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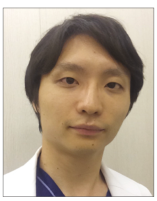
Impact of target lesion coronary calcium score on outcomes following drug-eluting stent implantation



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KEYWORDS

- calcified stenosis
- drug-eluting stent
- multislice computed tomography (MSCT)
- non-invasive imaging

Abstract

Aims: The aim of this study was to evaluate the impact of computed tomography scan-based coronary artery calcium scoring of the target lesion on outcomes following percutaneous coronary intervention using second-generation drug-eluting stents.

Methods and results: We retrospectively investigated 124 consecutive patients who underwent coronary artery calcium scoring prior to cobalt-chromium everolimus-eluting stent implantation. Eight-month clinical and angiographic outcomes were evaluated. Target vessel failure (TVF) was defined as a composite of cardiac death, target vessel myocardial infarction, and target vessel revascularisation. A significant difference in lesion calcium score was observed between patients with and without TVF (median 216.7 vs. 42.8, p=0.025). The area under the receiver operating characteristic curve for prediction using lesion calcium scoring was 0.74 (95% confidence interval [CI]: 0.53-0.94) for TVF. When using a cut-off value of 140, the sensitivity and specificity of the lesion calcium score for predicting TVF were 87.5% and 69.8%, respectively. Among the 103 patients with either no or mild angiographic calcification, 24 patients (23.3%) had a lesion calcium score ≥140 and they were at higher risk for TVF (20.8% vs. 1.3%, p=0.002).

Conclusions: Computed tomography-based detection of coronary artery calcification of the target lesion was associated with poor prognosis after cobalt-chromium everolimus-eluting stent implantation.

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Abbreviations

CAC	coronary artery calcification
CI	confidence interval
CoCr-EES	cobalt-chromium everolimus-eluting stents
CT	computed tomography
DES	drug-eluting stents
MI	myocardial infarction
PCI	percutaneous coronary intervention
QCA	quantitative coronary angiography
ROC	receiver operating characteristic
TLR	target lesion revascularisation
TVF	target vessel failure
TVR	target vessel revascularisation

Introduction

Coronary artery calcification (CAC) of the target lesion has been reported to be a risk factor for adverse events after percutaneous coronary intervention (PCI)[1-6]. Previous studies have evaluated CAC of the target lesion mainly using angiography. However, angiographic detection of CAC is characterised by poor sensitivity, with poor ability to detect small amounts of calcification[7,8], and is not quantitative. Computed tomography (CT) is the only non-invasive test with a high sensitivity and specificity for detection of CAC[9]. Using CT, small amounts of calcification can be detected, with its volume and density being easily quantified. The CT scan-based calcium score, which is calculated from the calcified plaque volume and the maximal calcium lesion density, was developed by Agatston et al[7]. This method has been demonstrated to be useful for evaluating cardiovascular risk[10-13]. Previously, we have reported that a high lesion calcium score was associated with worse outcomes following PCI using first-generation drug-eluting stents (DES)[14]. However, the impact of the target lesion calcium score on outcomes following PCI using second-generation DES is still unknown. The objective of this study was to elucidate the impact of the CT scan-based lesion calcium score on outcomes following PCI using cobalt-chromium everolimus-eluting stents (CoCr-EES).

Methods

The study population consisted of patients who underwent CoCr-EES (XIENCE V®, XIENCE PRIME®, or XIENCE Xpedition®; Abbott Vascular, Santa Clara, CA, USA) implantation to repair coronary lesions at our institution between October 2010 and December 2013. Among patients receiving CoCr-EES, those who also received an alternative stent type to the same lesion were excluded. Data of patients who underwent non-invasive coronary CT as part of a routine diagnostic process within six months before PCI were extracted and analysed. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients. The study was approved by the Medical Ethics Committee of Mitsui Memorial Hospital.

Detailed protocols of the CT scans are described in the **Supplementary Appendix**. All scans were analysed by an experienced cardiologist who was blinded to clinical follow-up data. Calcium scores for the target lesion and the whole coronary tree were calculated. Anatomical landmarks, such as side branches, were used to determine the target lesion on CT scans. The target lesion calcium score of the patients who underwent CoCr-EES implantation for more than two lesions was defined as the maximum lesion calcium score of the treated lesions.

Coronary angioplasty was performed using standard techniques[15,16]. Neither a scoring nor a cutting balloon was used in any of the lesions. Glycoprotein IIb/IIIa inhibitors were not used in any of the patients since they were not commercially available in Japan during the study period. CoCr-EES were available in diameters of 2.25 mm to 3.5 mm. The use of dual antiplatelet therapy was recommended for at least six months. Coronary angiograms obtained before stent implantation, after stent implantation, and eight months after implantation were analysed using a computer-based system (CMS software, version 6.0; Medis medical imaging systems, Leiden, the Netherlands). In-stent, proximal edge, and distal edge segments were analysed. Eight-month clinical outcomes of the study population were obtained from reviews of medical records. Target vessel failure (TVF) was defined as a composite of cardiac death, target vessel myocardial infarction (MI) and target vessel revascularisation (TVR). Definitions of angiographic parameters, angiographic outcomes, and clinical outcomes other than TVF are described in the **Supplementary Appendix**.

