JACC: ADVANCES VOL. 3, NO. 10, 2024

ORIGINAL RESEARCH

A Meta-Analysis of 3-Year Outcomes of Drug-Coated Balloons Versus Drug-Eluting Stents for Small-Vessel Coronary Artery Disease

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ABSTRACT

BACKGROUND Drug-coated balloons (DCBs) may be a viable alternative to drug-eluting stents (DES) for de novo small caliber coronary artery lesions. However, there remains a lack of data regarding the long-term efficacy of this approach.

OBJECTIVES The purpose of this study was to compare the rates of major adverse cardiovascular events (MACE) after 3-year follow-up among patients randomized to DCB versus DES for the treatment of small caliber coronary arteries with reference vessel diameter between 2 and 3 mm.

METHODS We systematically searched MEDLINE, EMBASE, and CENTRAL databases from their inception to July 2023 for randomized controlled trials comparing DCB versus DES for small caliber coronary artery disease. The primary end point was MACE at 3-year follow-up. Risk of bias was assessed using the Cochrane Risk of Bias Tool (RoB 2). Pooled risk ratios (RRs) and 95% CIs were estimated using random effects meta-analytic models.

RESULTS Four randomized controlled trials (n = 1,402) were included. In total, 706 patients were randomized to DCB and 696 to DES. Participants were mostly male (74%), with a mean/median age ranging from 60 to 68 years. Pooled data across trials for MACE showed wide CIs, with little indication of DES superiority over DCB (RR: 0.71; 95% CI: 0.36-1.41). Most individual components of MACE were inconclusive. There was a potential signal for a reduction of target vessel thrombosis with DCB compared to DES (RR: 0.25; 95% CI: 0.06-1.08).

CONCLUSIONS Although sample sizes are small, 3-year outcomes suggest that DCB may be a reasonable alternative to DES for the treatment of small coronary arteries. (JACC Adv. 2024;3:101204) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 1, 2024; revised manuscript received June 28, 2024, accepted July 8, 2024.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2024.101204

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CAD = coronary artery disease

DAPT = dual antiplatelet therapy

DCB = drug-coated balloon

DES = drug-eluting stent(s)

MACE = major adverse cardiovascular event

MI = myocardial infarction

PCI = percutaneous coronary intervention

RR = risk ratio

TLR = target lesion revascularization

TVR = target vessel revascularization

Percutaneous coronary intervention (PCI) in small caliber coronary artery disease (CAD) remains a challenge due to in-stent restenosis. Drug-eluting stents (DES) were designed to lower the risk of in-stent restenosis occurring with previously used bare-metal stents.[1] However, DES are still associated with high rates of restenosis and increased risks of adverse events in small caliber CAD.[2] Drug-coated balloons (DCBs) have been suggested as an alternative strategy. DCBs deliver a lipophilic drug to the arterial wall with a single balloon inflation.[3] The main advantages of DCBs are the absence of a permanent prosthesis, the remodeling of vessels, and a hortened duration of dual antiplatelet therapy (DAPT) which may be beneficial among patients at high risk of bleeding.[4] However, long-term clinical outcomes of DCB versus DES are limited. Therefore, our objective was to compare the rates of major adverse cardiovascular events (MACE) at 3 years of follow-up among patients enrolled in randomized controlled trials of DCB versus DES for the treatment of small caliber CAD.

METHODS

We conducted our systematic review and meta-analysis following a predefined study protocol and reporting as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[5] The protocol was publicly preregistered on Open Science Framework on July 4, 2023 (Center for Open Science).

DATA SOURCES AND SEARCH STRATEGY. Relevant studies were identified through a systematic search of the MEDLINE (via PubMed), Embase (via Ovid), and Cochrane CENTRAL databases from inception through July 5, 2023. Keywords, Medical Subject Headings terms, and EMTREE terms searched included those related to drug-coated balloon, drug-eluting stent, small CAD, angioplasty, and randomized clinical trial. The detailed search is reported in Supplemental Table 1. Publications identified in our search were imported into Covidence (Veritas Health Innovation Ltd), a software for systematic review management, and duplicates were removed.[6]

STUDY SELECTION. Two reviewers (A.D.A. and T.S.) independently screened the titles and abstracts of the identified publications using prespecified inclusion and exclusion criteria. Citations deemed potentially relevant by either reviewer were retrieved for full-text screening. Disagreements during full-text screening were resolved by consensus or the opinion of a third reviewer (T.Z.). Included articles were randomized controlled trials published in English or French that randomized patients with small caliber CAD to a DCB or DES treatment arm. For inclusion, studies had to report the primary outcome of interest or at least one of the secondary end points of interest (see below) and a minimum follow-up duration of 3 years. Editorials, reviews, and letters to the editor that did not include original data were excluded. Observational studies, case reports, and case series were also excluded.

