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ORIGINAL ARTICLE

Comparison of the vessel healing process after everolimus-eluting stent and bare metal stent implantations in patients with ST-elevation myocardial infarction

Hideki Yano[1,2] · Shigeo Horinaka[1] · Manami Watahik[1] · Tomoko Watanabe[1] · Toshihiko Ishimitsu[1]

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Abstract

Cobalt–chromium everolimus-eluting stent (CoCr EES) is associated with a lower rate of stent thrombosis even in patients with ST-elevation myocardial infarction (STEMI). However, the time-serial changes of endothelial coverage of the stent struts in the extremely early period have never been reported, especially in patients with STEMI. The aim of this study was to compare the vessel healing process between CoCr EES and cobalt–chromium bare metal stent (CoCr BMS) implantations using optical coherence tomography (OCT) in patients with STEMI. Sixty-three patients who had primary emergent percutaneous coronary intervention (PCI) with CoCr EES (42 patients) or CoCr BMS (21 patients) were enrolled in this study for 3 years. OCT was performed just after, 2 and 12 weeks after EES or BMS implantations. Time-serial changes in the neointimal coverage (NIC), the neointimal thickness, and malapposition of stent struts were evaluated. NIC of stent struts did not differ between CoCr EES (23.2%, 99.4%) and CoCr BMS (24.0%, 97.8%) at 2 weeks and 12 weeks after PCI, respectively. Thicknesses of the neointima on the stent strut was significantly thinner in CoCr EES (34.0 ± 13.8, 107.0 ± 32.4 μm) than in CoCr BMS (40.0 ± 14.6, 115.7 ± 33.8 μm) at 2 weeks and 12 weeks after PCI ($p = 0.011$, $p = 0.008$), respectively. The malapposition did not differ just after PCI, and was completely resolved at 12 weeks after PCI in both groups. Thrombus was significantly less in CoCr EES than in CoCr BMS at 2 weeks (19.0% vs 42.9%, $p < 0.01$), and decreased over time in both groups, but at 12 weeks, disappeared only in CoCr EES (CoCr EES: 0% vs. CoCr BMS: 4.8%, $p = 0.56$). This study demonstrated that NIC and apposition of the stent struts almost completed at 12 weeks after EES and BMS implantations, while the neointimal thickness on the stent struts were thinner in EES than in BMS. Moreover, thrombus was significantly less in EES than in BMS implantations 2 weeks after PCI, which may explain the lower rate of acute and subacute stent thrombosis of EES compared with BMS.

Keywords Everolimus-eluting stent · Optical coherence tomography · ST-elevation myocardial infarction · Neointimal thickness · Apposition · Stent strut coverage

Introduction

Drug-eluting stent DES) has been the most effective strategy for the prevention of restenosis after percutaneous coronary interventions PCI) in current clinical practice [1, 2]. However, excessive inhibition of neointimal formation can cause delayed vascular healing, and inadequate stent strut endothelial coverage after DES implantation is thought to be associated with late stent thrombosis LST) [3–7]. Second-generation DESs were developed to overcome this weak point while maintaining efficacy similar to first-generation DES. In fact, second-generation DES developed with newer alloys, biocompatible polymers, thinner struts, and different drug kinetics, have resulted in a reduction of LST [8–10]. Trials

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✉ Hideki Yano
hideki-y@dokkyomed.ac.jp

[1] Department of Cardiology and Nephrology, Dokkyo Medical University Hospital, Mibu, Tochigi 321-0293, Japan

[2] Department of Cardiology, Nasu Red Cross Hospital, Ohtawara, Tochigi 324-8686, Japan

and meta-analyzes have also indicated that shorter dual antiplatelet therapy might be safe with second-generation DES as opposed to first-generation DES [11, 12]. Moreover, it has been reported that significantly faster re-endothelialization < 14 days) is observed in rabbit iliac arteries with the everolimus-eluting stent EES) than with sirolimus-eluting stent [13].

An important histological predictor of LST is the neointimal coverage NIC) of stent struts, and the best morphometric predictor of LST is the ratio of uncovered-to-total stent struts evaluated by optical coherence tomography OCT), which has the resolution to identify the extent of stent strut tissue coverage [7, 14].

We reported that NIC of stent struts progressed to about 80% and malapposition of stent struts completely disappears at 4 weeks after EES implantation, and that NIC of stent struts is almost completed within 12 weeks [15].