STATISTICAL ANALYSIS

Categorical variables are presented as frequency and were compared using Fisher's exact test. Continuous variables are expressed as the mean±standard deviation or median (interquartile range), depending on their distribution, as assessed by visual inspection and Kolmogorov-Smirnov test, and were compared using the Student's t-test or Mann-Whitney U test. The receiver operating characteristic (ROC) curves were constructed to evaluate the discriminating power of the lesion calcium score in predicting adverse events. A cut-off point that maximises the sum of sensitivity and specificity was selected. Univariate logistic regression analyses were used to identify the variables associated with adverse events. Variables with $p<0.10$ in the univariate analyses were included in the multivariate logistic regression analysis to identify the independent predictors for adverse events. Values of $p<0.05$ were considered to be statistically significant, and all p-values were two-sided. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria)[17].

Results

During the study period, 421 patients with 572 *de novo* lesions underwent CoCr-EES implantation. Because of concomitant use of other types of stent, seven patients and 13 lesions were excluded. Among the 414 patients with 559 lesions, 131 patients (31.6%) with 156 lesions (27.9%) had undergone CT CAC scanning within six months before PCI. One patient without clinical follow-up and six patients without appropriate CT data at the time of analysis were excluded. This resulted in 124 patients with 149 lesions being evaluated.

Baseline patient characteristics are listed in **Table 1**. The mean age was 67.9±10.3 years. The median total calcium score was 420.5 (96.0-1,040.2). Baseline lesion and procedural characteristics are shown in **Table 2**. Moderate or severe angiographic calcification was observed in 24 lesions (16.1%). The median lesion calcium score of the overall population was 42.6 (4.8-180.1). The calcium scores of the lesions with angiographically moderate or severe calcification were significantly higher than those of the lesions without (328.2 [194.1-439.3] vs. 29.7 [3.2-111.4], p<0.001). Procedural and clinical success rates were both 100%. **Table 3** presents serial quantitative coronary angiographic data. Angiographic follow-up was performed in 134 lesions (89.9%). The angiographic in-segment binary restenosis rate was 6.7%. An eight-month clinical follow-up was performed for all patients **(Table 4)**. There was no death documented during that period. Myocardial infarction, TLR, and TVF occurred in three, six, and eight patients, respectively.

Table 1. Baseline patient characteristics.

Number of patients		124
Age, years		67.9±10.3
Male		103 (83.1)
BMI		24.1±3.5
Hypertension		96 (77.4)
Dyslipidaemia		112 (90.3)
Diabetes mellitus		52 (41.9)
Current smoker		19 (15.3)
Haemodialysis		8 (6.5)
Previous MI		12 (9.7)
Previous PCI		23 (18.5)
Previous CABG		6 (4.8)
Acute coronary syndrome		10 (8.0)
Multivessel disease		31 (25.0)
Baseline medication	Dual antiplatelet therapy	124 (100)
	Aspirin+clopidogrel	119 (96.0)
	Aspirin+ticlopidine	4 (3.2)
	Aspirin+prasugrel	1 (0.8)
	Statin	119 (96.0)
Total calcium score		420.5 [96.0-1,040.2]

Numbers are reported as n (%), mean±standard deviation, or median [interquartile range]. BMI: body mass index; CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention

Table 2. Baseline lesion and procedural characteristics.

Number of lesions		149
Target vessel	LMCA	4 (2.7)
	LAD	66 (44.3)
	LCX	48 (32.2)
	RCA	31 (20.8)
ACC/AHA classification	A	4 (2.7)
	B1	29 (19.5)
	B2	56 (37.6)
	C	60 (40.3)
Angiographic moderate/severe calcification		24 (16.1)
Bifurcation lesion		51 (34.2)
Average number of stents		1.18±0.44
Average stent diameter, mm		2.98±0.43
Total stent length, mm		25.4±12.6
Balloon-to-artery ratio		1.17±0.20
Maximum stent deployment pressure, atm		13.8±3.5
Rotablator use		3 (2.0)
Post-dilatation		76 (51.0)
Bail-out procedure		2 (1.3)
Lesion calcium score		42.6 [4.8-180.1]
Lesion success		149 (100)

Numbers are reported as n (%), mean±standard deviation, or median [interquartile range]. LAD: left anterior descending; LCX: left circumflex; LMCA: left main coronary artery; RCA: right coronary artery

Table 3. Results of quantitative coronary angiographic analysis.

