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Comparison of Ultrathin-Strut Sirolimus-Eluting Stents Versus Drug-Coated Balloons in Small Coronary Vessels: Real-World Data

Küçük Çaplı Koroner Arter Hastalığında Ultra-ince Strutlu Sirolimus Salınımlı Stent ile İlaç Kaplı Balon Tedavisinin Karşılaştırılması: Gerçek Yaşam Verileri

ABSTRACT

Objective: Drug-coated balloons (DCBs) and ultrathin-strut sirolimus-eluting stents (SES) are both treatment options for small-vessel coronary artery disease. However, comparative real-world data between these strategies are limited.

Method: In this single-center retrospective study, 178 consecutive patients with stable angina who underwent percutaneous coronary intervention with either a DCB (n = 89) or an ultrathin-strut SES (n = 89) between January 2017 and May 2025 were analyzed. Baseline demographics, angiographic and procedural features, and clinical outcomes were assessed. The primary outcome of this study was major adverse cardiac events (MACE), defined as a composite of target-lesion revascularization (TLR), long-term all-cause mortality, stroke, and myocardial infarction.

Results: Baseline characteristics were generally comparable, although SES-treated patients were older and had higher SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) scores. During a median follow-up of 293 days, MACE occurred in 2.2% of the DCB group and 5.6% of the SES group (P = 0.441). Rates of TLR, myocardial infarction, bleeding, and all-cause mortality were not significantly different. Kaplan–Meier analysis likewise demonstrated no significant difference in cumulative MACE between the two groups (log-rank P = 0.068).

Conclusion: In this real-world study, DCB treatment demonstrated similar safety and efficacy compared to ultrathin-strut SES for small-vessel coronary artery disease. DCB therapy may represent a viable alternative to DES in selected patients, supporting the "leave nothing behind" strategy.

Keywords: Drug-coated balloon, drug-eluting stent, sirolimus-eluting stent, small-vessel disease, ultrathin-strut

ÖZET

Amaç: İlaç kaplı balonlar (DCB) ve ultra-ince strut sirolimus salınımlı stentler (SES), küçük damar koroner arter hastalığının tedavisinde kullanılan iki seçenektir. Bu stratejilerin karşılaştırılması açısından gerçek yaşam verileri sınırlıdır.

Yöntem: Bu tek merkezli, retrospektif çalışmaya, Ocak 2017 ile Mayıs 2025 tarihleri arasında küçük damar koroner arter hastalığı nedeniyle perkütan koroner girişim uygulanan 178 hasta dahil edilmiştir. Hastaların 89'una DCB, 89'una ise ultra-ince strut SES uygulanmıştır. Başlangıç özellikleri, prosedürel ayrıntılar ve sonuçlar karşılaştırılmıştır. Birincil sonlanım noktası, tüm nedenlere bağlı ölüm, miyokard enfarktüsü, inme ve hedef lezyon revaskülarizasyonunu (TLR) içeren majör advers kardiyak olaylardır (MACE).

Bulgular: Başlangıç özellikleri ve komorbiditeler büyük ölçüde benzer olmakla birlikte, SES grubundaki hastaların daha yaşlı ve SYNTAX skorlarının daha yüksek olduğu görülmüştür. Medyan takip süresi 293 gün olarak bulunmuştur. MACE, DCB grubunda %2,2, SES grubunda ise %5,6 oranında saptanmıştır (P = 0,441). Tüm nedenlere bağlı mortalite, TLR, miyokard enfarktüsü ve majör kanama oranları benzer olarak bulunmuştur. Kaplan–Meier analizi, kümülatif MACE açısından anlamlı fark göstermemiştir (log-rank P = 0,068).

Sonuç: Bu gerçek yaşam kohortunda, küçük damar koroner arter hastalığının tedavisinde DCB, ince strutlu SES'e benzer güvenlik ve etkinlik sağlamıştır. DCB tedavisi, seçilmiş hastalarda ilaç-kalplı stentlere alternatif oluşturabilir ve "geride hiçbir şey bırakmama" stratejisini destekleyebilir.

