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ORIGINAL ARTICLE

BIO-PCI: DCB-First Revascularization with Multidisciplinary Secondary Prevention in Young Patients—A Retrospective Cohort Study

Onur Osman Şeker[1], Nihan Bahadır[2], Seçkin Dereli[2]

[1]Clinic of Cardiology, University of Health Sciences Türkiye, Samsun Training and Research Hospital, Samsun, Türkiye

[2]Department of Cardiology, Ordu University Faculty of Medicine, Ordu, Türkiye

ABSTRACT

Background: Coronary intervention targets a focal lesion but does not address the systemic and lifestyle factors that contribute to recurrent events, a gap that is rarely documented in young patients.

Aim: We evaluated 2 complementary domains of the BIO-percutaneous coronary intervention (PCI) framework in young patients with coronary artery disease (CAD): procedural and short-term clinical outcomes of a drug-coated balloon (DCB)-first revascularization strategy and longitudinal cardiometabolic and behavioral changes observed during multidisciplinary secondary prevention follow-up.

Study Design: Single-center retrospective cohort study.

Methods: We included 46 patients younger than 55 years with *de novo* CAD who underwent DCB-only PCI between September 2024 and April 2025, with a median follow-up of 14 months. Technical success was evaluated in all 48 patients who underwent DCB-first PCI. Paired cardiometabolic, behavioral, and sleep-related analyses and longitudinal clinical event assessment were performed in 46 patients who completed DCB-only PCI and had adequate baseline and follow-up data. We analyzed clinical events together with paired baseline-to-follow-up changes in body composition (assessed by bioelectrical impedance analysis), metabolic and inflammatory markers, lifestyle behaviors, and sleep quality, assessed using the Pittsburgh sleep quality index (PSQI).

Results: No cardiovascular deaths, myocardial infarctions, or target-lesion revascularizations were observed; 1 patient underwent target-vessel revascularization (2.2%), and technical success was achieved in 47 of 48 procedures (97.9%). Body weight decreased from 78 to 75 kg, low-density lipoprotein cholesterol from 100 to 80 mg/dL, glycated hemoglobin from 6.2% to 5.8%, and high-sensitivity C-reactive protein from 2.5 to 1.5 mg/L (all $p \leq 0.01$), with reductions in fat mass and visceral fat and preservation of skeletal muscle mass. The proportion of current smokers decreased from 50% to 22% (cessation rate, 56.5%), the proportion engaging in regular exercise increased from 35% to 65%, and the global PSQI score decreased from 8.2 to 6.1 (all $p<0.001$).

Conclusion: In this selected cohort of young patients, DCB-first PCI was technically successful in most procedures. Few clinical events and favorable within-patient changes in cardiometabolic, behavioral, and sleep-related measures were documented in the selected DCB-only longitudinal cohort. Because of the uncontrolled retrospective design, these observations do not establish clinical efficacy or safety and cannot be causally attributed to DCB treatment or the BIO-PCI framework. Prospective controlled studies are required to evaluate the incremental clinical value of this integrated approach.

Keywords: Drug-coated balloon, percutaneous coronary intervention, premature coronary artery disease, cardiometabolic risk, secondary prevention, sleep quality, BIO-PCI

INTRODUCTION

Coronary artery disease (CAD) continues to rank among the leading causes of morbidity and mortality worldwide. Although modern percutaneous coronary intervention (PCI) has markedly improved procedural and clinical outcomes, it addresses only a focal target within what is fundamentally a systemic disease. Over the long-term, outcomes depend as much on managing residual risk factors—including smoking, dyslipidemia, obesity, hypertension, diabetes, and physical inactivity—as on the revascularization procedure itself.[1]

Drug-coated balloons (DCBs) provide a "leave-nothing-behind" approach by delivering an antiproliferative agent without leaving a permanent metallic implant.[2] Growing evidence suggests that, following adequate lesion preparation, DCB-only treatment can yield favorable outcomes in carefully selected patients with *de novo* coronary disease while preserving future treatment options and avoiding permanent caging of the vessel.[3] Contemporary randomized trials, pooled analyses, and consensus statements increasingly support the broader use of DCBs beyond their conventional indications.[4-6]

Existing DCB studies have appropriately focused on procedural, vessel-level, and clinical outcomes.[3,6] However, particularly in young patients, the role of implant-avoiding revascularization should also be considered within the broader context of lifetime coronary disease management and sustained control of residual cardiovascular risk.

Address for Correspondence: Seçkin Dereli MD, Department of Cardiology, Ordu University Faculty of Medicine, Ordu, Türkiye
E-mail: drseckindereli@gmail.com **ORCID ID:** orcid.org/0000-0003-0090-3835

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The concept underlying BIO-PCI was inspired by educational initiatives and scientific discussions led by Professor Flavio Ribichini, emphasizing that coronary intervention should be integrated with optimization of the patient's biological and cardiovascular risk profile rather than viewed solely as a mechanical treatment of coronary stenosis.[7] This perspective is particularly relevant in young patients with premature CAD, in whom continued smoking, dyslipidemia, and physical inactivity remain major drivers of recurrent events despite successful revascularization.[8,9]

We therefore applied BIO-PCI as an integrated clinical framework comprising 2 complementary components. The first is a DCB-first, leave-nothing-behind revascularization strategy, used when anatomically and technically appropriate to minimize permanent metallic implant burden and preserve future treatment options, particularly in young patients. The second is longitudinal multidisciplinary management of residual cardiovascular risk through guideline-directed pharmacotherapy, lifestyle counseling, and continued patient-physician-team engagement. BIO-PCI does not introduce preventive therapies or risk-factor targets that differ from contemporary guidelines. Rather, its proposed distinction is that the revascularization decision and subsequent secondary prevention are planned from the outset as a continuous strategy for lifetime coronary disease management.