		Pre (n=149)	Post (n=149)	Follow–up (n=134)
Lesion length, mm		14.3 [9.2–23.2]	–	–
Reference diameter, mm	In–stent	–	3.02±0.48	2.88±0.50
	In–segment	2.69±0.59	2.95±0.58	2.86±0.57
Minimum lumen diameter, mm	In–stent	–	2.67±0.43	2.39±0.58
	In–segment	0.83±0.44	2.30±0.56	2.12±0.63
Diameter stenosis, %	In–stent	–	11.53±5.70	17.13±14.34
	In–segment	69.48±14.66	22.25±9.66	26.42±15.13
Acute gain, mm	In–segment	–	2.11±0.59	–
Late loss, mm	In–stent	–	–	0.26±0.41
	In–segment	–	–	0.18±0.51
Binary restenosis		–	–	9 (6.7)

Numbers are reported as n (%), mean±standard deviation, or median [interquartile range].

Table 4. Eight-month clinical outcomes.

Death	0 (0.0)
Myocardial infarction	3 (2.4)
Stroke	0 (0.0)
TVR	6 (4.8)
TLR	6 (4.8)
Stent thrombosis	1 (0.8)
TVF	8 (6.5)
Numbers are reported as n (%). TLR: target lesion revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation	

As depicted in **Figure 1**, there was a significant difference in the lesion calcium score between lesions and patients with and without adverse events. The ROC curves for the prediction of TLR and TVF are illustrated in **Figure 2**. When using a cut-off value of 140, the sensitivity and specificity of the lesion calcium score for predicting TVF were 87.5% (95% confidence interval [CI]: 47.3-99.7%) and 69.8% (95% CI: 60.6-78.0%), respectively. The positive predictive value was 16.7% (95% CI: 7.0-31.4%), while the negative predictive value was 98.8% (95% CI: 93.4-100%).

The baseline demographics of patients with and without a lesion calcium score ≥140 are shown in **Supplementary Table 1**. The patients with higher lesion calcium scores were significantly older (70.7±7.2 vs. 66.5±11.3, p=0.030). A numerically larger proportion of patients were on haemodialysis in the high lesion calcium score group (11.9% vs. 3.7%, p=0.12). The baseline lesion and procedural characteristics and the results of the quantitative coronary angiography (QCA) categorised by lesion calcium score are shown in **Supplementary Table 2** and **Supplementary Table 3**. The lesions with a higher calcium score were significantly longer (18.8 [9.5-28.2] mm vs. 12.7 [8.8-18.7] mm, p=0.015). The lesions with a higher calcium score had

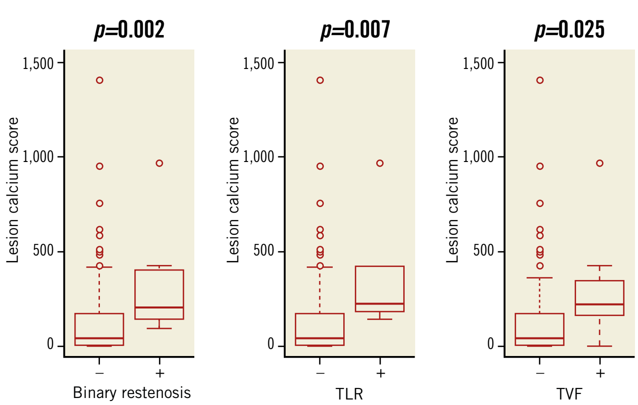

Figure 1. *Comparison of lesion coronary calcium score. There was a significant difference in the lesion calcium score between lesions with and without restenosis (median 202.4 vs. 41.1, p=0.002), patients with and without TLR (median 216.7 vs. 42.8, p=0.007), and patients with and without TVF (median 216.7 vs. 42.8, p=0.025). TLR: target lesion revascularisation; TVF: target vessel failure*

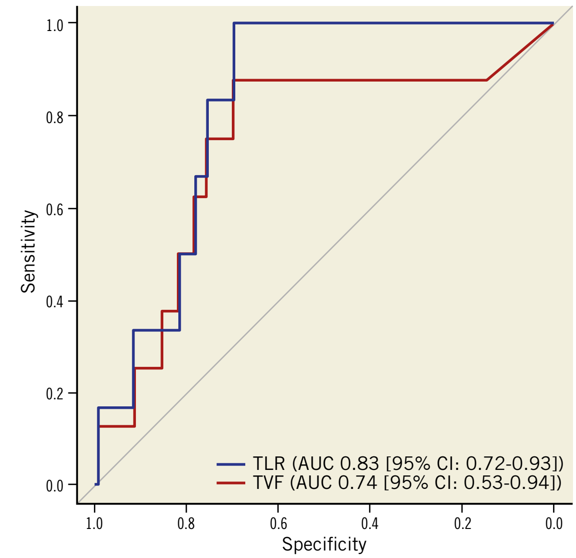

Figure 2. *Receiver operating characteristic curve for prediction of TLR and TVF using lesion calcium score. The AUC for prediction of TLR and TVF using the lesion calcium score was 0.83 (95% CI: 0.72-0.93) and 0.74 (95% CI: 0.53-0.94), respectively. AUC: area under the curve; TLR: target lesion revascularisation; TVF: target vessel failure*

