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Clinical impact of optical coherence tomography findings after drug-coated balloon treatment for patients with acute coronary syndromes

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Clinical impact of optical coherence tomography findings after drug-coated balloon
 treatment for patients with acute coronary syndromes

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- 39 Keywords: acute coronary syndrome, drug-coated balloon, optical coherence tomography,
- 40 target lesion failure, plaque morphology, thrombus

41 ¹

¹ Abbreviations

ACS, acute coronary syndrome; CN, calcified nodule; DCB, drug-coated balloon; DES, drug-eluting stent; FA, flow area; LA, lumen area; LRT, large residual thrombus; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; PE, plaque erosion; PR, plaque rupture; SRT, small residual thrombus; TA, thrombus area; TB, thrombus burden; TCFA, thin-cap fibroatheroma; TLF, target lesion failure; TV, thrombus volume

Highlights

- DCB is an option for specific lesion subsets in patients with ACS.
- Potential difficulties exist with angiography-based patient and lesion selection.
- Plaque morphology and residual TB may enable risk stratification.
- DCB could be considered an effective treatment for patients with PE.
- Stent implantation may be preferred if the residual TB is large in lesions with PR.

1 Abstract

2

3 **Background:** Drug-coated balloon (DCB) became a potential treatment option for patients

with acute coronary syndrome (ACS); however, factors associated with target lesion failure
 (TLF) remain uncertain.

- 6 **Methods:** This retrospective, multicentre, observational study included consecutive ACS
- 7 patients who underwent optical coherence tomography (OCT)-guided DCB treatment.
- 8 Patients were divided into two groups according to the occurrence of TLF, a composite of
- 9 cardiac death, target vessel-related myocardial infarction, and ischemia-driven target lesion
- 10 revascularisation.
- 11 **Results:** We enrolled 127 patients in this study. During the median follow-up period of 562
- 12 (IQR: 342–1,164) days, 24 patients (18.9%) experienced TLF, and 103 patients (81.1%) did
- 13 not. The cumulative 3-year incidence of TLF was 22.0%. The cumulative 3-year incidence of
- 14 TLF was the lowest in patients with plaque erosion (PE) (7.5%), followed by those with
- 15 rupture (PR) (26.1%) and calcified nodule (CN) (43.5%). Multivariable Cox regression
- 16 analysis revealed that plaque morphology was independently associated with TLF on pre-PCI
- 17 (percutaneous coronary intervention) OCT, and residual thrombus burden (TB) was
- 18 positively associated with TLF on post-PCI OCT. Further stratification by post-PCI TB
- 19 revealed a comparable incidence of TLF in patients with PR (4.2%) to that of PE if the culprit
- 20 lesion had a smaller post-PCI TB than the cut-off value (8.4%). TLF incidence was high in
- 21 patients with CN, regardless of TB size on post-PCI OCT.
- 22 **Conclusions:** Plaque morphology was strongly associated with TLF for ACS patients after
- 23 DCB treatment. Residual TB post-PCI might be a key determinant for TLF, especially in
- 24 patients with PR.
- 25

1 Introduction

2	New-generation drug-eluting stents (DES) have dramatically reduced the incidence of
3	restenosis. However, coronary stent implantation is accompanied by various risks of
4	intravascular complications, including stent thrombosis and in-stent restenosis [1, 2]. Recently,
5	drug-coated balloons (DCB) have been reported to be non-inferior to stent implantation for
6	small vessel coronary artery disease in chronic coronary syndrome (CCS) [3]. Several studies
7	have shown the usefulness of the DCB strategy in the setting of acute coronary syndrome
8	(ACS) [4, 5]. In addition, recent large-scale registry data has implied a lower risk of definite
9	thrombosis than DES [6]. Considering these findings, DCB could be an alternative treatment
10	option to stent implantation for specific lesion subsets not only in patients with CCS but in
11	those with ACS. Conversely, the previous studies on the efficacy of DCB for patients with ACS
12	showed the difficulty of lesion preparation and bail-out stenting rate were relatively high, even
13	in carefully selected patients [4, 5].
14	The application of optical coherence tomography (OCT) imaging allows the accurate
15	assessment of culprit lesion morphology and the optimisation of procedural results with its high
16	image resolution [7]. Plaque composition, thrombogenicity, and inflammation may drive
17	different outcomes following percutaneous coronary intervention (PCI) [8, 9]. However, no

18 studies have systematically assessed the factors related to clinical outcomes after DCB

19 treatment for patients with ACS. Therefore, this study aimed to investigate the prognostic risk

20	factors associated with target lesion failure (TLF) among ACS patients treated with DCB using
21	OCT.
22	
23	Methods
24	Study design
25	This retrospective, multicentre, observational study enrolled consecutive ACS
26	patients who underwent DCB treatment. The inclusion criteria were: (1) patients with ACS
27	who underwent OCT-guided PCI between Jan 2017 and Jan 2021; (2) patients whose culprit
28	lesions were treated with DCB; and (3) patients \geq 20 years old. Participating institutions,
29	exclusion criteria, and detailed definitions of ACS are described in the Supplemental
30	Material.
31	The study protocol complied with the Declaration of Helsinki and was approved by
32	the Ethics Committee of Kobe University Hospital. Informed consent was obtained as an opt-
33	out on the Division of Cardiovascular Medicine, Kobe University Graduate School of
34	Medicine website. This study was registered in the University Hospital Medical Information
35	Network Clinical Trial Registry (UMIN000049605).
36	

PCI procedure

38	In each institution, the DCB strategy was preferentially considered for lesions that
39	achieved optimal lesion preparation after balloon angioplasty or for those deemed unsuitable
40	for stent implantation (Supplemental Material). The information was ascertained from a
41	review of medical records.
42	
43	OCT image analysis and definitions
44	We retrospectively collected OCT images obtained before (pre-PCI) and
45	immediately after the index PCI (post-PCI) with a frequency-domain OCT (ILUMIEN, Abbot
46	Vascular, Santa Clara, CA, USA) or OFDI system (LUNAWAVE, Terumo, Tokyo, Japan).
47	The use of thrombus aspiration or pre-dilatation by a less than 2 mm balloon was allowed
48	before the OCT examination at pre-PCI.
49	Plaque morphology was classified into plaque rupture (PR), plaque erosion (PE), and
50	calcified nodule (CN) according to the previously established criteria (Figure 1A-C) [10].
51	Intra- or interobserver agreements for PR, PE, and CN were within the acceptable range
52	(intra-observer, kappa = 0.975 ; inter-observer, kappa = 0.959). Each plaque was classified
53	into one of the following three categories: (1) fibrous plaque, (2) lipid plaque, or (3) calcified
54	plaque [11]. Quantitative analysis was performed to evaluate flow area, lumen area, thrombus
55	area (TA), thrombus volume, and thrombus burden (TB) according to a previously validated
56	method [12]. Briefly, in each OCT frame, lumen area (LA) and flow area (FA) were