Accordingly, we conducted a single-center retrospective BIO-PCI cohort study examining 2 separate analytical domains. The procedural domain evaluated the feasibility and short-term clinical outcomes of a DCB-first strategy in young patients with *de novo* CAD. The longitudinal domain evaluated paired changes in body composition, metabolic and inflammatory markers, lifestyle behaviors, and sleep quality during continued medical treatment and multidisciplinary secondary prevention follow-up. These latter outcomes were not considered effects of DCB treatment. The study was exploratory and intended to provide real-world data for future prospective controlled investigations of the integrated BIO-PCI framework. The conceptual components of BIO-PCI and the distinct outcome domains evaluated in this study are summarized in Figure 1.

METHODS

Study Design, Patient Selection, and BIO-PCI Framework

This retrospective, single-center, observational cohort study included patients younger than 55 years with *de novo* CAD who underwent elective PCI using a DCB-first strategy at our institution between September 2024 and April 2025. Clinical follow-up was censored in May 2026.

The study was designed as a descriptive, hypothesis-generating pre-post cohort study with 2 prespecified analytical domains. The procedural domain evaluated procedural findings in patients undergoing DCB-first PCI, whereas the longitudinal domain assessed within-patient changes during multidisciplinary secondary prevention follow-up.

Following diagnostic coronary angiography, patients with *de novo* lesions considered suitable for a DCB-first strategy were counseled regarding the potential benefits and limitations of a leave-nothing-behind approach, the possibility of bailout stenting, and the local reimbursement status of DCB treatment. Eligibility for the DCB-first strategy was determined based on the clinical presentation, angiographic lesion characteristics, vessel size, feasibility of lesion preparation, and operator judgment.

Of 52 consecutive patients in whom a DCB-first strategy was discussed, 4 declined the proposed approach after shared decision-making. The remaining 48 patients underwent elective DCB-first PCI. One patient who required bailout stenting during the index procedure and 1 patient with insufficient baseline or follow-up data were subsequently excluded. Thus, the final analytical cohort comprised 46 patients treated exclusively with a DCB-only strategy.

In the present study, BIO-PCI was operationalized as an observational care framework integrating DCB-first, implant-avoiding revascularization with longitudinal guideline-directed secondary prevention.[1,10] Secondary prevention management began during the index hospitalization and included optimization of lipid-lowering, antihypertensive, and glucose-lowering therapy according to clinical indication; smoking cessation support; dietary counseling; weight management; physical activity recommendations; and assessment of sleep quality. Patients received an in-hospital dietitian consultation before discharge and were subsequently followed through the outpatient cardiology pathway. Face-to-face cardiology follow-up occurred at least 3 times per year. The 2 analytical domains of the framework are summarized in Figure 1.

Treatment objectives were based on contemporary cardiovascular prevention guidelines rather than uniform study-specific numerical targets. Follow-up was individualized according to clinical need and delivered through the standard cardiology outpatient pathway. BIO-PCI was not implemented as a prospectively standardized cardiac rehabilitation or patient education intervention, and adherence to individual components was not required for inclusion.

Smokers were advised to quit and, when appropriate, were referred to smoking cessation clinics, pulmonology, or primary care for behavioral and pharmacological support. Physical activity recommendations were provided in accordance with contemporary cardiovascular prevention guidelines and reinforced during outpatient follow-up.[1,10] Risk-factor counseling and reinforcement of lifestyle recommendations were provided individually during routine cardiology visits rather than through a structured patient education program. Each patient attended face-to-face cardiology visits at least 3 times per year; telephone and e-Nabız monitoring were not used. Per institutional practice, every patient underwent an in-hospital dietitian consultation during the index admission. After discharge, regular outpatient dietitian follow-up was not mandated and varied among patients; therefore, the proportion attending regular dietitian visits was reported as a lifestyle outcome rather than as a fixed protocol component. In addition, all patients were referred for a single closing dietitian visit at the end of follow-up for body composition assessment. Registered dietitians evaluated dietary habits, nutritional behaviors, and adherence to lifestyle recommendations.

This follow-up did not constitute a separate experimental lifestyle intervention program. Within the applied BIO-PCI framework, repeated

face-to-face cardiology visits and dietitian assessments represented the longitudinal patient-physician-team component accompanying the DCB-first procedural strategy.

Adherence to individual lifestyle recommendations was not an inclusion criterion. Uptake of dietitian follow-up, smoking cessation, exercise, and pharmacological risk-factor management was recorded during routine follow-up and analyzed as part of the BIO-PCI outcomes.

Eligible patients were identified from the institutional catheterization laboratory database. Demographic, clinical, angiographic, procedural, laboratory, body composition, and follow-up data were reviewed from electronic medical records, outpatient files, catheterization reports, and dietitian records.

Medication prescriptions at discharge were abstracted from medical records and reported by drug class. Subsequent changes in medication class or dose and objective measures of treatment adherence were not documented consistently enough to permit reliable longitudinal analysis. Similarly, smoking status, physical activity, dietary follow-up, and sleep-related measures were obtained from routine clinical documentation and patient reports and were not independently verified. Changes in medication dose, treatment persistence, and objective medication adherence were not captured consistently enough for reliable longitudinal analysis. Missing follow-up medication data were not imputed.

All procedures adhered to the principles of the Declaration of Helsinki, and the protocol received approval from the Non-Interventional Scientific Research Ethics Committee of Ordu University Faculty of Medicine (approval no: 2026/96, date: 16.02.2026). Given the retrospective nature of the study, written informed consent was not required and was waived.

Coronary Angiography and PCI Procedure

Coronary angiography and PCI were performed in accordance with prevailing clinical practice guidelines and current expert consensus on coronary revascularization and DCB use.[11,12] The revascularization approach, lesion preparation technique, and device selection were determined at the operator's discretion based on clinical, angiographic, and procedural factors.