worse angiographic outcomes (in-stent late loss, 0.46±0.62 mm vs. 0.17±0.18 mm, p<0.001; binary restenosis, 18.2% vs. 1.1%, p<0.001). **Supplementary Table 4** shows the eight-month clinical outcomes of the patients categorised by their lesion calcium score. TVF and TLR occurred more frequently in patients with a lesion calcium score ≥140 (TVF, 16.7% vs. 1.3%, p=0.002; TLR, 14.3% vs. 0.0%, p=0.0012). **Table 5** shows the results of the logistic regression analyses for TVF. Four variables (previous MI, previous PCI, previous coronary artery bypass grafting, and acute coronary syndrome at presentation) showed perfect separation and were not suitable for logistic regression analysis for TVF. A separate Fisher's exact test was performed to confirm that there were no significant differences or trends in the prevalence of these variables in patients with and without TVF and these variables were excluded from the multivariate analysis **(Supplementary Table 5)**. Multivariate analysis revealed that a lesion calcium score ≥140 was an independent predictor of TVF (adjusted odds ratio, 9.62; 95% CI: 1.03-90.0).

The baseline patient, lesion, and procedural characteristics and the results of QCA of the patients and lesions with either no or mild angiographic calcification categorised by lesion calcium score are shown in **Supplementary Table 6**, **Supplementary Table 7**, and **Supplementary Table 8**. Notably, among the 103 patients with either no or mild angiographic calcification, 24 lesions (23.3%) had a lesion calcium score ≥140. In this population, the sensitivity and specificity of a lesion calcium score ≥140 for predicting TVF were 83.3% (95% CI: 35.9-99.6%) and 80.4% (95% CI: 71.1-87.8%), respectively. The positive predictive value was 20.8% (95% CI: 7.1-42.2%), while the negative predictive value was

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Table 5. Logistic regression analysis for TVF.

	Univariate			Multivariate		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Lesion calcium score ≥140	16.2	1.92–137.0	0.011	9.62	1.03–90.0	0.047
Age, every 10 years	0.98	0.49–1.97	0.96			
Male sex	0.59	0.11–3.13	0.53			
BMI, every 1.0	0.97	0.78–1.21	0.78			
Hypertension	0.46	0.10–2.05	0.31			
Dyslipidaemia	0.73	0.08–6.52	0.78			
Diabetes mellitus	2.45	0.56–10.7	0.24			
Current smoker	0.78	0.09–6.71	0.82			
Haemodialysis	6.11	1.01–36.9	0.049	3.73	0.49–28.6	0.21
Multivessel disease	0.41	0.048–3.47	0.41			
Statin use	0.25	0.025–2.55	0.24			
Bifurcation lesion	2.63	0.60–11.5	0.20			
LL, every 1.0 mm	1.08	1.02–1.16	0.013	1.05	0.99–1.12	0.13
RD, every 0.5 mm	1.39	0.77–2.51	0.27			
Rotablator use	8.14	0.66–101.0	0.10			

BMI: body mass index; CABG: coronary artery bypass grafting; CI: confidence interval; LL: lesion length; MI: myocardial infarction; PCI: percutaneous coronary intervention; RD: reference diameter; TVF: target vessel failure

98.7% (95% CI: 93.1-100%). Among this population, the patients with a lesion calcium score ≥140 still had a significantly higher rate of TVF compared to the lesions with less calcium (20.8% vs. 1.3%, p=0.002) **(Supplementary Table 9)**.

Discussion

In this retrospective cohort study, the lesion calcium score differed significantly between the patients with and without adverse events. ROC analysis revealed that the lesion calcium score is predictive of adverse events following CoCr-EES implantation. A calcium score of more than 140 was an independent predictor of adverse events.

The presence of CAC has been reported to be associated with adverse events during the balloon angioplasty, bare metal stent, and first-generation DES era[1-4,18]. The introduction of second-generation DES successfully reduced the rate of adverse events compared with bare metal stents and first-generation DES[19-21]; however, calcified lesions remained a challenge. *Post hoc* analyses of several trials had shown that CAC is a risk factor for adverse events after second-generation stent implantation[5,6]. Our study confirmed this result using a different modality for CAC detection.

