Thrombogenicity of Platinum–Chromium Everolimus-Eluting Stent Is Comparably Low to That of Cobalt–Chromium Everolimus-Eluting Stent in the Subacute Phase of Acute Myocardial Infarction

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Background: Population science has shown similar outcomes between cobalt–chromium everolimus-eluting stent (CoCr-EES) and platinum–chromium everolimus-eluting stent (PtCr-EES). However, subclinical intracoronary thrombus following implantation of CoCr-EES or PtCr-EES in acute myocardial infarction (AMI) has not been explored.

Methods: We performed coronary angioscopy (CAS) 13 ± 2 days after stent implantation: 47 stents in 46 lesions from 42 patients with AMI (male 90%, mean age 64 ± 13 years). The degree of thrombus adhesion and yellow plaque severity were compared between CoCr-EES (26 stents from 22 patients) and PtCr-EES (21 stents from 20 patients). The degree of thrombus adhesion was graded: grade 0 (none), no thrombus; grade 1 (focal), several spotty thrombi; grade 2 (diffuse), thrombus extending between the struts. Yellow plaque severity was graded: grade 0, white; grade 1, light yellow; grade 2, yellow; grade 3, intensive yellow.

Results: Thrombus grade was similar (CoCr-EES: grade 0, 4%; grade 1, 50%; grade 2, 46%; PtCr-EES: grade 0, 19%; grade 1, 38%; grade 2, 43%, P = 0.46). Yellows plaque grade was also similar between CoCr-EES (grade 0, 0%; grade 1, 23%; grade 2, 19%; grade 3, 58%) and PtCr-EES (grade 0, 0%; grade 1, 19%; grade 2, 29%; grade 3, 52%, P = 0.88).

Conclusions: Extent of subclinical intracoronary thrombus was comparable between CoCr-EES and PtCr-EES in the subacute phase of AMI, associated with equally severe yellow plaque lesions. Thrombogenicity of PtCr-EES may be similarly low to that of CoCr-EES in patients with AMI.

Key words: acute myocardial infarction, angioscopy, cobalt–chromium everolimus-eluting stent, platinum–chromium everolimus-eluting stent

Introduction

Population science has shown similar outcomes between the cobalt–chromium everolimus-eluting stent (CoCr-EES, Abbott Park, Abbott Vascular, IL, USA) and the platinum–chromium everolimus-eluting stent (PtCr-EES, Boston Scientific, Natick, MA, USA) in patients with stable and unstable angina pectoris.1 Based on these outcomes, CoCr-EES and PtCr-EES have often been used in the clinical setting.2 CoCr-EES has demonstrated a lower rate of early stent thrombosis compared to bare-metal stents (BMS) in patients with acute myocardial infarction (AMI).3 However, intracoronary status following the implantation these stents in the subacute phase of AMI has not been explored.

Coronary angioscopy (CAS) can evaluate macroscopic intravascular status in full color and the detection power of thrombus is better than with the other imaging devices.4 Therefore, we compared the degree of subclinical intracoronary thrombus between CoCr-EES and PtCr-EES in the subacute phase in patients with AMI using CAS.
Methods

Patients
This study examined 47 second-generation drug-eluting stents (DES) placed in 42 patients (age 64 ± 13 years, male 90%) presenting with AMI due to de novo lesions in native coronary arteries from November 2013 to January 2016. The patients who received staged percutaneous coronary intervention or follow-up coronary angiography 2 weeks after the initial percutaneous coronary intervention were included in this study. Patients received follow-up CAS as well as angiography 13 ± 2 days after stent implantation and were divided into two groups based on DES type: 26 CoCr-EESs in 22 patients and 21 PtCr-EESs in 20 patients. All patients received clopidogrel (75 mg/day) or prasugrel (3.75 mg/day) (in addition to aspirin (100 mg/day) during follow-up. Glycoprotein IIb/IIIa inhibitors were not used as they are not approved for stable angina pectoris in Japan. The Medical Ethics Committee of Kansai Rosai Hospital approved the study, and all patients provided written informed consent.

Angiographic and angioscopic follow-up
Coronary angiography was performed after administration of unfractionated heparin (5000 IU) into the radial or femoral artery via the inserted sheath and of isosorbide dinitrate (2.5 mg) into the coronary artery. Angioscopy was subsequently performed using a Fullview NEO angioscope catheter (FiberTech, Tokyo, Japan), the detailed specifications and usage of which have been previously described.\(^5\)\(^,\)\(^6\) Briefly, the optical fiber was placed at the distal segment of the coronary artery and was manually pulled back from the distal edge of the stent to the proximal edge under careful angioscopic and angiographic guidance. Angioscopic images consisted of 3000 pixels with full color and were digitally stored for offline analysis.