DATA EXTRACTION. Data were extracted independently by two reviewers (A.D.A. and T.S.) following an intention-to-treat approach into a pilot-tested database, with disagreements resolved by consensus or by a third reviewer (T.Z.) if consensus could not be achieved. Screening and data extraction were performed using Covidence.

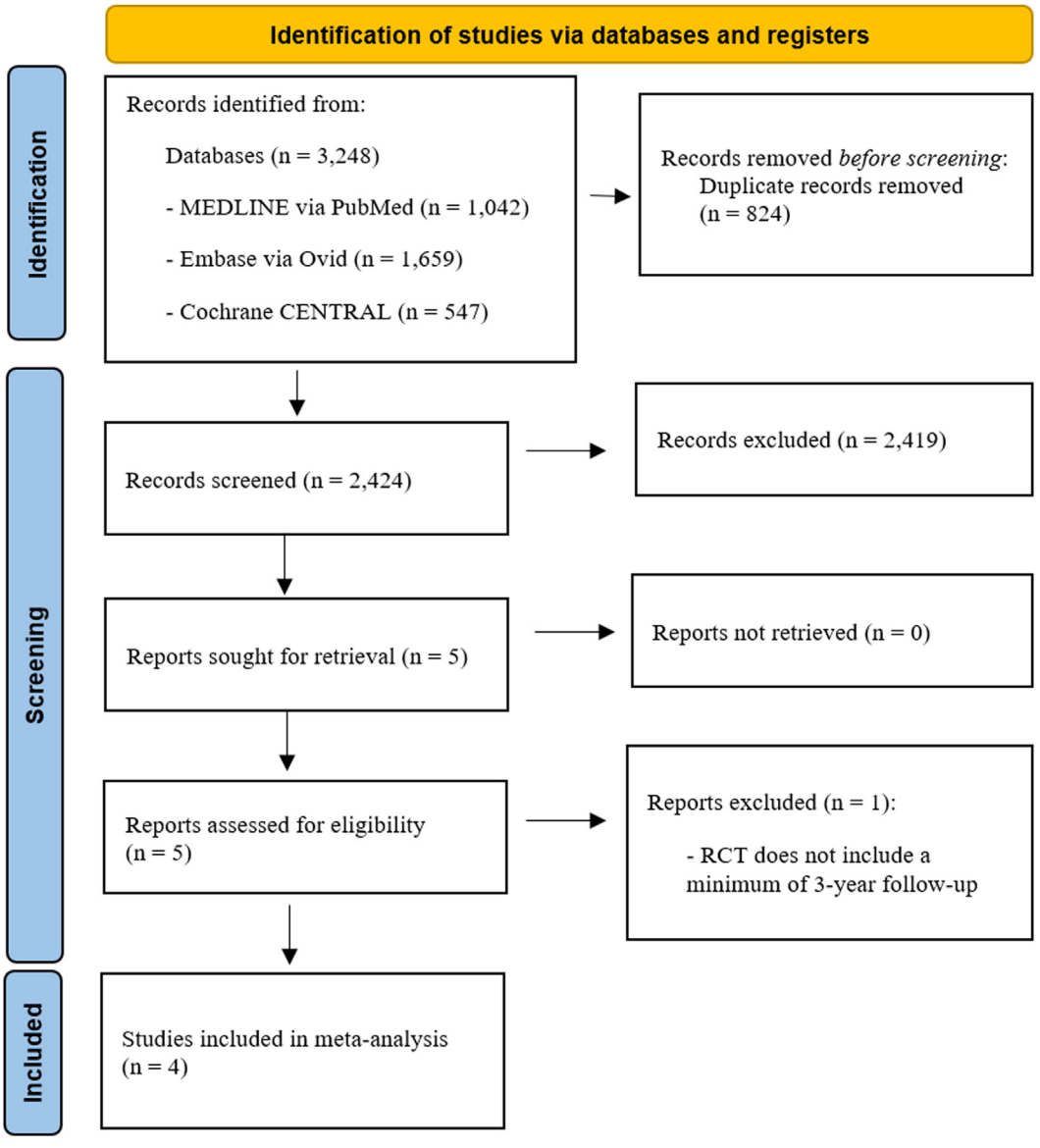
OUTCOMES. Our prespecified primary clinical outcome was MACE, a composite end point that included cardiac or all-cause death, myocardial infarction (MI), target lesion revascularization (TLR), or target vessel revascularization (TVR), recording the definition of MACE used in each study. Our prespecified secondary outcomes were the individual components of the composite end point and target vessel thrombosis.

QUALITY ASSESSMENT. The risk of bias for included randomized controlled trials was assessed independently by two reviewers (A.D.A. and T.S.) using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB 2), with disagreements resolved by consensus. All eligible randomized controlled trials were included in the systematic review and meta-analysis regardless of quality.