Several methods for evaluating lesion CAC have been used in previous studies, with angiographic evaluation being used most frequently. Only the original diagnostic invasive coronary angiography is required for evaluation and there is no need for additional radiation exposure. However, since the sensitivity for detecting CAC is low, a small amount and low density of CAC is difficult to detect[7,8]. In the present study, a number of patients with either no or mild angiographic calcification had lesion calcium scores greater than 140, and they were at high risk for adverse events. This suggests that coronary angiography alone is not enough to detect the amount and density of calcium that has a negative impact on outcomes following PCI. Notably, patients with a lesion calcium score <140 had only one TVF event with no TLR, which was considerably lower compared with previous studies evaluating the efficacy of CoCr-EES in general[22,23]. This also indicates the usefulness of CT for detection of lesion CAC that affects the outcomes following PCI.

CT is the only non-invasive test for CAC detection that is highly accurate[11]. The calcium score of the target lesion can be calculated easily using dedicated software[9]. Our data indicate that the evaluation of CAC using CT is useful for determining patients and lesions with a poor prognosis. Yet, it is not cost-effective to perform CAC scoring in every patient who opts for PCI. However, given the established utility of CAC scanning and CT angiography in diagnosing coronary artery diseases[24], the number of patients who undergo cardiac CT during their initial diagnostic process is increasing. In the present study, 31.6% of the patients who underwent CoCr-EES implantation at a *de novo* lesion had undergone CAC scanning within six months before PCI. When we plan PCI for such patients, reviewing the initial CT data to confirm the calcium burden of the target lesion may provide the physician and the patient with additional information about future adverse events. The present study suggests a calcium score of 140 as a threshold for identifying patients at risk for adverse events; however, the sample size of this study was small and further studies are needed to confirm this result.

Methods to minimise the impact of CAC are still not known. Statins have been investigated as a potential anticalcification drug. However, prospective randomised controlled trials have shown that statins do not prevent CAC progression and may even increase CAC[25,26]. Rotational atherectomy may be one solution, but a prospective randomised controlled trial showed that the use of rotational atherectomy was associated with higher late lumen loss with no impact on clinical outcomes[27]. Additional studies are required to elucidate the optimal strategies to improve the outcomes of patients with calcified coronary lesions.

Whether stent implantation itself has any effect on the progression of the underlying calcification is also not known. The present study showed that CT can accurately quantify lesion CAC prior to stent implantation, but evaluation of lesion CAC after stent implantation is almost impossible due to blooming and motion artefacts[28]. Bioresorbable vascular scaffolds, which are radiolucent, have been developed and are now being used in daily practice. Previous reports revealed that a clear CT image of the target lesion can be obtained even after bioresorbable vascular scaffold implantation[29,30]. Serial CT analyses may be useful to investigate the behaviour of lesion calcification after bioresorbable vascular scaffold implantation.

Limitations

The present study has several limitations. First, the sample size was small and adverse events occurred in less than ten patients. The results of the QCA showed that lesions with higher lesion calcium score had worse angiographic outcomes. Together with the results of the previous studies[1-6,14,18], it is plausible to conclude that the lesion CAC detected by CT is associated with poor outcomes following PCI. However, the multivariate analyses conducted may be inadequate and confounding biases may not have been fully excluded. Second, this study was a retrospective single-centre study. The study population consisted of patients who underwent coronary CT during their initial diagnostic process at our institution. Thus, applying these results to the general population undergoing PCI may be inappropriate. The CT scans were performed within six months before PCI, not just before PCI. The amount of calcium may have changed by the time of PCI and may have influenced the outcomes in some cases. Third, we did not consider the distribution of CAC within the lesion. Eccentric calcification is associated with less acute gain compared with concentric calcification[1]. Intimal and medial calcification has been reported to be associated with different pathophysiology[31], and spotty calcification has been reported to be associated with vulnerable plaques and progression of atherosclerosis[32,33]. Not only the volume and density, but also the distribution and types of CAC within the lesion, might have an impact on outcomes after PCI. Fourth, because we analysed patients who underwent only CoCr-EES implantation, the result cannot be extrapolated to other types of DES. Finally, this was a *post hoc* analysis and the results should be considered hypothesis-generating rather than causal.

Conclusions

CT-based detection of CAC of the target lesion was associated with poor prognosis after CoCr-EES implantation. Coronary angiography alone may not be enough to detect the calcification that has a negative impact on outcomes following PCI; CT may provide additional information about future adverse events. CT images, if present, should be carefully reviewed when planning PCI.

Impact on daily practice

The result of the present study suggests that coronary angiography alone is not enough to detect the amount and density of calcium that has a negative impact on outcomes following PCI and that CT can provide additional information about future adverse events. A cut-off lesion calcium score of 140 may be useful in detecting patients who are at higher risk for adverse events. CT images, if present, should be carefully reviewed when planning PCI.