However, our study was limited to patients presenting with stable coronary artery disease who underwent elective percutaneous coronary intervention PCI) to de novo lesions. Patients with ST-elevation myocardial infarction STEMI) were excluded. Activation of platelets and the coagulation cascade has been reported in patients with STEMI. Thus, the risk of stent thrombosis ST) after PCI may be higher in patients with STEMI than in those with stable coronary artery disease [16, 17]. However, OCT findings in the extremely early periods such as 2 or 12 weeks after EES implantation in patients with STEMI have never been reported.

Therefore, the present study evaluated the vascular healing defined as neointimal formation and malapposition of the stent struts by OCT evaluation at just after, 2 and 12 weeks after EES compared with BMS implantation in patients with STEMI.

Methods

Study patients and design

This was a retrospective, non-randomized, and observational study conducted in two centers examining patients with STEMI. Patients who underwent PCI within 12 h after onset of symptoms and confirmed elevation of ST segment in electrocardiogram were enrolled. STEMI was defined as high-grade stenosis/occlusion of a native coronary artery as seen on diagnostic coronary angiography after intracoronary injection of a nitrate, and presenting with ECG changes as well as the elevation of serum cardiac marker (creatine kinase MB fraction at least twice the upper normal limit).

Patients were recruited at two centers: Nasu Red Cross Hospital and Dokkyo Medical University Hospital, between November 2012 and July 2017.

Enrollment period was shown in Fig. 1. Total number of the STEMI was 502 patients who received either CoCr EES (420 patients) or CoCr BMS (82 patients) in the two study institutions during this period. In these patients, 71 patients with multi-vesseldisease who underwent emergent percutaneous coronary intervention (PCI) of STEMI lesions using the cobalt–chromium EES (XIENCE Alpine, Abbott Vascular, Santa Clara, CA, USA) and Multi-Link Vision BMS (Abbott Vascular, Santa Clara, CA, USA) were enrolled in this study. After receiving informed consent, we performed staged PCI to the residual lesion 2 weeks after the first index PCI and conducted follow-up CAG after 12 weeks thereafter. As shown in Figs. 2 and 3, patients refused to join in this study and 5 patients were excluded due to failure of OCT examination after PCI. The remaining 63 patients were analyzed in this study.

Optimal results were obtained at the index procedure using OCT. Time-series OCT was performed to assess the percentage of NIC on the stent struts in the first-implanted CoCr EES or CoCr BMS 2 weeks after primary PCI while treating another residual lesion, and 12 weeks after primary PCI while undergoing follow-up CAG. EES or BMS was selected by the physician's discretion. The study protocol was approved by the institutional review board of our institute, and written informed consent was obtained from all patients before the procedure.

Procedures were performed following current clinical practice. Aspirin (loading dose 200 mg) and clopidogrel (loading dose of 300 mg) were administered before PCI. Patients received unfractionated heparin which was used to maintain an activated clotting time of 250 s or longer during PCI. After PCI, clopidogrel (75 mg/day) and aspirin (100 mg) were prescribed for the study period.

Left main trunk lesions, bifurcation lesions requiring 2 stents, severe chronic kidney disease, unsuccessful PCI, unsuitable lesions for OCT proximal vessel size > 3.5 mm or proximal lesions < 10 mm from the ostium of each artery), chronic total occlusions, and in-stent restenosis were excluded from this study. Quantitative coronary angiography QCA) analysis was conducted as previously described [18].

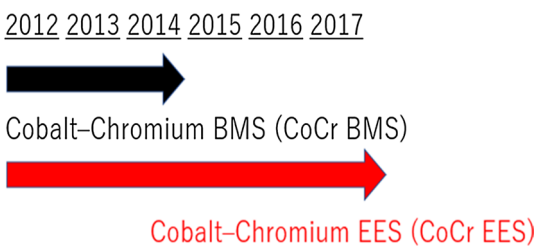
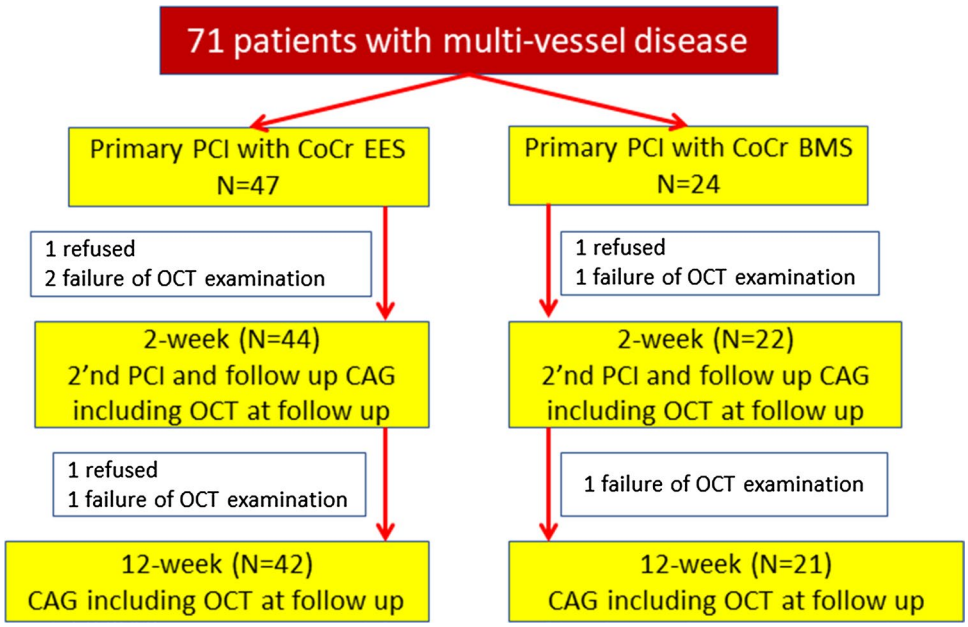


Fig. 1 Enrollment period of the sirolimus-eluting stent (SES) and the everolimus-eluting stent (EES)

Fig. 2 Study chart flow



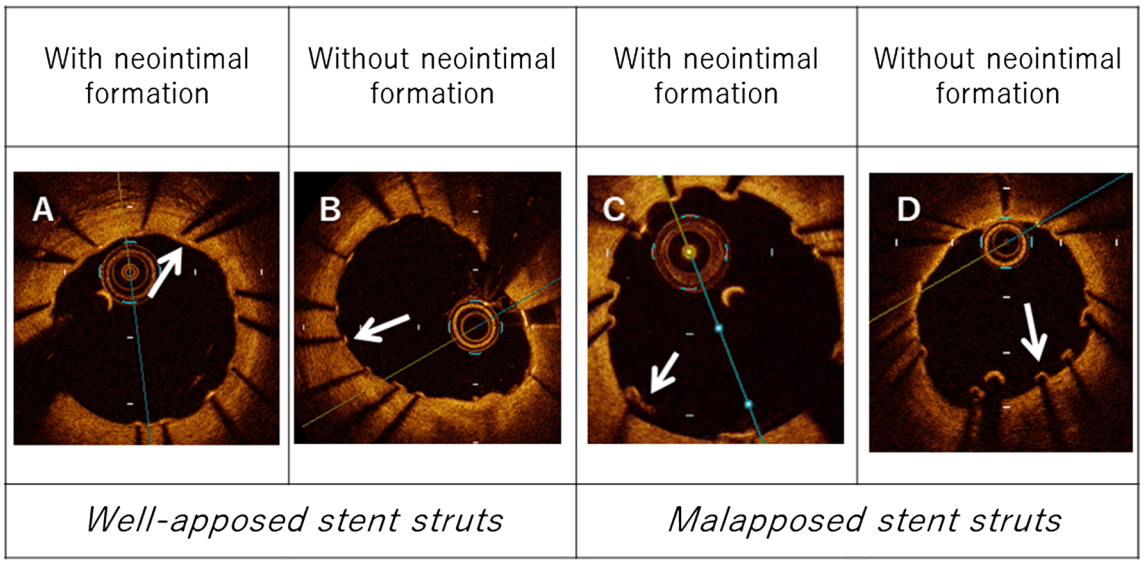


Fig. 3 Representative optical coherence tomography images of some case examples of good coverage, non-coverage, and malapposition. **a** Well-apposed stent struts with neointima formation. **b** Well-apposed stent struts without neointima formation. **c** Malapposed stent struts with neointima formation. **d**Malapposed stent struts without neointima formation

Angiographic restenosis was defined as more than 50% of the %DS in the QCA analysis.

OCT image protocol and analysis

OCT was performed using the frequency-domain OCT system (C7-XR™ Intravascular Imaging System and Dragonfly™ OCT catheter; St. Jude Medical, St. Paul, MN, USA) with a motorized pull-back system at 20 mm/s and rotation speed of 100 frames/s, using a non-occlusive technique. Cross-sectional OCT images were analyzed at 1-mm intervals (every 5 frames).

