Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Data Sharing Statement

The REC-CAGEFREE I trial is planning to continue follow-up until 2032. Individual participant data is available upon request from the authors. Any relevant inquiry should be emailed to Dr. Ling Tao (Email: lingtaofmmu@qq.com)

Supplementary Methods

1. The recommendation of DCB angioplasty

The procedural maneuvers of DCB should adhere to the recommendations of the German Consensus Group on DCB interventions [1] and the Third Report of the International DCB Consensus Group. [2]

1. With or without a Plain Old Balloon Angioplasty (POBA), a pre-dilatation prior to DCB angioplasty shall be performed with a non-compliant balloon, cutting balloon, or scoring balloon at 0.8-1.0 balloon/vessel size ratio.

2. After lesion preparation, a 5- to 10-minute observational period should be conducted, followed by an angiogram to ensure satisfactory lesion preparation, which consists of the following criteria:

1) ≤30% residual stenosis (visual);

2) Thrombolysis In Myocardial Infarction (TIMI) flow grade 3; and

3) the absence of a flow-limiting dissection (NHLBI type D, E, and F).

Randomization should ONLY be conducted when successful pre-dilatation is confirmed.

3. Subsequently, the DCB, on each side longer than the lesion by at least 2-3 mm to avoid geographical mismatch, is inflated at nominal pressure for ~45 seconds. In cases where subjects experience TIMI flow<3, severe dissection (type D, E, and F), or visual residual stenosis>30% (visual) post-DCB, a rescue DES is implanted mandatorily for bailout treatment.

2. Covariate adjusted analysis

The pre-specified covariables included in the adjusted analyses are age (continuous), sex (binary), hypertension (binary), hyperlipidemia (binary), diabetes (binary), smoking status (categorical), history of CVD (binary), stroke (binary), and clinical presentation (categorical).

A propensity score with treatment as the dependent variable (1 for the DCB group and 0 for the DES group) and all covariates listed above as independent variables were conducted through a logistic regression model with a random effect for the center. Then, an Inverse Probability Treatment Weighting (IPTW) analysis (weighted KM) was performed to estimate the covariate-adjusted difference in cumulative primary outcome rate between the treatment groups in the ITT population, with its one-sided 95%CI estimated.

3. Win ratio analysis

The unmatched win ratio method was employed to analyze the hierarchical composite endpoint of DoCE, which consists of three time-to-event outcomes including cardiovascular death, target vessel myocardial infarction, and clinically and physiologically indicated target lesion

revascularization. The endpoints will be evaluated by clinical importance in hierarchical order as follows. This hierarchy was established based on previous studies. [3,4]

- Time to cardiovascular death
- Time to target vessel myocardial infarction
- Time to clinically and physiologically indicated target lesion revascularization

Following Pocock et al's methodology [5], in the unmatched win ratio approach, each patient in the DCB group is compared with each patient in the DES group; therefore, there were a total of 1,133 * 1,139 paired comparisons. The algorithm for calculating the unmatched win ratio analysis is described as follows:

Step 1: All pairs (1,133 * 1,139 patient pairs) will be compared for the time until death, truncated at 720 days. If both participants die, the "winner" will be the one who had a longer time until death. If one participant dies but another does not, the "winner" will be the one who had a longer censored time. Otherwise, the match is tied and then go to Step 2.

Step 2: The tied pairs from the previous step will be compared for the time until a target vessel myocardial infarction, which is truncated at 720 days. If both participants have a target vessel myocardial infarction, the "winner" will be the one who had a longer time until an event. If one participant has an event but another does not, the "winner" will be the one who had a longer censored time. Otherwise, the match is tied and then go to Step 3.

Step 3: Repeat Step 2 for the outcome of clinically and physiologically indicated target lesion revascularization.

The unmatched win ratio was calculated as the total number of wins in the DCB group divided by the total number of wins in the DES group. The point estimate, together with 95% CI of the win ratio, is estimated using the *WINS* package (Version 1.3.3) in R statistical software version 4.2.1 (R Project for Statistical Computing). The p value in the win ratio analysis was from the method based on U-statistics described by Dong et al [6].

4. Definitions of study endpoints

4.1. Definition of Death

Death is defined according to Standardized End Point Definitions for Coronary Intervention Trials -The Academic Research Consortium-2 Consensus Document (ARC-2) [7]

Type of Death	Definition
Cardiovascular mortality	1. Death due to proximate cardiac cause, e.g. myocardial infarction, cardiac tamponade, worsening heart failure, and endocarditis.
	2. Death caused by non-coronary, non-CNS vascular conditions such as pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease.
	3. Death from vascular CNS causes • From hemorrhagic stroke • From ischemic stroke
	4. All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure.
	5. Sudden or unwitnessed death defined as non-traumatic, unexpected fatal event occurring within 1h of the onset of symptoms in an apparently healthy subject. If death is not witnessed, the definition applies when the victim was in good health 24h before the event.
	6. Death of unknown cause.
Non-cardiovascular mortality	7. Death of a primary cause that is clearly related to another condition (e.g. trauma, cancer, suicide).