Conflict of interest statement

K. Tanabe is a member of the Advisory Board for Abbott Vascular Japan and receives honoraria for lectures from Abbott Vascular and Toshiba Medical Systems. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix. Computed tomography protocol. Definitions of angiographic parameters and outcomes. Definition of clinical outcomes.

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The supplementary data are published online at: www.asiaintervention.org

Supplementary data

Supplementary Appendix. Computed tomography scan protocol

Patients were scanned in a supine position from the level of the pulmonary arteries through the base of the heart. Patients with a heart rate >60 beats/min were advised to consume propranolol 20 mg orally two hours before scanning. Scanning was performed using prospective electrocardiogram gating with gantry rotation time of 350 msec, detector collimation of 320 mm by 0.5 mm, tube voltage of 120 kV, and tube current of 200 mA. The data set was reconstructed with a small field of view tightly confined around the heart. Coronary artery calcification was quantified with an Agatston coronary calcium score equivalent adapted for multidetector computed tomography, using a workstation with a standard built-in algorithm (ZioStation version 2.1.5; Ziosoft, Redwood City, CA, USA) [9].

Definitions of angiographic parameters and outcomes

Proximal and distal edge segments included up to 5 mm from either side of the in-stent segment. Late lumen loss was defined as the difference between the minimal lumen diameter after completion of the stenting procedure and that which was measured eight months after implantation. Binary restenosis was defined as stenosis >50% of the reference diameter in the segment. Angiographic severe calcification was defined as radiopacities seen without cardiac motion before contrast injection, and moderate calcification was defined as radiopacities noted only during the cardiac cycle before contrast injection [34].

Definitions of clinical outcomes

Non-fatal myocardial infarction (MI) included spontaneous and periprocedural MI. Spontaneous MI was defined as an increase in the level of troponin or creatine kinase-MB by more than the upper limit of normal, and periprocedural MI was defined as an increase in the level of troponin or creatine kinase-MB after PCI by more than three times the upper limit of normal [35]. Target vessel revascularisation and target lesion revascularisation were defined as repeat percutaneous or surgical interventions for the treated vessel and lesion, respectively. Stent thrombosis was defined as definite or probable stent thrombosis using Academic Research Consortium definitions [36].

Supplementary Table 1. Patient characteristics by lesion calcium score.

	Calcium score <140 (n=82)	Calcium score ≥140 (n=42)	*p*-value
Age, years	66.5±11.3	70.7±7.2	0.030
Male	70 (85.4)	33 (78.6)	0.45
BMI	24.1±3.5	24.1±3.7	0.98
Hypertension	61 (74.4)	35 (83.3)	0.36
Dyslipidaemia	56 (68.3)	30 (71.4)	0.84
Diabetes mellitus	31 (37.8)	21 (50.0)	0.25
Current smoker	14 (17.1)	5 (11.9)	0.60
Haemodialysis	3 (3.7)	5 (11.9)	0.12
Previous MI	9 (11.0)	3 (7.1)	0.75
Previous PCI	17 (20.7)	6 (14.3)	0.47
Previous CABG	4 (4.9)	2 (4.8)	1.00
Acute coronary syndrome	9 (11.0)	1 (2.4)	0.16
Multivessel disease	20 (24.4)	11 (26.2)	0.83
Baseline medication			
Dual antiplatelet therapy	82 (100)	42 (100)	0.74
Aspirin+clopidogrel	79 (96.3)	40 (95.2)	
Aspirin+ticlopidine	2 (2.4)	2 (4.8)	
Aspirin+prasugrel	1 (1.2)	0 (0.0)	
Statin	78 (95.1)	41 (97.6)	0.66
Total calcium score	152.3 [34.4–477.5]	1,162.3 [658.7–2,014.8]	<0.001

Numbers are reported as n (%), mean±standard deviation, or median (interquartile range). BMI: body mass index; CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention

Supplementary Table 2. Baseline lesion and procedural characteristics by lesion calcium score.

	Calcium score <140 (n=102)	Calcium score ≥140 (n=47)	*p*-value
Target vessel			0.16
LMCA	3 (2.9)	1 (2.1)	
LAD	42 (41.2)	24 (51.1)	
LCX	26 (25.5)	5 (10.6)	
RCA	31 (30.4)	17 (36.2)	
ACC/AHA classification			0.0016
A, n (%)	4 (3.9)	0 (0.0)	
B1, n (%)	26 (25.5)	3 (6.4)	
B2, n (%)	40 (39.2)	16 (34.0)	
C, n (%)	32 (31.4)	28 (59.6)	
Angiographic moderate/severe calcification	3 (2.9)	21 (44.7)	<0.001
Bifurcation	32 (31.4)	19 (40.4)	0.35
Average number of stents, n	1.11±0.34	1.34±0.56	0.002
Average stent diameter, mm	2.99±0.44	2.97±0.41	0.81
Total stent length, mm	22.8±11.4	31.0±13.4	<0.001
Balloon-to-artery ratio	1.15±0.16	1.21±0.27	0.11
Maximum stent deployment pressure, atm	13.5±3.6	14.6±3.4	0.087
Post-dilatation	51 (50.0)	25 (53.2)	0.86
Rotablator use	0 (0.0)	3 (6.8)	0.034
Bail-out procedure	2 (2.0)	0 (0.0)	1.00
Lesion calcium score	13.2 [0.0–43.4]	252.4 [195.9–416.4]	<0.001

