Smooth arterial healing after paclitaxel-coated balloon angioplasty for in-stent restenosis assessed by optical frequency domain imaging

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Abstract

Aims: Our aim was to evaluate visual and qualitative changes of intimal tissue by optical frequency domain imaging (OFDI) after paclitaxel-coated balloon (PCB) angioplasty.

Methods and results: We conducted a prospective observational study of 38 Japanese patients undergoing PCB angioplasty for in-stent restenosis at a single institute from February 2014 to June 2015. The scheduled follow-up coronary angiography (CAG) was performed six to nine months after PCI. Intravascular imaging assessment was performed twice, immediately following PCB angioplasty and during follow-up CAG, using an OFDI system. During the study period, PCB angioplasty was performed on 38 patients and OFDI assessment was performed in all 38 cases at the time of angioplasty. Follow-up CAG was performed in 22 patients and qualitative OFDI assessment was performed in 12 patients. The average follow-up period was 6.3±1.4 months. The minimum lumen area measured by OFDI immediately following balloon angioplasty and at follow-up was 4.8±1.5 mm^2 and 4.2±1.9 mm^2, respectively. The neointimal area immediately following angioplasty and at follow-up was 2.7±1.6 mm^2 and 2.9±0.9 mm^2, respectively. Late luminal loss six months after angiography was 0.6 mm^2. In the 22 follow-up patients, repeat ISR was seen in four patients (18%). Qualitative OFDI assessment at six months showed smooth healed neointimal tissue with a homogeneous appearance, which had been an uneven surface at the time of angioplasty.

Conclusions: After PCB angioplasty, the arterial healing process, as assessed by OFDI, shows smooth neointimal tissue by six months.

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Introduction

The paclitaxel-coated balloon (PCB) is a useful device for percutaneous coronary intervention (PCI). PCB angioplasty is performed mainly to ISR lesions and in small vessel disease. Previous studies have shown its favourable clinical outcomes and arterial healing process[1]. However, the visual changes of the arterial healing process in real-world patients have not yet been examined. We therefore sought to assess changes of the intima after PCB angioplasty using the high-resolution optical frequency domain imaging (OFDI) system.

Methods

STUDY DESIGN

We conducted a prospective observational study of 38 Japanese patients undergoing PCB (SeQuent® Please; B. Braun, Melsungen, Germany) angioplasty for ISR at a single institute from February 2014 to June 2015. All ISR lesions were predilated using the Lacrosse NSE balloon (Goodman Co. Ltd., Aichi, Japan). The scheduled follow-up CAG was performed at six to nine months after PCI. When patients reported chest pain, a follow-up CAG was performed earlier than the scheduled date.

METHODS OF OFDI ACQUISITION

Intravascular imaging assessment was performed twice, just after PCB angioplasty and at the time of follow-up CAG, using the OFDI system (Terumo Corp., Tokyo, Japan). OFDI imaging uses a non-occlusive technique at an image acquisition rate of 158 frames/s during an automated pullback at a speed of 40 mm/s. The pullback was performed during continuous intracoronary injection of contrast medium through the ≥6 Fr guiding catheter using an injection pump at a flow rate of 3.0 ml/s for the left coronary artery and 2.5 ml/s for the right coronary artery for four seconds.

STATISTICAL ANALYSIS

Discrete data are presented as frequencies and/or percentages and continuous variables are presented as mean±SD.

Results

From February 2014 to June 2015, PCB angioplasty was performed on 38 patients with ISR, and OFDI assessment was performed in all 38 cases at the time of angioplasty. Baseline data of the study participants are shown in **Table 1**. For the 38 patients with ISR, the rate of previously implanted stents that were bare metal stents (BMS) was 26.3% (n=10), first-generation DES was 7.9% (n=3), and second-generation DES was 65.8% (n=25). Next, follow-up CAG was performed in 22 patients and qualitative OFDI assessment was performed in 12 patients. The average follow-up period was 6.3±1.4 months. The minimum lumen area measured by OFDI immediately following balloon angioplasty and at follow-up was 4.8±1.5 mm^2 and 4.2±1.9 mm^2, respectively. The neointimal area following angioplasty and at follow-up was 2.7±1.6 mm^2 and 2.9±0.9 mm^2, respectively **(Table 2)**. Late luminal loss at six months after angiography was 0.6 mm^2. In the 22 follow-up patients, repeat ISR was seen in four patients (18%). Over a six-month period, qualitative

Table 1. Patient characteristics.

Number of patients		38
Number of lesions		38
Mean age, years		70.6±9.9
Male		34 (89.5%)
Coronary risk factors	HTN	35 (92.1%)
	DM	29 (76.3%)
	Dyslipidaemia	27 (71.1%)
	Smoking	15 (39.5%)
	Haemodialysis	5 (13.2%)
Multiple ISR history		14 (36.8%)
Target vessels	LAD	18 (47.4%)
	LCX	6 (15.8%)
	RCA	14 (36.8%)
Previous stents	BMS	10 (26.3%)
	1st DES	3 (7.9%)
	2nd DES	25 (65.8%)

BMS: bare metal stents; DES: drug-eluting stents; DM: diabetes mellitus; ISR: in-stent restenosis; HTN: hypertension; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery

OFDI assessment showed a smoothened surface of healed neointimal tissue with a homogeneous appearance in all 12 cases. This surface was jagged and uneven in appearance at the time of angioplasty **(Figure 1A, Figure 1B)**.