STATISTICAL ANALYSIS. Pooled risk ratios (RRs) and corresponding 95% CIs for DCB versus DES were estimated using DerSimonian and Laird random effects meta-analytic models with inverse variance weighting and Jackson and modified Knapp-Hartung method extensions. Meta-analysis was only conducted for outcomes reported by at least three sufficiently homogeneous trials to ensure meaningful interpretation.

The presence of statistical heterogeneity was estimated using the I^2 and τ^2 statistics. Sensitivity analyses were conducted using a Mantel-Haenszel fixed effects approach and by excluding studies at high risk of bias. Publication bias was not assessed because there were <10 randomized controlled trials included. All analyses were conducted using the meta package in R, version 4.2.3.

FIGURE 1 Overview of Study Selection



PRISMA flow diagram of RCTs of DCB versus DES for small caliber coronary artery disease. The systematic review was conducted with *Covidence*. Four studies were included in the meta-analysis. DCB = drug-coated balloon; DES = drug-eluting stent; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT = randomized controlled trial.

RESULTS

Our systematic search identified 3,248 potentially eligible records (Figure 1). A total of 2,424 records remained after removing duplicates. Of the 5 full-text articles retrieved, 4 randomized controlled trials met our inclusion criteria, with the remaining randomized controlled trial excluded due to insufficient follow-up duration.

STUDY AND TREATMENT CHARACTERISTICS. Included articles were published between 2015 and 2023 (Table 1). All included trials were multicenter studies and had a follow-up duration of 36 months. Three trials were open label except the BELLO (Balloon Elution and Late Loss Optimization) trial, a single-blind blind trial in which patients but not physicians were blinded to assigned treatment.[12] In all trials, outcomes were assessed blind to treatment

TABLE 1 Study Characteristics of Randomized Studies Comparing DCB Versus DES for Small Caliber Coronary Arteries

Study, Years	Sample Size	Study Design	Country	MACE Definition	Inclusion Criteria	Total Follow-Up (Mo)
BASKET-SMALL 2,[4,7] 2018/2020	758	Multicenter	Germany, Austria, Switzerland	Composite of cardiac death, nonfatal MI, TVR	Patients with indication for PCI either due to ACS, chronic angina pectoris, or silent ischemia, angiographic lesions in native coronary arteries with a diameter of 2 mm to less than 3 mm	36
PICCOLETO-II,[8,9] 2020/2023	232	Multicenter	Italy	Composite of cardiac death, all MIs, TVR	Age ≥18 y, hospitalized patient for small CAD or ACS, with indication for PCI, RVD with a diameter between 2.00 and 2.75 mm and stenosis >70%	36
RESTORE SVD,[10,11] 2020/2023	230	Multicenter	China	Composite of cardiac death, target vessel MI, ischemia-driven TLR	Age ≥18 y, presenting stable or unstable angina or recent stabilized MI, had only 1 lesion in the target small vessel with a visual stenosis of ≥70% or ≥50% complicated by evidence of ischemia before PCI, lesion length limited to <26 mm, visual diameters of target lesions limited to ≥2.25 and ≤ 2.75 mm	36
BELLO,[12,13] 2012/2015	182	Multicenter	Italy	Composite of death, MI, TVR	Age ≥18 y, with diagnosis of stable or unstable angina or documented silent ischemia, maximum of 2 angiographically significant de novo lesions <25 mm in length in native coronary arteries with a visually estimated RVD <2.8 mm	36

ACS = acute coronary syndrome; CAD = coronary artery disease; DCB = drug-coated balloon; DES = drug-eluting stent; MACE = major adverse cardiovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; RVD = reference vessel diameter; TLR = target lesion revascularization; TVR = target vessel revascularization.

assignment. The four trials combined accounted for 1,402 participants with 706 participants randomized to DCB and 696 participants to DES, with BASKET-SMALL 2 (Basel Stent Kosten Effektivitäts Trial Drug Eluting Balloons vs Drug Eluting Stents in Small Vessel Interventions) trial being the largest trial included in our study.[7]

Table 2 summarizes the baseline characteristics of the patients in the trials. Participants were mostly male (74%), and the mean/median age ranged from 60 to 68 years. Patient characteristics were generally well balanced. In the PICCOLETO-II (Drug Eluting Balloon Efficacy for Small Coronary Vessel Disease Treatment) trial, there was an imbalance in the proportion of patients with renal failure between each intervention arm (3.3% in DCB and 10.6% in DES).[8] In the BASKET-SMALL-2 trial, there was a higher proportion of men in the DCB group than in the DES group (77% and 70%).[7] In the RESTORE SVD (Restore Small-Vessel Disease) trial, there was a larger proportion of patients in the DCB group who had type 2 diabetes (20.2% in DCB and 10.3% in DES). This trial had the