57	measured, and then the thrombus area (TA) was calculated as LA minus FA (Figure 1D). The
58	LA was traced using the proprietary analysis software in the imaging frames where the
59	luminal border was visible in at least three out of four image quadrants. In frames with
60	difficulties in luminal border detection in more than one quadrant, the LA was extrapolated
61	from the nearest proximal or distal frame with a visible lumen contour. Thrombus volume
62	was calculated as the mean TA multiplied by the thrombus length, and TB (%) was calculated
63	as mean TA (mm ²) divided by mean LA (mm ²) \times 100%. Inter- and intra-observer agreements
64	for measuring TB on calcified nodules were within the acceptable range (intra-observer,
65	0.933; inter-observer, 0.891 at pre-PCI; intra-observer, 0.928; inter-observer, 0.862 at post-
66	PCI). A detailed methodology of OCT image analysis is described in the Supplemental
67	Material.
68	
69	Outcomes
70	The primary outcome of the study was TLF, which was a composite of cardiac death,
71	target vessel-related myocardial infarction, and ischaemia-driven target lesion
72	revascularisation (TLR). The detailed definitions of outcomes are described in the
73	Supplemental Material. Cardiovascular events were ascertained from a review of medical
74	records and confirmed by direct contact with the patients, their families, or physicians.
75	

76 Statistical analysis

77	Categorical variables are presented as numbers (percentages) and were compared
78	with a chi-square test or Fisher's exact test. Continuous variables are expressed as
79	mean±standard deviation (SD) or median (interquartile range [IQR]) and were compared
80	using the Student's t-test or the Mann-Whitney U test based on their distributions. Chi-square
81	or Fisher exact tests for categorical outcomes with more than 2 degrees of freedom were
82	applied for testing overall differences, and post-hoc tests for controlling type 1 error using
83	Bonferroni correction were performed if the overall test was significant. Statistical
84	significance was set at p value < 0.05 . If the p value of the overall test was < 0.05 , then a two-
85	group post-hoc comparison was performed using the Mann-Whitney U test or the
86	independent samples Student's t-test for continuous outcomes, and chi-square or Fisher exact
87	test for categorical outcomes; the test result was considered significant if the p value was
88	<0.017 (i.e., 0.05 of 3). Receiver operating characteristic (ROC) analysis was used to
89	determine the optimal cutoff value of TB at post-PCI associated with TLF. The cumulative
90	incidence of clinical events was estimated by the Kaplan-Meier method, and the differences
91	between groups were assessed with the log-rank test. Cox regression analysis was used to
92	identify independent factors associated with TLF for all the variables evaluated in this study.
93	Variables were adopted in the multivariable analysis if the p values in the univariable analysis
94	were less than 0.15, and the stepwise algorithm was used for variable selection. Age and sex

95	were also included as variables in the multivariable analysis owing to their clinical relevance
96	and potential confounding effects. Although they did not show a significant association with
97	the dependent variable (p-value < 0.15), their inclusion was important for proper adjustment
98	of important covariates and consideration of potential effect modifiers. We used multiple
99	models if there were significant correlations among adjusted covariables. To assess
100	intraobserver and interobserver variabilities, categorical data were compared using Cohen's
101	kappa coefficient, and Lin's concordance correlation coefficient was used for continuous
102	data. All statistical analyses were performed using the Microsoft R open software version
103	3.4.1 (R Development Core Team, Vienna, Austria).
104	
105	Results
106	Study population
107	Of 496 ACS patients who underwent OCT-guided PCI from Jan 2017 to Jan 2021,
108	312 patients were treated with stents, 21 patients with in-stent restenosis or stent thrombosis,
109	
	6 patients with shock status, 2 patients with target lesion in a left main coronary artery, 10
110	b patients with shock status, 2 patients with target lesion in a left main coronary artery, 10 patients with missing data, 5 patients with insufficient OCT data quality, and 13 patients with
110 111	b patients with shock status, 2 patients with target lesion in a left main coronary artery, 10 patients with missing data, 5 patients with insufficient OCT data quality, and 13 patients with undetermined culprit plaque morphology were excluded. Finally, a total of 127 ACS patients
110 111 112	6 patients with shock status, 2 patients with target lesion in a left main coronary artery, 10 patients with missing data, 5 patients with insufficient OCT data quality, and 13 patients with undetermined culprit plaque morphology were excluded. Finally, a total of 127 ACS patients who underwent PCI with DCB were enrolled (Figure 2). The reasons for choosing treatment
110 111 112 113	6 patients with shock status, 2 patients with target lesion in a left main coronary artery, 10 patients with missing data, 5 patients with insufficient OCT data quality, and 13 patients with undetermined culprit plaque morphology were excluded. Finally, a total of 127 ACS patients who underwent PCI with DCB were enrolled (Figure 2). The reasons for choosing treatment using a DCB were as follows: 25 lesions (19.7%) with very small vessel coronary disease; 1

114	patient (0.8%) scheduled for non-cardiac surgery; 59 patients (46.5%) with a high risk of
115	bleeding complications; 23 lesions (16.4%) considered to develop stent fracture easily; and
116	65 lesions (51.2%) with bifurcation. The remaining 27 lesions (21.3%) were treated with
117	DCB because the operator considered optimal lesion preparation was successfully achieved
118	with balloon dilatation. During the median follow-up period of 562 (IQR: 342-1,164) days,
119	24 patients (18.9%) experienced TLF, and 103 patients (81.1%) did not. The overall
120	cumulative 3-year incidence of TLF was 22.0%.
121	
122	Comparison of baseline patient, lesion, and procedural characteristics between TLF and
123	non-TLF groups
124	The baseline patient, lesion, and procedural characteristics are shown in Table 1.
125	Patients with TLF had a significantly higher prevalence of chronic kidney disease and
126	haemodialysis and had lower estimated Glomerular Filtration Rate (eGFR) levels than those
127	in the non-TLF group. The peak value of CK was significantly higher, and the left ventricular
128	ejection fraction was significantly lower in patients with TLF than those with non-TLF. The
129	two groups had similar rates of patients with high bleeding risk and duration of dual
130	antiplatelet therapy after PCI. Additionally, the location of the culprit lesion was identical

132	severe calcification than those in the non-TLF group. All procedural characteristics were
133	comparable between the two groups.