Numbers are reported as n (%), mean±standard deviation, or median (interquartile range). LAD: left anterior descending; LCX: left circumflex; LMCA: left main coronary artery; RCA: right coronary artery

Supplementary Table 3. Results of QCA by lesion calcium score.

	Calcium score <140 (n=102)	Calcium score ≥140 (n=47)	*p*-value
Lesion length, mm	12.7 [8.8–18.7]	18.8 [9.5–28.2]	0.015
Pre-procedure			
RVD, mm	2.71±0.58	2.63±0.61	0.44
MLD, mm	0.79±0.45	0.92±0.43	0.098
%DS	71.3±14.6	65.6±14.3	0.028
Post-procedure			
RVD, mm			
In-stent	3.02±0.50	3.03±0.44	0.89
In-segment	2.94±0.58	2.95±0.58	0.91
MLD, mm			
In-stent	2.70±0.45	2.59±0.37	0.15
In-segment	2.32±0.60	2.25±0.48	0.51
%DS			
In-stent	10.3±4.9	14.1±6.5	<0.001
In-segment	21.7±9.7	23.5±9.5	0.30
Acute gain, mm	1.91±0.50	1.67±0.44	0.005
Follow-up			
RVD, mm			
In-stent	2.67±0.98	2.59±0.81	0.64
In-segment	2.90±0.59	2.79±0.54	0.31
MLD, mm			
In-stent	2.53±0.45	2.10±0.70	<0.001
In-segment	2.24±0.52	1.86±0.74	0.001
%DS			
In-stent	13.5±6.6	24.5±21.5	<0.001
In-segment	22.6±9.0	34.2±21.1	<0.001
Late loss, mm			

In-stent	0.17±0.18	0.46±0.62	<0.001
In-segment	0.10±0.35	0.36±0.71	0.004
Binary restenosis	1 (1.1)	8 (18.2)	<0.001

Values are n (%), mean±standard deviation, or median (interquartile range).

MLD: minimum lumen diameter; QCA: quantitative coronary angiography; RVD: reference vessel diameter; %DS: % diameter stenosis

Supplementary Table 4. Eight-month clinical outcomes by lesion calcium score.

	Calcium score <140 (n=82)	Calcium score ≥140 (n=42)	*p*-value
Death	0 (0.0)	0 (0.0)	NA
Myocardial infarction	1 (1.3)	2 (4.8)	0.27
Stroke	0 (0.0)	0 (0.0)	NA
TVR	0 (0.0)	6 (14.3)	0.0012
TLR	0 (0.0)	6 (14.3)	0.0012
Stent thrombosis	0 (0.0)	1 (2.4)	0.34
TVF	1 (1.2)	7 (16.7)	0.002

Numbers are reported as n (%).

TLR: target lesion revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation

Supplementary Table 5. Fisher's exact test for variables that showed perfect separation.

	TVF (-) (n=116)	TVF (+) (n=8)	*p*-value
Previous MI	12 (10.3)	0 (0.0)	1.00
Previous PCI	23 (19.8)	0 (0.0)	0.35
Previous CABG	6 (5.2)	0 (0.0)	1.00
Acute coronary syndrome	10 (8.6)	0 (0.0)	1.00

Numbers are reported as n (%).

BMI: body mass index; CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention; TVF: target vessel failure

Supplementary Table 6. Patient characteristics of those with no or mild angiographic calcification.

	Calcium score <140 (n=79)	Calcium score ≥140 (n=24)	
Age, years	66.1±11.3	71.1±6.0	0.038
Male	67 (84.8)	2 (91.7)	0.51
BMI	24.2±3.5	24.8±4.0	0.46
Hypertension	58 (73.4)	20 (83.3)	0.42
Dyslipidaemia	72 (91.1)	22 (91.7)	1.00
Diabetes mellitus	29 (36.7)	15 (62.5)	0.034
Current smoker	13 (16.5)	3 (12.5)	0.76
Haemodialysis	3 (3.8)	1 (4.2)	1.00
Previous MI	8 (10.1)	3 (12.5)	0.72
Previous PCI	16 (20.3)	5 (20.8)	1.00
Previous CABG	4 (5.1)	1 (4.2)	1.00
Acute coronary syndrome	9 (11.4)	0 (0.0)	0.11
Multivessel disease	18 (22.8)	8 (33.3)	0.30
Baseline medication			
Dual antiplatelet therapy	79 (100)	24 (100)	NA
Aspirin+clopidogrel	76 (96.2)	23 (95.8)	0.66
Aspirin+ticlopidine	2 (2.5)	1 (4.2)	
Aspirin+prasugrel	1 (1.3)	0 (0.0)	
Statin	75 (94.9)	23 (95.8)	1.00
Total calcium score	148.3 [31.1–442.1]	911.0 [630.3–1,301.7]	< 0.001

Numbers are reported as n (%), mean±standard deviation, or median (interquartile range).