TABLE 2 Demographic and Clinical Characteristics of Participants Randomized to DCB Versus DES

							Previous			CAD		
Study (Year)	Age (y) (Mean/Median[a])	Male (%)	Diabetes (%)	Hypertension (%)	Dyslipidemia (%)	Current Smoker (%)	MI (%)	PCI (%)	CABG (%)	Stable (%)	ACS (%)	LVEF (Median)
BASKET-SMALL 2 (2020)[4]												
DCB	67	77	32	85	69	22	42	62	10	70	29	60
DES	68	70	35	89	70	20	35	64	9	73	27	60
PICCOLETO-II (2023)[9]												
DCB	64[a]	70	38	65	61	20	38	50	3	54	46	58
DES	66[a]	77	35	67	55	17	30	53	4	56	44	58
RESTORE SVD (2023)[11]												
DCB	60	66	40	67	53	29	22	39	0	31	69	61
DES	61	77	42	75	49	32	25	33	1	29	71	60
BELLO (2015)[13]												
DCB	65	80	43	80	79	16	51	58	10	76	24	NR
DES	66	77	38	82	79	11	36	42	13	78	22	NR

[a]Used for numbers relating to median age.

CABG = coronary artery bypass graft; LVEF = left ventricular ejection fraction; NR = not reported; other abbreviations as in Table 1.

highest number of participants with acute coronary syndrome (ACS), accounting for over one-third of all participants with ACS (42%) (**Table 2**). The RESTORE SVD trial also included an additional arm of 32 participants with very small vessel disease, which we excluded from our analysis.[10] The reference vessel diameter was between 1.78 and 2.81 mm (**Table 3**).

The devices used varied across trials (Supplemental Table 2). Both of the BELLO trial's devices were coated with paclitaxel. Supplemental Tables 3 and 5 show that the BELLO trial had the highest inflation pressure for DES as well as the greatest bailout stenting rate. For all trials reporting lumen diameter stenosis at baseline and post-procedure, DES led to more substantial decreases of stenosis postprocedure (**Table 4**).

QUALITY ASSESSMENT. We rated the PICCOLETO-II trial to be at low risk of bias and the 3 other trials as having some concerns due to deviation from intended intervention domain. In the BELLO and RESTORE SVD trials, 9.9% and 3.5% of patients, respectively, required bailout bare-metal stent implantation (Supplemental Table 5). In the BASKET-SMALL 2 trial, 5.1% of patients from the DCB group were treated with a combination of DCB and stents (mostly DES), and these patients had higher rates of MACE at 12 months than those treated with DCB only.[7] Additionally, 1 participant in the RESTORE SVD trial was treated with 2 stents.[10] A summary of the RoB 2 results stratified by risk domain is reported in Supplemental Figure 1.

EFFICACY AND SAFETY END POINTS. The overall pooled RR for MACE for DCB versus DES was 0.71 (95% CI: 0.36-1.41) (**Figure 2**). Benefits for MACE were observed with DCB in the BELLO trial (RR: 0.47; 95% CI: 0.26-0.86) and the PICCOLETO-II trial (RR: 0.51; 95% CI: 0.26-1.00). **Figure 3** suggests a potential reduction in the risk of target vessel thrombosis with DCB (RR: 0.25; 95% 0.06-1.08). Meta-analytic results were inconclusive for cardiac death (Supplemental Figure 2), all-cause mortality (Supplemental Figure 3), MI (**Figure 4**), and TLR (Supplemental Figure 4). A meta-analysis could not be conducted for TVR as only two trials reported this outcome. **Table 5** shows that the rates of TVR were slightly higher in the DES group of the BASKET-SMALL 2 trial (7.9% for DCB and 8.5% for DES), but rates in the BELLO trial were almost double in the DES group than in the DCB group (3.3% for DCB and 6.5% for DES).

SENSITIVITY ANALYSES. Similar results were obtained using fixed effects meta-analytic models (Supplemental Figures 5 to 10).

TABLE 3 Vessel and Lesion Characteristics Prior to Percutaneous Coronary Intervention

Study (Year)	Reference Vessel Diameter (mm)	Lumen Diameter Stenosis at Baseline (%)	Lesion Length (mm)
BASKET-SMALL 2 (2020)[4]			
DCB	NR	NR	NR
DES	NR	NR	NR
PICCOLETO-II (2023)[9]			
DCB	2.23 ± 0.4	75 ± 17	13.5 ± 7.3
DES	2.18 ± 0.4	76 ± 15	14.0 ± 6.9
RESTORE SVD (2020)[11]			
DCB	2.11 ± 0.27	69.6 ± 9.3	10.5 ± 4.8
DES	2.21 ± 0.29	71.0 ± 10.5	10.8 ± 5.2
BELLO (2015)[13]			
DCB	2.41 ± 0.34	72.1 ± 10.1	15.3 ± 7.5
DES	2.41 ± 0.40	72.8 ± 9.3	14.9 ± 8.0

Values are mean ± SD.
Abbreviations as in **Tables 1 and 2**.