4.2. Definition of Stroke

Classified by TIA, ischemic stroke, hemorrhagic stroke, and indeterminate [8,9]

Cerebrovascular Accident (CVA)/Stroke: A stroke is defined as a sudden onset of focal neurological deficits due to vascular lesions of the brain that persist for >24 hours. Any neurological symptom that lasts < 24 hours is classified as a transient ischemic attack (TIA). Stroke results from either of two types of cerebral vascular disturbance: ischemia or hemorrhage.

Ischemic stroke: Infarction caused by focal occlusion or stenosis of single or multiple intracranial or extracranial arteries.

Hemorrhagic stroke: Infarction caused by nontraumatic intraparenchymal, intraventricular, or subarachnoid hemorrhage.

Indeterminate: Insufficient information to determine stroke of ischemic or hemorrhagic origin.

Transient ischemic attack (TIA): TIAs are focal neurologic abnormalities of sudden onset and brief duration (i.e., lasting less than 24 hours) that reflect dysfunction in the distribution of the affected artery. TIAs include transient monocular blindness (e.g., amaurosis fugax defined as a transient episode of monocular blindness, or partial blindness, lasting ten minutes or less) and transient hemispheric attacks.

4.3. Definition of Myocardial infarction

4.3.1. Target Vessel Myocardial Infarction
Myocardial Infarction is not clearly attributable to a non-target vessel.
4.3.2. Non-target Vessel Myocardial Infarction
Myocardial Infarction is clearly attributable to a non-target vessel.
4.3.3. Spontaneous Myocardial infarction (according to Fourth universal definition of myocardial infarction 2018) [10]

MI type 1
Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL and with at least one of the following: • Symptoms of acute myocardial ischemia; • New ischemic ECG changes; • Development of pathological Q waves; • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic aetiology; • Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.
MI type 2
Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute coronary athero-thrombosis, requiring at least one of the following: • Symptoms of acute myocardial ischemia • New ischemic ECG changes; • Development of pathological Q waves; Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology.
MI type 3
Patients who suffer cardiac death, with symptoms suggestive of myocardial ischemia accompanied by presumed new ischemic ECG changes or ventricular fibrillation, but die before blood samples for biomarkers can be obtained, or before increases in cardiac biomarkers can be identified, or MI is detected by autopsy examination.
MI type 4a: MI related to PCI (<48 hours post PCI)
Adjudicated per SCAI definition only, see below.

MI type 4b:
A subcategory of PCI-related MI is stent/scaffold thrombosis, type 4b MI, as documented by angiography or autopsy using the same criteria utilized for type 1 MI. It is important to indicate the time of the occurrence of the stent/scaffold thrombosis in relation to the timing of the PCI procedure.
MI type 4c:
Occasionally MI occurs and—at angiography, in-stent restenosis, or restenosis following balloon angioplasty in the infarct territory—is the only angiographic explanation since no other culprit lesion or thrombus can be identified. This PCI-related MI type is designated as type 4c MI, defined as focal or diffuse restenosis, or a complex lesion associated with a rise and/or fall of cTn values above the 99th percentile URL applying, the same criteria utilized for type 1 MI.
MI type 5: CABG-related MI 48h after the index procedure
Adjudicated per SCAI definition only, see below.

4.3.4. Peri-procedural MI after PCI or CABG (<48 hours post- PCI or CABG) according to the Consideration of a New Definition of Clinically Relevant Myocardial Infarction After Coronary Revascularization - An Expert Consensus Document from the Society for Cardiovascular Angiography and Interventions (SCAI 2013) definition [11]

- For patients with normal baseline cardiac biomarkers, any of the following criteria:
    - CK-MB ≥10×ULN or cTn (I or T) ≥70×ULN OR
    - CK-MB ≥ 5×ULN or cTn (I or T) ≥35×ULN may be accepted in combination with any of the following:
        - New pathologic Q-waves in ≥2 contiguous leads
        - OR: new persistent LBBB
- For patients with elevated baseline cardiac biomarkers, any of the following criteria:
    - When biomarker levels are stable or falling, there should be new CK-MB elevation by an absolute increment of ≥10×ULN (or ≥70×ULN for cTnI or T) from the previous nadir level
    - When biomarker levels have not been shown to be stable or falling, there should be a further rise in CK-MB or troponin beyond the most recently measured value by an absolute increment of ≥10×ULN in CK-MB or ≥70×ULN in cTn plus new ST-segment elevation or depression plus signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension.

Note: Any peri-procedural MI that occurred due to the PCI that was performed prior to randomization is considered a baseline clinical presentation rather than an event.