Our definition of optimal stent expansion referred to the MUSIC criteria which outlines intravascular ultrasound criteria of optimal stent expansion. In brief, the criteria are as follows: in-stent minimum lumen area ≥ 90% of the average reference lumen area, symmetric stent expansion defined by minimum lumen diameter/maximum lumen diameter ≥ 0.7 [19]. Strut apposition was considered significant when the distance between strut and vessel wall was greater than

200 µm and had the length ≥ 600 µm in the first-generation drug-eluting stents with thick struts > 140 µm) and thick polymer 13–22 µm) [20]. Tissue prolapse was defined as the distance from the stent strut to the greatest extent of protrusion ≥ 100 µm [21]. Edge dissection was defined as disruption of the lumen vessel surface in within 5 mm of the stent edge. OCT guidance was used to determine the need of further balloon dilatation for sub-optimal stent expansion and/or significant malapposition and tissue prolapse, and further stent implantation was implemented in cases of edge dissections extending beyond 200 µm [22].

Finally, in view of these OCT indicators, we defined the optimal acute result of PCI by angiographic findings of TIMI grade 3.

Quantitative measurements of OCT images were performed offline throughout the length of the stent by an independent investigator blinded to patient and procedural information using specific software for analysis (LightLab Imaging, Westford, MA, USA).

For serial comparison, cross-sectional OCT images were analyzed at 2 and 12 weeks after stent implantation. A total of 1446 cross-sectional images which depicted 15,803 stent struts had good image quality for analysis. Stent and lumen contours were semi-automatically outlined, and stent and luminal cross-sectional areas CSA), neointimal hyperplasia NIH) thickness, NIC and apposition of the stent struts were evaluated for the entire circumference of the vessel (Fig. 3). Quantitative analysis was performed in each individual strut along the entire stented segment. A fully covered stent strut was defined as complete coverage of the stent strut on the luminal side by visible neointima, with thickness greater than 10 µm which is the limit of current axial resolution of the available OCT system. This means that neointimal thickness has to be at least 10 µm to be detected by the OCT [23]. Thus, struts were graded as covered > 10 µm tissue thickness) or uncovered < 10 µm thickness). NIH thickness was manually perpendicularly calculated as the luminal surface of NIH minus the outer edge of stent strut. Mean values were reported in this study. Images of every frame were evaluated to detect the presence of thrombi in the vessel lumen. Intracoronary thrombi were identified as any unusual mass protruding beyond the stent struts into the lumen with signal-free shadowing or signal attenuation [24]. Strut malapposition was defined as separation of the stent strut surface from the inner vessel wall by a distance greater than 100 µm in EES [25, 26] instead of 200 µm [20] in this study. The reason was that CoCr EES with thin polymer thickness (4 µm) and CoCr BMS were same platform with a thin strut thickness of 81 µm. The malapposition rate was calculated as the number of malapposed struts divided by total number of struts in each series. These analyzes of cross-sectional area were excluded when they included bifurcations, which could not be distinguished by OCT images.

Statistical analysis

All calculated data are expressed as the mean ± SD. One-way repeated analysis of variance, which was subsequently subjected to a post-hoc analysis (Scheffe's test) for multiple comparisons, was used to determine the statistical significance of differences. Chi-squared test was used for analyzing categorical variables with percentages. Statistical analysis was conducted with a commercially available statistical software program (StatView Version 5.0; Abacus Concepts, Berkeley, CA, USA). Statistical significance was accepted at $p < 0.05$.

Results

Baseline characteristics

Sixty-three patients were enrolled to receive either EES ($n = 42$) or CoCr BMS ($n = 21$). Door-to-balloon time and left ventricular ejection fraction did not differ between both groups (Table 1). Baseline patient and angiographic characteristics, medication, procedural and lesion characteristics were also comparable between both groups (Tables 1, 2).

Serial change of OCT findings

A total of 63 stented lesions could be evaluated by OCT without any serious complications. The typical OCT images just after, and at 2 and 12 weeks after PCI are shown in Fig. 4, respectively. OCT data just after PCI are summarized in Table 3 and serial change of OCT data were also shown in Supplementary Tables one and two. Outcome of OCT data at 2 and 12 weeks after PCI are summarized in Tables 4 and 5, respectively. NIC of the stent struts at 2 weeks after PCI were 23.2% and 24.0% in EES and BMS groups, respectively ($p = 0.61$, Table 4), and 99.3% (EES) and 97.8% (BMS) at 12 weeks after PCI ($p = 0.28$, Table 5). Thicknesses of the neointima was significantly thinner in EES than in BMS at 2 and 12 weeks after PCI (2 weeks: 34.0 ± 13.8 µm vs. 40.0 ± 14.6 µm, $p = 0.011$, Table 4, 12 weeks: 107.0 ± 32.4 µm vs. 115.7 ± 33.8 µm, $p = 0.008$, Table 5. Malapposition was 8.4% and 10.0% just after PCI in the EES and BMS groups, respectively ($p = 0.18$, Table 3), and was not observed at 12 weeks after PCI in both groups (Table 5). Thrombus was significantly less in EES (19.0%) than in BMS (42.9%) at 2 weeks after PCI ($p = 0.006$, Table 4, and reduced over time in both groups, but only completely disappeared at 12 weeks in the EES group (EES: 0% vs. BMS: 4.8%, $p = 0.56$, Table 5. Stent edge dissections were 19.0% and 23.8% in EES and BMS just after PCI,