Angioscopic analysis
Angioscopic images were analyzed to determine the following: (1) degree of thrombus adhesion and (2) yellow plaque severity. Thrombus was defined based on the criteria adopted by the European Working Group on Coronary Angioscopy.\(^7\) Moreover, the degree of thrombus adhesion was graded: grade 0 (none), no thrombus; grade 1 (focal), several spotty thrombi; grade 2 (diffuse), thrombus extending between the struts (Fig. 1). Yellow plaque severity was graded: grade 0, white; grade 1, light yellow; grade 2, yellow; grade 3, intensive yellow.\(^8\) The estimated inter- and intra-observer \(\kappa\) coefficient for evaluating the degree of thrombus adhesion were 0.86 and 0.89, respectively.

Statistical analysis
All results are expressed as mean ± SD unless otherwise stated. Continuous variables with and without homogeneity of variance were analyzed by Student’s t-test and Welch t-test, respectively. Categorical variables were analyzed with Fisher’s exact test for 2×2 comparisons. For more than 2×2 comparisons, the Mann–Whitney test was used. Statistical significance was defined as \(P<0.05\). All calculations were performed using IBM SPSS Statistics Version 20 (IBM Corp., Armonk, NY, USA).

Results
Patients
Patient characteristics were comparable among CoCr-EES and PtCr-EES groups except for frequency of diabetes mellitus (Table 1). Medication use at the time of CAS follow-up was similar between CoCr-EES and PtCr-EES (Table 2). Laboratory data were not significantly different between CoCr-EES and PtCr-EES (Table 3). Lesion and procedural characteristics are shown in Table 4. There were no
### Table 1 Patients’ characteristics

|                | CoCr-EES | PtCr-EES | P value |
|----------------|----------|----------|---------|
| No. of patients| 22       | 20       |         |
| Age, years     | 63 ± 13  | 67 ± 12  | 0.30    |
| Male, n (%)    | 21 (96)  | 17 (85)  | 0.27    |
| Prior PCI, n (%)| 2 (9)    | 2 (10)   | 0.66    |
| OMI, n (%)     | 2 (9)    | 0 (0)    | 0.27    |
| Multivessel disease, n (%)| 11 (50) | 10 (50) |         |
| Hypertension*, n (%)| 22 (100) | 20 (100) | –       |
| Dyslipidemia*, n (%)| 22 (100) | 20 (100) | –       |
| Diabetes mellitus†, n (%)| 3 (14) | 9 (45) | 0.025   |
| Current smoking, n (%)| 10 (46) | 9 (45) | 0.98    |
| Hemodialysis, n (%)| 0 (0)    | 0 (0)    | –       |

Data are presented as mean ± SD or number (%).

*Receiving antihypertensive medication, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg.

†Treatment with medication, total cholesterol ≥220 mg/dL, low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol ≤40 mg/dL, or triglycerides ≥150 mg/dL.

‡Oral agent or insulin treatment or HbA1c ≥6.5%.

CoCr-EES: cobalt–chromium everolimus-eluting stent; OMI: old myocardial infarction; PCI: percutaneous coronary intervention; PtCr-EES: platinum–chromium everolimus-eluting stent

### Table 2 Medication use

|                | CoCr-EES | PtCr-EES | P value |
|----------------|----------|----------|---------|
| Aspirin, n (%)  | 22 (100) | 20 (100) | –       |
| Ticlopidine, n (%)| 1 (5)    | 0 (0)    | 0.52    |
| Clopidogrel, n (%)| 18 (82)  | 19 (95)  | 0.20    |
| Prasugrel, n (%) | 3 (14)   | 1 (5)    | 0.34    |
| Warfarin, n (%)  | 0 (0)    | 0 (0)    | –       |
| DOAC, n (%)      | 0 (0)    | 1 (5)    | 0.48    |
| ACE inhibitor, n (%)| 16 (73) | 12 (60) | 0.38    |
| ARB, n (%)       | 3 (14)   | 5 (25)   | 0.29    |
| β-blocker, n (%) | 19 (85)  | 12 (60)  | 0.052   |
| Calcium antagonist, n (%)| 3 (14) | 2 (10) | 0.55    |
| Statin, n (%)    | 22 (100) | 18 (90)  | 0.22    |
| Furosemide, n (%)| 2 (9)    | 4 (20)   | 0.29    |
| EPA, n (%)       | 10 (46)  | 8 (40)   | 0.72    |

Data are presented as number (%).

ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; CoCr-EES: cobalt–chromium everolimus-eluting stent; DOAC: direct oral anticoagulant; EPA: eicosapentaenoic acid; PtCr-EES: platinum–chromium everolimus-eluting stent.

### Table 3 Laboratory data

|                | CoCr-EES | PtCr-EES | P value |
|----------------|----------|----------|---------|
| On admission   |          |          |         |
| White blood cell, ×10^9/μL | 10.8 ± 3.4 | 10.8 ± 3.4 | 0.96    |
| Hemoglobin, g/dL | 14.4 ± 1.8 | 14.4 ± 1.9 | 0.98    |
| Platelet, ×10^9/μL  | 233 ± 53  | 252 ± 111 | 0.46    |
| Creatinine, mg/dL | 0.94 ± 0.21 | 0.83 ± 0.20 | 0.11    |
| eGFR, mg/dL      | 63.9 ± 14.0 | 72.9 ± 18.7 | 0.085   |
| Total cholesterol, mg/dL | 187 ± 46  | 205 ± 50  | 0.24    |
| HDL cholesterol, mg/dL | 43 ± 10   | 47 ± 14   | 0.29    |
| LDL cholesterol, mg/dL | 122 ± 38  | 129 ± 36  | 0.55    |
| Triglyceride, mg/dL   | 114 ± 38  | 129 ± 36  | 0.26    |
| HbA1c, %          | 6.0 ± 0.8  | 6.7 ± 1.6  | 0.070   |
| BNP, pg/mL        | 208 ± 296  | 110 ± 148  | 0.19    |
| CRP, mg/dL        | 0.35 ± 0.52 | 1.3 ± 3.6  | 0.25    |
| Maximum CK, U/L   | 2711 ± 2058 | 3201 ± 3477 | 0.58    |
| Maximum CK-MB, U/L| 248 ± 201 | 304 ± 344 | 0.53    |

Data are presented as mean ± SD. BNP: brain natriuretic peptide; CK: creatine phosphokinase; CoCr-EES: cobalt–chromium everolimus-eluting stent; CRP, C-reactive protein; eGFR: estimated glomerular filtration rate; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PtCr-EES: platinum–chromium everolimus-eluting stent.

### Table 4 Lesion and procedural characteristics

|                | CoCr-EES | PtCr-EES | P value |
|----------------|----------|----------|---------|
| Number of lesions| 25       | 21       |         |
| Target vessel, n (%) |         |          | 0.23    |
| LAD            | 11 (44)  | 12 (57)  |         |
| LCX            | 3 (12)   | 0 (0)    |         |
| RCA            | 11 (44)  | 9 (43)   |         |
| Type B2/C*, n (%)| 21 (84)  | 20 (95)  | 0.23    |
| Bifurcation, n (%) | 7 (28)  | 9 (43)   | 0.29    |
| Number of stents| 26       | 21       |         |
| Follow-up duration, days | 13 ± 2  | 13 ± 2   | 0.17    |
| Distal protection, n (%) | 13 (50) | 7 (33)   | 0.25    |
| Aspiration, n (%) | 22 (85)  | 20 (95)  | 0.25    |
| Pre-dilatation, n (%) | 6 (23)  | 10 (48)  | 0.078   |
| Pre-dilatation balloon diameter, mm | 2.6 ± 0.5 | 2.6 ± 0.4 | 0.75   |
| Pre-dilatation balloon pressure, atm | 10 ± 4  | 11 ± 3   | 0.60    |
| Stent diameter, mm | 3.3 ± 0.4 | 3.2 ± 0.4 | 0.55    |
| Stent length, mm | 23 ± 10  | 27 ± 9   | 0.11    |
| Stent pressure, atm | 11 ± 3   | 10 ± 1   | 0.41    |
| Post-dilatation, n (%) | 17 (65) | 14 (67)  | 0.93    |
| Post-dilatation balloon diameter, mm | 3.5 ± 0.6 | 3.1 ± 0.9 | 0.22   |
| Post-dilatation balloon pressure, atm | 16 ± 3  | 14 ± 5   | 0.25    |

Data are presented as mean ± SD or n (%). *Based on the American College of Cardiology/American Heart Association Classification. CoCr-EES: cobalt–chromium everolimus-eluting stent; PtCr-EES: platinum–chromium everolimus-eluting stent.

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**Thrombogenicity of PtCr-EES Versus CoCr-EES**

During the post-dilatation, the number of thrombus grade 2 and 3 was similarly distributed between the two groups (Fig. 3). Thrombus grade was similarly distributed between CoCr-EES and PtCr-EES groups (Fig. 2). Yellow plaque grade 2 and 3 was also similar between the two groups (Fig. 3). Representative cases are shown in Figs. 4 and 5.