4.4. Definition of Revascularization

Revascularization is defined according to Standardized End Point Definitions for Coronary Intervention Trials -The Academic Research Consortium-2 Consensus Document (ARC-2) [7]

Classification	Definition

Target lesion	The target lesion is defined as the treated segment including the 5-mm margin proximal and distal to the stent
Target lesion revascularization (TLR)	Target lesion revascularization is defined as a repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion.
Target vessel	The target vessel is defined as the entire major intervened coronary vessel, including side branches.
Target vessel revascularization (TVR)	Target vessel revascularization is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel including the target lesion.
Target vessel non–target lesion revascularization	Target vessel nontarget lesion revascularization is defined as any repeat percutaneous intervention or surgical bypass of the target vessel for pre-existing disease, disease progression or other reasons unrelated to the target lesion as defined above.
Non-Target Lesion Revascularization (Non-TLR)	Any revascularization in the target vessel for a lesion other than the target lesion is considered a non-TLR.
Non-Target Vessel Revascularization (Non-TVR)	Revascularization of the vessel identified and treated as the non-target vessel at the time of the index procedure.

Clinically and physiologically indicated revascularization (CPI-TLR/TVR)
A revascularization is considered clinically and physiologically indicated if associated with any of the following (Hierarchically):

1. Positive invasive functional ischemia test (e.g. FFR, iFR). When invasive functional assessment is available, use the following hierarchy:
   a) Core laboratory–reported fractional flow reserve ≤0.80 or instant wave-free ratio ≤0.89.
   b) Site-reported fractional flow reserve ≤0.80 or instant wave-free ratio ≤0.89.
   c) Core laboratory–reported angiography-derived fractional flow reserve ≤0.80.
2. Angiographic diameter stenosis ≥50% (by core laboratory QCA based on the average of multiple views) and positive non-invasive ischemia test (e.g. dobutamine stress test, nuclear test, exercise test, FFR-CT).
3. Angiographic diameter stenosis ≥50% (by core laboratory QCA based on the average of multiple views) and ischemic symptoms (stable angina or acute coronary syndrome).
4. Angiographic diameter stenosis ≥70% (by core laboratory QCA based on the average of multiple views).
5. Angiographic diameter stenosis ≥70% (by core laboratory QCA based on the worst view).

Additional notes:

- In case a revascularization occurs in a vessel and the core laboratory-reported angiography-derived fractional flow reserve > 0.80, and the target lesions have a core

laboratory-reported angiographic diameter stenosis ≥70% by QCA based on multiple views, the revascularization will be considered as non-clinically indicated.

- When the diameter stenosis is <50%, the presence of severe ischemic signs and symptoms (e.g., acute myocardial infarction) would also confirm the diagnosis of a clinically indicated revascularization.

4.5. Definition of Bleeding

Bleeding Academic Research Consortium (BARC) definition [12] for Bleeding is used in the primary analyses.

Type 0:	No evidence of bleeding
Type 1:	Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a health-care professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a health-care professional.
Type 2:	Any overt, actionable sign of haemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: • Requiring medical or percutaneous intervention guided by a health care professional includes (but is not limited to) temporary/permanent cessation of a medication, coiling, compression, local injection • Leading to hospitalization or an increased level of care • Prompting evaluation, defined as an unscheduled visit to a healthcare professional resulting in diagnostic testing (laboratory or imaging)
Type 3:	Type 3a: • Overt bleeding plus haemoglobin drop of 3 to < 5 g/dL (provided haemoglobin drop is related to bleed). • Any transfusion with overt bleeding. Type 3b: • Overt bleeding plus haemoglobin drop ≥5 g/dL (provided haemoglobin drop is related to bleed), • Cardiac tamponade, • Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/haemorrhoid), • Bleeding requiring intravenous vasoactive agents. Type 3c:

	• Intracranial haemorrhage (does not include microbleeds or haemorrhagic transformation, does include intraspinal), Subcategories confirmed by autopsy or imaging or lumbar puncture, • Intraocular bleed compromising vision.
Type 4:	CABG-related bleeding, • Perioperative intracranial bleeding within 48 h, • Reoperation after closure of sternotomy for the purpose of controlling bleeding, • Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period, • Chest tube output more than or equal to 2L within a 24-h period.
Type 5:	Fatal bleeding Type 5a: • Probably fatal bleeding; no autopsy or imaging confirmation but clinically suspicious Type 5b: • Definite fatal bleeding is bleeding that is directly observed (either by clinical specimen – blood, emesis, stool, etc. – or by imaging) or confirmed on autopsy.

4.6. Definition of Stent (device) Thrombosis

Stent (device) thrombosis is defined according to Standardized End Point Definitions for Coronary Intervention Trials -The Academic Research Consortium-2 Consensus Document (ARC-2) [7].

A thrombosis within the segment of DCB is considered as stent thrombosis.

Classification	**Criteria**
Definite stent (device) thrombosis	1. Angiographic confirmation of stent (device) thrombosis
	The presence of a thrombus that originates in the stent (device) or in the segment 5 mm proximal or distal to the stent (device) that was used during the index PCI or in a side branch originating from the treated segment and the presence of at least 1 of the following criteria:
	Acute onset of ischemic symptoms at rest
	New electrocardiographic changes suggestive of acute ischemia
	Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous myocardial infarction)
	2. Pathological confirmation of stent (device) thrombosis
	Evidence of recent thrombus within the stent (device) was used during the index PCI determined at autopsy

	Examination of tissue retrieved following thrombectomy (visual/histology)
Probable (device) thrombosis	Regardless of the time after the index procedure, any myocardial infarction that is related to documented acute ischemia in the territory of the implanted stent (device) without angiographic confirmation of stent (device) thrombosis and in the absence of any other obvious cause.

Supplementary Tables

Table S1. List of Sites

No.	Site	Number of enrollments
1	Xijing Hospital	609
2	Zhuzhou Central Hospital	195
3	The Southwest Hospital of AMU	182
4	Ankang City Central Hospital	165
5	Xiangtan Central Hospital	115
6	China-Japan Union Hospital of Jilin University	93
7	The First Affiliated Hospital of USTC	83
8	The First Hospital of Kunming	83
9	Tangshan Workers Hospital	71
10	West China Hospital Sichuan University	67
11	The Second Affiliated Hospital of Nanchang University	67
12	The Second Xiangya Hospital of Central South University	67
13	Renmin Hospital of Wuhan University	32
14	Tianjin 4th Central Hospital	30
15	The Fourth Affiliated Hospital of China Medical University	29
16	Beijing Friendship Hospital	28
17	Yantai Yuhuangding Hospital	27
18	The First Affiliated Hospital of Bengbu Medical College	27
19	The Affiliated Hospital of Qingdao University	24
20	Tongji Hospital Tongji Medical College of HUST	24
21	Hunan Provincial People's Hospital	24
22	Shanxi Cardiovascular Hospital	23
23	Fuwai Central China Cardiovascular Hospital	21
24	Changzheng Hospital	20
25	Jiangxi Provincial People's Hospital	19
26	The First Affiliated Hospital of Nanchang University	17
27	Ganzhou People's Hospital	17
28	The Affiliated Hospital of Xuzhou Medical University	16
29	Shanghai Sixth People's Hospital	13
30	Yan'an Hospital of Kunming City	12
31	Shanxi Bethune Hospital	11
32	Xiangyang Central Hospital	10
33	Zhongnan Hospital of Wuhan University	10
34	Third People's Hospital of Xuzhou	9
35	Shaanxi Provincial People's Hospital	5
36	Lanzhou University Second Hospital	5

37	Tianjin Medical University General Hospital	5
38	Changhai Hospital	5
39	Nanjing First Hospital	3
40	Jiangsu Province Hospital	3
41	The Third Xiangya Hospital of Central South University	3
42	The First Hospital of China Medical University	2
43	First Affiliated Hospital of Kunming Medical University	1

Table S2. Inclusion and exclusion criteria

Inclusion criteria
1. Indicated for PCI either due to acute or chronic coronary syndrome
2. Patients with *de novo*, non-complex lesion and underwent successful pre-dilatation
3. Able to complete the follow-up and compliant with the prescribed medication
Non-complex PCI is defined as meeting all the following criteria:
1) planned treated lesions/vessels <3, planned DES or DCB <3, or planned total DES/DCB length≤60 mm; 2) Bifurcations not requiring treatment in both main and side branch; 3) Non-left main lesion; 4) Non-venous or arterial graft lesion; 5) Non-chronic total occlusion; and 6) Not requiring atherectomy
Successful pre-dilatation is defined as fulfilling all the following criteria:
1) Achieving Thrombolysis In Myocardial Infarction (TIMI) flow grade 3
2) Without National, Heart, Lung, and Blood Institute (NHLBI) classification defined dissections type D, E, and F
3) Residual stenosis ≤30% after balloon pre-dilation (visual assessment)
4) Without serious complications requiring the termination of PCI
Exclusion criteria
1. Under the age of 18
2. Unable to provide informed consent
3. Patient is a woman who is pregnant or nursing
4. Known contraindication to medications such as Aspirin, Heparin, antiplatelet drugs, or contrast
5. Currently participating in another trial and not yet at its primary endpoint
6. Concurrent medical condition with a life expectancy of less than 2 years
7. Previous intracranial haemorrhage
8. In-stent restenosis requiring revascularization
9. Atrial fibrillation required chronic use of anticoagulation
10. Prior CABG
11. Cardiogenic shock