DISCUSSION

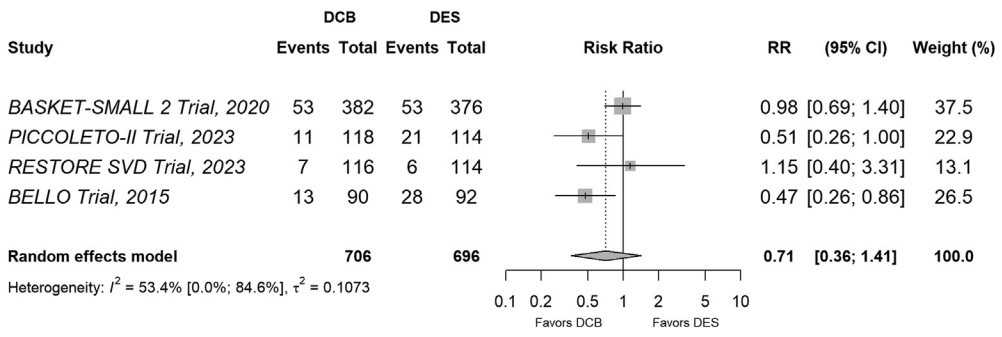
Our study was designed to compare the outcomes of DCB versus DES in small caliber CAD at 3-year follow-up in terms of MACE, cardiac death, all-cause death, MI, TLR, TVR, and target vessel thrombosis. When data were pooled across trials for MACE, CIs were wide, but there was little evidence that DES was superior to DCB (**Central Illustration**). Due to limited data, analyses of individual components of MACE remained inconclusive. However, there was a potential signal for a reduction of target vessel thrombosis with DCB compared to DES. Our results suggest that

TABLE 4 Stenosis Characteristics and Device Length in All Included Randomized Studies Comparing DCB Versus DES

Study (Year)	Stenosis in-Lesion (%)	Stenosis in-Segment (%)	Device Length (mm)
BASKET-SMALL 2 (2020)[4,a]			
DCB	NR	NR	23.9 ± 11.7
DES	NR	NR	23.2 ± 12.9
PICCOLETO-II (2023)[9,b]			
DCB	21.4 ± 22	29.6 ± 16	21.8 ± 8.2
DES	13.1 ± 18	26.8 ± 12	18.3 ± 6.9
RESTORE SVD (2020)[11]			
DCB	19.9 ± 8.8	19.8 ± 8.8	21.0 ± 4.9
DES	11.9 ± 6.0	12.6 ± 6.4	20.4 ± 5.8
BELLO (2015)[13]			
DCB	1.6 ± 0.3	1.5 ± 0.3	25.6 ± 6.3
DES	2.0 ± 0.3	1.7 ± 0.4	18.5 ± 5.6

Values are mean ± SD. [a]Reported mean number of devices used in: 1.68 ± 0.82 DCB; 1.26 ± 0.55 DES. [b]Reported mean number of devices used: 1.03 DCB; 1.12 DES.
Abbreviations as in **Tables 1 to 3**.

FIGURE 2 Meta-Analysis of MACE With DCB Versus DES



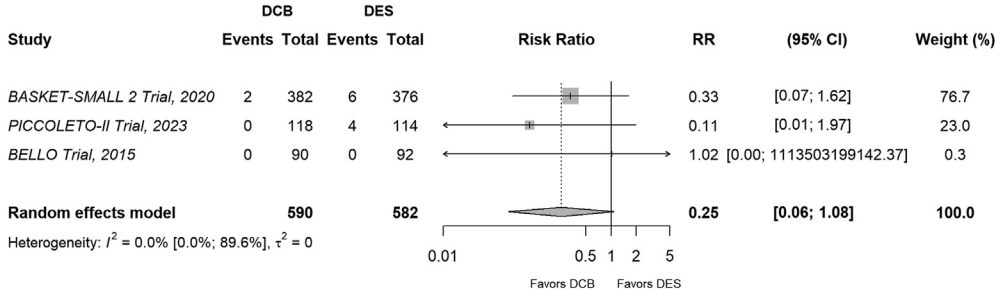
Forest plot of the relative risks of MACE with DCB versus DES for small caliber coronary artery disease at 3-year follow-up. The forest plot was made with R, version 4.2.3. MACE = major adverse cardiovascular event; RR = risk ratio; other abbreviations as in Figure 1.

DCB may be a reasonable alternative to DES for PCI in small CAD.