135 Comparison of pre-PCI OCT findings between TLF and non-TLF groups

136	Table 2 summarises pre- and post-PCI OCT findings. The plaque morphology of the
137	culprit lesions significantly differed between the two groups (p=0.002). The lesions in the
138	TLF group had a significantly lower prevalence of PE compared with those in the non-TLF
139	group (12.5% vs 47.6%, p=0.002). The prevalence of CN in the TLF group was higher than
140	that in the non-TLF group (33.3% vs 14.6%, p=0.04), but it was not statistically significant.
141	Regarding the qualitative analysis of pre-PCI OCT findings, there were significant
142	differences in the prevalence of lipid, fibrous, and calcified plaques. The lesions with TLF
143	had a significantly higher prevalence of TCFA, macrophage, and cholesterol crystal (TCFA,
144	54.2% vs 26.2%, p=0.008; macrophage, 75.0% vs 50.5%, p=0.03; cholesterol crystal, 62.5%
145	vs 31.1%, p=0.004). As for the pre-PCI OCT measurements, reference area, minimum FA,
146	and % area stenosis were not different between the two groups. Regarding thrombus analysis
147	at pre-PCI, mean TA, TB and TV tended to be higher in the TLF group; however, there was
148	no statistically significant difference between the two groups (mean TA, 0.40 [0.10–1.42] vs
149	0.21 [0–0.58], p=0.06; TB, 15.53 [3.01–30.39] vs 8.03 [0–17.18], p=0.07; TV, 2.45 [0.27–
150	65.16] vs 0.98 [0–3.68], p=0.08) (Table 2).

152	Comparison of post-PCI OCT findings between TLF and non-TLF groups
153	Table 2 also shows post-PCI OCT findings. Minimum FA and acute FA gain were
154	not significantly different, whereas % area stenosis was significantly higher in the TLF group.
155	Mean TA, TB, and TV were significantly higher in the TLF group than in the non-TLF group
156	(mean TA, 0.43 [0.28–0.92] vs 0.15 [0–0.40], p<0.001; TB, 9.23 [4.85–18.89] vs 3.6 [0–
157	9.14], p<0.001; TV, 2.3 [0.38–9.87] vs 0.67 [0–1.90], p=0.0014, p<0.001). Additionally, in
158	the TLR group compared with the non-TLR group, there was a smaller reduction of TB
159	during the PCI procedure (23.9 [0-44.6] vs 57.8 [25.9-78.8], p=0.02). The prevalence and
160	severity of dissections after PCI were comparable between the two groups.
161	The post-PCI OCT findings according to plaque morphology are shown in Supplemental
162	Table 1. The residual TB at post-PCI was highest in patients with PR among the three groups.
163	
164	Factors associated with TLF
165	Clinical outcomes during a median follow-up period of 562 (IQR: 342-1164) days
166	are summarised in Table 3. The results of the univariable and multivariable Cox regression
167	analysis for patient and lesion characteristics, pre-PCI OCT findings, and post-PCI OCT
168	findings associated with TLF are summarised in Table 4. The multivariable patient and lesion
169	characteristics model showed that there were no variables significantly associated with TLF.

170	At Cox regression analysis of pre-PCI OCT findings, the univariate analysis showed that
171	plaque morphology (p=0.020), TCFA (HR: 2.86, 95%CI: 1.28–6.39, p=0.01), macrophage
172	(HR: 2.77, 95%CI: 1.10–6.99, p=0.03), cholesterol crystal (HR: 3.43, 95%CI: 1.50–7.85,
173	p=0.04), lipid index (HR: 1.02, 95%CI: 0.99–1.05, p=0.10), and TB (HR: 1.02, 95%CI: 1.02–
174	1.04, p=0.048) were positively associated with TLF. Additionally, the multivariable pre-PCI
175	OCT findings model showed that plaque morphology was an independent predictor of TLF
176	(p<0.001). Specifically, compared to PR, PE was associated with a lower risk of TLF (HR:
177	0.46, 95%CI: 0.11-0.87, p=0.025), and CN was associated with a higher risk of TLF (HR:
178	4.27, 95%CI: 1.02-17.8, p=0.038). At pre-PCI OCT findings, minimum FA, calcification
179	measurements, and thrombus measurements were not independently associated with TLF.
180	The Kaplan–Meier curve demonstrated that the cumulative 3-year incidence of TLF in
181	patients with PE was significantly lower than those with PR (7.5% vs 26.1%, HR: 4.85,
182	95%CI: 1.38–17.04, p=0.01) or CN (7.5% vs 43.5%, HR: 6.40, 95%CI: 1.70–24.1, p=0.006)
183	(Figure 3A).
184	In the Cox regression analysis of post-PCI OCT findings, the multivariable analysis
185	(post-PCI OCT findings model) showed that TB (HR: 1.08, 95%CI: 1.04–1.12, p<0.001) was
186	independently associated with TLF, and % area stenosis (HR: 1.17, 95%CI: 0.998-1.37,
187	p=0.053) tended to be related to TLF, but was not statistically significant. ROC analysis of
188	TB at post-PCI showed that the cutoff value of this parameter for identifying patients with

189 subsequent TLF was 8.4% (sensitivity, 70.8%, specificity, 68%; area under the curve, 0.72,
190 95% CI: 0.60–0.84).

