43.7 ± 11.6%, $p = 0.01$. Three dissections (8.6%) were incompletely healed at 6-month OCT follow-up. None of the EDs caused cardiac events during the 6-month follow-up, however, 1 ED-patient had target lesion revascularization with PCI and DES-implantation in extension of the scheduled OCT-control.

Conclusions: OCT-detected EDs were frequent after stent implantation due to NSTEMI, and the majority of these EDs healed without leading to an adverse prognosis at 6 months.

1. Introduction

Percutaneous coronary intervention (PCI) with stent implantation is the standard treatment for coronary artery stenosis. High-pressure stenting techniques sought to secure sufficient expansion and apposition are increasingly performed in order to reduce the risk of later stent failure. However, such implantation techniques in combination with plaque formation at the stent borders represents a risk of inducing edge dissections (ED) [1]. The transition point between the rigid stent and the unstented reference segment constitutes the basis for high tensile vessel wall stress [2].

EDs have been associated with post-procedure ischemic complications, as these unfavourable vessel wall features accompanied by concomitant plaque disruption with exposure of its prothrombotic content may cause slow and turbulent flow and promote thrombosis and/or vessel closure [3–5].

Optical coherence tomography (OCT) is a high-resolution intravascular imaging modality, which enables in-vivo evaluation of the immediate stenting result including possible vessel wall injury following PCI [6,7]. OCT is increasingly adopted in the catheterization laboratories [8], and as a consequence, EDs are progressively recognized. It is a challenging task to define, which OCT-detected angiographically silent adverse features that warrants additional intervention. The spontaneous healing course of untreated OCT-detected EDs and their association with later adverse events remains limited elucidated [9–12].

The purpose of the present study was to; (1) assess the incidence of EDs in a non-ST segment elevation myocardial infarction (NSTEMI) patient-population using OCT; (2) compare the ED-rate obtained by

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OCT versus intravascular ultrasound (IVUS); (3) characterize and compare patients with- versus without ED; (4) evaluate and compare morphometric and morphological characteristics at the reference segment sites in dissected versus non-dissected edges by using a combination of post-procedure OCT and IVUS, and (5) to evaluate the spontaneous healing course of EDs at 6-month by using OCT-assessment.

2. Methods

2.1. Patients, study design and procedures

This study included serial OCT (post-procedure and 6-month follow-up) data and post-procedure IVUS data from the OCTACS trial [13].

The OCTACS trial was designed as a prospective, single center, randomized trial comparing the influence of OCT-guided versus angio-guided implantation of the third-generation biolimus-eluting biodegradable polymer stent (Nobori®, Terumo, Tokyo, Japan) (N-BES) on 6-month strut coverage in patients indicating PCI due to NSTEMI. The inclusion period was August 2011 to May 2013. The detailed study protocol is provided in the main publication [13]. Briefly, patients were eligible if they were ≥18 and <80 years old, had been diagnosed with a NSTEMI, and had a culprit lesion with visually more than 50% diameter de novo stenosis on angiography, requiring treatment with a drug-eluting stent (DES). Exclusion criteria were life expectancy of less than one year; left main disease; extremely narrowed, calcified and/or tortuous culprit vessels unsuitable for intravascular imaging; very long lesions (>45 mm) due to the limited pullback length of the OCT system; bifurcation lesions, and; plasma creatinine >170 μmol/L.

Prior to the index-procedure, patients were loaded with a 300 mg dose of aspirin and a loading dose of 180 mg of ticagrelor. Also, an unfractionated heparin dose (70 IU/kg) was administered at the PCI-procedure. Stents were implanted according to standard techniques. The operators visually estimated angiographic variables, including choice of stent size. Direct stenting without prior balloon dilation was allowed. Full lesion coverage by implantation of one or more stents was attempted.

Post stenting, after obtaining an angiographic optimal result, eligible patients for this study were randomly assigned 1:1 to either: (1) angio-guided PCI or (2) OCT-guided PCI.

Patients randomized to angio-guided PCI had so-called "documentary" OCT and IVUS after completion of the intervention. It was not possible to blind the operator, investigator or patient for the allocated implantation technique, but the operator was blinded to the post-procedure OCT- and IVUS-images, as the operator screen-sides were turned off, and the entire pullbacks remained uncommented on.

Prespecified per protocol OCT criteria regarding stent expansion, stent apposition, residual stenosis and EDs determined whether or not additional intervention was indicated in the OCT-guided group. Specifically, a "significant ED" was defined as an ED causing a minimal luminal area (MLA) <4 mm^2. The degree of optimization based upon image findings was left to the discretion of the operator.

The study complies with the declaration of Helsinki, and the institutional review board approved the study (Ethical Committee project-ID: S-20110030, Danish Data Agency project ID: 2011-41-6020, ClinicalTrials.gov: NCT02272283), and written informed consent was obtained from all patients.

2.2. Optical coherence tomography image acquisition and analysis

OCT imaging of the target lesion was performed both post-procedure and at 6-month follow-up using a frequency-domain OCT system (C7-XR™ or Ilumien™ OCT system; LightLab Imaging, Inc., St. Jude Medical, St. Paul, MN, USA). Following administration of 200 μg intracoronary nitroglycerin (and a 5000 IU unfractionated heparin dose in follow-up procedures), the imaging was performed. A 2.7 Fr C7 Dragonfly™ Imaging Catheter (LightLab Imaging, Inc., St. Jude Medical, St. Paul, MN, USA), flushed with 20 ml undiluted contrast was used. Contrast media was flushed continuously through the guiding catheter during image acquisition. Motorized pullback OCT imaging was performed at a pullback rate of 20 mm/s throughout the target vessel. Stent edges were used as landmarks.