PREVIOUS META-ANALYSES. A previous meta-analysis examined DCB and DES for small vessel coronary disease.[14] The study included both single-arm studies and randomized controlled trials, with no restriction on follow-up duration. The meta-analysis included 37 studies with follow-up duration ranging from 6 to 60 months. The investigators concluded that DCBs are a favorable alternative to DES.[14] However, the wide range of follow-up durations made it difficult to determine the long-term safety and efficacy of DCB compared to DES. Our meta-analysis sought to specifically examine the 3-year outcomes of DCB versus DES use in randomized controlled trials.

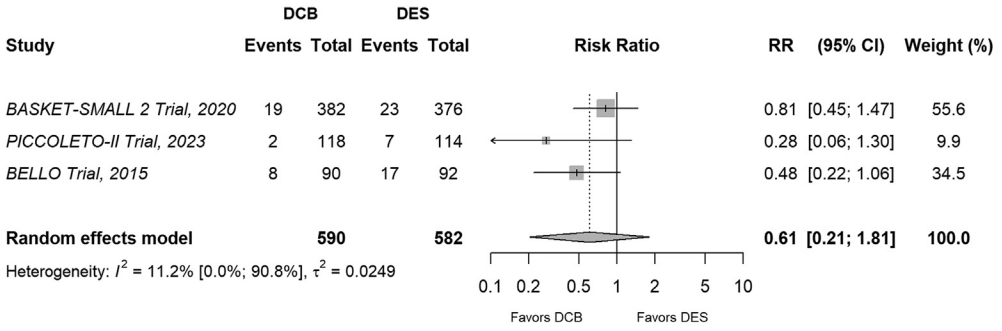
DRUG-ELUTING STENTS. DES were designed to lower the risk of in-stent restenosis caused by bare-metal stents. They release antiproliferative drugs into the arterial wall and prevent restenosis by inhibiting tissue growth. The antiproliferative drugs, such as everolimus, paclitaxel, and zotarolimus, are eluted in a sustained manner. The same drugs that coat DES also cause delayed healing of the endothelium, wounded by stent implantation.[15] The risk of developing in-stent restenosis is higher among patients with diabetes due to increased blood viscosity, caused by elevated fibrinogen production, and aggressive vascular cell proliferation.[16-18] Vessel and lesion characteristics also have a role in the in-stent restenosis process. The high metal/vessel ratio in small vessels, caused by long or numerous stents, provokes neointimal hyperplasia.[18-20] The most preventable cause of in-stent restenosis is stent underexpansion.[21] Predilatation needs to be performed with a balloon shorter than the DES, and post-dilatation also needs to be performed.[16] Stent

FIGURE 3 Meta-Analysis of Target Vessel Thrombosis With DCB Versus DES



Forest plot of the relative risks of target vessel thrombosis with DCB versus DES for small caliber coronary artery disease at 3-year follow-up. The forest plot was made with R, version 4.2.3. Abbreviations as in Figures 1 and 2.

FIGURE 4 Meta-Analysis of MI With DCB Versus DES



Forest plot showing the relative risks of MI with DCB versus DES for small caliber coronary artery disease at 3-year follow-up. The forest plot was made with R, version 4.2.3. MI = myocardial infarction; other abbreviations as in Figures 1 and 2.

thrombosis can occur because coagulation factors are activated in response to the mechanical damage.[22] It is frequently associated with underexpansion of the stent, improper stent strut placement to the vessel wall, edge dissection, and malapposition. The high inflation pressure needed for post-dilatation of the stent increases the risk of edge dissection, requiring bailout stenting in some cases.[23] Therefore, it is crucial that the procedure is conducted optimally to prevent adverse events.[24]

DRUG-COATED BALLOONS. Paclitaxel-coated balloons are the most commonly used DCBs. The PICCOLETO trial (2010) was the first study to compare DCB versus DES for small caliber CAD. It was known that DCBs reduce neointimal proliferation and reduce the risk of in-stent restenosis.[25,26] DCBs quickly deliver paclitaxel, a lipophilic drug, to the vessel wall in a uniform way.[27] DCBs require a longer inflation time than DES for the drug to be eluted and delivered to the vessel.[23] Excipients added such as iopromide (in the SeQuent Please DCB in BASKET-SMALL 2 trial), dextran (Elutax SV in PICCOLETO-II trial), and shellac (Restore DCB in RESTORE SVD trial) act as drug carriers.[27] As soon as the balloon is inflated, most of the drug is released, contrary to the sustained release of DES. DCB advantages include better vascular remodeling, lowered risk of restenosis and thrombosis, and decreased rates of bleeding-related complications due to shortened dual antiplatelet therapy (DAPT).[12,26,28]

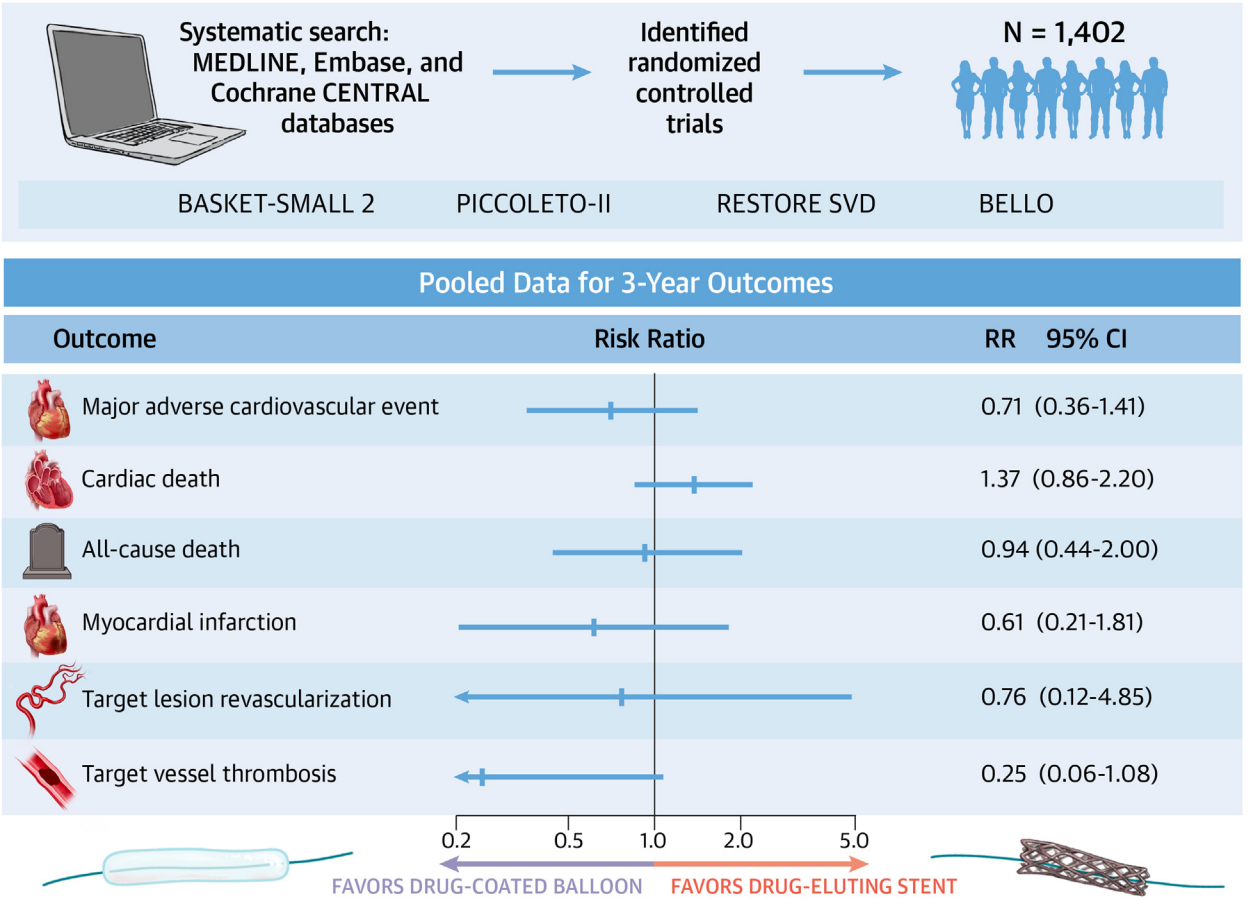
DUAL ANTIPLATELET THERAPY. DAPT is a crucial component of treatment for patients undergoing PCI,

TABLE 5 Outcomes of Efficacy and Safety of Randomized Studies Comparing DCB Versus DES at 3 Years[a]

Study (Year)	MACE	Cardiac Death	All-Cause Death	MI	TLR	TVR	Target Vessel Thrombosis
BASKET-SMALL 2 (2020)[4]							
DCB	53 (13.9%)	17 (4.5%)	28 (7.3%)	19 (5.0%)	NR	30 (7.9%)	2 (0.5%)
DES	53 (14.1%)	13 (3.5%)	27 (7.2%)	23 (6.1%)	NR	32 (8.5%)	6 (1.6%)
PICCOLETO II (2023)[9]							
DCB	11 (9.3%)	2 (1.7%)	4 (3.4%)	2 (1.7%)	9 (7.6%)	NR	0
DES	21 (18.4%)	1 (0.9%)	4 (3.5%)	7 (6.1%)	15 (13.2%)	NR	4 (3.5%)
RESTORE SVD (2020)[11]							
DCB	7 (6.0%)	NR	NR	NR	7 (6.0%)	NR	NR
DES	6 (5.3%)	NR	NR	NR	3 (2.6%)	NR	NR
BELLO (2015)[13]							
DCB	13 (14.4%)	2 (2.2%)	2 (2.2%)	8 (8.9%)	6 (6.7%)	3 (3.3%)	0
DES	28 (30.4%)	1 (1.1%)	5 (5.4%)	17 (18.5%)	12 (13.0%)	6 (6.5%)	0

Values are n (%). [a]All comparisons were not statistically significant.
Abbreviations as in Tables 1 and 2.

CENTRAL ILLUSTRATION **Meta-Analysis of Outcomes of Drug-Coated Balloons Versus Drug-Eluting Stents in Small-Vessel Coronary Artery Disease**



Dobromir Angheluta A, et al. JACC Adv. 2024;3(10):101204.

Meta-analytic results of MACE, cardiac death, all-cause death, MI, TLR, and target vessel thrombosis. Target vessel revascularization could not be included in the meta-analysis due to lack of data. TLR = target lesion revascularization; other abbreviations as in **Figures 2 and 4**.

especially with DES.[29] DAPT reduces ischemic events risk such as MI and cardiovascular mortality at the expense of increasing bleeding risk.[24] Shortening DAPT duration is an attractive advantage of DCB use, especially for patients at high risk of bleeding such as those with chronic kidney disease.[30] Patients treated with a DCB are typically prescribed DAPT for only a only a 1 month period instead of the usual 6 months when a DES is placed. The absence of permanent implantation of a stent diminishes the thrombotic risk. The incidence of bleeding complications rises with increasing intensity and duration of antiplatelet treatment.[24] Both the 2016 American College of Cardiology/American Heart Association and the 2017 European Society of Cardiology guidelines recommend 6 to 30 months of DAPT after DES implantation for stable CAD patients with low bleeding risk. Stable CAD patients with high bleeding risk might be considered for up to 3 months of DAPT after DES implantation, while ACS patients are usually prescribed DAPT for 12 months (if not at high bleeding risk) or 6 months (if at high bleeding risk).[24] In the trials included in this meta-analysis, DAPT was tailored to the interventional strategy. Individuals receiving DCB were prescribed DAPT for 1 month, whereas those with DES received at least 6 months. For patients with bailout stenting, 3 months of DAPT were required for treatment combining DCBs with bare-metal stents and 6 months when combined with DES.[7,8,10,12]

STUDY LIMITATIONS. Our study has several potential limitations. First, included trials used slightly different definitions of MACE. Second, there were differences in the DCB and DES devices utilized across the trials. However, all DCBs were coated with paclitaxel, and DES drugs are typically of similar safety and efficacy.[31] Third, the trial sample sizes were small, highlighting the need for larger cohorts. With only four included trials, many of our treatment estimates were accompanied by wide 95% CIs. Fourth, the enrolled trial populations were disproportionally male, and the generalizability of our results to women is unclear. Fifth, there is the potential for competing risks for our analyses of cardiac death, MI, and TLR. Future studies should aim to analyze individual patient-level data to address this issue. Finally, little information concerning DAPT protocols used in the trials was reported. Since DAPT is an essential element of PCI, its use and duration should be detailed in all trials examining the efficacy of treatments for small caliber CAD.

CONCLUSIONS

Our study was designed to compare long-term outcomes at 3-year follow-up in randomized controlled trials treating small caliber coronary arteries with DCB and DES. When data were pooled across trials for MACE, CIs were wide, but there was little indication that DES was superior to DCB. Most individual components of MACE were associated with small sample sizes and large CIs and were therefore inconclusive. However, there was a potential signal for a reduction of target vessel thrombosis with DCB compared to DES. Overall, our findings suggest that DCB is a reasonable alternative to DES for treating small caliber CAD.

ACKNOWLEDGMENT The authors would like to thank Genevieve Gore, liaison librarian at McGill University, for her assistance with constructing the search strategy.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Ms Seirafi was supported by the Ivan Racheff Scholarship, funded through the McGill University Faculty of Medicine and Health Sciences Research Bursary Program (Montréal, Québec, Canada). Dr Filion is supported by a Senior salary support award from the *Fonds de recherche du Québec - santé* and a William Dawson Scholar award from McGill University (Montréal, Québec, Canada). Dr Eisenberg holds a James McGill Professorship from McGill University (Montréal, Québec). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

PATIENT CARE AND PROCEDURAL SKILLS: DCB is a reasonable alternative to DES for small CAD. There is a potential signal for a reduction in MACE and target vessel thrombosis with DCB compared to DES at 3-year follow-up. Larger trials are needed to definitively compare DCB versus DES in patients with for small CAD.

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KEY WORDS drug-coated balloon, drug-eluting stent, meta-analysis, randomized controlled trial, small coronary artery disease, systematic review

APPENDIX For supplemental tables and figures, please see the online version of this paper.