The left anterior descending, left circumflex, and right coronary arteries served as target vessels. For each lesion, we documented its location; presence of bifurcation or ostial involvement; lesion length;

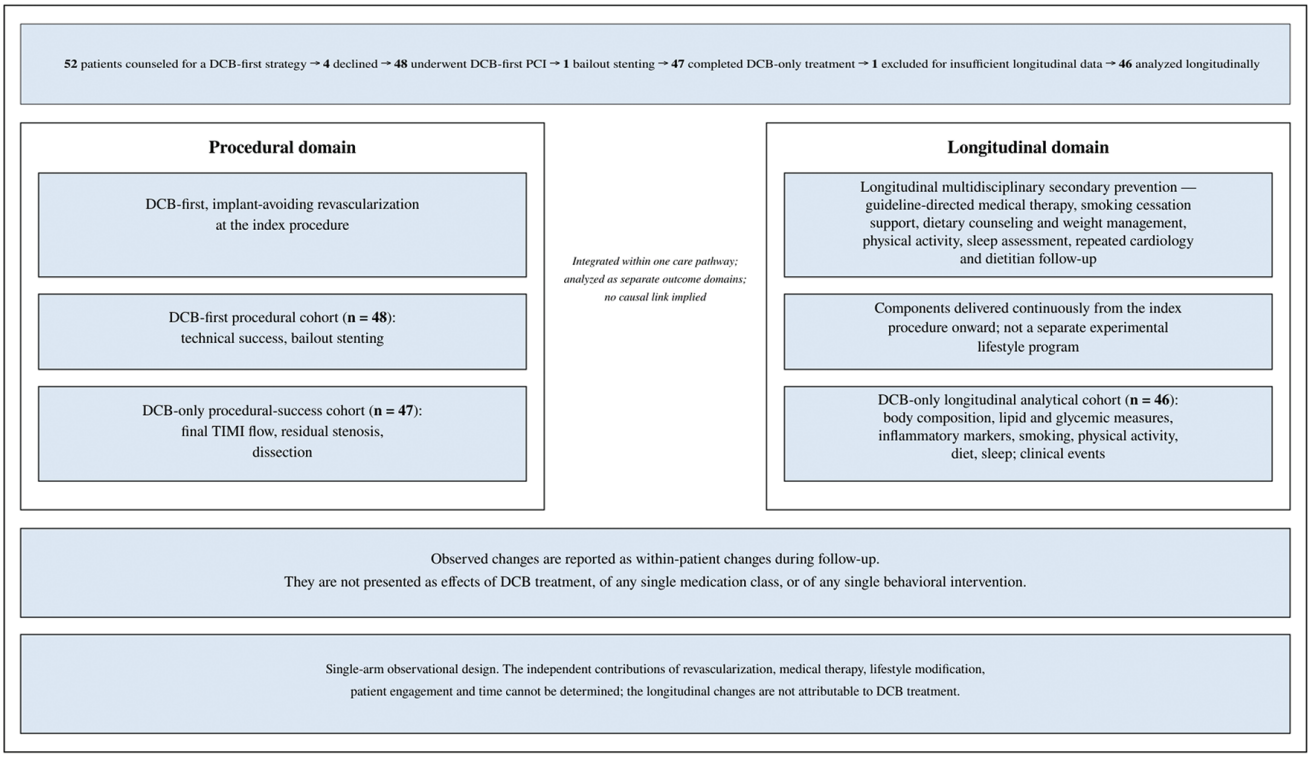

Figure 1. The BIO-percutaneous coronary intervention (PCI) framework: procedural and longitudinal domains. The upper band summarizes the study flow: 52 patients counseled for a drug-coated balloon (DCB)-first strategy, 4 declined, 48 underwent DCB-first PCI, 1 required bailout stenting, 47 completed DCB-only treatment, 1 was excluded for insufficient longitudinal data, and 46 were analyzed longitudinally. The diagram then separates the two analytical domains of the framework. The procedural domain comprises DCB-first, implant-avoiding revascularization at the index procedure, with technical success and bailout stenting reported for the DCB-first procedural cohort (n=48) and the final angiographic findings for the DCB-only procedural-success cohort (n=47). The longitudinal domain comprises multidisciplinary secondary prevention—guideline-directed medical therapy, smoking-cessation support, dietary counseling and weight management, physical activity, sleep assessment, and repeated cardiology and dietitian follow-up, delivered continuously from the index procedure onward rather than as a separate experimental program—with cardiometabolic, behavioral and sleep measures and clinical events reported for the DCB-only longitudinal analytical cohort (n=46). The two domains are integrated within a single care pathway but analyzed separately; no arrow links the procedural domain to the longitudinal outcomes. In this single-arm observational cohort the independent contributions of revascularization, medical therapy, lifestyle modification, patient engagement and time cannot be determined, and the longitudinal changes are not attributable to DCB treatment

degree of calcification; presence of chronic total occlusion; reference vessel diameter; and percentage diameter stenosis.

Adequate lesion preparation was considered mandatory before DCB application. When clinically indicated, semicompliant, non-compliant, scoring, and cutting balloons, as well as rotational atherectomy, were used for lesion preparation. A DCB-only approach was adopted only when lesion preparation produced an acceptable angiographic result, defined as adequate coronary flow, no flow-limiting dissection, and an acceptable degree of residual stenosis.

In selected cases, fractional flow reserve (FFR) and intravascular ultrasound (IVUS) were performed when clinical or angiographic findings warranted their use. FFR was used to assess the physiological significance of intermediate coronary stenoses,[13] whereas IVUS was used for lesion characterization, vessel sizing, plaque morphology assessment, and procedural planning.[11,12]

Paclitaxel-coated and sirolimus-coated balloons were used during the study period. For each procedure, balloon diameter and length, inflation pressure and duration, and the number of devices used were recorded. Paclitaxel-coated and sirolimus-coated balloons were selected according to device availability and operator judgment; balloon coating was neither randomized nor assigned according to a study protocol.

Definitions and Outcomes

Technical success was defined as successful delivery and inflation of the DCB, resulting in a satisfactory final angiographic outcome, defined as thrombolysis in myocardial infarction (TIMI) grade 3 flow with no flow-limiting dissection and no need for bailout stenting. This endpoint was evaluated in the DCB-first procedural cohort (n=48); no single composite measure of procedural or clinical success was applied to the overall BIO-PCI strategy.

On angiography, coronary dissections were graded as none, type A, or type B. At the completion of the procedure, residual diameter stenosis and final TIMI flow grade were documented.

Clinical endpoints recorded during follow-up included cardiovascular death, myocardial infarction, target-lesion revascularization (TLR), and target-vessel revascularization (TVR). Major adverse cardiovascular events (MACEs) were defined as a composite of cardiovascular death, myocardial infarction, and clinically driven TLR.

Clinical events were ascertained through review of institutional electronic medical records, hospitalization records, outpatient cardiology files, and catheterization laboratory records through May 2026. All 46 patients in the final longitudinal analytical cohort had at least 12 months of follow-up and complete paired data for the reported outcomes. One patient from the 48-patient DCB-first procedural cohort had insufficient baseline or follow-up information and was therefore excluded from the longitudinal analysis. Clinical events were not independently adjudicated or systematically verified through an external or national registry.

Study outcomes were organized into 2 analytically distinct domains. Procedural feasibility and technical success were evaluated in the DCB-first procedural cohort of 48 patients, including the patient who required bailout stenting. Clinical, cardiometabolic, behavioral, and sleep-related outcomes were evaluated in the final DCB-only longitudinal cohort of 46 patients. Cardiometabolic and behavioral changes were considered outcomes observed during multidisciplinary secondary prevention follow-up and were not attributed to the DCB procedure itself.

No endpoint was prospectively registered or used for sample-size determination. For reporting clarity, technical success and within-patient changes in body weight and low-density lipoprotein cholesterol (LDL-C) were designated as the principal descriptive outcomes. This post-hoc hierarchy was established for organizational purposes and does not confer confirmatory status. All other cardiometabolic, body composition, inflammatory, behavioral, and sleep-related outcomes were considered secondary exploratory outcomes.

Cardiometabolic and Lifestyle Assessment

Baseline evaluation was performed around the time of the index procedure, and the corresponding follow-up assessment—including laboratory testing, body composition analysis, the Pittsburgh sleep quality index (PSQI), and lifestyle measures—was conducted at a single closing study visit no earlier than 12 months after the index procedure (range, 12-21 months; median, 14 months). Cardiometabolic variables assessed at both time points included body weight, body mass index, blood pressure, heart rate, lipid profile, glycated hemoglobin (HbA1c), renal function indices, and high-sensitivity C-reactive protein (hs-CRP). Because the index procedures were performed between September 2024 and April 2025 and closing visits were scheduled according to clinical availability, the interval between the index procedure and paired follow-up assessment ranged from 12 to 21 months (median, 14 months); the final closing visit was performed in May 2026.

Body composition was measured using a multifrequency bioelectrical impedance analyzer (InBody 770; InBody Co., Ltd., Seoul, South Korea) according to a standardized protocol. Recorded measures included body fat percentage, fat mass, visceral fat level, and skeletal muscle mass. Lifestyle measures included smoking status and cessation, participation in exercise, weekly exercise duration, and clinically meaningful weight loss. Current smoking was defined as any tobacco use within the previous 30 days, whereas smoking cessation was defined as self-reported abstinence at the follow-up visit. Regular exercise was defined as at least 150 minutes of moderate-intensity physical activity per week, which consisted primarily of walking in this cohort; weekly exercise duration was recorded in minutes. Weight-loss categories were defined as reductions of at least 5% and 10% from baseline body weight.

Sleep quality was assessed using the PSQI, which is routinely administered to patients undergoing coronary intervention at Ordu University Training and Research Hospital.[14,15] The global PSQI score, proportion of poor sleepers (PSQI >5), self-reported sleep duration, and subjective sleep quality and sleep latency components were assessed at baseline and follow-up.

Smoking status, physical activity, dietary behavior, and sleep quality were based on patient self-reports documented during routine follow-up and were not independently verified using biochemical

markers, wearable devices, detailed dietary records, actigraphy, or polysomnography.

Statistical Analysis

Continuous variables are reported as mean (standard deviation) or median [interquartile range (IQR)], as appropriate. Normality was assessed using the Shapiro-Wilk test, and categorical variables were summarized as counts and percentages. For paired continuous variables with an approximately normal distribution, within-patient mean differences and 95% confidence intervals (CIs) were estimated using paired t-tests. For paired continuous variables that deviated from normality, the Wilcoxon signed-rank test was used, and the Hodges-Lehmann estimator was used to estimate within-patient median differences with 95% CIs. Paired binary endpoints were compared using the McNemar test, and 95% CIs for within-patient differences in paired proportions were calculated using Newcombe's score-based method for paired data. Statistical significance was defined as a 2-sided $p<0.05$. Proportions for clinical events are reported with exact (Clopper-Pearson) binomial 95% CIs.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 30.0 (IBM Corp., Armonk, NY, USA).

Because this was a retrospective, hypothesis-generating cohort study, no formal a priori sample size calculation was performed. The sample size was determined by the number of consecutive patients available during the predefined study period and by the eligibility and follow-up criteria described above. No confirmatory endpoint was used for sample-size determination. No adjustment for multiple comparisons was applied. Except for the defined principal outcomes, all analyses were considered exploratory, and nominal p values were interpreted descriptively rather than as confirmatory evidence.

RESULTS

Among 52 consecutive patients for whom an elective DCB-first strategy was discussed, 4 declined the proposed strategy after shared decision-making. Of the remaining 48 patients who underwent DCB-first PCI, 1 required bailout stenting during the index procedure, and 1 had insufficient baseline or follow-up data. The final analytical cohort therefore comprised 46 patients treated with a DCB-only strategy and followed within the BIO-PCI framework (Figure 1).

Baseline Characteristics

A total of 46 patients were included in the final analytical cohort. The mean age was 40±6 years, and 37 patients (80.4%) were male. Cardiovascular risk factors were common: 23 patients (50.0%) were current smokers, 25 (54.3%) had hyperlipidemia, 15 (32.6%) were obese, 14 (30.4%) had hypertension, and 12 (26.1%) had diabetes mellitus. A family history of premature CAD was present in 14 patients (30.4%), and the mean body mass index was 27±4 kg/m^2. At hospital discharge, most patients received guideline-directed secondary prevention therapy, including a statin in 39 patients (84.8%), aspirin and a P2Y12 inhibitor in all patients, ezetimibe in 10 (21.7%), and a beta-blocker in 29 (63.0%); detailed medical therapy is shown in Table 1. Guideline-directed lipid-lowering therapy was prescribed and recommended for all patients. The 7 patients (15.2%) not receiving a statin at discharge had declined statin treatment despite counseling, and no patient had a documented contraindication.

Most patients presented with stable angina pectoris (37, 80.4%), whereas 9 (19.6%) had silent ischemia. Among patients with angina, the majority were in Canadian Cardiovascular Society class II (20, 54.1%). Left ventricular ejection fraction was preserved (60%±5%). Baseline laboratory values, including mean LDL-C of 100±30 mg/dL and HbA1c of 6.2%±1.0%, are shown in Table 1.

Lesion and Procedural Characteristics

The left anterior descending artery was the most frequently targeted vessel (25, 54.3%), followed by the right coronary artery (12, 26.1%) and left circumflex artery (9, 19.6%). Most lesions were located in the proximal segment (28, 60.9%). Calcified lesions were present in 9 patients (19.6%), and chronic total occlusions were present in 5 (10.9%). The mean reference vessel diameter was 3.0±0.5 mm, and the mean lesion length was 25±10 mm (Table 2).

Lesion preparation was performed in all patients, most commonly using semicompliant (89.1%) and non-compliant (69.6%) balloons; scoring or cutting balloons and rotational atherectomy were used less frequently. FFR and IVUS were used in 14 (30.4%) and 16 (34.8%) patients, respectively (Table 2). Paclitaxel-coated balloons were used in 41 patients (89.1%) and sirolimus-coated balloons in 5 (10.9%), with a median of 1 balloon per patient (IQR, 1-2) (Table 2).

Among the 48 patients who underwent elective DCB-first PCI, technical success of the DCB-only procedure was achieved in 47 (97.9%), whereas bailout stenting was required in 1 patient (2.1%). The final DCB-only analytical cohort consisted of 46 patients.

In the full DCB-first procedural cohort, technical success was achieved in 47 of 48 patients (97.9%; exact 95% CI, 88.9-99.9%), and bailout stenting was required in 1 of 48 patients (2.1%; exact 95% CI, 0.1-11.1%). Among the 47 patients in whom the DCB-only procedure was completed, final TIMI grade 3 flow was restored in all 47 (100%; exact 95% CI, 92.5-100%). Residual diameter stenosis greater than 25% was present in 5 patients (10.6%; exact 95% CI, 3.5-23.1%), and non–flow-limiting type A or B dissection was present in 7 (14.9%; exact 95% CI, 6.2-28.3%). No flow-limiting dissections occurred (0%; exact 95% CI, 0.0-7.5%) (Table 3). Lesion, device, and procedural characteristics for the full DCB-first procedural cohort (n=48) are presented in Table 2.

Cardiometabolic Changes

From baseline to follow-up, body weight decreased from 78±12 to 75±11 kg, and body mass index decreased from 27.0±4.0 to 26.0±3.8 kg/m^2 (both $p<0.001$). Body fat percentage, fat mass, and visceral fat level also decreased significantly, whereas skeletal muscle mass remained unchanged ($p=0.21$). Systolic and diastolic blood pressure and heart rate also decreased significantly. Lipid values were lower at follow-up, with significant reductions in total cholesterol (180±40 to 150±35 mg/dL), LDL-C (100±30 to 80±25 mg/dL), and triglycerides, whereas high-density lipoprotein cholesterol (HDL-C) remained unchanged ($p=0.45$). HbA1c decreased from 6.2%±1.0% to 5.8%±0.8% ($p=0.003$), and hs-CRP decreased from 2.5±3.0 to 1.5±2.0 mg/L ($p=0.01$), while renal function remained stable (Table 4).

Table 1. Baseline characteristics, laboratory findings, and discharge medical therapy (DCB-only longitudinal analytical cohort, n=46)

Variable	Value
Age (years)	40±6
Sex (male)	37 (80.4%)
Height (cm)	170±8
Body weight (kg)	78±12
Body mass index (kg/m^2)	27±4
Current smoking (%)	23 (50.0%)
Hypertension (%)	14 (30.4%)
Diabetes mellitus (%)	12 (26.1%)
Hyperlipidemia (%)	25 (54.3%)
Family history of premature coronary artery disease (%)	14 (30.4%)
Obesity (%)	15 (32.6%)
Clinical and laboratory characteristics	
Stable angina pectoris (%)	37 (80.4%)
Silent ischemia (%)	9 (19.6%)
CCS angina class I	7 (18.9%)
CCS angina class II	20 (54.1%)
CCS angina class III	10 (27.0%)
LVEF (%)	60±5
Hemoglobin (g/dL)	14.0±1.5
Serum creatinine (mg/dL)	0.9±0.2
eGFR (mL/min/1.73 m^2)	90±20
Total cholesterol (mg/dL)	180±40
LDL cholesterol (mg/dL)	100±30
HDL cholesterol (mg/dL)	45±12
Triglycerides (mg/dL)	150±70
HbA1c (%)	6.2±1.0
hs-CRP (mg/L)	2.5±3.0
Medical therapy at discharge	
Statin	39 (84.8%)
Ezetimibe	10 (21.7%)
Aspirin	46 (100%)
P2Y12 inhibitor	46 (100%)
DAPT duration (months)	3 (IQR 1-6)
Beta-blocker	29 (63.0%)
ACE inhibitor/ARB/ARNI	32 (69.6%)
SGLT2 inhibitor	13 (28.3%)
GLP-1 receptor agonist	6 (13.0%)
Metformin	11 (23.9%)
Insulin	4 (8.7%)
Number of antihypertensive agents	1 (IQR 0-2)