Quantitative OCT analysis was performed using the LightLab OCT Imaging proprietary software (Offline Review Workstation, LightLab Imaging, Inc., St. Jude Medical, St. Paul, MN, USA).

The reference segments 5 mm adjacent to the distal and the proximal stent edges were assessed frame by frame (every 0.2 mm) by one dedicated OCT-analyst. Stent borders were defined as the first and the last cross sections of the stented segment where struts were visible. The peri-stent region consisted of the first frame immediately following the stent border (0.2 mm apart).

Edge dissections were defined as disruptions of the arterial lumen surface with visible flap [14]. The longitudinal extension of the dissection was measured by adding consecutive frames with the feature.

Specific morphometric parameters in form of: [A] dissection arc, [B] flap length, [C] flap root thickness, and potential [D] dissection cavity (depth and area) were calculated to estimate the magnitude of each dissection. Also, the "effective lumen area" (referring to the smallest "true" lumen at the dissection site) [E], and the "actual lumen area" (referring to the "true" lumen plus possible false lumen (cavity) or "behind flap area" caused by the dissection) [F] were traced, in order to estimate the significance of the possible lumen compromise. These morphometric parameters were measured at the frame of the dissection site, where the ED had the largest circumferential extent (i.e. the widest dissection arc and the largest dissection flap).

Further, the depth of the dissection was characterized as: [G] intimal (limited to the intimal layer), [H] medial (extending into the media of the vessel wall), and [I] adventitial (extending through the external elastic membrane) (Fig. 1).

The plaque type at the distal and proximal reference segments was qualitatively assessed and characterized as: [A] fibrous (homogeneous signal rich), [B] fibro-calcified (signal rich with defined borders), [C] lipid-calcific (signal poor where focal calcified plaques were heterogeneous in appearance and/or without defined borders), or lipid-rich (signal poor with diffuse borders). In lipid-rich plaques, the thickness of the fibrous cap was measured at the thinnest point in order to classify them as thick-cap fibroatheromas (ThCFA, >65 μm) [D] or thin-cap fibroatheromas (TCFA, <65 μm) [E] [15]. A normal vessel wall was characterized by a preserved 3-layered architecture comprising the evidence of intimal, medial, and adventitial layers [F] (Fig. 2).

2.3. Intravascular ultrasound imaging and analysis

All IVUS acquisitions were performed after stent implantation and intracoronary administration of 200 μg nitroglycerin using an Atlantis™ SR Pro 40 MHz catheter and an ILab system (Boston Scientific, Natick, MA, USA). The IVUS catheter was advanced ≥10 mm distal to the stented segment, and imaging was performed using an automatic pullback device throughout the stent to the proximal reference segment site at a frame rate of 30 frames/s and a pullback speed of 0.5 mm/s.

IVUS pullbacks were analyzed off-line by one dedicated IVUS-analyst using the planimetry echoPlaque 4.0 Analysis Software (INDEC Medical Systems, CA, USA) at 1 mm intervals at the reference segments.

Dissections were tears in the reference segment plaque parallel to the vessel wall with visualization of blood flow in the false lumen/behind flap [16].

The lumen cross sectional area (CSA) was measured as the area bounded by the luminal vessel contour, and the external elastic membrane (EEM) CSA was measured at the leading edge of the adventitia. The plaque- and media (P&M) CSA was calculated as the EEM CSA minus the lumen CSA. Plaqueburden was defined as P&M CSA divided by the EEM CSA.

2.4. Statistical analysis

The statistical analysis was performed with SPSS 22.0 software (SPSS, Chicago, IL, USA).

Categorical variables were compared with chi-square statistics or with the Fisher's exact test.

Continuous variables were compared with the Student's *t*-test or with non-parametric testing, depending on the distribution of the data.

A binary logistic regression analysis was performed to identify predictors for MLA < 4 mm^2 at ED-edges at 6-month follow-up. Kappa statistics (κ) was performed to determine consistency between different analysts (analyst A versus analyst B) on the presence of EDs, the depth of EDs, and the underlying plaque type in dissected reference segments. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

3.1. Study cohort

In total, 100 patients were enrolled in the study. One patient suffered from a severe stenting induced non-edge culprit vessel dissection. Due to subsequent hemodynamic instability, this patient was excluded from further invasive imaging evaluation. OCT system failure occurred in two cases, and only IVUS was carried out, leaving 97 patients with 97 de novo coronary lesions for baseline OCT interpretation. During follow-up, 10 patients withdrew their informed consent, and declined the scheduled invasive re-examination at 6-month. Furthermore, four additional patients were excluded prior to 6-month invasive follow-up for various reasons (in one patient it was impossible to flush the target vessel at follow-up, one patient developed severe cognitive deficits and was excluded from invasive follow-up due to protocol-related and ethical reasons, one patient developed a subacute stent thrombosis, and one patient suffered from a cardiac death), and in one patient poor technical quality/flush prevented sufficient OCT assessment at 6-month, leaving a total of 82 patients for complete OCT baseline and follow-up evaluation. There were no significant differences in baseline characteristics between patients with versus without scheduled 6-month OCT-control.