191	According to this cutoff value, each patient group based on the plaque morphology
192	of culprit lesions was further divided into large (LRT: TB at post-PCI > 8.4%) or small (SRT:
193	TB at post-PCI \leq 8.4%) residual thrombus groups. The incidence of TLF in patients with PR
194	with LRT, PR with SRT, PE with LRT, PE with SRT, CN with LRT, and CN with SRT was
195	46.2%, 3.9%, 5.9%, 5.7%, 50%, and 29.4%, respectively. In-hospital TLR was required in
196	three out of 26 (11.5%) PR patients with LRT, whereas in one out of 101 (1.0%) remaining
197	patients (Supplemental Table 2). In the analysis for Supplemental Table 3, each comparison
198	was performed for each category of the variable, using PE with SRT, PR with SRT, or CN
199	with SRT as the reference category. The Kaplan-Meier curve with log-rank analysis
200	demonstrated that the cumulative 3-year incidence of TLF in patients with PR with LRT, CN
201	with LRT, and CN with SRT was significantly higher than that in those with PE with SRT
202	(47.9% vs 9.0%, HR: 10.52, 95%CI: 2.35–47.08, p=0.0021, 58.3% vs 9.0%, HR: 8.42,
203	95%CI: 1.40–50.43, p=0.020, 33.9% vs 9.0%, HR: 5.44, 95%CI: 1.06–28.04, p=0.043,
204	respectively). In contrast, the cumulative 3-year incidence of TLF in patients with PR with
205	SRT and PE with LRT was comparable with that in those with PE with SRT (4.2% vs 9.0%,
206	HR: 0.63, 95%CI: 0.057-6.94, p=0.71; 5.9% vs 9.0%, HR: 0.94, 95%CI: 0.085-10.37,

207 p=0.96, respectively). The cumulative 3-year incidence of TLF in patients with CN with LRT,

208	CN with SRT, and PR with LRT was significantly higher than that in those with PR with SRT
209	(58.3% vs 4.2%, HR: 13.39, 95%CI: 1.39-128.8, p=0.03; 33.9% vs 4.2%, HR: 8.66, 95%CI:
210	1.01-74.1, p=0.04; 47.9% vs 4.2%, HR: 16.74, 95%CI: 2.17-129.0, p=0.007, respectively).
211	Conversely, those with PE with LRT and PE with SRT were comparable with those with PR
212	with SRT (5.9% vs 4.2%, HR: 1.49, 95%CI: 0.09-23.9, p=0.78; 9.0% vs 4.2%, HR: 1.59,
213	95%CI: 0.14-17.6, p=0.71, respectively). The cumulative 3-year incidence of TLF in patients
214	with CN and LRT was comparable to that in patients with CN and SRT (58.3% vs 33.9%,
215	HR: 1.55, 95%CI: 0.37–6.48, p=0.55) (Figure 3B, Supplemental Table 3). Representative
216	cases are described in Figure 4.
217	
218	Discussion
219	To the best of our knowledge, this is the first study evaluating factors associated with

220 TLF after DCB treatment for patients with ACS using OCT. The main findings of the current study can be summarised as follows: (1) overall, 3-year cumulative incidence of TLF in 221 patients with ACS after DCB treatment was 22.0%; (2) regarding pre-PCI OCT findings, 222 plaque morphology was an independent predictor of TLF. Specifically, compared to PR, PE 223 was associated with a lower risk of TLF, and CN was associated with a higher risk of TLF; 224 (3) regarding post-PCI OCT findings, residual TB after DCB treatment was independently 225 226 associated with TLF; (4) the overall incidence of TLF was significantly lower in patients with

227	PE than in those with PR and CN. However, when further stratified by post-PCI TB, the
228	incidence of TLF in patients with PR was comparable to that of PE if the culprit lesion had a
229	smaller TB than the cutoff value (8.4%). Conversely, the incidence of TLF was high in
230	patients with CN regardless of the size of the TB. These findings indicate the potential
231	implication of detailed OCT assessment at pre- and post-PCI for the risk stratification of ACS
232	patients undergoing DCB treatment.
233	Mangner et al. reported the clinical outcome of ACS patients with small vessel
234	coronary artery disease treated with DCB versus DES [13]. They reported that, at 3 years,
235	there was no difference in the incidence of TVR between ACS patients treated with DCB and
236	those with DES (10.1% and 8.4%, respectively). The REVELATION trial was a prospective
237	randomised trial comparing DCB with DES for STEMI patients with large coronary artery
238	disease [4]. They reported that DCB showed no significant difference in late lumen loss, and
239	TLR rate at 9 month was as low as 3% (2 out of 58 patients). Considering these data, DCB
240	could be an alternative treatment option to stent implantation for specific lesion subsets in
241	patients with ACS. However, the REVELATION trial applied strict inclusion criteria that the
242	subjects were registered only if the residual stenosis was <50% after thrombus aspiration or
243	balloon pre-dilatation. Another study (PEPCAD NSTEMI trial) investigating the efficacy of
244	DCB compared with coronary stents in the setting of NSTEMI included only patients who
245	had small thrombus on angiography and excluded patients with large angiographical

246	thrombus [5]. However, despite such strict inclusion criteria, the bail-out stenting rate of
247	these trials was relatively high; 18.3% (11 out of 60 patients) and 15.4% (19 out of 123
248	patients) for the REVELATION and PEPCAD NSTEMI trials, respectively. Considering the
249	bail-out stenting rate of around 5% in previous studies that mainly enrolled patients with CCS
250	[3], these data indicate potential difficulties of the angiography-based patient and lesion
251	selection for the effective treatment with DCB-only strategy in ACS patients. However, no
252	study has directly assessed the risk factors associated with a worse prognosis among ACS
253	patients after DCB treatment. Thus, we investigated prognostic factors independently
254	associated with subsequent TLF among ACS patients after DCB treatment.
255	In the present study, we tried to evaluate the qualitative and quantitative
256	characteristics of ACS culprit lesions for a more accurate risk stratification. For this purpose,
257	we applied OCT evaluation for culprit plaque morphology and residual TB. Patient and lesion
258	characteristics were not associated with TLF; however, plaque morphology at pre-OCT was
259	independently associated with TLF. Recently, several studies have indicated the potential
260	utility of intravascular imaging to determine potential lesion subsets that could be effectively
261	treated with anti-thrombotic therapy without stenting. Jia et al. demonstrated the feasibility of
262	adopting anti-thrombotic therapy without stenting for STEMI patients caused by PE [14].
263	However, the EROSION study included only patients who had ACS culprit lesions with mild
264	to moderate stenosis (%DS<70%) after thrombus aspiration. Among 103 patients diagnosed