Table 1 Baseline patient characteristics in the CoCR EES and CoCr BMS groups

	CoCr EES ($N = 42$)	CoCr BMS ($N = 21$)	p value
Age, year	65.2 ± 6.9	66.2 ± 7.3	0.576
Male	29 (69.0%)	15 (71.4%)	0.353
Body Mass Index (kg/m^2)	24.4 ± 5.3	24.8 ± 6.2	0.689
Hypertension (%)	30 (71.4%)	14 (66.7%)	0.276
Hyperlipidemia (%)	22 (53.7%)	12 (57.1%)	0.320
Diabetes mellitus (%)	19 (45.2%)	8 (38.1%)	0.101
Estimated glomerular filtration rate (eGFR) < 60 (%)	14 (33.3%)	8 (38.1%)	0.201
Current smoker (%)	17 (40.4%)	8 (38.0%)	0.430
Ejection fraction (%)	45.9 ± 9.4	48.0 ± 7.8	0.149
Door-to-balloon time (min)	80.3 ± 9.7	83.8 ± 8.8	0.185
The medications just before PCI			
ACEI/ARB (*n*)	28 (66.7%)	13 (62.0%)	0.217
Calcium channel blockers (*n*)	14 (33.3%)	8 (38.1%)	0.307
Beta blockers (*n*)	8 (19.0%)	5 (23.8%)	0.226
Statins (*n*)	17 (40.4%)	9 (42.9%)	0.579
Nicolandil (*n*)	5 (11.9%)	2 (9.5%)	0.336
DAPT (*n*)	42 (100%)	21 (100%)	1.000

Data are expressed as numbers (%) or mean ± SD

AP angina pectoris, *OMI* old myocardial infarction, *ACEI* angiotensin-converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *DAPT* dual antiplatelet therapy

Table 2 Lesion characteristics in the CoCR EES and CoCr BMS groups

	CoCr EES ($N = 42$)	CoCr BMS ($N = 21$)	p value
Target lesion			
LMT	0	0	1.000
LAD	18 (42.9%)	10 (47.6%)	0.239
LCX	8 (19.0%)	3 (14.3%)	0.215
RCA	16 (38.0%)	8 (38.1%)	0.902
Multi vessel disease			
Two-vessel disease	20 (47.6%)	13 (61.9%)	0.120
Three-vessel disease	22 (52.4%)	8 (38.1%)	0.107
ACC/AHA lesion types (*n*)			
A/B1	17 (40.4%)	9 (42.9%)	0.457
B2/C	25 (59.5%)	12 (57.1%)	0.436
Mean reference diameter (mm)	2.97 ± 0.27	3.01 ± 0.30	0.786
Lesion length (mm)	21.80 ± 8.24	20.90 ± 6.03	0.272
Minimum lumen diameter (mm)	0.08 ± 0.10	0.07 ± 0.09	0.710
Percent stenosis diameter (%)	98.10 ± 9.30	97.40 ± 9.30	0.675
Number of stents implanted per patient	1.10 ± 0.16	1.05 ± 0.18	0.496
Stent diameter (mm)	3.13 ± 0.23	3.11 ± 0.25	0.305
Stent length (mm)	22.88 ± 7.37	22.43 ± 9.30	0.197
Maximum inflation pressure (atm)	16.0 ± 1.8	15.8 ± 1.9	0.695

Data are expressed as numbers (%) or mean ± SD

RCA right coronary artery, *LAD* left anterior descending artery, *LCx* left circumflex artery, *ACC/AHA* American College of Cardiology/American Heart Association