Discussion

Drug-coated balloon (DCB) angioplasty is mainly performed for small vessel disease and in-stent restenosis. Previous studies have shown favourable clinical outcomes using DCB for in-stent restenosis when compared with plain balloon angioplasty and drug-eluting stents[1]. Long-term safety has also been shown. PCB angioplasty showed similar favourable clinical outcomes to DES implantation for the treatment of DES restenosis in complex situations[2]. We sought to assess the healing process of PCB angioplasty by OFDI, as this process is key for a favourable clinical outcome.

In our study, predilatation using the Lacrosse NSE balloon was performed in all cases. This balloon catheter contains three triangular nylon elements (width, 0.014″, height, 0.015″) which are free-floating on the outside of the balloon surface, and attached proximal and distal to a 13 mm balloon length[3]. Dilatation using the Lacrosse NSE balloon creates a scoring effect into the intimal tissue through

Table 2. Quantitative OFDI findings.

	Pre PCI	Post PCB	6-month follow-up
Minimal lumen area (mm^2)	1.1±0.5	4.8±1.5	4.2±1.9
Minimal stent area (mm^2)	6.0±2.3	7.5±2.7	7.2±2.5
Neointimal area (mm^2)	4.9±2.2	2.7±1.6	2.9±0.9

OFDI: optical frequency domain imaging; PCB: paclitaxel-coated balloon; PCI: percutaneous coronary intervention
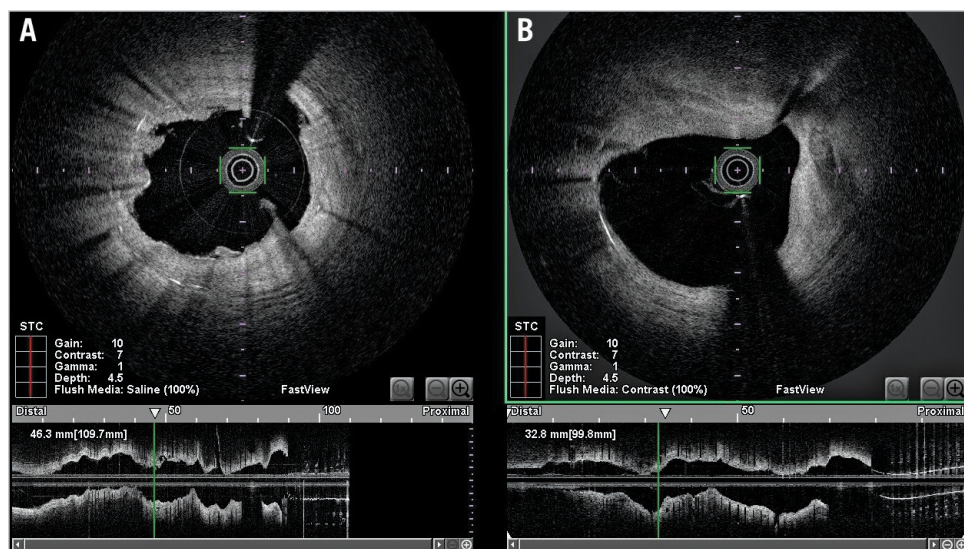
Figure 1. *Examples of qualitative findings by OFDI. A) OFDI image shows a jagged and uneven surface at the time of balloon angioplasty. B) Six months after balloon angioplasty, OFDI image shows a smoothened surface of healed neointimal tissue with a homogeneous appearance.*

a focused transmission of force through the elements. Several types of scoring balloon are available, and the scoring effect is useful for predilatation of calcified or hard plaque lesions. Because we used this balloon for predilatation in all ISR cases, OFDI showed a jagged, uneven surface at the time of PCB angioplasty. However, over six months this surface smoothened and a homogeneous neointima covered the stent strut very well in all cases. To our knowledge, this is the first study to evaluate visually how the intimal tissue changes following PCB angioplasty in real-world patients. Treatment of BMS ISR with PCB leaves significantly fewer stent struts uncovered at nine-month follow-up[4]. A previous study evaluated the PCB healing process by counting the number of covered or uncovered stent struts, and measuring the thickness of the intima[5]. However, our study focused on visual evaluation using a high-resolution OFDI system, which has been developed to overcome the limitations of conventional time-domain optical coherence tomography[6]. It enables the precise measurement of the vasa vasorum area in coronary arteries[7]. Our findings are in agreement with previous reports[8], which show that even dissection and intimal injury by scoring balloon inflation can be smoothly healed after PCB angioplasty.

Study limitations

This study has limitations related to study design and methods of data collection. First, the sample size was relatively small. It was a non-randomised study where all confounding factors and biases could not be eliminated. There is a possibility of substantial selection bias with regard to patient selection, as well as the experience and dedication of the operators.

Conclusions

After PCB angioplasty for ISR, the arterial healing process assessed by OFDI results in a smooth surface by six months.

Impact on daily practice

Paclitaxel-coated balloons have been widely used for treatment of in-stent restenosis. The present study showed a smooth arterial healing process after angioplasty. This finding might be applicable to native coronary artery disease, e.g., coronary dissection. Paclitaxel-coated balloons might help to avoid unnecessary metal stent implantation.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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