265	as PE, 32 patients (31% of patients with PE) were excluded because of the presence of >70%
266	of stenosis. Additionally, balloon angioplasty was not permitted before and after the
267	enrollment; instead, aggressive anti-thrombotic therapy was required with over 60% of use of
268	glycoprotein IIb/IIIa inhibitor and 100% of dual antiplatelet therapy with aspirin and
269	Ticagrelor. On the other hand, a higher degree of percentage of area stenosis was associated
270	with worse clinical outcome [15]. Since many of ACS culprit lesions have >70% of stenosis
271	after thrombus aspiration and increased risk of bleeding in the real-world ACS population, we
272	considered the need for data on the safety and the efficacy of DCB treatment followed by
273	standard dual antiplatelet therapy (aspirin plus clopidogrel or prasugrel) in a real-world
274	patient database. In the current study, 15.7% of patients who underwent DCB treatment for
275	ACS required TVR. This finding aligns with a previous study where 10.1% of ACS patients
276	underwent TVR following DCB treatment. However, it is worth noting that the prevalence of
277	ST-elevated myocardial infarction was 44.1% in the present study compared to 7% in the
278	previous study [13]. Additionally, we found that patients with PE had a feasible clinical
279	outcome after DCB treatment in the real-world ACS population, while those with CN had a
280	worse clinical outcome. The previous studies investigating clinical outcomes of DES strategy
281	for PR, PE, and CN patients showed the incidence of TLF was 7%, 12%, and 38% at 3 years,
282	respectively [8, 16]. While direct comparisons between the clinical outcomes of the DCB
283	strategy in the present study and those of DES in the previous study should not be made, it is

284	worth noting that the clinical outcomes of DCB treatment for patients with PE and CN (with
285	incidences of TLF at 5.8% and 34.8%, respectively) appeared to be similar to those of DES.
286	However, the clinical outcome of DCB treatment for patients with PR (with an incidence of
287	TLF at 25%) appeared to be worse than that of DES in the previous study.
288	To benefit the most from DCB, the infiltration of paclitaxel released from the DCB is
289	essential. Although multiple factors have been reported to affect its infiltration, plaque
290	component and physical barrier are currently considered two major components. Previous
291	studies demonstrated that the deposition of paclitaxel in the human aorta is inversely
292	proportional to the lipid content. The lipid content in atherosclerotic plaques weakens the
293	effectiveness of lipophilic drugs. In the present study, TCFA was more frequent and lipid
294	index tended to be larger in lesions with TLF. Conversely, the extracellular matrix, which is
295	abundant in PE plays a crucial role in the distribution and retention of lipophilic drugs.
296	Because drugs bind to histone proteins for transmembrane transportation, these proteins can
297	promote drug delivery and retention [17]. Regarding calcified plaque, Fanelli et al. found that
298	DCBs were ineffective in lesions with severe calcification, and corresponding tests proposed
299	that calcium inhibited drug absorption [18]. Considering different characteristics of plaque
300	components among plaque morphology, lesions with PE might respond better to DCB than
301	those with PR and CN.

302	Another important factor of prognosis after DCB treatment for ACS patients was
303	different physical barrier by thrombus and different thrombogenicity according to lesion
304	morphology. In a previous experimental study, thrombus positioned between stent and vessel
305	wall could decrease diffusion, retention, and uptake of drug, inhibiting effective drug delivery
306	to the vessel wall [19]. Therefore, a reduced or inhomogeneous drug distribution could occur
307	after DCB treatment for thrombus-rich lesions. Indeed, in the current study, residual TB at
308	post-OCT and not at pre-OCT was strongly related with TLF. Interestingly, in patients with
309	PR, residual TB after PCI stratified the future risk of TLF, while PE had a low incidence and
310	CN had a high incidence of TLF regardless of residual TB. In general, a ruptured site releases
311	highly thrombogenic substrates such as lipid and tissue factors [20]. Conversely, eroded
312	plaques do not contain a large necrotic core but exhibit a proteoglycan-rich matrix and
313	smooth muscle cells, which have less tissue factor and inflammation, resulting in lower local
314	thrombogenicity [20]. We currently speculate that such a difference in local thrombogenicity
315	between lesions with PR and those with PE might affect the extent of residual thrombus, its
316	time course afterwards, and different outcomes after DCB treatment. In the EROSION study,
317	anti-thrombotic therapy decreased most of the residual thrombus in PE during the initial 1
318	month [14]. We found that lesions with PE had a favourable prognosis regardless of the
319	extent of the residual thrombus. These data may indicate that the residual thrombus in lesions
320	with PE might follow a relatively favourable time course regardless of its volume in patients

321	with ACS. On the other hand, PR had high thrombogenicity, which may induce progressive
322	thrombus development after the DCB treatment [20]. Large residual thrombus could decrease
323	FA, and disturbance of blood flow caused by luminal narrowing might induce further
324	thrombus development, especially in lesions with PR [21]. Considering that in-hospital TLR
325	was required in 3 out of 26 (11.5%) PR patients with LRT, whereas 1 out of 101 (1.0%) in the
326	remaining patients, stent implantation might be preferred if residual thrombus volume after
327	PCI is large, especially in lesions with PR.
328	
329	Limitations
330	First, as a retrospective study, our results are subject to selection bias. More
331	specifically, the registry included only those patients who could complete their treatment only
332	with DCB according to the operator's discretion. Therefore, the issue of selection bias cannot
333	be avoided. Second, there was a lack of pathological assessment; we identified some OCT
334	features associated with TLF; however, we could not reveal what the OCT features indicated
335	pathologically. Especially the signal attenuation caused by a large red thrombus can
336	potentially mask the vessel wall, obstructing thrombus measurements. However, OCT is the
337	ideal modality to evaluate intracoronary thrombus in vivo. We used a previously published
338	method for these cases, which showed adequate feasibility and reproducibility [12].
330	

340 Conclusion	
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341	Plaque morphology at pre-PCI OCT was strongly associated with TLF for ACS
342	patients after DCB treatment. Additionally, post-PCI residual TB might be an important
343	factor, especially in patients with PR. Detailed OCT assessment at pre- and post-PCI may
344	have implications for the risk stratification of ACS patients undergoing DCB treatment.
345	
346	
347	Acknowledgement: None
348	
349	Ethics approval and informed consent: The study protocol complied with the Declaration
350	of Helsinki and was approved by the Ethics Committee of Kobe University Hospital.
351	Informed consent was obtained as an opt-out on the Division of Cardiovascular Medicine,
352	Kobe University Graduate School of Medicine website. This study was registered in the
353	University Hospital Medical Information Network Clinical Trial Registry
354	(UMIN000049605).
355	
356	Data statement:
357	The data that support the findings of this study are available from the corresponding author,
358	HO, upon reasonable request.