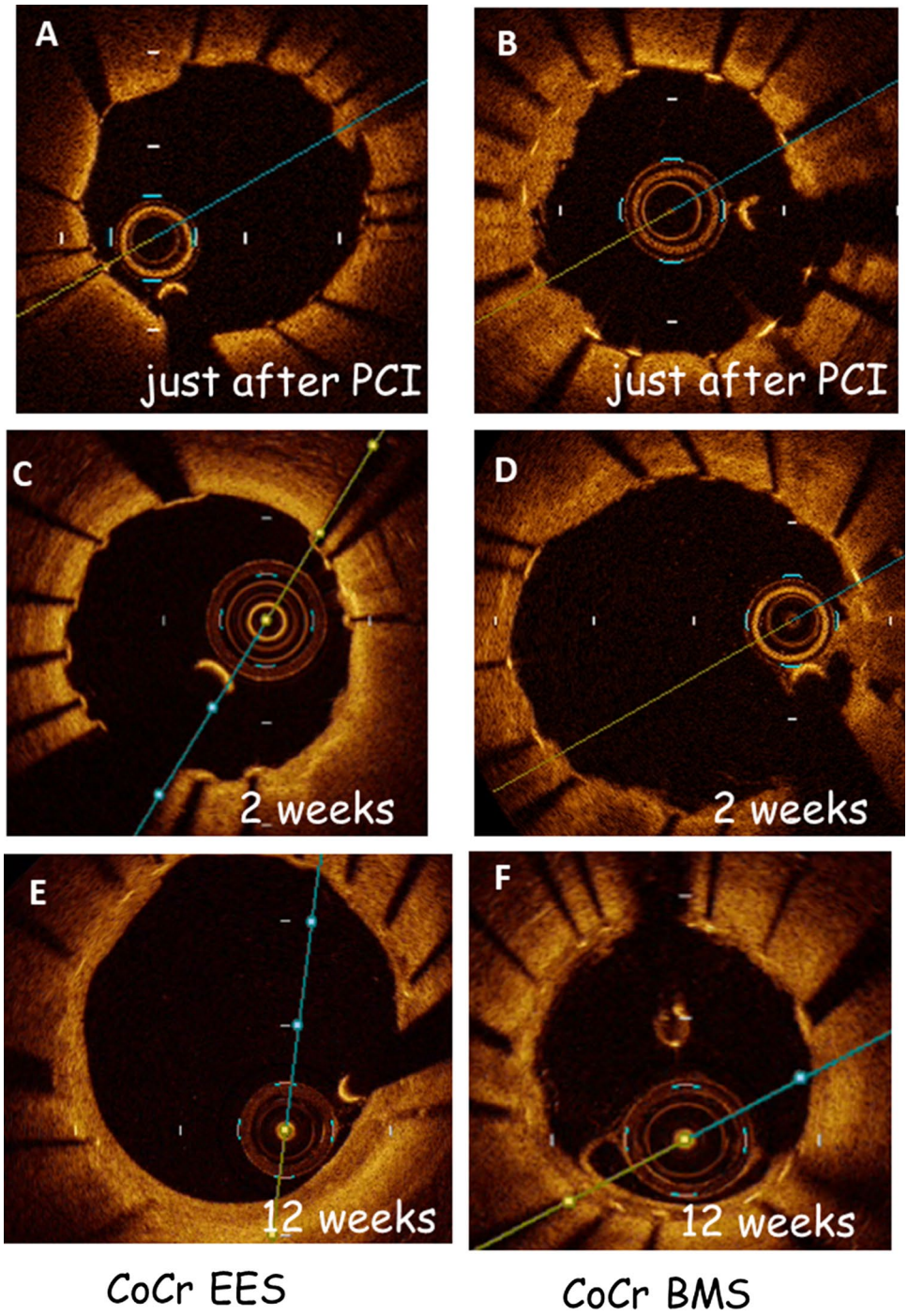


Fig. 4 Representative serial optical coherence tomography images. A: Just after CoCr EES implantation. B: Just after CoCr BMS implantation. The greater amount of thrombus was observed on the vessel lumen surface just after intervention in the CoCr BMS than in CoCr EES. C: 2 weeks after CoCr EES implantation, a few stent struts were covered with the neointima. D: 2 weeks after CoCr BMS implantation, four-fifth of its struts were covered with the thinner neointima. E: 12 weeks after CoCr EES implantation, its struts were almost completely covered with the high-signal neointima. F: 12 weeks after CoCr EES implantation, its struts were almost completely covered with the high-signal neointima

Table 3 Optical coherence tomography findings just after PCI in the CoCR EES and CoCr BMS groups

	CoCr EES ($N = 42$)	CoCr BMS ($N = 21$)	p value
Lumen area (mm^2)	7.9 ± 1.8	7.5 ± 1.7	0.578
Malapposition at post-PCI (%)	8.4 ± 2.5	10.0 ± 2.2	0.175
Stent edge dissection	8 (19.0%)	5 (23.8%)	0.128
Presence of thrombus	39 (92.8%)	19 (90.4%)	0.662