Data are presented as mean±SD, median (IQR), or n (%). CCS angina class percentages are calculated among patients with angina (n=37). ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, ARNI: Angiotensin receptor–neprilysin inhibitor, CCS: Canadian Cardiovascular Society, DAPT: Dual antiplatelet therapy, eGFR: Estimated glomerular filtration rate, GLP-1: Glucagon-like peptide-1, HbA1c: Glycated hemoglobin, HDL: High-density lipoprotein, hs-CRP: High-sensitivity C-reactive protein, LDL: Low-density lipoprotein, LVEF: Left ventricular ejection fraction, SD: Standard deviation, SGLT2: Sodium-glucose cotransporter 2

Lifestyle and Sleep Changes

Favorable changes from baseline were observed in self-reported lifestyle behaviors. The proportion of current smokers decreased from 50% to 22% ($p<0.001$), corresponding to a cessation rate of 56.5% among baseline smokers. Regular exercise participation increased

Table 2. Lesion, device, and procedural characteristics (DCB-first procedural cohort, n=48)

Variable	Value
Target vessel	
LAD	26 (54.2%)
LCX	9 (18.8%)
RCA	13 (27.1%)
Lesion location	
Proximal	29 (60.4%)
Mid	15 (31.3%)
Distal	4 (8.3%)
Bifurcation lesion (%)	5 (10.4%)
Ostial lesion (%)	5 (10.4%)
Long lesion (%)	18 (37.5%)
Calcified lesion (%)	9 (18.8%)
CTO (%)	5 (10.4%)
Reference vessel diameter (mm)	3.0±0.5
Lesion length (mm)	25±10
Diameter stenosis (%)	70±10
Lesion preparation and procedural characteristics	
Predilatation	48 (100.0%)
Semi-compliant balloon (%)	42 (87.5%)
Non-compliant balloon (%)	34 (70.8%)
Scoring balloon (%)	1 (2.1%)
Cutting balloon (%)	7 (14.6%)
Rotational atherectomy (%)	7 (14.6%)
FFR assessment performed (%)	15 (31.3%)
IVUS assessment performed (%)	16 (33.3%)
Drug-coated balloon characteristics	
Paclitaxel-coated balloon	43 (89.6%)
Sirolimus-coated balloon	5 (10.4%)
DCB diameter (mm)	2.75±0.51
DCB length (mm)	24.2±9.6
Inflation pressure (atm)	7.0±2.1
Inflation duration (seconds)	70±40
Number of DCBs used	1 (IQR 1-2)

Data are presented as mean±SD, median (IQR), or n (%) (n=48). Long lesion was defined as a lesion length >20 mm; chronic total occlusion as an estimated occlusion duration ≥3 months; and a calcified lesion as moderate or severe angiographic calcification. atm: Atmospheres, CTO: Chronic total occlusion, DCB: Drug-coated balloon, FFR: Fractional flow reserve, IQR: Interquartile range, IVUS: Intravascular ultrasound, LAD: Left anterior descending artery, LCX: Left circumflex artery, RCA: Right coronary artery, SD: Standard deviation

from 35% to 65%, and median weekly exercise duration increased from 0 to 150 minutes (both p<0.001). Clinically meaningful weight loss of at least 5% and 10% was achieved by 35% and 12% of patients, respectively. Self-reported PSQI scores also improved at follow-up: the mean global PSQI score decreased from 8.2±2.4 to 6.1±2.2, and the proportion of poor sleepers (PSQI >5) decreased from 72% to 49% (both p<0.001), accompanied by an increase in self-reported sleep duration (Table 5).

Table 3. Angiographic and procedural outcomes

Variable	n (%); exact 95% CI
DCB-first procedural cohort (n=48)	
Technical success	47 (97.9%); exact 95% CI, 88.9-99.9
Bailout stenting	1 (2.1%); exact 95% CI, 0.1-11.1
DCB-only procedural-success cohort (n=47)	
Final TIMI 3 flow	47 (100%); exact 95% CI, 92.5-100
Final residual diameter stenosis >25%	5 (10.6%); exact 95% CI, 3.5-23.1
Type A/B (non-flow-limiting) dissection	7 (14.9%); exact 95% CI, 6.2-28.3
Flow-limiting dissection	0 (0%); exact 95% CI, 0.0-7.5

Data are presented as n (%) using the denominator indicated for each cohort. Procedural outcomes are reported separately for the DCB-first procedural cohort (n=48), which includes the one patient who required bailout stenting, and the final DCB-only procedural-success cohort (n=47). Exact two-sided 95% confidence intervals for proportions were calculated using the Clopper-Pearson method. TIMI: Thrombolysis in myocardial infarction, CI: Confidence interval, DCB: Drug-coated balloonS

Clinical Outcomes

Over a median follow-up of 14 months (range, 12-21 months), no cardiovascular deaths or myocardial infarctions occurred. No patient required TLR, whereas TVR was performed in 1 patient (2.2%) (Table 6). Given the small longitudinal cohort of 46 patients and the low event count, the corresponding exact (Clopper-Pearson) 95% CIs were wide: 0-7.7% for cardiovascular death, myocardial infarction, and TLR (0 of 46), and 0.1-11.5% for TVR (1 of 46, 2.2%). In the full 48-patient DCB-first procedural cohort, technical success was achieved in 47 of 48 patients (97.9%; exact 95% CI, 88.9-99.9%), and bailout stenting occurred in 1 of 48 (2.1%; exact 95% CI, 0.1-11.1%). These estimates were imprecise because of the small cohort size and low event count.