Table S3. Study endpoints

Primary endpoint
Device-oriented Composite Endpoint (DoCE), defined as a nonhierarchical composite clinical endpoint of cardiac death, target vessel myocardial infraction (TV-MI), and clinically and physiologically indicated target lesion revascularization (CPI-TLR)
Secondary endpoints
1. Individual components of the DoCE
2. Patient-oriented composite endpoint (PoCE) *PoCE is a nonhierarchical composite clinical endpoint of all-cause death, any stroke, any MI, and any revascularization*
3. Individual components of the PoCE
4. Target vessel failure (TVF) *Target vessel failure is a nonhierarchical composite clinical endpoint of cardiac death, TV-MI, and clinically and physiologically indicated target vessel revascularization (CPI-TVR)*
5. Clinically and physiologically indicated target vessel revascularization
6. Net adverse clinical events (NACE) *NACE is a nonhierarchical composite clinical endpoint of all-cause death, any stroke, any MI, any revascularization, and BARC-defined type 3 or 5 bleeding events*
7. Definite/Probable Stent thrombosis rates according to ARC-II classification
8. BARC type 3 or 5 bleeding events
9. BARC type 2, 3 or 5 bleeding events
10. BARC defined type 2 bleeding events
11. Device success rate
12. Procedure success rate
13. Clinically relevant ischemic or bleeding events *Clinically relevant ischemic or bleeding events is defined as the hierarchical composite clinical endpoint of any death, any stroke, any MI, BARC type 3 bleeding events, any revascularization, and BARC type 2 bleeding events*

Commented [DW1]: *Hierarchical composite endpoint is not listed here.*

Table S4. Medications at discharge and follow-up in the ITT population

Antiplatelet medication	DCB (N=1,133)	DES (N=1,139)	p value
Aspirin			
Discharge	1,055/1,130 (93.4%)	1,062/1,138 (93.3%)	0.969
1 month	1,039/1,128 (92.1%)	1,046/1,135 (92.2%)	0.966
3 months	969/1,122 (86.4%)	994/1,134 (87.7%)	0.362
6 months	887/1,122 (79.1%)	945/1,132 (83.5%)	0.007
12 months	790/1,108 (71.3%)	850/1,119 (76.0%)	0.013
24 months	609/1,090 (55.9%)	651/1,108 (58.8%)	0.172
Indobufen			
Discharge	56/1,130 (5.0%)	53/1,138 (4.7%)	0.740
1 month	51/1,128 (4.5%)	52/1,135 (4.6%)	0.945
3 months	49/1,122 (4.4%)	54/1,134 (4.8%)	0.653
6 months	48/1,122 (4.3%)	57/1,132 (5.0%)	0.394
12 months	51/1,108 (4.6%)	54/1,119 (4.8%)	0.804
24 months	16/1,090 (1.5%)	17/1,108 (1.5%)	0.898
Clopidogrel			
Discharge	695/1,130 (61.5%)	689/1,138 (60.5%)	0.639
1 month	704/1,128 (62.4%)	696/1,135 (61.3%)	0.594
3 months	694/1,122 (61.9%)	698/1,134 (61.6%)	0.883
6 months	676/1,122 (60.2%)	705/1,132 (62.3%)	0.323
12 months	619/1,108 (55.9%)	672/1,119 (60.1%)	0.045
24 months	411/1,090 (37.7%)	422/1,108 (38.1%)	0.854
Ticagrelor			
Discharge	432/1,130 (38.2%)	446/1,138 (39.2%)	0.638
1 month	416/1,128 (36.9%)	430/1,135 (37.9%)	0.621
3 months	404/1,122 (36.0%)	421/1,134 (37.1%)	0.581
6 months	362/1,122 (32.3%)	397/1,132 (35.1%)	0.159
12 months	260/1,108 (23.5%)	307/1,119 (27.4%)	0.032
24 months	88/1,090 (8.1%)	100/1,108 (9.0%)	0.425
Single antiplatelet therapy			
Discharge	22/1,130 (1.9%)	24/1,138 (2.1%)	0.784
1 month	44/1,128 (3.9%)	47/1,135 (4.1%)	0.771
3 months	109/1,122 (9.7%)	91/1,134 (8.0%)	0.158
6 months	220/1,122 (19.6%)	137/1,132 (12.1%)	<0.001
12 months	374/1,108 (33.8%)	291/1,119 (26.0%)	<0.001
24 months	856/1,090 (78.5%)	901/1,108 (81.3%)	0.103
Dual antiplatelet therapy			
Discharge	1,108/1,130 (98.1%)	1,113/1,138 (97.8%)	0.676
1 month	1,083/1,128 (96.0%)	1,088/1,135 (95.9%)	0.855
3 months	1,003/1,122 (89.4%)	1,038/1,134 (91.5%)	0.083

6 months	875/1,122 (78.0%)	982/1,132 (86.7%)	<0.001
12 months	670/1,108 (60.5%)	792/1,119 (70.8%)	<0.001
24 months	133/1,090 (12.2%)	144/1,108 (13.0%)	0.575

* Number (%) in patients in whom medications were assessed.

PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitors.

Table S5. Definition of Per-Protocol Population

Reasons	Patients (%)
DCB group	**N = 1133**
No protocol violation	1113 (98.2%)
Not fulfilling the inclusion and exclusion criteria	12 (1.1%)
Atrial fibrillation requiring chronic oral anticoagulation	2 (0.2%)
Prior intracranial hemorrhage	2 (0.2%)
In-stent restenosis	5 (0.4%)
Planned numbers of vessel to be treated ≥3	1 (0.1%)
Planned numbers of lesions to be treated ≥3	2 (0.2%)
Planned DES or DCB implanted ≥3	2 (0.2%)
Planned total DES or DCB length >60 mm	2 (0.2%)
Not fulfilling the criteria of successful pre-dilatation	1 (0.1%)
Residual stenosis >30% after balloon pre-dilation (visual)	1 (0.1%)
Dissection type D, E, or F	1 (0.1%)
Not adherent to the assigned device (DCB)	3 (0.3%)
Lost to follow-up or withdrew consent	6 (0.5%)
DES group	**N = 1139**
No protocol violation	1118 (98.2%)
Not fulfilling the inclusion and exclusion criteria	10 (0.9%)
Atrial fibrillation requiring chronic oral anticoagulation	2 (0.2%)
Prior intracranial hemorrhage	1 (0.1%)
In-stent restenosis	5 (0.4%)
Planned numbers of lesions to be treated ≥3	1 (0.1%)
Planned DES or DCB implanted ≥3	1 (0.1%)
Planned total DES or DCB length >60 mm	1 (0.1%)
Not fulfilling the criteria of successful pre-dilatation	1 (0.1%)
Residual stenosis >30% after balloon pre-dilation (visual)	1 (0.1%)
Not adherent to the assigned device (DES)	3 (0.3%)
Lost to follow-up or withdrew consent	8 (0.7%)

Table S6. Clinical outcomes at 2 years in the per-protocol and as-treated analyses

Per protocol	**DCB (N=1,113)**	**DES (N=1,118)**	**Difference, % (95%CI)**	**p value**
Device-oriented composite endpoint *	71/1113 (6·4)	37/1118 (3·3)	3·08 (1·30, 4·86)	<0·001
Cardiovascular death	26/1113 (2·3)	14/1118 (1·3)	1·09 (-0·02, 2·19)	0·053
Target-vessel myocardial infarction	21/1113 (1·9)	17/1118 (1·5)	0·38 (-0·70, 1·46)	0·494
Clinically and physiologically indicated target lesion revascularization	34/1113 (3·1)	13/1118 (1·2)	1·93 (0·72, 3·13)	0·002
As-treated	**DCB (N=1,012)**	**DES (N=1,232)**	**Difference, % (95%CI)**	**p value**
Device-oriented composite endpoint †	60/1012 (6·0)	49/1229 (4·0)	1·96 (0·13, 3·79)	0·036
Cardiovascular death	22/1012 (2·2)	18/1229 (1·5)	0·71 (-0·41, 1·84)	0·215
Target-vessel myocardial infarction	15/1012 (1·5)	24/1229 (2·0)	-0·46 (-1·54, 0·63)	0·404
Clinically and physiologically indicated target lesion revascularization	33/1012 (3·3)	15/1229 (1·2)	2·08 (0·81, 3·36)	0·001

* For the between-group difference in DoCE, the upper boundary of the one-sided 95% confidence interval was 4·58 percentage points, and the p value for noninferiority was 0·670.

† For the between-group difference in DoCE, the upper boundary of the one-sided 95% confidence interval was 3·49 percentage points, and the p value for noninferiority was 0·220.