Anahtar Kelimeler: İlaç kaplı balon, ilaç salınımlı stent, sirolimus salınımlı stent, küçük damar hastalığı, ince strut

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

Berhan Keskin
Aykun Hakgör
Atakan Dursun
Aysel Akhundova
Mehmet Beşiroğlu
Beytullah Çakal
Hacı Murat Güneş
Oğuz Karaca
Ekrem Güler
İrfan Barutçu
Bilal Boztosun

Department of Cardiology, İstanbul Medipol University, Medipol Mega University Hospital, İstanbul, Türkiye

Corresponding author:
Berhan Keskin
✉ berhankeskin92@gmail.com

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Although drug-eluting stents (DES) are a well-established treatment option for small coronary vessel disease, in-stent restenosis and adverse events remain significant concerns in this patient population (1). Several randomized controlled trials have demonstrated that drug-coated balloons (DCBs) provide comparable efficacy to DES with respect to adverse events, including target-lesion revascularization (TLR), mortality, myocardial infarction, and bleeding (2–8). DCBs may offer additional advantages, such as enabling shorter durations of dual antiplatelet therapy (DAPT), avoiding the need for overly long or multiple stents in extensive coronary artery disease (CAD), and providing greater flexibility, particularly in calcified or tortuous coronary vessels (9). Despite the favorable outcomes reported in randomized controlled trials, data reflecting real-world results are critically important at this stage.

Advances in drug-eluting stent technology have aimed to further reduce in-stent restenosis and adverse outcomes in small-vessel CAD. Innovations such as ultrathin struts, enhanced biocompatibility, and the use of bioresorbable materials have been employed to lower complications such as stent thrombosis, inflammation, and in-stent restenosis (ISR) (10). ISR remains a particularly significant concern in small-vessel disease. The Orsiro sirolimus-eluting coronary stent (SES) (Biotronik, Buelach, Switzerland), with an ultrathin strut thickness of 60 μm for diameters ≤ 3 mm, is designed to provide improved flexibility and deliverability, as well as to promote earlier endothelialization, potentially reducing in-stent restenosis rates (10). Owing to these properties, Orsiro coronary stents have attracted particular interest in patients with small-vessel disease. Subgroup analyses from several previous studies on small-vessel disease (11–15), including the BIO-RESORT trial (Randomized Trial Comparing Three Contemporary Drug-Eluting Stents with Different Polymer Coatings in All-Comers Patients Undergoing PCI) (11) and BIO-FLOW II trial (Randomized Trial of the Orsiro Biodegradable Polymer Sirolimus-Eluting Stent Versus Xience Everolimus-Eluting Stent in Patients With CAD) (12), have demonstrated that the Orsiro ultrathin-strut coronary stent is associated with lower TLR rates and, in the BIO-FLOW II trial, even reduced mortality (12). These findings highlight the potential advantages of ultrathin-strut SES over second-generation everolimus-eluting DES in small-vessel coronary artery disease, particularly regarding adverse events such as target lesion revascularization.

Previous studies and randomized clinical trials on drug-coated balloons have primarily used first- or second-generation DES as comparators rather than ultrathin-strut SES (2–8). Moreover, the effectiveness of DCBs in real-world settings for small-vessel coronary artery disease needs to be fully established. Therefore, this study aims to compare the Orsiro ultrathin-strut coronary stent with DCB treatment in small-vessel coronary artery disease in terms of clinical outcomes.

Materials and Methods

Study Population

This single-center, retrospective study included patients who underwent DCB or ultrathin-strut SES treatment for small-vessel coronary artery disease due to stable angina pectoris between January 1, 2017 and May 31, 2025. Patients were consecutively enrolled, and the following strict exclusion criteria were applied:

ABBREVIATIONS

ACEi	Angiotensin-converting enzyme inhibitors
AF	Atrial fibrillation
ARBs	Angiotensin II receptor blockers
ARNi	Angiotensin receptor neprilysin inhibitor
BARC	Bleeding Academic Research Consortium
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CHF	Congestive heart failure
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
DAPT	Dual antiplatelet therapy
DCB	Drug-coated balloon
DES	Drug-eluting stents
DM	Diabetes mellitus
HDL	High-density lipoprotein
HT	Hypertension
ISR	In-stent restenosis
LDL	Low-density lipoprotein
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiac events
MRA	Mineralocorticoid receptor antagonist
PASP	Pulmonary artery systolic pressure
PCI	Percutaneous coronary intervention
QCA	Quantitative coronary angiography
SES	Sirolimus-eluting stents
TIMI	Thrombolysis in myocardial infarction
TLR	Target-lesion revascularization
TVR	Target vessel restenosis

- Percutaneous coronary intervention (PCI) for small-vessel disease involving chronic total occlusion or a bifurcation segment (n = 11)
- Acute coronary syndrome or shock requiring inotropic support (n = 5)
- Severe anemia (hemoglobin < 8 mg/dL) (n = 2)
- Active malignancy (n = 1)
- End-stage renal disease with glomerular filtration rate < 30 mL/min/1.73 m2 or maintenance dialysis (n = 3)
- Severe valvular heart disease (n = 2)
- Missing data (n = 12)
- Bail-out DES implantation after DCB application due to flow-limiting dissection or recoil (n = 3).

After applying these criteria, the remaining patients constituted the study cohort (Figure 1). Baseline characteristics, laboratory values, medications, and imaging data were obtained from the hospital information system and patient files, and recorded anonymously. Transthoracic echocardiographic examinations were performed at discharge using a Vivid E95 ultrasound device (General Electric Vingmed Ultrasound, Milwaukee, WI). The evaluated parameters were left ventricular ejection fraction (LVEF) by visual estimation, pulmonary artery systolic pressure (PASP) using the Bernoulli equation based on tricuspid regurgitant jet velocity, and valvular pathologies.

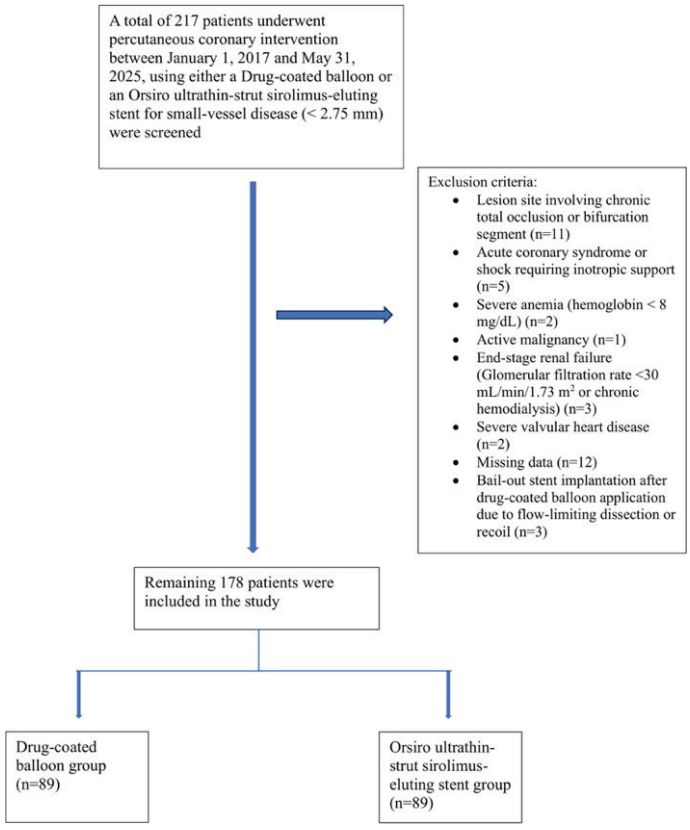

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patient selection.

Given the retrospective design of this study, the risk of selection bias cannot be excluded, as lesion characteristics may have influenced the decision between DES and DCB implantation. To reduce this potential bias, consecutive patient enrollment was applied. Lesion complexity was characterized by reporting the SYNTAX I score, which integrates factors such as calcification, tortuosity, and lesion length. Furthermore, the presence of LMCA stenting, device length (as a surrogate for lesion length), and the number of diseased vessels were also reported, thereby providing detailed information on lesion characteristics in the cohort.

The study was approved by Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee (Approval Number: E-10840098-202.3.02-5214, Date: 14.08.2025), and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients at admission and prior to invasive procedures, allowing the use of their data for scientific purposes.

Procedural Details

Loading doses of aspirin (300 mg) and clopidogrel (600 mg) were administered to all patients prior to the procedure. A left or right radial arterial approach was used in all cases. Pre-dilation of lesions with a plain balloon (balloon-to-vessel ratio 1:1) was routinely performed, and adjunctive devices such as scoring or cutting balloons, rotational atherectomy, intravascular lithotripsy, or orbital atherectomy were used when necessary. Following pre-dilation, a drug-coated balloon or an ultrathin-strut SES sized 1:1 was deployed. The following paclitaxel-coated balloons were used in the DCB procedures: Pantera Lux® (Biotronik AG, Buelach, Switzerland), Essential Pro® paclitaxel-coated balloon (iVascular, Barcelona, Spain), Elutax® paclitaxel-coated balloon (Aachen Resonance GmbH, Aachen, Germany), Agent™ sirolimus-coated balloon (Boston Scientific, Marlborough, MA, USA), IN.PACT® Admiral paclitaxel-coated balloon (Medtronic, Minneapolis, MN, USA), SeQuent® Please NEO paclitaxel-coated balloon (B. Braun Melsungen AG, Berlin, Germany), and Danubio® paclitaxel-coated balloon (Minvasys, Gennevilliers, France). For DCB procedures, balloon inflation at nominal pressure was maintained for at least 60 seconds. Procedural success was defined as ≤ 30% residual stenosis, restoration of Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow, and absence of flow-limiting dissection. A re-evaluation was performed after a five-minute waiting period, following the administration of an intracoronary vasodilator, to exclude vessel recoil or other complications. Bail-out DES implantation was performed in unsuccessful DCB cases according to predefined criteria. In the DES group, routine post-dilation with non-compliant balloons was carried out. When additional interventions for other lesions were required, these were generally performed during the same procedure; however, in cases where excessive contrast administration or prolonged procedural time was anticipated, a staged approach was preferred. Following PCI, all participants were prescribed dual antiplatelet therapy with aspirin and clopidogrel for a minimum of six months.

Definitions and Outcomes

Definitions were based on the consensus document of the Drug-Coated Balloon Academic Research Consortium (16). Small-vessel coronary artery disease was defined as a reference vessel diameter < 2.75 mm. In this study, vessel diameter was primarily determined by quantitative coronary angiography (QCA). When QCA was not feasible, visual estimation by experienced interventional cardiologists was performed. The primary outcome was major adverse cardiac events (MACE), defined as a composite of all-cause death, any myocardial infarction, stroke, and target-lesion revascularization. Each component of MACE was also analyzed individually. Significant bleeding events were classified according to the Bleeding Academic Research Consortium (BARC) criteria, with type 3 to 5 bleeding considered clinically relevant (17). Follow-up data were collected through review of hospital records and outpatient clinic visits, and, when necessary, by structured telephone contact with patients or their relatives.

Statistical Analysis

The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test, supported by visual inspection of histograms. Categorical variables were summarized as counts and percentages, while continuous variables were presented as mean ± standard deviation if normally distributed, or as median with interquartile ranges otherwise.

Comparisons between the DCB and ultrathin-strut SES groups were performed using the independent samples t-test or Mann–Whitney U test for continuous data, depending on distribution. For categorical comparisons, the Chi-square test or Fisher's exact test was applied.

Table 1. Comparison of drug-coated balloon (DCB) and ultrathin-strut sirolimus-eluting stent (Orsiro) groups regarding baseline clinical characteristics, comorbidities, and medications

Variables	DCB (n = 89)	Orsiro (n = 89)	p
Baseline clinical characteristics and comorbidities			
Age (years)	57.4 ± 11.2	61.9 ± 9.0	0.003
Male sex	79 (88.8%)	80 (89.9%)	1.000
Smoking	47 (52.8%)	50 (56.2%)	0.763
Hypertension	65 (73.0%)	65 (73.0%)	1.00
Diabetes mellitus	42 (47.2%)	43 (48.3%)	1.00
Chronic kidney disease	2 (2.2%)	7 (7.9%)	0.171
Congestive heart failure	3 (3.4%)	7 (7.9%)	0.329
Chronic obstructive pulmonary disease	3 (3.4%)	0	0.244
Previous cerebrovascular accident	1 (1.1%)	0	1.00
Atrial fibrillation	6 (6.7%)	4 (4.5%)	0.745
Peripheral arterial disease	0	1 (1.1%)	1.00
Pre-existing coronary artery disease	37 (41.6%)	29 (32.6%)	0.277
Previous PCI	35 (39.3%)	25 (28.1%)	0.154
Previous CABG	3 (3.4%)	5 (5.6%)	0.718
Medications during Follow-up			
ß-blocker usage	69 (77.5%)	85 (95.5%)	0.001
ACEi/ARB usage	58 (65.2%)	61 (68.5%)	0.750
Statin usage	89 (100%)	88 (98.9%)	1.00
SGLT-2i usage	25 (28.1%)	27 (30.3%)	0.869
MRA usage	3 (3.4%)	4 (4.5%)	1.00
ARNI usage	2 (2.2%)	0	0.477
Insulin usage	6 (6.7%)	10 (11.2%)	0.432
DAPT duration (months)	15.8 ± 18.5	12.2 ± 12.7	0.139

ACEi, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin II receptor blocker; ARNI: Angiotensin receptor neprilysin inhibitor; CABG, Coronary artery bypass graft surgery; DAPT, Dual antiplatelet therapy; MRA, Mineralocorticoid receptor antagonist; PCI, Percutaneous coronary intervention; SGLT-2i, Sodium-glucose cotransporter-2 inhibitor.

Time-to-event outcomes, including cumulative incidence of MACE, were analyzed with Kaplan–Meier survival curves, and statistical differences were evaluated using the log-rank test. All statistical analyses were conducted with Python 3.11 (Python Software Foundation, Wilmington, DE, USA). A two-sided p-value < 0.05 was considered statistically significant.

Results

A total of 178 patients were included in this study, with 89 in each group (DCB vs. ultrathin-strut SES). The ultrathin-strut SES group was older (61.9 ± 9.0 vs. 57.4 ± 11.2 years, P = 0.003), while gender distribution (male: 88.8% vs. 89.9%, P = 1.00) and smoking prevalence (52.8% vs. 56.2%, P = 0.763) were similar. Comorbidities, including hypertension (HT), atrial fibrillation (AF), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), chronic kidney disease (CKD), prior cerebrovascular accident, and peripheral arterial disease, did not differ between groups (Table 1). Rates of pre-existing CAD (41.6% vs. 32.6%, P = 0.277), previous percutaneous coronary intervention (39.3% vs. 28.1%, P = 0.154), and previous coronary artery bypass grafting (CABG) (3.4% vs. 5.6%, P = 0.718) were also comparable (Table 1).

The use of medications, including statins, angiotensin-converting enzyme inhibitors (ACEi)/angiotensin II receptor blockers (ARBs), angiotensin receptor neprilysin inhibitor (ARNi), mineralocorticoid receptor antagonists (MRAs), sodium-glucose cotransporter-2 inhibitors (SGLT-2i), and insulin during follow-up, was similar between groups, except for ß-blockers, which were more frequently prescribed in the ultrathin-strut SES group (95.5% vs. 77.5%, P = 0.001) (Table 1). Mean DAPT durations did not differ significantly (15.8 ± 18.5 vs. 12.2 ± 12.7 months, P = 0.139).

Laboratory parameters at admission were comparable between groups, including hemoglobin (14.2 ± 1.7 vs. 13.7 ± 1.8 g/dL, P = 0.079), creatinine (0.9 ± 0.2 vs. 1.0 ± 0.3 mg/dL, P = 0.174), hemoglobin A1c, C-reactive protein (CRP) values, and lipid profile (total cholesterol, low-density lipoprotein [LDL]-cholesterol, high-density lipoprotein [HDL]-cholesterol, triglycerides). The ultrathin-strut SES group had a lower albumin level, with borderline statistical significance (4.3 ± 0.4 vs. 4.7 ± 0.2, P = 0.041) (Table 2). Left ventricular ejection fraction at discharge was slightly lower in the ultrathin-strut SES group (55.2 ± 11.1% vs. 58.9 ± 7.6%, P = 0.013) (Table 2).

Table 2. Comparison of laboratory and echocardiographic parameters between drug-coated balloon (DCB) and ultrathin-strut sirolimus-eluting stent (Orsiro) groups

Variables	DCB (n = 89)	Orsiro (n = 89)	p
Laboratory parameters			
Hemoglobin (g/dL)	14.2 ± 1.7	13.7 ± 1.8	0.079
WBC (cell count/L)	(8.2 ± 2.3) ×10^3	(8.5 ± 2.4) ×10^3	0.460
Platelets (cell count/mcL)	(238.7 ± 57.7) ×10^3	(241.8 ± 62.5) ×10^3	0.731
CRP (mg/dL)	5.5 ± 8.7	7.7 ± 13.3	0.390
Creatinine (mg/dL)	0.9 ± 0.2	1.0 ± 0.3	0.174
Urea (mg/dL)	31.0 ± 10.6	37.2 ± 19.0	0.069
AST (IU/L)	28.5 ± 27.5	24.5 ± 20.0	0.463
ALT (IU/L)	29.2 ± 17.1	22.1 ± 9.5	0.027
Albumin (g/dL)	4.7 ± 0.2	4.3 ± 0.4	0.041
Sodium (mEq/L)	139.1 ± 3.1	138.2 ± 2.5	0.084
Potassium (mEq/L)	4.3 ± 0.4	4.2 ± 0.4	0.389
Hemoglobin A1c (%)	6.7 ± 1.3	6.5 ± 1.6	0.624
Total cholesterol (mg/dL)	189.1 ± 50.1	184.2 ± 54.3	0.726
LDL cholesterol (mg/dL)	118.0 ± 47.4	111.0 ± 49.3	0.368
HDL cholesterol (mg/dL)	42.1 ± 9.7	41.5 ± 12.1	0.806
Triglycerides (mg/dL)	197.8 ± 122.1	212.0 ± 165.6	0.703
TSH (mIU/L)	1.9 ± 1.0	1.9 ± 1.2	0.860
Echocardiographic parameters			
Left ventricular ejection fraction (%)	58.9 ± 7.6	55.2 ± 11.1	0.013
Pulmonary artery systolic pressure (mmHg)	26.4 ± 5.8	25.3 ± 5.5	0.507

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; CRP, C-reactive protein; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; TSH, Thyroid-stimulating hormone; WBC, White blood cell count.

Regarding angiographic characteristics, the number of diseased vessels was similar between groups (2.0 ± 0.8 vs. 2.2 ± 0.7, P = 0.109). However, the ultrathin-strut SES group had a higher SYNTAX I score (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) (18.9 ± 0.5 vs. 13.8 ± 10.3, P = 0.002), indicating more complex anatomic disease (Table 3). Device diameters were comparable (2.4 ± 0.3 vs. 2.4 ± 0.1 mm, P = 0.304), but device length was greater in the ultrathin-strut SES group (32.0 ± 8.1 vs. 25.7 ± 5.5 mm, P < 0.001) (Table 3). In the DCB group, 83 (93.3%) patients received paclitaxel-coated balloons, while six (6.7%) received sirolimus-coated balloons.

The median follow-up for the overall patient population was 293 (170–456) days, ranging from 71 to 2807 days, and was similar between groups (296 (189–456) vs. 256 (158–456) days, P = 0.906). The primary outcome, MACE, occurred in 5.6% of patients in the ultrathin-strut SES group and 2.2% in the DCB group (P = 0.441) (Table 3, Figure 2). Rates of all-cause mortality, TLR, cerebrovascular accident, and myocardial infarction were also comparable (Table 3, Figure 2). No cases of procedural mortality or early (< 30 days) mortality occurred in either group. Coronary angiography during follow-up was performed in six patients (6.7%) in the DCB group and seven (7.9%) in the ultrathin-strut SES group, with identical rates of TLR and restenosis > 50% (2.2% vs. 2.2%, P = 1.00). BARC type 3–5 bleeding occurred in one patient (1.1%) in each group (P = 1.00) (Table 3, Figure 2). Kaplan–Meier analysis did not demonstrate a statistically significant difference in cumulative MACE between the groups (log-rank P = 0.068) (Figure 3).

Discussion

Small-vessel coronary artery disease is associated with a higher incidence of restenosis despite advancements in DES technology, with target vessel failure reported in over 40% of patients at 10-year follow-up (18). Drug-coated balloons emerged as an alternative after studies consistently demonstrated superior outcomes compared with plain balloon angioplasty (19). Whereas DES exert their effect through controlled, sustained release of antiproliferative drugs, DCBs act via rapid drug uptake by the vessel wall to achieve persistent drug bioavailability (1). Consequently, adequate lesion preparation and, when necessary, the use of adjunctive devices—such as cutting balloons, scoring balloons, and rotational atherectomy—are critical for optimal drug delivery. Sufficient balloon inflation time (≥ 30 seconds) is also essential to ensure adequate drug transfer (1). In the first PICCOLETO trial (Paclitaxel-Coated Balloon Versus Drug-Eluting Stent for the Treatment of Small Coronary Vessels) (20) for small-vessel disease, DCB use was associated with higher MACE and target vessel restenosis (TVR) rates within six months, leading to early trial termination. However, only 25% of patients in that study underwent pre-dilation before DCB deployment, and the unfavorable outcomes were attributed to insufficient lesion preparation.

Table 3. Comparison of angiographic characteristics and outcomes between drug-coated balloon (DCB) and ultrathin-strut sirolimus-eluting stent (Orsiro) groups

Variables	DCB (n = 89)	Orsiro (n = 89)	p
Angiographic characteristics			
Diseased vessel number	2.0 ± 0.8	2.2 ± 0.7	0.109
Device length (mm)	25.7 ± 5.5	32.0 ± 8.1	<0.001
Device diameter (mm)	2.4 ± 0.3	2.4 ± 0.1	0.304
SYNTAX I score	13.8 ± 10.3	18.9 ± 10.5	0.002
Patients with LMCA stent	19 (21.3%)	26 (29.2%)	0.301
Outcomes			
Follow-up duration (days)	256 (158, 456)	296 (189, 456)	0.906
Procedural mortality	0	0	1.00
30-day mortality	0	0	1.00
MACE	2 (2.2%)	5 (5.6%)	0.441
All-cause mortality	0	3 (3.4%)	0.244
Target-lesion revascularization	2 (2.2%)	2 (2.2%)	1.00
Cerebrovascular accident	0	0	1.00
Myocardial infarction	0	0	1.00
BARC type 3-5 bleeding	1 (1.1%)	1 (1.1%)	1.00

BARC, Bleeding Academic Research Consortium; LMCA, Left main coronary artery; MACE, Major adverse cardiac events.

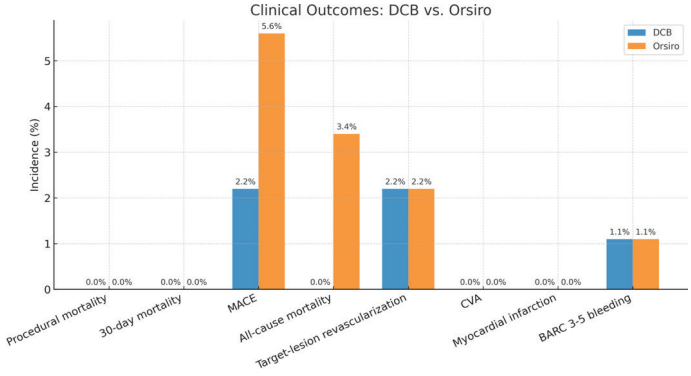

Figure 2. Clinical outcomes in the drug-coated balloon and Orsiro ultrathin-strut sirolimus-eluting stent groups.

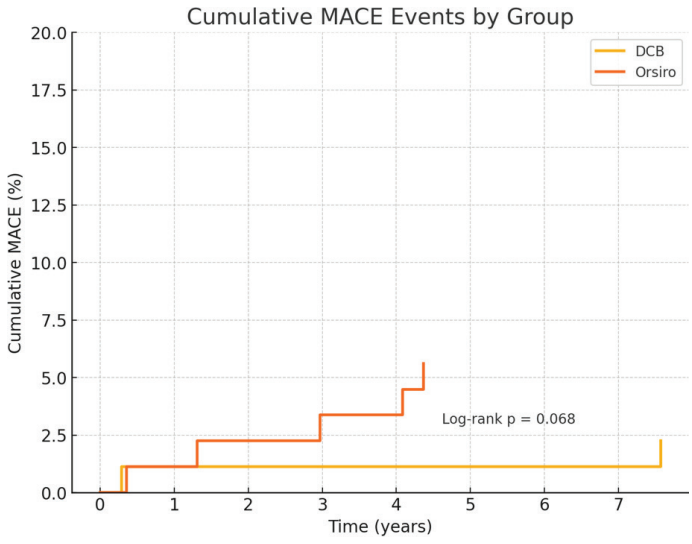

Figure 3. Kaplan-Meier curves depicting cumulative major adverse cardiac events (MACE) events during follow-up in the drug-coated balloon and Orsiro ultrathin-strut sirolimus-eluting stent groups.

Subsequent randomized controlled trials were designed to evaluate the non-inferiority of DCBs compared with DES in small-vessel CAD. In the BELLO trial (Balloon Elution and Late Loss Optimization) (3), DCBs were compared with first-generation DES, with pre-dilation prior to DCB performed in 97% of cases. Although MACE and TLR rates were similar at six months, DCB use was associated with lower MACE rates at three years (3). Later trials compared DCBs with second-generation DES in small-vessel CAD. In the BASKET-SMALL 2 trial (Basel Stent Kosten Effektivitäts Trial–Small Vessels 2), MACE, cardiovascular death, myocardial infarction, and TVR were similar between DCB and DES groups at both 12 months and three years (4, 5). The RESTORE SVD trial (Randomized Comparison of the Restenosis Rate Between Drug-Eluting Stent and Drug-Coated Balloon in Small Vessel Coronary Artery Disease) also demonstrated comparable efficacy of the two devices at 12- and 24-month follow-up (6). Similarly, the PICCOLETO II trial (Paclitaxel-Coated Balloon Versus Drug-Eluting Stent for the Treatment of Small Coronary Vessels II) (7) and the study by Yu et al. (8) reported no significant differences in MACE, myocardial infarction, and TVR at 12 months. Angiographic outcomes were also evaluated in these randomized clinical trials. In the PICCOLETO II trial (7), late lumen loss was lower in the DCB group, although minimal lumen diameter at six months was comparable between groups. Similarly, Yu et al.(8) reported no significant difference in late lumen loss at nine months. Meta-analyses have also

demonstrated comparable long-term clinical outcomes between DCBs and DES (19, 21, 22). However, the use of DCBs for de novo lesions in non-small coronary vessels has not been adequately investigated, despite promising findings from observational studies (23, 24). Further randomized trials with long-term follow-up are warranted before definitive conclusions can be reached for this patient subset.

Drawbacks of DES include early and late stent thrombosis, long-term inflammatory reactions, reduced flexibility and deliverability—particularly in tortuous or calcified vessels—ISR, and the requirement for prolonged DAPT (9). DCBs may overcome many of these limitations. For example, stent thrombosis is not a concern with DCB treatment. Enhanced deliverability and flexibility can facilitate and shorten procedures while reducing procedural complications. By preserving the vessel's natural flexibility, DCBs may be particularly advantageous in situations where vessel mobility is critical, such as in tortuous segments and bifurcation lesions. Furthermore, DCB use eliminates stent-related complications such as malapposition and fracture, and is especially beneficial for diffuse coronary lesions by avoiding the need for excessively long stents, which may increase restenosis risk and complicate potential future coronary artery bypass grafting (9). Although newer-generation DES have demonstrated high efficacy and safety even in patients with diffuse CAD (25), the "leave nothing behind" strategy offered by DCB therapy remains appealing to clinicians for the reasons outlined above. Real-world studies are essential to validate clinical trial findings and strengthen confidence in their application.

DCB treatment may also allow for shorter DAPT duration and potentially reduce bleeding risk, particularly in patients at high risk for bleeding. Cortese et al.(26) demonstrated lower BARC type 3–5 bleeding events in patients receiving single antiplatelet therapy after DCB treatment, without compromising efficacy compared with those receiving DAPT following DCB application. However, clinical trials have not demonstrated superiority of DCB over DES in terms of bleeding outcomes in patients with small-vessel disease. In our study, DAPT duration and bleeding rates were comparable between groups. The high proportion of DES use in other coronary segments and the potential presence of extensive CAD in patients with small-vessel involvement may explain these findings. Real-world practice may not always align with theoretical expectations; nevertheless, bleeding rates could be reduced in patients with isolated small-vessel disease treated exclusively with DCB.

Coronary dissection after DCB application is a common phenomenon, occurring in up to 40% of cases. However, these dissections usually do not impair distal flow and may be left untreated. In the study by Gitto et al. (27), target lesion failure rates at two years were similar between patients without dissection and those with untreated dissections in the absence of flow limitation. Current guidelines likewise recommend leaving non-flow-limiting dissections untreated (1). Regarding device type, previous studies suggest that the choice of DCB—paclitaxel-coated versus sirolimus-coated—does not significantly affect outcomes. This finding is supported by the comparative study of Vlieger et al. (28), the randomized clinical trial by Ahmad et al. (29), and the meta-analysis by Shin et al. (30).

Several studies have investigated the potential advantages of the Orsiro SES (Biotronik, Buelach, Switzerland), particularly in small-vessel disease. While some studies (31, 32) found no significant difference between ultrathin-strut SES and second-generation DES, other investigations, including randomized-controlled trials and meta-analyses, have reported superior outcomes with ultrathin-strut SES compared with second-generation DES in this patient population (10–15). Previous randomized controlled trials comparing DCBs have primarily used first- or second-generation DES as comparators. To our knowledge, this is the first study to compare DCBs with ultrathin-strut SES in small-vessel coronary artery disease with respect to clinical outcomes. Our findings suggest that DCBs offer a comparable efficacy and safety profile to ultrathin-strut DES; however, larger randomized studies with longer follow-up are warranted to confirm these results. The presence of longer lesion lengths and higher SYNTAX scores in the ultrathin-strut SES group should be considered when interpreting the results of this study. More complex anatomic disease may contribute to higher TLR rates and poorer clinical outcomes, potentially creating a pre-existing disadvantage for the ultrathin-strut SES group. Nevertheless, this study demonstrated comparable efficacy of the two devices in small-vessel coronary artery disease and reflected real-world practice, in which clinicians tend to prefer DES implantation in the setting of more complex CAD rather than DCB.

Limitations

This study has various limitations. First, it was conducted at a single center using a retrospective design, which may introduce selection and information bias. To minimize this risk, patients were enrolled consecutively. Second, the sample size was modest, reducing statistical power to detect differences in infrequent clinical outcomes. Third, although baseline characteristics were generally well balanced, residual confounding from unmeasured variables cannot be excluded. Because of the very low number of MACE events (n = 7), Cox regression analysis with hazard ratios and confidence intervals could not be reliably performed, and survival comparisons were therefore limited to Kaplan–Meier curves with log-rank testing. Finally, the median follow-up duration was less than one year, and longer-term differences between treatment strategies may not have been captured.

Conclusion

In this real-world, retrospective analysis of patients with small-vessel coronary artery disease, treatment with drug-coated balloons demonstrated comparable efficacy and safety outcomes to ultrathin-strut sirolimus-eluting stents. Rates of MACE, all-cause mortality, target-lesion revascularization, and major bleeding were similar between the two strategies. Larger randomized trials with extended follow-up are warranted to confirm these observations and further define the optimal revascularization strategy for small-vessel coronary artery disease.

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