BMI: body mass index; CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention

Supplementary Table 7. Baseline lesion and procedural characteristics of lesions with no or mild angiographic calcification.

	Calcium score <140 (n=99)	Calcium score ≥140 (n=26)	*p*-value
Target vessel			0.57
LMCA	3 (3.0)	0 (0.0)	
LAD	39 (39.4)	13 (50.0)	
LCX	26 (26.3)	4 (15.4)	
RCA	31 (31.3)	9 (34.6)	
ACC/AHA classification			0.022
A	4 (4.0)	0 (0.0)	
B1	26 (26.3)	3 (11.5)	
B2	38 (38.4)	6 (23.1)	
C	31 (31.3)	17 (65.4)	
Bifurcation lesion	31 (31.3)	12 (46.2)	0.17
Average number of stents, n	1.11±0.35	1.38±0.64	0.004
Average stent diameter, mm	3.00±0.44	3.00±0.41	0.97
Total stent length, mm	23.0±11.5	32.7±12.2	<0.001
Balloon-to-artery ratio	1.15±0.16	1.26±0.33	0.018
Maximum stent deployment pressure, atm	13.5±3.6	13.9±3.7	0.62
Post-dilatation	49 (49.5)	11 (42.3)	0.66
Rotablator use	0 (0.0)	0 (0.0)	NA
Bail-out procedure	2 (2.0)	0 (0.0)	1.00
Lesion calcium score	12.9 [0.0–42.8]	217.5 [172.5–277.5]	<0.001

Numbers are reported as n (%), mean±standard deviation, or median (interquartile range). LAD: left anterior descending; LCX: left circumflex; LMCA: left main coronary artery; RCA: right coronary artery

Supplementary Table 8. Results of QCA of lesions with no or mild angiographic calcification.

	Calcium score <140 (n=99)	Calcium score ≥140 (n=26)	*p*-value
Lesion length, mm	12.5 [8.9–18.7]	22.8 [14.8–27.6]	0.003
Pre-procedure			
RVD, mm	2.73±0.58	2.56±0.65	0.22
MLD, mm	0.80±0.45	0.88±0.46	0.45
%DS	71.1±14.5	67.1±16.2	0.22
Post-procedure			
RVD, mm			
In-stent	3.03±0.50	2.98±0.41	0.62
In-segment	2.95±0.58	2.87±0.51	0.53
MLD, mm			
In-stent	2.71±0.45	2.58±0.36	0.17
In-segment	2.33±0.59	2.15±0.44	0.17
%DS			
In-stent	10.4±4.8	13.2±5.4	0.012
In-segment	21.5±9.5	24.8±9.2	0.12
Acute gain, mm	1.91±0.50	1.70±0.46	0.058
Follow-up			
RVD, mm			
In-stent	2.70±0.96	2.67±0.69	0.89
In-segment	2.91±0.59	2.82±0.50	0.49
MLD, mm			
In-stent	2.54±0.45	2.12±0.70	<0.001
In-segment	2.25±0.52	1.89±0.73	0.007
%DS			
In-stent	13.6±6.6	24.3±20.7	<0.001
In-segment	22.7±9.1	34.3±20.7	<0.001
Late loss, mm			

In-stent	0.17±0.18	0.44±0.62	0.001
In-segment	0.10±0.35	0.26±0.71	0.11
Binary restenosis	1 (1.0)	5 (19.2)	0.0014

Values are n (%) or mean±standard deviation.

MLD: minimum lumen diameter; QCA: quantitative coronary angiography; RVD: reference vessel diameter; %DS: % diameter stenosis

Supplementary Table 9. Eight-month clinical outcomes of lesions with no or mild angiographic calcification.

	Calcium score <140 (n=79)	Calcium score ≥140 (n=24)	*p*-value
Death	0 (0.0)	0 (0.0)	NA
Myocardial infarction	1 (1.3)	2 (8.3)	0.14
Stroke	0 (0.0)	0 (0.0)	NA
TVR	0 (0.0)	4 (16.7)	0.002
TLR	0 (0.0)	4 (16.7)	0.002
Stent thrombosis	0 (0.0)	1 (4.2)	0.23
TVF	1 (1.3)	5 (20.8)	0.002

Numbers are reported as n (%).

TLR: target lesion revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation