ORIGINAL ARTICLE

Procedural characteristics and cardiovascular outcomes in patients undergoing drug-coated balloon angioplasty for de novo lesions in large coronary arteries: an observational study

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Abstract

Limited data exist regarding drug-coated balloon (DCB) treatment in de novo large coronary arteries. We sought to demonstrate procedural characteristics, residual stenosis, and clinical outcomes following DCB angioplasty for de novo lesions in large versus small coronary arteries. The study included 184 consecutive patients with 223 de novo coronary lesions undergoing paclitaxel DCB angioplasty between January 2019 and August 2020, who were divided according to whether the DCB diameter was ≥ 3.0 mm (large group, $n=58$) or <3.0 mm (small group, $n=125$). The large group had a higher proportion of acute coronary syndrome more commonly with ostial, bifurcation, and calcified lesions in large vessels and received lesion preparation with more frequent use of scoring or cutting balloons and atherectomy devices compared to the small group. Postprocedural angiographic diameter stenosis was smaller in the large group compared to the small group (31% [22–37] vs. 35% [26–42], $p=0.032$), and intravascular ultrasound revealed no significant difference in postprocedural area stenosis between the groups ($66.2 \pm 7.7\%$ vs. $67.9 \pm 7.8\%$; $p=0.26$). The median follow-up duration was 995 days. The incidence of a composite of all-cause death, myocardial infarction, stroke, or target lesion revascularization was similar between the groups (log-rank $p=0.41$) and was influenced by the presence of acute coronary syndrome and anemia but not by DCB diameter. The rate of cardiovascular outcomes after DCB treatment was comparable in de novo large and small coronary arteries. Notably, well-planned lesion preparation with intravascular imaging guidance was prevalent in large vessels.

Keywords Coronary artery disease · Drug-coated balloon · Intravascular ultrasound · Percutaneous coronary intervention

Abbreviations

CI	Confidence interval
DCB	Drug-coated balloon
EEM	External elastic membrane
IVUS	Intravascular ultrasound
MI	Myocardial infarction
MLA	Minimal lumen area
PCI	Percutaneous coronary intervention

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Introduction

While drug-eluting stents have made remarkable advancement in the field of percutaneous coronary intervention (PCI) during these decades, drug-coated balloons (DCB) have been used in specific types of coronary lesions, including in-stent restenosis, de novo lesions in small vessels, and bifurcation lesions [1]. DCB treatment involves the property of local antiproliferative drug delivery while leaving no metal behind, offering the potential to prevent restenosis without an elevated thrombotic risk [2]. Thus, DCB angioplasty is an encouraging alternative therapy for coronary artery disease.

However, there are concerns regarding elastic recoil, flow-limiting dissection, and hematoma linked to acute vessel closure immediately after DCB angioplasty, unlike drug-eluting or bare-metal stent implantation. While previous trials showed the clinical feasibility of DCB treatment in de novo small coronary vessels [3], there are limited data

on DCB use in de novo large arteries. Therefore, we sought to demonstrate procedural characteristics, residual stenosis, and clinical outcomes following DCB angioplasty for de novo lesions in large versus small coronary arteries.

Methods

Patients

This observational study was conducted using data from the clinical and intravascular imaging database of the Koseikai Takai Hospital cardiac catheterization lab. Between January 2019 and August 2020, 314 patients with 445 coronary lesions underwent PCI with DCB catheters. The study comprised 184 consecutive patients with 223 coronary de novo lesions who underwent PCI using DCBs. The baseline characteristics and procedures were obtained from the database. PCI procedures were guided by intravascular imaging according to current practice guidelines [4, 5]. The lesions to treat were selected at the operator's discretion after the diagnostic angiogram, and careful lesion preparation, with scoring balloons or atherectomy devices if needed, was highly encouraged during PCI. The study patients underwent angioplasty using the paclitaxel DCB SeQuent Please (B. Braun, Melsungen, Germany). The patients were divided into two groups based on whether the DCB diameter was ≥ 3.0 mm (large group) or < 3.0 mm (small group). All patients received treatment with aspirin and a $P2Y_{12}$ inhibitor, unless oral anticoagulants had been prescribed previously.

The study complied with the Declaration of Helsinki, and written informed consent was obtained from all patients before PCI.

Angiography and intravascular ultrasound

After intracoronary administration of nitroglycerine, angiography was performed during the procedure to evaluate the coronary arteries. The reference vessel diameter, minimal lumen diameter, percent diameter stenosis, and angiographic lesion length were measured based on diastolic frames in a single view showing the smallest minimal lumen diameter without foreshortening the target lesion. Quantitative coronary angiography analysis at pre- and post- procedures was performed offline by two independent operators. Moderate calcification was defined as radiopacities noted only during the cardiac cycle before contrast injection, and severe calcification was defined as radiopaque densities noted without cardiac motion before contrast injection and generally involving both sides of the arterial wall.

Intravascular ultrasound (IVUS) or other imaging modalities were used at the discretion of the operators after the diagnostic angiography. Two commercially available IVUS catheters with 60 MHz transducers were used in the present study: OptiCross HD (Boston Scientific, Natick, MA, USA) and AltaView (Terumo, Tokyo, Japan). IVUS examinations were conducted before PCI, after lesion preparation, and after DCB angioplasty. IVUS was utilized to determine the indication of a debulking device and scoring or cutting balloon, and to select balloon size and length using a motorized transducer pullback. Quantitative grayscale IVUS analysis was performed using QIvus 3.0 (Medis, Leiden, The Netherlands) to measure cross-sectional lumen and external elastic membrane (EEM) areas at proximal and distal references and in the target lesions, according to the American College of Cardiology consensus statement [6]. Plaque plus media area was calculated as EEM area minus lumen area. Plaque burden (%) was calculated as (plaque plus media area) divided by the EEM area. The remodeling index was expressed as the EEM area at the minimal lumen area (MLA) site divided by the average EEM area of the proximal and distal reference segments. To evaluate lumen stenosis, the percent area stenosis (%) was measured as (mean reference lumen area minus MLA) divided by the mean reference lumen area. To assess the circularity of the cross section, the lumen eccentricity index was calculated as the minimal lumen diameter divided by the maximal lumen diameter derived from the same cross section [7]. The lumen asymmetry index was calculated as one minus the minimal lumen diameter divided by the maximal lumen diameter throughout an entire lesion. Volumetric quantification of atheroma in the target lesion, including total atheroma volume and percent atheroma volume, was assessed according to the expert consensus documents [8]. The presence of dissection was defined as a linear rim of tissue with a width ≥ 0.20 mm and a clear separation. The intramural hematoma was characterized by an accumulation of blood within the medial space, displacing the internal elastic membrane inward and EEM outward by echolucent material in the media.

Clinical endpoints

The primary endpoint was a composite endpoint, including all-cause death, non-fatal myocardial infarction (MI), stroke, or target lesion revascularization. MI was defined by the fourth universal definition of myocardial infarction [9]. Periprocedural MI was defined as target vessel MI within 48 h after the index procedure. Stroke was defined as symptomatic stroke with the rapid onset of a focal or global neurological deficit lasting ≥ 24 h. Target lesion revascularization was defined as any revascularization for a stenosis within the target lesion. The clinical outcome data were obtained by reviewing the patient records.

Statistical analysis

Categorical variables were presented as counts (percentages), while continuous variables were presented as mean ± standard deviation or medians and interquartile (interquartile range [first quartile–third quartile]). Categorical variables were compared between the two groups with the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared between the groups using the unpaired t-test or Mann–Whitney U test, based on the data distribution. The Shapiro–Wilk test was used to assess the normality of continuous data. Kaplan–Meier survival curves with time-to-event data after the index procedure were generated and compared using the long-rank test (Mantel-Cox). The difference in the clinical event rate between the two groups was compared using Cox proportional hazard models, with a report of the hazard ratio, 95% confidence interval (CI), and p value. A multivariate Cox proportional hazards model was used to determine the independent determinants of the primary endpoint. The candidate predictor variables included acute coronary syndrome (unstable angina or acute MI), hemodialysis, C-reactive protein, and hemoglobin of < 11.0 g/dL, which were significant predictors in univariate analysis. In addition, the patients in the large group were divided into calcified and noncalcified subgroups based on the absence or presence of angiographically moderate or severe calcification. Baseline characteristics, procedures, and the incidence of the primary endpoint were examined in calcified versus noncalcified subgroups.

Statistical analysis was performed using SPSS statistical software (version 24.0, SPSS Inc., Chicago, IL, USA). A p value of < 0.05 was considered statistically significant.

Results

Baseline characteristics and procedures

The median age was 73.0 years (66.5–79.0) and 77.0% were male. The median period of clinical follow-up was 995 days (765–1155). Out of 184 patients with 223 lesions, we excluded one patient with one lesion in whom a DCB catheter did not completely cross the target lesion. Then, the patients undergoing DCB treatment in de novo coronary lesions were classified as the large group ($n = 58$) or the small group ($n = 125$). Baseline patient and lesion characteristics are provided in Table 1 and Fig. 1. The large group, compared to the small group, had a higher proportion of acute coronary syndrome and a lower prevalence of diabetes and was more commonly treated for ostial, bifurcation, and calcified lesions in large vessels. The large group included more type B2 or C lesions according to the American

College of Cardiology/American Heart Association classification than the small group (62.1% vs. 39.2%; $p = 0.004$).

As shown in Table 2 and Fig. 1, the median DCB diameter was 3.0 mm (3.0–3.5) in the large group and 2.5 mm (2.0–2.5) in the small group. The large group underwent lesion preparation with more frequent use of scoring or cutting balloons (77.6% vs. 54.4%; $p = 0.003$) and atherectomy devices (43.1% vs. 4.0%; $p < 0.001$) compared to the small group.

Angiography

As shown in Table 3, quantitative coronary angiography analysis showed reference vessel diameter was 2.81 mm (2.41–3.13) in the large group and 1.89 mm (1.66–2.12) in the small group. Postprocedural percent diameter stenosis was smaller in the large group than in the small group (31% [22–37] vs. 35% [26–42]; $p = 0.032$). The incidence of angiographic dissection was not different between the groups (20.7% vs. 16.0%; $p = 0.53$).

Intravascular ultrasound

As shown in Table 4, preprocedural IVUS revealed that the large group had larger plaque burden in the proximal reference segment and at the MLA site and greater percent area stenosis in the target lesion with more frequent attenuated plaques than the small group. Postprocedural IVUS analysis with volumetric quantification showed no significant differences in percent area stenosis (66.2 ± 7.7% vs. 67.9 ± 7.8%; $p = 0.26$) and percent atheroma volume (54.2 ± 7.6% vs. 55.3 ± 8.2%; $p = 0.48$) between the large and small groups. The incidence of dissection (61.7% vs. 70.1%; $p = 0.42$) and hematoma (17.0% vs. 32.8%; $p = 0.083$) after PCI did not differ significantly between the two groups. In terms of lumen circularity, IVUS analysis showed a similar postprocedural eccentricity and asymmetry index between the groups, but the mean increase in the asymmetry index was lower in the large group compared to the small group (Supplementary Table 1).

Clinical data

In our cohort, the large group underwent follow-up computed tomography or invasive angiography more frequently (Supplementary Fig. 1) and discontinued dual antiplatelet therapy earlier than the small group (Supplementary Fig. 2). As shown in Fig. 2 and Supplementary Table 2, there was no difference in the rate of the primary endpoint between the large group and the small group (log-rank $p = 0.41$). In the patient-level cohort, univariate analysis revealed that acute coronary syndrome, hemodialysis, C-reactive protein, and anemia (hemoglobin of < 11.0 g/dL) were associated with

Table 1 Baseline patient and lesion characteristics

	Large (≥ 3.0 mm) $n=58$	Small (< 3.0 mm) $n=125$	p Value
Age, years	70.5 (61.0–78.0)	75.0 (69.0–79.0)	0.054
Male	48 (82.8%)	93 (74.4%)	0.26
Body-mass index, kg/m^2	24.1 (22.1–25.8)	23.9 (21.5–26.1)	0.49
Body-mass index ≥ 25.0	25 (43.1%)	50 (50.0%)	0.75
Smoker	39 (67.2%)	70 (56.0%)	0.20
Current smoker	15 (25.9%)	18 (14.4%)	0.066
Diabetes	21 (36.2%)	73 (58.4%)	0.007
Insulin-treated diabetes	3 (5.2%)	14 (11.2%)	0.28
Dyslipidemia	43 (74.1%)	98 (78.4%)	0.57
Hypertension	47 (81.0%)	104 (83.2%)	0.84
Acute coronary syndrome (culprit)	11 (19.0%)	9 (7.2%)	0.023
Prior myocardial infarction	15 (25.9%)	33 (26.4%)	1.00
Multivessel disease	30 (51.7%)	77 (61.6%)	0.26
Prior stroke	5 (8.6%)	15 (12.0%)	0.62
Peripheral artery disease	15 (25.9%)	26 (20.8%)	0.45
Hemodialysis	4 (6.9%)	9 (7.2%)	1.00
Malignancy	5 (8.6%)	18 (14.4%)	0.34
Ejection fraction, %	57 (49–63)	61 (50–66)	0.20
Ejection fraction ≤ 40%	6 (10.5%)	8 (6.5%)	0.38
Blood test			
Triglyceride, mg/dL	122 (84–158)	111 (78–163)	0.44
HDL cholesterol, mg/dL	55 (42–65)	54 (45–63)	0.84
LDL cholesterol, mg/dL	102 (73–127)	77 (62–109)	0.006
eGFR, mL/min	64.0 (54.8–76.8)	62.3 (48.9–71.5)	0.12
C-reactive protein, mg/dL	0.12 (0.05–0.26)	0.08 (0.05–0.17)	0.16
Hemoglobin, g/dL	13.9 ± 1.8	13.5 ± 1.8	0.13
Hemoglobin < 11.0 g/dL	4 (6.9%)	11 (8.8%)	0.78
Medication at discharge			
Aspirin	57 (98.3%)	119 (95.2%)	0.43
P2Y$_{12}$ inhibitor	56 (96.6%)	125 (100%)	0.099
Anticoagulant	4 (6.9%)	12 (9.6%)	0.78
Statin	57 (98.3%)	121 (96.8%)	1.00
Target vessel			0.002
Right coronary	15 (25.9%)	36 (28.8%)	0.73
Left main	3 (5.2%)	0	0.031
Left anterior descending	28 (48.3%)	46 (36.8%)	0.15
Left circumflex	10 (17.2%)	43 (34.4%)	0.022
Graft	2 (3.4%)	0	0.099
Angiographic morphology			
Ostial	16 (27.6%)	5 (4.0%)	< 0.001
Proximal	25 (43.1%)	7 (5.6%)	< 0.001
Moderate or severe calcification	25 (43.1%)	31 (24.8%)	0.016
Eccentric	6 (10.3%)	6 (4.8%)	0.20
Angulated	3 (5.2%)	6 (4.8%)	1.00
Bifurcation	35 (60.3%)	28 (22.4%)	< 0.001
Thrombus	3 (5.2%)	3 (2.4%)	0.38
Chronic total occlusion	1 (1.7%)	6 (4.8%)	0.43
Type B2/C lesion	36 (62.1%)	49 (39.2%)	0.004

eGFR estimated glomerular filtration rate, *HDL* high density lipoprotein, *LDL* low density lipoprotein
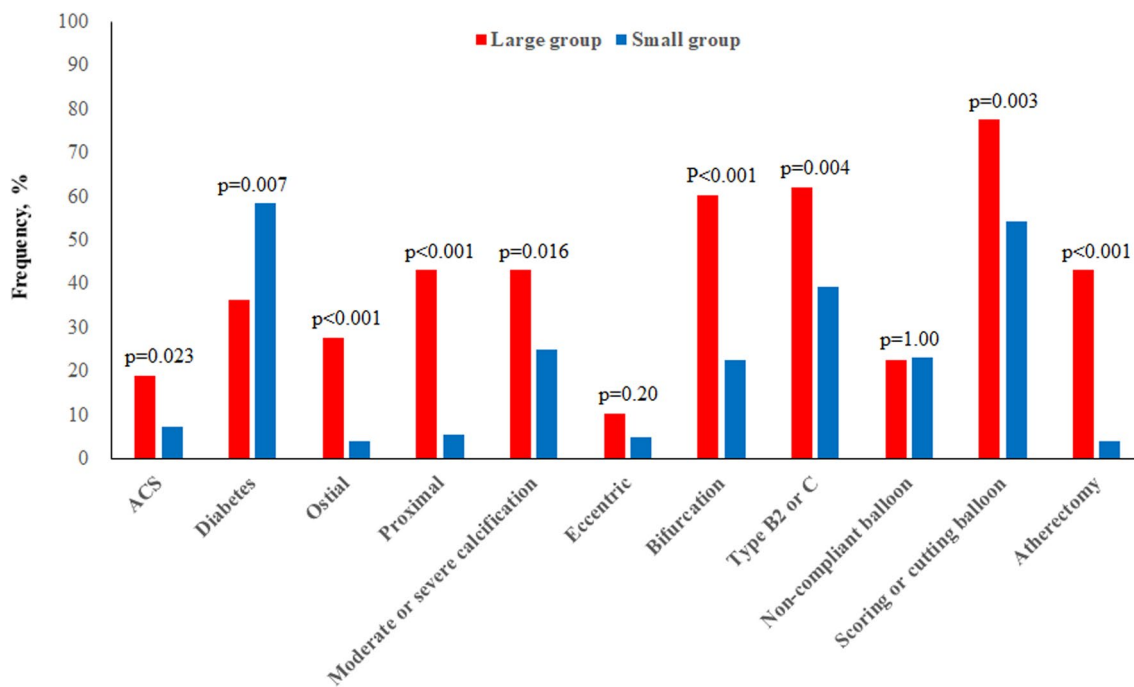
Fig. 1 Patients, lesions, and procedures in the large and small groups. Atherectomy includes rotational and orbital atherectomy, or directional coronary atherectomy. *ACS* acute coronary syndrome

Table 2 Procedures

	Large (≥ 3.0 mm) $n = 58$	Small (< 3.0 mm) $n = 125$	p Value
Radial access	49 (84.5%)	110 (88.0%)	0.64
Lesion preparation			
Non-compliant balloon	13 (22.4%)	29 (23.2%)	1.00
Scoring/cutting balloon use	45 (77.6%)	68 (54.4%)	0.003
Predilatation pressure, atm	10 (6–12)	10 (6–12)	0.77
Atherectomy*	25 (43.1%)	5 (4.0%)	< 0.001
Rotational/orbital atherectomy	5 (8.6%)	5 (4.0%)	0.29
Directional coronary atherectomy	20 (34.5%)	0	< 0.001
DCB treatment			
Minimal diameter of DCB, mm	3.0 (3.0–3.5)	2.5 (2.0–2.5)	< 0.001
Total length of DCB, mm	15 (15–20)	20 (20–26)	< 0.001
Pressure of DCB angioplasty, atm	7 (7–8)	7 (6–8)	0.57
Total inflation time of DCB, sec	50 (45–300)	80 (60–300)	0.22
Hybrid strategy of DCB and stent	1 (1.7%)	3 (2.4%)	1.00
Bailout stenting	0	3 (2.4%)	0.55
Intravascular imaging guidance	57 (98.3%)	110 (88.0%)	0.023
Intravascular ultrasound use	54 (93.1%)	107 (85.6%)	0.22

*Atherectomy includes rotational atherectomy, orbital atherectomy, or directional coronary atherectomy. *DCB* drug-coated balloon

the primary endpoint. However, the DCB diameter did not show an association with the primary endpoint. In the study patients, multivariate analysis identified acute coronary syndrome (hazard ratio 4.06; 95% CI 1.75–9.44; $p = 0.001$) and

anemia (hazard ratio 5.25; 95% CI 1.87–14.75; $p = 0.002$) as predictors of the primary endpoint (Table 5). Notably, the incidence of the primary endpoint in the large group was not different between in patients with and without

Table 3 Angiographic findings

	Large (≥ 3.0 mm) n = 58	Small (< 3.0 mm) n = 125	p Value
Pre angiography			
Reference vessel diameter, mm	2.81 (2.41–3.13)	1.89 (1.66–2.12)	< 0.001
Minimal lumen diameter, mm	1.15 (0.80–1.47)	0.73 (0.57–0.96)	< 0.001
% diameter stenosis, %	59 (50–70)	61 (51–71)	0.53
Angiographic lesion length, mm	10.1 (7.0–13.3)	11.3 (7.5–15.3)	0.46
Post angiography			
Reference vessel diameter, mm	2.92 (2.55–3.34)	1.97 (1.80–2.21)	< 0.001
Minimal lumen diameter, mm	1.99 (1.61–2.47)	1.25 (1.08–1.45)	< 0.001
% diameter stenosis, %	31 (22–37)	35 (26–42)	0.032
Angiographic lesion length, mm	7.5 (4.5–11.3)	7.6 (4.7–11.8)	0.75
Angiographic acute gain, mm	0.87 (0.42–1.22)	0.51 (0.28–0.79)	< 0.001
Post angiographic dissection	12 (20.7%)	20 (16.0%)	0.53

Angiographic acute gain was calculated as postprocedural minimal lumen diameter minus preprocedural minimal lumen diameter

angiographically moderate or severe calcification (Supplementary Table 3, Supplementary Table 4, Supplementary Fig. 3).

Discussion

The main findings of the present study were as follows: (1) in this observational study, the rate of cardiovascular outcomes after DCB treatment was comparable in de novo large and small coronary arteries, although the large group exhibited more acute coronary syndrome and more often involved ostial, bifurcation, and calcified lesions in large vessels; (2) well-planned lesion preparation followed by DCB use with intravascular imaging guidance was prevalent in de novo large vessels; and (3) the incidence of cardiovascular outcomes was not associated with DCB diameter but was influenced by the presence of acute coronary syndrome and anemia in our cohort.

While there are limited data on DCB treatment for de novo lesions in large vessels, previous studies demonstrated the safety and efficacy of DCB strategies in specific patient populations or types of coronary lesions. The randomized PEPCAD NSTEMI trial showed that treatment of de novo coronary lesions with DCBs that were 2.81 ± 0.49 mm in diameter was non-inferior to treatment with drug-eluting or bare-metal stents regarding 9-month target lesion failure in patients with non-ST-segment elevation MI [10]. In the PEPCAD NSTEMI trial, all-cause death occurred in 4.7% and target lesion reintervention occurred in 1.2% of patients undergoing DCB treatment at 9 months, which were comparable to the clinical performance observed in the large group of our study.

Another study, the DEBUT trial, demonstrated that PCI with DCB only for de novo lesions was superior to

bare-metal stent implantation in terms of major adverse cardiac events at 9 months in patients with high bleeding risk, and two-thirds of the DCB-only group were treated using DCBs that were ≥ 3.0 mm in diameter [11]. Moreover, Uskela et al. reported that the 12-month rates of major adverse cardiovascular events were 7.1% in patients with stable coronary artery disease and 12% in patients with acute coronary syndrome [12]. These trials support the feasibility of DCB strategies in the treatment of de novo lesions in large coronary arteries.

Despite the absence of scaffolding material like drug-eluting stents or bioresorbable vascular scaffolds, we observed favorable angiographic findings in the large group. Previous studies also showed the efficacy of DCB treatment without coronary stents in hemodialysis patients [13] and patients with bifurcation lesions [14]. Our study demonstrated that angiographic percent diameter stenosis after PCI was approximately 30% in the large group. According to the current international DCB consensus [5], our study demonstrated that acceptable angiographic findings, defined as residual stenosis ≤ 30%, were more frequently achieved in the large group compared to the small group. Obviously, intravascular imaging guidance is considered to be indisputable in DCB treatment, as it provides an assessment of lesion morphology and can be utilized in adequate lesion preparation leading to optimal DCB angioplasty. According to expert consensus documents, intracoronary imaging modalities have a key role in the minimizing risk of complications [15]. Our study also provides preprocedural and postprocedural intravascular imaging data with volumetric IVUS quantification in patients undergoing DCB treatment for de novo lesions. The large group, compared to the small group, exhibited larger postprocedural MLA (4.5 mm^2 [3.5–6.1] vs. 2.4 mm^2 [1.8–2.7]; $p < 0.001$) and a greater initial lumen gain, as measured by the postprocedural MLA

Table 4 Intravascular ultrasound measurement

	Large ($\geq$ 3.0 mm)	Small ($<$ 3.0 mm)	p Value
Pre-IVUS	$n=51$	$n=80$	
Proximal reference EEM area, mm^2	13.8 (9.1–17.7)	7.4 (6.0–8.8)	< 0.001
Proximal reference lumen area, mm^2	4.9 (3.5–8.3)	3.9 (2.6–4.5)	< 0.001
Proximal reference plaque burden, %	57.1 ± 17.4	49.9 ± 14.6	< 0.001
Distal reference EEM area, mm^2	12.6 (10.0–16.4)	5.0 (4.1–6.5)	< 0.001
Distal reference lumen area, mm^2	6.5 (5.0–8.0)	2.8 (2.4–3.6)	< 0.001
Distal reference plaque burden, %	45.2 ± 14.0	43.1 ± 11.3	0.35
MLA, mm^2	2.0 (1.8–2.6)	1.3 (1.2–1.5)	< 0.001
EEM area at the MLA site, mm^2	12.4 (8.5–15.0)	5.2 (4.3–6.6)	< 0.001
P&M area at the MLA site, mm^2	8.7 (6.0–12.2)	3.8 (2.9–5.2)	< 0.001
Plaque burden at the MLA site, %	80.1 (76.3–85.9)	74.1 (68.4–79.3)	< 0.001
Remodeling index at the MLA site	0.89 ± 0.18	0.89 ± 0.18	0.90
> 1.00	12 (23.5%)	21 (26.3%)	0.84
% area stenosis, %	81.6 (76.5–86.4)	77.1 (72.5–80.9)	0.001
Lumen volume, mm^3	51.1 (32.6–79.2)	24.4 (15.4–40.6)	< 0.001
EEM volume, mm^3	144.2 (90.6–227.5)	62.8 (42.2–111.4)	< 0.001
Total atheroma volume, mm^3	91.6 (52.8–155.3)	38.9 (24.8–70.1)	< 0.001
Percent atheroma volume, %	63.0 ± 9.2	61.4 ± 8.6	0.32
IVUS lesion length, mm	10.8 (7.7–14.5)	10.8 (7.9–17.2)	0.71
IVUS attenuated plaque > 90°	12 (23.5%)	5 (6.3%)	0.007
IVUS calcified plaque > 90°	20 (39.2%)	37 (46.3%)	0.47
Post-IVUS	n = 47	n = 67	
Proximal reference EEM area, mm^2	14.5 (11.1–19.3)	8.3 (6.5–10.1)	< 0.001
Proximal reference lumen area, mm^2	6.7 (5.1–9.7)	4.2 (3.4–4.9)	< 0.001
Proximal reference plaque burden, %	51.4 ± 10.6	49.2 ± 11.0	0.28
Distal reference EEM area, mm^2	13.1 (9.2–17.5)	5.7 (4.7–7.1)	< 0.001
Distal reference lumen area, mm^2	6.4 (5.3–9.1)	3.5 (2.6–4.0)	< 0.001
Distal reference plaque burden, %	46.4 ± 12.1	44.2 ± 11.0	0.31
MLA, mm^2	4.5 (3.5–6.1)	2.4 (1.8–2.7)	< 0.001
EEM area at the MLA site, mm^2	13.1 (9.2–17.7)	6.3 (5.4–7.6)	< 0.001
P&M area at the MLA site, mm^2	8.3 (5.5–11.6)	4.0 (3.3–5.2)	< 0.001
Plaque burden at the MLA site, %	62.8 (57.2–69.9)	63.4 (59.5–68.9)	0.80
Remodeling index at the MLA site	0.96 ± 0.12	0.93 ± 0.16	0.40
% area stenosis, %	66.2 ± 7.7	67.9 ± 7.8	0.26
Lumen volume, mm^3	76.4 (47.5–106.8)	35.6 (23.7–63.4)	< 0.001
EEM volume, mm^3	169.0 (119.5–246.8)	84.2 (52.5–150.4)	< 0.001
Total atheroma volume, mm^3	80.9 (57.5–140.8)	45.6 (28.8–90.4)	< 0.001
Percent atheroma volume, %	54.2 ± 7.6	55.3 ± 8.2	0.48
IVUS lesion length, mm	10.7 (8.3–14.5)	12.4 (8.3–19.9)	0.51
Post IVUS dissection	29 (61.7%)	47 (70.1%)	0.42
Post IVUS hematoma	8 (17.0%)	22 (32.8%)	0.083
Pre- and post-IVUS	n = 45	n = 52	
IVUS lumen gain, mm^2	2.1 (1.2–3.6)	1.0 (0.5–1.3)	< 0.001
Δ lumen volume, mm^3	20.8 (11.0–33.6)	8.6 (4.1–15.7)	< 0.001
Δ vessel volume, mm^3	14.5 (5.0–31.1)	7.2 (2.3–14.3)	0.013
Δ atheroma volume, mm^3	0.3 (−7.8 to 4.3)	−0.6 (−4.0 to 2.9)	0.93
Δ percent atheroma volume, %	−8.8 ± 7.3	−6.9 ± 4.8	0.12

Δ (delta) indicates post-treatment score minus pre-treatment score. *EEM* external elastic membrane, *IVUS* intravascular ultrasound, *MLA* minimal lumen area, *P & M* plaque plus media