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465	Figure	legends

467	Figure 1:	Representative	OCT in	1ages of	plaque mor	phology an	d assessment	method of
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- 468 LA, FA, and TA
- 469 A) Plaque rupture, B) Plaque erosion, C) Calcified nodule, D) Assessment method of LA, FA,
- 470 and TA: TB=8.4 (%). FA, flow area; LA, lumen area; OCT, optical coherence tomography;
- 471 TA, thrombus area; TB, thrombus burden
- 472

473	Figure	2:	Study	flowchart
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- 474 ACS, acute coronary syndrome; OCT, optical coherence tomography; PCI, percutaneous
- 475 coronary intervention; DCB, drug-coated balloon, TLF: target lesion failure
- 476
- 477

478 Figure 3: Kaplan–Meier curves for the cumulative incidence of TLF

- 479 A) Kaplan–Meier curves stratified by culprit plaque morphology; B) Kaplan–Meier curves
- 480 stratified by culprit plaque morphology and residual TB after PCI.
- 481 CI, confidence interval; CN, calcified nodule; HR, hazard ratio; LRT, large residual
- 482 thrombus; PE, plaque erosion; PCI, percutaneous coronary intervention; PR, plaque rupture;
- 483 SRT, small residual thrombus; TLF, target lesion failure; TB, thrombus burden
- 484

485 **Figure 4: Representative cases**

486 A) A representative case of PE

- 487 A 49-year-old woman presented with STEMI.
- 488 1) Baseline CAG showed a total occlusion in the proximal LAD. OCT images (a-c) indicated
- 489 PE with thrombus. 2) CAG showed a 30% stenosis after PCI, and OCT images (a–c) showed
- 490 a large residual thrombus after DCB (white arrowhead). The residual TB was 10.1%. 3)
- 491 Twelve months later, CAG and OCT images (a–c) showed no significant stenosis without
- 492 thrombus. The minimal FA increased from 4.6 to 5.1 mm².

493 **B)** A representative case of PR with SRT

- 494 An 89-year-old man presented with STEMI.
- 1) Baseline CAG showed severe stenosis in the middle LAD. OCT images (a-c) indicated PR
- 496 with thrombus. *Indicates PR. 2) After PCI with DCB, CAG showed no significant stenosis,
- 497 and OCT images (a–c) showed a small residual thrombus (white arrowhead). The residual TB
- 498 was 1.3%. 3) Twelve months later, CAG and OCT images (a–c) showed no significant
- 499 stenosis without thrombus. The minimal FA increased from 3.6 to 5.3 mm².

500 C) A representative case of PR with LRT

- 501 A 59-year-old man presented with STEMI.
- 502 1) Baseline CAG showed a total occlusion in the middle RCA. OCT images (a-c) indicated
- 503 PR with thrombus. *Indicates PR. 2) After PCI with DCB, CAG showed a 30% stenosis, and

504	OCT images (a–c) showed a large residual thrombus (white arrowhead). The residual TB is
505	15.4%. 3) Six months later, the patient had effort-related chest pain. CAG and OCT showed
506	severe stenosis at the lesion previously treated with DCB. The minimal FA decreased from
507	$3.1 \text{ to } 0.7 \text{ mm}^2$.
508	CAG, coronary angiography; DCB, drug-coated balloon; LAD, left anterior descending
509	artery; LRT, large residual thrombus; OCT, optical coherence tomography; PE, plaque
510	erosion; PR, plaque rupture; RCA, right coronary artery; SRT, small residual thrombus;
511	STEMI, ST-segment elevation myocardial infarction
512	

Variable	All lesions (n=127)	TLF (n=24)	non-TLF (n=103)	P value
Median follow-up period	562 (342–1,164)	101 (229–340.75)	727 (456–1,206)	< 0.001
Baseline patient characteristics				
Age (yr.)	69.0±12.4	69.0±9.2	69.0±13.0	0.99
Sex male, n (%)	92 (72.4%)	19 (79.2%)	73 (70.9%)	0.42
Hypertension, n (%)	90 (70.9%)	19 (79.2%)	71 (68.9%)	0.32
Dyslipidemia, n (%)	81 (63.8%)	15 (62.5%)	66 (64.1%)	0.89
Diabetes Mellitus, n (%)	61 (48.0%)	15 (62.5%)	46 (44.7%)	0.12
Current smoker, n (%)	39 (31.5%)	6 (25.0%)	33 (33%)	0.45
Prior PCI, n (%)	17 (13.4%)	4 (16.7%)	13 (12.6%)	0.60
Chronic Kidney Disease, n (%)	58 (45.7%)	16 (66.7%)	42 (40.8%)	0.02
Haemodialysis, n (%)	11 (8.7%)	5 (20.8%)	6 (5.8%)	0.02
LVEF (%)	55.0±7.4	49.3±14.4	56.9±10.3	0.004
High bleeding risk, n (%)	59 (46.5%)	10 (41.7%)	49 (47.6%)	0.66
Clinical presentation				0.67
uAP, n (%)	25 (19.7%)	3 (12.5%)	22 (21.4%)	
NSEMI, n (%)	46 (36.2%)	9 (37.5%)	37 (35.9%)	
STEMI, n (%)	56 (44.1%)	12 (50.0%)	44 (42.7%)	
Laboratory data				
estimated GFR, ml/min/1.73 m ²	59.1±23.6	51.3±28.2	60.9±22.0	0.07
LDL level, mg/dl	112.1±36.1	96.1±34.3	116.1±35.4	0.13
HbA1c, %	6.7±3.8	6.5±1.2	6.7±4.1	0.74
Peak CK, IU/L	372 (153.5–1,207.3)	1092 (200.3–1,997.5)	324 (142–935.3)	0.03

Table 1. Baseline patient, lesion and procedural characteristics

Medications at discharge				
Statin, n (%)	117 (92.1%)	21 (87.5%)	96 (93.2%)	0.40
Type of antiplatelet				0.68
Clopidogrel, n (%)	9 (7.1%)	2 (8.3%)	7 (6.8%)	
Prasugrel, n (%)	118 (92.9%)	22 (91.7%)	96 (93.2%)	
Duration of DAPT, months	5.24±2.79	5.75±3.75	5.13±2.53	0.33
Baseline lesion characteristics				
Target vessel: LAD/ LCX/ RCA, %	41.7/ 28.3/ 29.9	37.5/ 20.8/ 41.7	42.7/ 30.1/ 27.2	0.39
Lesion location: Proximal/ mid/ distal, %	37.0/ 35.4/ 27.6	45.8/ 25.0/29.2	35.0/ 37.9/ 27.2	0.45
Calcification, n (%)	42 (33.1%)	12 (50.0%)	30 (29.1%)	0.051
Bifurcation, n (%)	65 (51.2%)	12 (50.0%)	53 (51.5%)	0.90
Multivessel disease, n (%)	55 (43.3%)	12 (50.0%)	43 (41.7%)	0.47
Pre-TIMI flow grade 0/1, n (%)	46 (36.2%)	10 (41.7%)	36 (35.0%)	0.54
Post-TIMI flow grade 3, n (%)	127 (100%)	24 (100%)	103 (100%)	1.0
Procedural characteristics				
Thrombectomy, n (%)	40 (31.5%)	10 (41.7%)	30 (29.1%)	0.24
Rotational atherectomy, n (%)	15 (11.8%)	5 (20.8%)	10 (9.7%)	0.13
Orbital atherectomy, n (%)	6 (4.8%)	1 (4.2%)	5 (4.9%)	0.88
Pre-dilatation balloon diameter, mm	$2.62{\pm}0.60$	2.57±0.74	2.63±0.56	0.64
Pre-dilation balloon maximum pressure, atm	11.6±5.90	10.4±5.76	11.8±5.85	0.41
DCB diameter, mm	2.76±0.45	2.80±0.52	2.76±0.44	0.69
DCB length, mm	25.2±11.7	22.3±6.31	25.9±12.5	0.18
DCB inflation pressure, atm	7.7±2.8	8.07±2.26	7.65±2.90	0.61