DISCUSSION

This study evaluated 2 distinct but complementary components of the BIO-PCI framework in young patients with *de novo* CAD. First, the DCB-first procedural strategy achieved a high technical success rate, with bailout stenting required in only 1 of 48 patients and few clinical events during follow-up. Second, paired longitudinal analyses in the 46-patient DCB-only longitudinal cohort documented favorable cardiometabolic, behavioral, and self-reported sleep-related changes during continued medical treatment and multidisciplinary secondary prevention follow-up. These longitudinal changes should not be

Table 4. Longitudinal cardiometabolic measures: baseline and follow-up

Variable	Baseline	Follow-up	Change (95% CI)	p value (test)
Body weight (kg)	78±12	75±11	-3.0 (-3.8 to -2.2)	<0.001 (Paired t-test)
BMI (kg/m^2)	27.0±4.0	26.0±3.8	-1.0 (-1.3 to -0.7)	<0.001 (Paired t-test)
Body fat percentage (%)	25±6	23±6	-2.0 (-3.1 to -0.9)	0.001 (Paired t-test)
Fat mass (kg)	20±6	17±6	-3.0 (-3.9 to -2.1)	<0.001 (Paired t-test)
Visceral fat level (score, 1-59)	10 (7-13)	8 (5-11)	-2.0 (-3.0 to -1.0)	0.002 (Wilcoxon signed-rank test)
Skeletal muscle mass (kg)	30±4	30.5±4	+0.5 (-0.3 to +1.3)	0.21 (Paired t-test)
Systolic blood pressure (mmHg)	125±12	120±10	-5.0 (-8.8 to -1.2)	0.01 (Paired t-test)
Diastolic blood pressure (mmHg)	78±8	75±7	-3.0 (-5.7 to -0.3)	0.03 (Paired t-test)
Heart rate (beats/min)	78±10	72±8	-6.0 (-10.0 to -2.0)	0.004 (Paired t-test)
Total cholesterol (mg/dL)	180±40	150±35	-30 (-39 to -21)	<0.001 (Paired t-test)
LDL cholesterol (mg/dL)	100±30	80±25	-20 (-27 to -13)	<0.001 (Paired t-test)
HDL cholesterol (mg/dL)	45±12	46±12	+1.0 (-1.6 to +3.6)	0.45 (Paired t-test)
Triglycerides (mg/dL)	150±70	120±60	-30 (-48 to -12)	0.002 (Paired t-test)
HbA1c (%)	6.2±1.0	5.8±0.8	-0.4 (-0.66 to -0.14)	0.003 (Paired t-test)
Serum creatinine (mg/dL)	0.90±0.20	0.88±0.20	-0.02 (-0.07 to +0.03)	0.38 (Paired t-test)
eGFR (mL/min/1.73 m^2)	90±20	92±20	+2.0 (-1.0 to +5.0)	0.18 (Paired t-test)
hs-CRP (mg/L)	2.5±3.0	1.5±2.0	-1.0 (-1.8 to -0.2)	0.01 (Paired t-test)

Data are presented as mean±SD or median (IQR), as appropriate (n=46). p values are from paired t-tests or Wilcoxon signed-rank tests, as appropriate; p<0.05 was considered statistically significant. Change values are within-patient mean (or median) differences with 95% confidence intervals; all paired comparisons included 46 patients. p values were obtained with the paired t-test for normally distributed paired continuous differences and the Wilcoxon signed-rank test for non-normally distributed paired continuous differences. BMI: Body mass index, eGFR: Estimated glomerular filtration rate, HbA1c: Glycated hemoglobin, HDL: High-density lipoprotein, hs-CRP: High-sensitivity C-reactive protein, LDL: Low-density lipoprotein, SD: Standard deviation

Table 5. Self-reported lifestyle and sleep measures: baseline and follow-up

Variable	Baseline	Follow-up	Change (95% CI)	p value (Test)
Current smoking status	50%	22%	-28 (-42 to -14)	<0.001 (McNemar test)
Smoking cessation	–	56.5%	–	–
Regular exercise participation	35%	65%	+30 (+15 to +45)	<0.001 (McNemar test)
Weekly exercise duration (min/week)	0 (IQR 0-60)	150 (IQR 60-210)	+150 (+120 to +180)	<0.001 (Wilcoxon signed-rank test)
Regular outpatient dietitian follow-up	20%	50%	+30 (+13 to +47)	0.001 (McNemar test)
≥5% weight loss	–	35%	–	–
≥10% weight loss	–	12%	–	–
Global PSQI score	8.2±2.4	6.1±2.2	-2.1 (-2.9 to -1.3)	<0.001 (Paired t-test)
PSQI >5 (%)	72%	49%	-23 (-38 to -8)	<0.001 (McNemar test)
Sleep duration (h/night)	5.8±1.1	6.7±0.9	+0.9 (+0.5 to +1.3)	<0.001 (Paired t-test)
Subjective sleep quality component	2.0±0.7	1.3±0.6	-0.7 (-1.0 to -0.4)	<0.001 (Paired t-test)
Sleep latency component	1.8±0.8	1.2±0.7	-0.6 (-0.9 to -0.3)	0.001 (Paired t-test)

Data are presented as mean±SD, percentages, or median, as appropriate (n=46). Smoking cessation is expressed as a proportion of baseline smokers (n=23); weekly exercise duration is presented as the median (IQR). Sleep quality was assessed with the PSQI, on which higher scores indicate poorer sleep. p values are from paired t-tests, the McNemar test, or the Wilcoxon signed-rank test, as appropriate; $p<0.05$ was considered statistically significant. A dash (–) indicates not applicable. Change values are within-patient differences with 95% confidence intervals; all paired comparisons included 46 patients. p values were obtained with the McNemar test for paired binary outcomes, the paired t-test for normally distributed paired continuous differences, and the Wilcoxon signed-rank test for non-normally distributed paired continuous differences. Regular outpatient dietitian follow-up refers to continued attendance at scheduled outpatient dietitian visits; the baseline column reflects the early post-discharge period. An in-hospital dietitian consultation during the index admission and a single closing dietitian visit for body-composition assessment at the end of follow-up were performed in all patients and are not included in this variable. PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation, IQR: Interquartile range