Table S7. Clinical outcomes of other secondary outcomes in the ITT population

	DCB (N=1,133)	DES (N=1,139)	Difference, % (95%CI)	p value
Peri-procedural Outcomes				
Device success	1142/1266 (90.2)	1261/1263 (99.8)	-9.64 (-11.40, -8.06)	<0.001
Device failure	124/1,266 (9.8%)	2/1,263 (0.2%)	9.64 (8.06, 11.40)	<0.001
Bailout stenting	114/1,266 (9.0%)	0/1,263 (0.0%)	9.00 (7.52, 10.71)	<0.001
Replace device	10/1,266 (0.8%)	2/1,263 (0.2%)	0.63 (0.08, 1.30)	0.038
Procedure success	1010/1133 (89.1)	1126/1139 (98.9)	-9.71 (-11.72, -7.85)	<0.001
Procedure failure	123/1,133 (10.9%)	13/1,139 (1.1%)	9.71 (7.85, 11.72)	<0.001
Device failure	114/1,133 (10.1%)	2/1,139 (0.2%)	9.89 (8.21, 11.78)	<0.001
DoCE within 7 days	15/1,133 (1.3%)	11/1,139 (1.0%)	0.36 (-0.56, 1.31)	0.438
Cardiovascular death	3/1,133 (0.3%)	1/1,139 (0.1%)	0.18 (-0.27, 0.69)	0.373
TV-MI	12/1,133 (1.1%)	10/1,139 (0.9%)	0.18 (-0.67, 1.06)	0.675
Peri-procedural MI	10/1,133 (0.9%)	9/1,139 (0.8%)	0.09 (-0.72, 0.92)	0.823
CPI-TLR	2/1,133 (0.2%)	1/1,139 (0.1%)	0.09 (-0.34, 0.56)	0.624
Definite or probable stent thrombosis	1/1,133 (0.1%)	2/1,139 (0.2%)	-0.09 (-0.56, 0.34)	>0.999
Bleeding Outcomes				
BARC type 2, 3, or 5 bleeding events	73/1133 (6.5)	83/1139 (7.3)	-0.82 (-2.92, 1.27)	0.440
BARC type 2 bleeding events	58/1133 (5.2)	58/1139 (5.1)	0.05 (-1.78, 1.87)	0.961
Clinically relevant ischemic or bleeding events*	165692 (12.8)	203521 (15.8)	0.81 (0.66, 1.00)	0.054

*Clinically relevant ischemic or bleeding events is a hierarchical composite endpoint of any death, any stroke, any MI, BARC type 3 bleeding events, any revascularization, and BARC type 2 bleeding events, compared with the Win ratio method. The total number of Wins (proportion) in each group, unmatched win ratio (95%CI), and p value are displayed.

Table S8. Number of patients with adverse events according to the Common Terminology Criteria for Adverse Events (CTCAE) in the ITT population

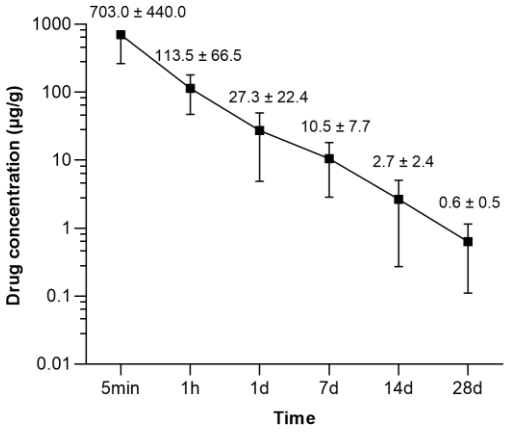
System Organ Class	DCB (N = 1,133)	DES (N = 1,139)	p value
Blood and lymphatic system disorders	6 (0·5%)	6 (0·5%)	0·993
Cardiac disorders	657 (58·0%)	625 (54·9%)	0·134
Chest pain	582 (51·4%)	553 (48·6%)	0·179
Ear and labyrinth disorders	4 (0·4%)	6 (0·5%)	0·753
Endocrine disorders	1 (0·1%)	0 (0·0%)	0·499
Eye disorders	17 (1·5%)	18 (1·6%)	0·877
Gastrointestinal disorders	240 (21·2%)	225 (19·8%)	0·399
General disorders and administration site conditions	185 (16·3%)	167 (14·7%)	0·272
Immune system disorders	6 (0·5%)	9 (0·8%)	0·443
Hepatobiliary disorders	6 (0·5%)	4 (0·4%)	0·547
Infections and infestations	83 (7·3%)	63 (5·5%)	0·081
Injury, poisoning and procedural complications	36 (3·2%)	26 (2·3%)	0·191
Investigations	205 (18·1%)	190 (16·7%)	0·374
Metabolism and nutrition disorders	56 (4·9%)	79 (6·9%)	0·044
Musculoskeletal and connective tissue disorders	92 (8·1%)	91 (8·0%)	0·909
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	27 (2·4%)	35 (3·1%)	0·313
Nervous system disorders	168 (14·8%)	153 (13·4%)	0·340
Psychiatric disorders	33 (2·9%)	39 (3·4%)	0·487
Renal and urinary disorders	21 (1·9%)	26 (2·3%)	0·472
Reproductive system and breast disorders	2 (0·2%)	3 (0·3%)	>0·999
Respiratory, thoracic and mediastinal disorders	323 (28·5%)	295 (25·9%)	0·162
Skin and subcutaneous tissue disorders	270 (23·8%)	256 (22·5%)	0·444
Surgical and medical procedures	3 (0·3%)	11 (1·0%)	0·033
Vascular disorders	75 (6·6%)	63 (5·5%)	0·277

Adverse events include serious adverse events. Patients with multiple events of one type were counted once.