- 517 Values are expressed as average±standard deviation, median (25th, 75th percentiles) or n (%)
- 518 PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; uAP, unstable angina pectoris; NSTEMI, non-ST elevation
- 519 myocardial infarction; STEMI, ST-elevation myocardial infarction; GFR, Glomerular Filtration Rate; LDL, low-density lipoprotein; CK,
- 520 creatinine kinase; DAPT, dual antiplatelet therapy; TIMI, Thrombolysis in Myocardial Infarction; DCB, drug-coated balloon

522

523

Table 2. OCT findings

Variables	All lesions (n=127)	TLF (n=24)	non-TLF (n=103)	P value
Pre-PCI OCT findings				
Plaque morphology				0.002
Plaque rupture, n (%)	52 (40.9%)	13 (54.2%)	39 (37.9%)	
Plaque erosion, n (%)	52 (40.9%)	3 (12.5%)	49 (47.6%)	
Calcified nodule, n (%)	23 (18.1%)	8 (33.3%)	15 (14.6%)	
Qualitative analysis				
Plaque characteristics				0.003
Fibrous plaque, n (%)	32 (25.2%)	1 (4.2%)	31 (30.1%)	
Lipid plaque, n (%)	75 (59.1%)	15 (62.5%)	60 (58.3%)	
Calcified plaque, n (%)	20 (15.7%)	8 (33.3%)	12 (11.7%)	
TCFA, n (%)	40 (31.5%)	13 (54.2%)	27 (26.2%)	0.008
Macrophage, n (%)	70 (55.1%)	18 (75.0%)	52 (50.5%)	0.03
Cholesterol crystal, n (%)	47 (37.0%)	15 (62.5%)	32 (31.1%)	0.004
Microchannels, n (%)	24 (19.0%)	5 (20.8%)	19 (18.5%)	0.79
Thrombus, n (%)	98 (77.2%)	21 (87.5%)	77 (74.8%)	0.18
Quantitative analysis				
Reference area, mm ²	4.99 ± 2.18	5.55 ± 2.22	4.89 ± 2.14	0.17
Minimal flow area, mm ²	1.16 ± 0.66	1.21 ± 0.57	1.15 ± 0.68	0.73
% area stenosis, %	73.6 ± 15.2	75.6 ± 11.9	73.2 ± 15.9	0.48
Lipid index	1228.6 ± 1410.4	1679.1 ± 1532.2	1126.1 ± 1360.5	0.09
Maximum calcium thickness, µm	448.7 ± 650.0	656.8 ± 753.7	403.4 ± 616.3	0.10
Maximum calcium arc, degree, °	71.9 ± 109.3	102.3 ± 124.4	65.2 ± 104.4	0.15
Calcium length, mm	2.73 ± 5.09	4.45 ± 5.40	2.35 ± 4.94	0.12
Mean thrombus area, mm ²	0.23 (0-0.63)	0.40 (0.10–1.42)	0.21 (0-0.58)	0.06
Thrombus burden, %	8.5 (0-22.2)	15.53 (3.01-30.39)	8.03 (0-17.18)	0.07
Thrombus volume, mm ³	1.04 (0-4.34)	2.45 (0.27-65.16)	0.98 (0-3.68)	0.08

Post-PCI OCT findings				
Minimal flow area, mm ²	3.56 ± 1.20	3.34 ± 0.96	3.61 ± 1.24	0.35
% area stenosis, %	33.3 ± 17.3	43.1 ± 18.5	31.1 ± 16.2	0.003
Acute flow area gain, mm ²	2.40 ± 1.26	2.47 ± 1.32	2.11 ± 0.91	0.23
Mean thrombus area, mm ²	0.22 (0-0.47)	0.43 (0.28–0.92)	0.15 (0-0.40)	< 0.001
Thrombus burden, %	4.5 (0-22.2)	9.23 (4.85–18.89)	3.60 (0-9.14)	< 0.001
Thrombus volume, mm ³	0.88 (0-2.74)	2.30 (0.38–9.87)	0.67 (0-1.90)	0.001
Reduction of thrombus burden*, %	52.1 (3.8–75.3)	33.8 (0-44.6)	57.8 (25.9–78.8)	0.02
Dissection (intimal, medial), n (%)	48 (10, 38) (37.8%)	9 (2, 7) (37.5%)	39 (8, 31) (37.9%)	1.0
Length of the dissection, mm	2.14 ± 3.37	2.25 ± 4.59	1.92 ± 2.92	0.67
Maximal arc of the dissection, °	39.6 ± 61.4	33.8 ± 62.2	37.2 ± 59.4	0.81
Linear rim of tissue with a width >200 μ m, n (%)	28 (58.3%)	4 (44.4%)	24 (61.5%)	0.46
Hematoma, n (%)	6 (4.7%)	1 (4.2%)	5 (4.9%)	0.92

526 Values are expressed as average±standard deviation, median (25th, 75th percentiles) or n (%)

527 * Reduction of thrombus burden was calculated for 98 lesions (21 lesions in the TLF group and 77 lesions in the non-TLF group).