Table 4 Outcomes of optical coherence tomography 2 weeks after PCI in the CoCR EES and CoCr BMS groups

	2 weeks after implantation of CoCr EES or BMS		
	CoCr EES $N = 42$	CoCr BMS $N = 21$	p value
Follow-up OCT			
Lumen area (mm^2)	7.1 ± 1.3	6.7 ± 1.2	0.410
Neointimal thickness (μm)	34.0 ± 13.8	40.0 ± 14.6	0.011
Well-apposed stent struts			
With neointimal formation (%)	23.2 ± 8.0	24.0 ± 6.8	0.612
Without neointimal formation (%)	76.9 ± 7.0	75.8 ± 6.4	0.471
Malapposed stent struts			
With neointimal formation (%)	0.1 ± 0.2	0.2 ± 0.1	0.878
Without neointimal formation (%)	1.2 ± 0.6	1.0 ± 0.3	0.799
Stent edge dissection	1 (2.3%)	1 (4.8%)	0.276
Presence of thrombus	8 (19.0%)	9 (42.9%)	< 0.001

Table 5 Outcomes of optical coherence tomography 12 weeks after PCI in the CoCR EES and CoCr BMS groups

	12 weeks after implantation of CoCr EES or BMS		
	CoCr EES $N = 42$	CoCr BMS $N = 21$	p value
Follow-up OCT			
Lumen area (mm^2)	6.6 ± 1.9	6.7 ± 1.5	0.531
Neointimal thickness (μm)	107.0 ± 32.4	40.0 ± 14.6	0.008
Well-apposed stent struts			
With neointimal formation (%)	99.4 ± 0.6	97.8 ± 0.5	0.283
Without neointimal formation (%)	0.7 ± 0.4	2.2 ± 0.4	0.141
Malapposed stent struts			
With neointimal formation (%)	0	0	0.878
Without neointimal formation (%)	0	0	0.432
Stent edge dissection	0	0	1.000
Presence of thrombus	0 (0%)	1 (4.8%)	0.558

respectively (Table 3). However, these were completely resolved at 12 weeks after PCI (Table 5). Moreover, other relevant findings of OCT were also shown in Supplementary Tables 3 and 4.

Clinical outcomes

No major adverse cardiac events such as target vessel revascularization, cardiac death, nonfatal myocardial infarction and ST were observed for 12 weeks after primary PCI (Table 6).

Discussion

To our knowledge, there is no report comparing the process of vascular healing between CoCr EES and CoCr BMS at 2 and 4 weeks after PCI in STEMI patients by use of OCT. This study shows that the stent struts were rapidly covered by neointima from 2 to 12 weeks EES: 76.0% vs. BMS: 73.8%) and almost completely covered within 12 weeks in both groups. The stent struts were also completely apposed within 12 weeks in both groups. Interestingly, thrombus was more frequently observed in BMS than in EES at 2 weeks after PCI, but disappeared in both groups 12 weeks after PCI. Previously, we reported that NIC of stent struts was almost completed at 12 weeks after XIENCE stent implantation in 35 patients who received elective PCI for stable coronary disease [15]. Although the present and previous studies included different patient characters, those studies had similar results.

On the other hand, with first-generation DES such as sirolimus-eluting stent, it has been reported that, at 2 years after implantation, uncovered struts were observed in 3.2% [27] or 6.5% [28, 29] and in-stent thrombus was seen in almost 30% [1, 30] by OCT. In addition, a comparative OCT study between first-generation and second-generation DES showed similar suppression of the NIH, while uncovered and malapposed struts significantly improved in the second-generation DES compared with the first-generation DES 2 months after implantation [31]. Furthermore, the ENDEAVOR OCT study showed that NIC and apposition were almost complete at 3 months after implantation of the zotarolimus-eluting second-generation DES. This favorable vascular response might be a result of rapid drug-elution and a biocompatible polymer [32]. The progression of restenosis has been shown to have different mechanisms between DES and BMS. In BMS, neointimal hyperplasia is greatest at 6 months, and lumen enlargement occurs from 6 months to 3 years after implantation [33]. In contrast, first-generation DES exhibited a potent antiproliferative effect of the neointimal hyperplasia for a few months. In the J-Cypher registry which evaluated the real-world outcomes of the first-generation sirolimus-eluting stent SES), the target lesion revascularization rate was 5.5% at 1 year, 8.1% at 2 years, and 10% at 3 years after

Table 6 Incidence of MACE 2 and 12 weeks after PCI in the CoCR EES and CoCr BMS groups

	2 weeks			12 weeks		
	CoCr BMS	CoCr BMS	*p* value	CoCr BMS	CoCr BMS	*p* value
MACE	0 (0%)	0 (0%)	1.00	0 (0%)	0 (0%)	1.00
TLR	0 (0%)	0(0%)	1.00	0 (0%)	0 (0%)	1.00
TVR	0 (0%)	0 (0%)	1.00	0 (0%)	0 (0%)	1.00
Stent thrombosis	0 (0%)	0 (0%)	1.00	0 (0%)	0 (0%)	1.00
MI	0 (0%)	0 (0%)	1.00	0 (0%)	0 (0%)	1.00
Cardiac death	0 (0%)	0 (0%)	1.00	0 (0%)	0 (0%)	1.00

SES implantation [34]. In contrast, EES has not shown such an increasing rate of revascularization—the so-called "late catch-up phenomenon"—over 5-years of follow-up [35]. Thus, the target lesion revascularization rate may be lower with EES compared to BMS for several years even in patients with STEMI. In fact, we have reported that EES was associated with improved outcomes—specifically, significant reductions in target lesion revascularization and ST—compared with BMS out to 2 years [36].

Although ST occurs infrequently, it remains catastrophic and associated with high mortality [37]. ST might be induced by the coronary slow flow, delayed healing, stent malapposition and underexpansion, small-stent diameter, long length, dissection, and failure to inhibit platelet adhesion and aggregation [38, 39]. Moreover, it has been suggested that acute coronary syndrome is an independent predictor of ST [40]. Although ST is not necessarily related to the stent malapposition, the coronary vasospasm frequently occurred, and it triggered acute coronary occlusion after PCI in patient with acute myocardial infarction. This tends to cause the stent malapposition in the chronic phase. However, the fluorinated copolymer coating used on the XIENCE stent has been shown to be highly biocompatible, thromboresistant, and haemocompatible [41]. Thus, the late-acquired malapposition might occur less.

Histopathology of human autopsy has demonstrated that delayed healing defined as incomplete NIC strongly correlates with LST after DES implantation [42]. However, this phenomenon has not been observed in BMS [43]. Therefore, NIC of struts after stent implantation may play a protective role against LST and might be an important parameter in determining the optimal duration of DAPT [7, 14]. Recently, a number of second-generation DESs have been approved to include information on DAPT discontinuation at 1 or 3 months after PCI in their IFUs. Furthermore, based on clinical evidence from second-generation DES including XIENCE, the ACC/AHA guidelines regarding DAPT were updated in March 2016 with a Class IIb recommendation that DAPT discontinuation after 3 months may be reasonable in patients with stable ischemic heart disease with high bleeding risk [44]. This study might support the possibility for shorter DAPT durations with the XIENCE stent even in patients with STEMI, since the stent struts were almost completely covered by the neointima and apposed at 3 months after implantation. Otsuki et al. also reported that an apposition area was not observed in the OCT image at 6-, 9- and 12-months after EES implantation, respectively [45].

This favorable NIC may be induced by the XIENCE stent platform, the biocompatible polymer, the anti-proliferative drug, and a thin strut 81 μm) configuration which may result in less vascular injury during stent implantation and may accelerate re-endothelialization [24, 46]. Furthermore, it has been demonstrated that re-endothelialization of the XIENCE stent is faster than other DESs in a rabbit iliac artery model [13].

Study limitations

There are potential limitations to our data. First, the participating Institutions were limited to only two centers and patients were non-randomly and retrospectively selected, so selection bias may have influenced our results. Second, the number of enrolled patients was small; however, more than 15,000 stent struts were evaluated for NIH, NIC, and malapposition. Third, the evaluation of NIH quality might be important to better understand LST, but the present study cannot clarify this as current OCT technology haslimitations in its ability to differentiate between fibrin or microthrombi and healthy neointima. Fourth, it is difficult to precisely distinguish the border between fibrin and neointima. Finally, LST after DES is not always related to lack of stent coverage, vessel remodeling, and in-stent thrombus. Other mechanisms might be implicated such as in-stent or in-segment plaque rupture and occlusive restenosis with neoatherosclerosis.

Conclusion

This study demonstrated that near-complete NIC and apposition of stent struts were achieved at 12 weeks after EES stent implantation. Thrombus was less frequently observed in EES than in BMS at 2 weeks after PCI in patients with

STEMI, which may explain lower rates of acute and subacute ST of EES compared with BMS.

Compliance with ethical standards

Conflict of interest The authors indicated no potential conflicts of interest.

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