Fig. 2 Cumulative incidence of a composite endpoint of death, MI, stroke, or TLR. *MI* myocardial infarction, *TLR* target lesion revascularization
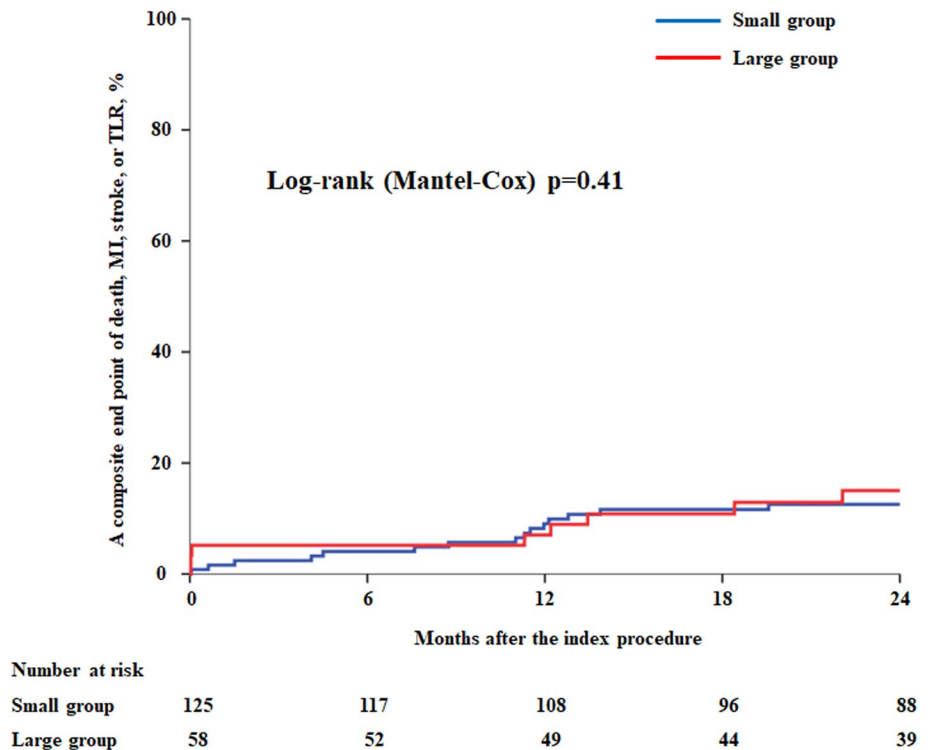

Table 5 Predictors of the primary endpoint in the patient-level multivariate analysis

	Hazard ratio (95% CI)	p Value
Acute coronary syndrome (culprit)	4.06 (1.75–9.44)	0.001
Hemodialysis	2.43 (0.85–6.99)	0.099
C-reactive protein, mg/dL	1.13 (0.89–1.43)	0.33
Anemia (hemoglobin < 11.0 g/dL)	5.25 (1.87–14.75)	0.002

The univariate analysis demonstrated that the candidate predictor variables included acute coronary syndrome, hemodialysis, C-reactive protein, and hemoglobin of < 11.0 g/dL. The multivariate analysis showed that the presence of acute coronary syndrome and anemia was associated with the primary endpoint. *CI* confidence interval

minus the preprocedural MLA (2.1 mm^2 [1.2–3.6] vs. 1.0 mm^2 [0.5–1.3]; $p < 0.001$). Although changes in atheroma volume during PCI were nearly imperceptible in both the large and small groups (0.3 mm^3 [-7.8–4.3] and −0.6 mm^3 [−4.0 to 2.9], respectively), the volumetric IVUS analysis revealed that balloon angioplasty in the large group had a greater effect on enlargement in lumen volume (20.8 mm^3 [11.0–33.6] vs. 8.6 mm^3 [4.1–15.7]; $p < 0.001$).

This study has limitations. First, the sample size is small. Larger prospective studies are needed to further investigate the efficacy and safety of DCB treatment in de novo large coronary lesions. Nonetheless, the present study provides unprecedented data on angiography and volumetric quantification by intravascular imaging as well as clinical outcomes following DCB treatment for de novo coronary lesions. Second, the study did not include patients in whom operators dismissed DCB angioplasty for suboptimal results after lesion preparation, because the study included patients undergoing PCI using DCB catheters. Finally, the selection of patients and lesions is biased. The large group more commonly had ostial, bifurcation, and calcified lesions, which were possibly unsuitable for drug-eluting stents. Thus, DCB angioplasty may be an available alternative even for complex lesions in de novo large arteries under lesion preparation using scoring or cutting balloons and atherectomy devices with intravascular ultrasound guidance.

Conclusions

In our cohort, the rate of cardiovascular outcomes after DCB angioplasty was comparable in de novo large and small coronary arteries. Particularly, DCB treatment in large vessels was characterized by well-planned lesion preparation with intravascular imaging guidance. Prospective studies with larger sample sizes are needed to further evaluate the effectiveness of DCB angioplasty in de novo large coronary arteries.

Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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