**Angioscopic findings**

Thrombus grade was similarly distributed between CoCr-EES and PtCr-EES groups (Fig. 2). Yellow plaque grade was also similar between the two groups (Fig. 3). Representative cases are shown in Figs. 4 and 5.
Fig. 2 Distribution of Thrombus Grade. Fifty percent of CoCr-EES demonstrated grade 1 thrombus; most of remaining stents showed grade 2. Forty-three percent of PtCr-EES demonstrated grade 2 thrombus; while 38% and 19% of PtCr-EES showed grade 1 and grade 0, respectively. There were no significant differences between CoCr-EES and PtCr-EES (P = 0.46 by Mann–Whitney test).

CoCr-EES: cobalt–chromium everolimus-eluting stents; PtCr-EES: platinum–chromium everolimus-eluting stents.

Fig. 3 Distribution of Yellow Plaque Grade. Yellow Plaque grade was scored as grade 3 in 58% of CoCr-EES and 52% of PtCr-EES. There were no significant differences between CoCr-EES and PtCr-EES groups (P = 0.88, Mann–Whitney test).

CoCr-EES: cobalt–chromium everolimus-eluting stents; PtCr-EES: platinum–chromium everolimus-eluting stents.

Fig. 4 A representative case of AMI with cobalt–chromium everolimus-eluting stent implantation. (A) Initial coronary angiography of left anterior descending artery. Angiography shows subtotal occlusion with filling defect in the mid part of left anterior descending artery (red arrows). (B) Final coronary angiography just after percutaneous coronary intervention. Percutaneous coronary intervention was performed with thrombus aspiration and CoCr-EES (3.5*28 mm) implantation. (C) Follow-up coronary angiography 2 weeks after stent implantation. Angiography shows the patency of the CoCr-EES implantation site. (D) CAS images of CoCr-EES implantation site. Angioscopy demonstrates focal thrombi and intensive yellow plaques from the proximal to distal stented segment (a–c).

AMI: acute myocardial infarction; CAS: coronary angioscopy; CoCr-EES: cobalt–chromium everolimus-eluting stents; Dotted red line: CoCr-EES (3.5*28 mm) implantation site; GW: guidewire.
Thrombogenicity of PtCr-EES Versus CoCr-EES

Discussion

In this study, we demonstrate that (1) thrombus grade was similar between CoCr-EES and PtCr-EES in the subacute phase of AMI and (2) yellow plaque grade was also similar between CoCr-EES and PtCr-EES.

The components of CoCr-EES and PtCr-EES were similar regarding drug and polymer; furthermore, strut thickness and width were comparable in spite of the difference of the material in the stent struts. However, to the best of our knowledge, there has been no published data regarding the difference of thrombogenicity between cobalt–chromium and platinum–chromium. It is suggested that thrombogenicity of CoCr-EES and PtCr-EES may be similar because thrombus grades in the subacute phase of AMI were similar in our study.

It has previously been reported that thrombogenicity of CoCr-EES was lower than that of BMS, which was thought to be due to an anti-thrombotic effect of fluoropolymer. In this study, the degree of thrombus seen with PtCr-EES was similar to that of CoCr-EES and thus the anti-thrombotic effect of PtCr-EES may be mainly caused by fluoropolymer.

CoCr-EES demonstrated a lower incidence of early stent thrombosis than BMS for AMI patients. Previous CAS studies showed that the incidence of thrombus adhesion of yellow color was higher at the stent implantation site compared to that of white color, and the rate of thrombus adhesion increased as yellow color grade became more severe. PtCr-EES can be safely and effectively used for patients with AMI similar to CoCr-EES because it showed similar degree of thrombus adhesion to the lesion of similar yellow plaque grade.

Limitations

This study has several limitations. First, this was a single-center, non-randomized, observational study with a small sample size. Second, CAS cannot evaluate the entire stented segment. Third, the frequency of diabetes mellitus was different between CoCr-EES and PtCr-EES. Although no report to date has shown a relationship between diabetes mellitus and early stent thrombosis, there is a possibility that the difference impacted on the angiographic findings. However, we could not adjust the patient background due to the limited sample size in this observational study. Finally, a relationship between degree of thrombus and future adverse clinical events was not clear for this study, and further investigation is necessary.
Conclusions

Extent of subclinical intracoronary thrombus was comparable between CoCr-EES and PtCr-EES in the subacute phase of AMI, associated with equally severe yellow plaque lesions. Thrombogenicity of PtCr-EES may be similarly low to that of CoCr-EES in patients with AMI.

Disclosure Statement

There is no conflict of interest.

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