528 PCI, percutaneous coronary intervention; OCT, optical coherence tomography; PR, plaque rupture; PE, plaque erosion; CN, calcified nodule;

529 TCFA, thin cap fibroatheroma

530

Table 3. Clinical outcomes

Variable	No. of patients (%)
Cardiac death, n, (%)	4 (3.2%)
Target vessel MI, n, (%)	2 (1.6%)
Target lesion revascularisation, n, (%)	19 (15.0%)
Target lesion revascularisation in hospital, n, (%)	4 (3.1%)
Target lesion failure, n, (%)	24 (18.9%)

534 Values are expressed as n (%)

535 MI, myocardial infarction

537 Table 4. Uni- and Multivariable Cox regression analysis of patient and lesion characteristics, pre-PCI OCT findings and post-PCI OCT

538 findings associated with TLF

variable	Univariate, HR	P value	value Multivariable model 1		Multivariable model 2	
	(95%CI)		HR (95%CI)	P value	HR (95%CI)	P value
Patient and lesion characteristics						
models						
Age	1.01 (0.97–1.03)	0.96	1.01 (0.97–1.05)	0.79	0.99 (0.96–1.04)	0.86
Sex male	1.60 (0.60-4.28)	0.35	1.76 (0.57–5.42)	0.32	1.75 (0.58–5.26)	0.32
Diabetes Mellitus	1.85 (0.81-4.22)	0.15	1.21 (0.49–2.99)	0.68	1.24 (0.50–3.08)	0.64
Chronic Kidney Dysfunction	2.67 (1.14-6.24)	0.02			1.85 (0.69-4.93)	0.22
Haemodialysis	3.02 (1.12-8.13)	0.03	1.96 (0.58–6.57)	0.28		
LVEF (per 5%)	0.78 (0.66–0.93)	0.0051	0.90 (0.72–1.12)	0.35	0.86 (0.71–1.05)	0.13
Calcification	2.03 (0.91-4.51)	0.08	1.50 (0.57–3.95)	0.42	1.79 (0.73–4.38)	0.20
Pre-PCI OCT findings models	, , , , , , , , , , , , , , , , , , , ,		Multivariable model 3			
Plaque morphology (reference: PR)	-	0.020	-	< 0.001		
PE	(0.21 [0.06–0.72])	(0.014)	(0.46 [0.11–0.87])	(0.025)		
CN	(1.32 [0.55–3.18])	(0.54)	(4.27 [1.02–17.8])	(0.038)		
TCFA	2.86 (1.28-6.39)	0.010	2.21 (0.68-8.27)	0.17		
Macrophage	2.77 (1.10-6.99)	0.03	1.47 (0.42–3.87)	0.46		
Cholesterol crystal	3.43 (1.50–7.85)	0.004	2.51 (0.86-8.32)	0.14		
Lipid index (per 100)	1.02 (0.99–1.05)	0.10	1.03 (0.99–1.03)	0.18		
Minimum flow area	1.02 (0.58–1.80)	0.94				
% area stenosis (per 5 %)	1.012 (0.98–1.04)	0.41				
Reference vessel area	1.12 (0.95–1.33)	0.19				
Thrombus burden (per 1%)	1.02 (1.02–1.04)	0.048	1.02 (0.99–1.05)	0.15		
Post-PCI OCT findings models			Multivariable model 4			
Minimum flow area	0.84 (0.58–1.21)	0.35				
% area stenosis (per 5 %)	1.21 (1.07–1.37)	0.002	1.17 (0.998–1.37)	0.053		

Reference vessel area	1.16 (0.97–1.39)	0.11	1.10 (0.857–1.42)	0.45	
Thrombus burden (per 1%)	1.09 (1.053–1.13)	< 0.001	1.08 (1.042–1.12)	< 0.001	
Reduction of thrombus burden, % (per 10)	0.97 (0.938–1.00)	0.06	0.99 (0.96–1.03)	0.70	

541 Multivariable model 1 was adjusted for age, sex, diabetes mellitus, haemodialysis, LVEF, and calcification. Multivariate model 2 was adjusted

542 for age, sex, diabetes mellitus, chronic kidney disease, LVEF and calcification. Multivariate model 3 was adjusted for plaque morphology,

543 TCFA, macrophages, cholesterol crystals, lipid index, and thrombus burden at pre-PCI OCT. Multivariate model 4 was adjusted for % area

544 stenosis, reference vessel area, thrombus burden, and reduction of thrombus burden on post-PCI OCT. PCI, percutaneous coronary intervention;

545 OCT, optical coherence tomography; TLF, target lesion failure; HR, hazard ratio; CI, confidence interval; LVEF, left ventricular ejection

546 fraction; CK, creatine kinase; PR, plaque rupture; CN, calcified nodule; PE, plaque erosion; TCFA, thin cap fibroatheroma

Figure 1: Representative OCT images of plaque morphology and assessment method of LA, FA, and TA on OCT image.



d) Assessment method of LA, FA, and TA



Figure 2: Study flowchart





Figure 3 (A): Kaplan–Meier curves showing the cumulative incidence of TLF stratified by culprit plaque morphology

(B): Kaplan–Meier curves showing the cumulative incidence of TLF stratified by culprit plaque morphology and residual thrombus burden after PCI

	G	roups	Cumulative incidence of TLF at 3 years (95%CI)				
(%) 100		CN with LRT	58.3% (0.233–0.944)				
	-	 CN with SRT 	33.9% (0.152–0.647)				
		PR with LRT 47.9% (0.306–0.688)					
	-	 PR with SRT 	4.2% (0.006–	0.261)			
80		PE with LRT	5.9% (0.009-	-0.35)			
	-	 PE with SRT 	9.0% (0.022–	0.329)			
60	Log-rar	nk p<0.001		CN with LRT: 58.3%			
40			·	PR with LRT: 47.9%			
20				CN with SR1: 33.9%			
				PE with SRI: 9.0%			
0				PE with LRT: 5.9%			
0		12	24 30	β (Months)			
Number at risk		_		(
CN with LRI 6	,	5	3 1				
DR with I RT 26		10	8 7	,			
PR with SRT 26	, }	21	15 1	2			
PE with LRT 17	,	13	10 9	-			
PE with SRT 35	5	28	11 8	5			

Figure 4. Representative cases

A) A representative case of PE with LRT

1) CAG and OCT images at pre PCI



2) CAG and OCT images at post PCI



3) CAG and OCT images 12 months after PCI



- B): A representative case of PR with SRT
 - 1) CAG and OCT images at pre PCI



2) CAG and OCT images at post PCI



3) CAG and OCT images 12 months after PCI



- C) A representative case of PR with LRT
 - 1) CAG and OCT images at pre PCI



2) CAG and OCT images at post PCI



3) CAG and OCT images 6 months after PCI