Supplementary Figures

Figure S1. Characteristics of the paclitaxel-coated balloon used and the graphic representation of the 28-day paclitaxel tissue levels in rabbit abdominal aorta

Device	Company	Drug	Excipient	Dose (mg/mm^2)	Coatings feature	Drug retention
Swide	Shenqi Medical, China	Paclitaxel	Iopromide	3	Crystalline, size <2um	28 days



Based on previous study findings, the IC50 values of paclitaxel for human smooth muscle cell proliferation ranged between 0.0014-0.002ug/g,[13] and endothelial cell proliferation ranged between 0.0017-0.0068ug/g.[14] The paclitaxel-coated balloon utilized in the current study demonstrated tissue concentrations of paclitaxel exceeding these levels for at least 28 days.

Figure S2. KM curves of DoCE and its components in the per-protocol population at 2 years

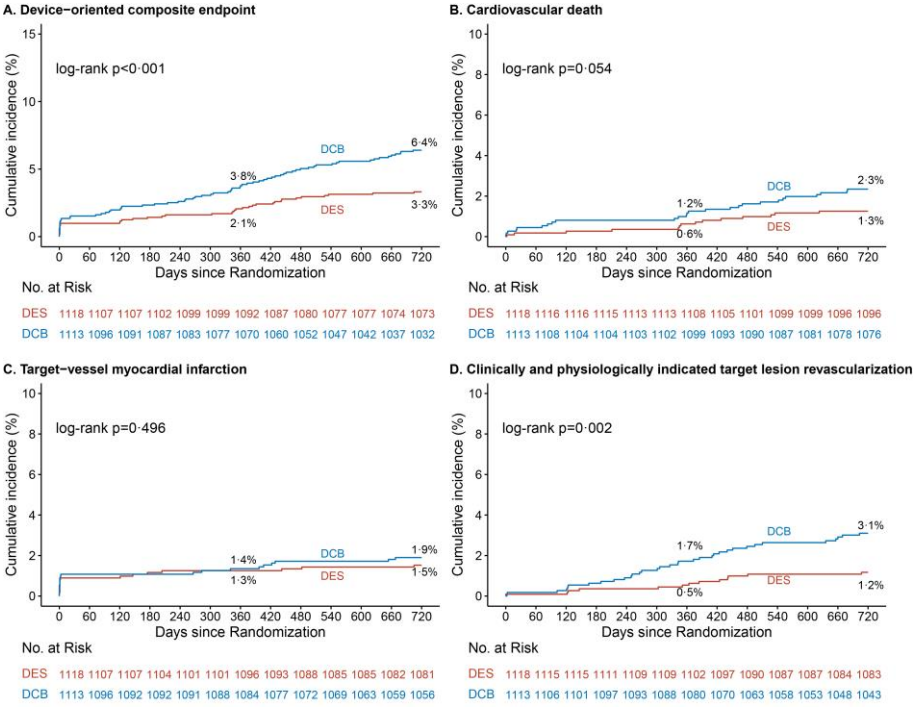
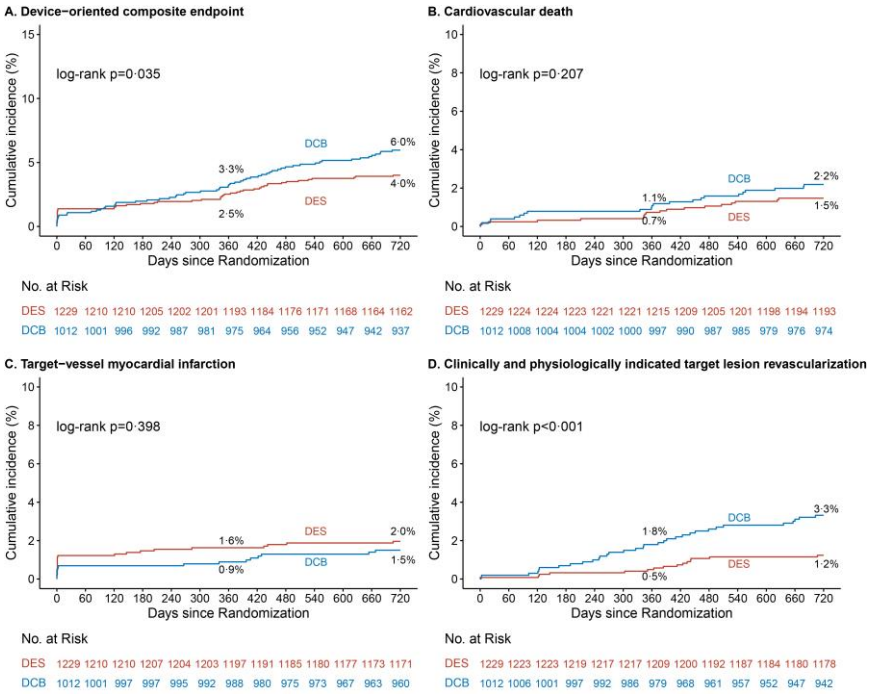


Figure S3. KM curves of DoCE and its components in the as-treated population at 2 years



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