Table 6. Clinical outcomes

Variable	n (%); exact 95% CI
Follow-up duration	14 months (range 12-21)
Cardiovascular death	0 (0.0%); exact 95% CI, 0.0-7.7
Myocardial infarction	0 (0.0%); exact 95% CI, 0.0-7.7
Target lesion revascularization	0 (0.0%); exact 95% CI, 0.0-7.7
Target vessel revascularization	1 (2.2%); exact 95% CI, 0.1-11.5
Major adverse cardiovascular events	0 (0.0%); exact 95% CI, 0.0-7.7

Data are presented as median (range) or n (%) (n=46). Exact two-sided 95% confidence intervals for proportions were calculated using the Clopper-Pearson method. CI: Confidence interval

interpreted as effects of DCB treatment. Rather, their evaluation reflects the BIO-PCI premise that implant-avoiding revascularization and lifetime management of residual coronary risk should be pursued together while remaining analytically distinct.

Our procedural findings are consistent with the growing body of evidence supporting DCB-only treatment in selected *de novo* lesions.[3] Among the 48 elective DCB-first procedures, technical success was achieved in 47 (97.9%), with bailout stenting required in 1 patient. In the final DCB-only analytical cohort, all patients had final TIMI grade 3 flow and no flow-limiting dissection. These findings are consistent with reported DCB-only *de novo* cohorts, in which low long-term TVR rates and MACE rates comparable to or lower than those reported with drug-eluting stents have been described.[4,16] Real-world all-comers registries have likewise reported low 1-year TLR rates following DCB treatment.[17] DCB outcomes depend heavily on meticulous lesion preparation and an acceptable final angiographic result, including preserved flow, absence of flow-limiting dissection, and limited residual stenosis.[2,5] No clear device-related differences in procedural success or short-term clinical events were observed between paclitaxel-coated and sirolimus-coated balloons. However, the study was neither designed nor adequately powered to compare these balloon technologies, and no conclusions regarding their comparative efficacy, safety, or equivalence can be drawn.

Although mortality and major clinical events were low, young age does not eliminate the risk of recurrent disease. Patients with premature CAD carry a substantial burden of recurrent events and repeat revascularization, and even very young PCI populations have non-trivial rates of MACE and cerebrovascular events.[9] This residual risk is driven largely by persistent, modifiable risk factors rather than by the treated lesion itself, underscoring the need to address risk beyond the treated vessel in this population.[1,10]

Body weight, body mass index, fat mass, and visceral fat decreased while skeletal muscle mass was preserved, suggesting a favorable change in body composition rather than simple weight loss; inflammatory markers also decreased at follow-up. These cardiometabolic changes occurred in the setting of guideline-directed medical therapy, dietary counseling, lifestyle modification, repeated clinical follow-up, and dietitian involvement. The reduction in LDL-C is compatible with the expected effects of lipid-lowering therapy, particularly statins and ezetimibe, whereas changes in HbA1c and body weight may have been influenced by glucose-lowering agents, including sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists, prescribed at discharge in 28.3% and 13.0% of patients, respectively, as well as by dietary and physical activity changes. Similarly, the reduction in blood pressure may reflect antihypertensive

treatment. The decline in hs-CRP may have been influenced by statin therapy, weight reduction, smoking cessation, improved metabolic control, or non-specific temporal variation. Because medications were prescribed according to clinical indication rather than assigned according to a study protocol, their independent contributions cannot be separated from those of lifestyle modification, multidisciplinary follow-up, or other temporal effects in this retrospective single-arm cohort. Accordingly, these findings should be interpreted as longitudinal changes in risk factors observed during contemporary secondary prevention rather than as effects of DCB treatment or evidence of an incremental BIO-PCI effect.

They represent descriptive within-patient observations that may generate hypotheses for prospective comparative studies, in which the independent contributions of revascularization strategy, medical therapy, lifestyle modification, and multidisciplinary follow-up can be evaluated.

The BIO-PCI framework should not be interpreted as a fully standardized intervention distinct from usual care. Its secondary prevention components were guideline-based and individualized, and their intensity and uptake varied among patients. Without a usual-care comparator or prospectively defined measures of adherence, the incremental contribution of the integrated framework cannot be determined.

The low observed event frequencies should not be interpreted as evidence of clinical efficacy or safety. The exact CIs were wide, and even outcomes with no observed events had an upper 95% confidence limit of 7.7%. The study was neither designed nor powered to evaluate comparative clinical outcomes.

The direction of the longitudinal changes observed in this cohort is broadly consistent with findings from previous studies of cardiac rehabilitation and structured secondary prevention. A meta-analysis of randomized trials after PCI found that exercise-based rehabilitation improved exercise capacity and angina-related outcomes, although evidence for reductions in major clinical events remained inconclusive.[18] In EUROACTION, nurse-coordinated multidisciplinary preventive care improved lifestyle and cardiovascular risk-factor management compared with usual care.[19] Similarly, RESPONSE-2, which added nurse-coordinated community-based lifestyle programs to guideline-based hospital care after acute coronary syndrome and/or revascularization, increased the proportion of patients achieving improvement in at least 1 lifestyle-related risk factor from 26% to 37%.[20] The favorable changes in physical activity, smoking, body weight, and metabolic risk markers observed in our cohort are directionally consistent with these findings. However, the present follow-up was not a prespecified formal cardiac rehabilitation program, lacked a usual-care comparator, and included concomitant medication optimization. Therefore, this concordance supports the potential relevance of sustained multidisciplinary secondary prevention after PCI but does not establish an independent BIO-PCI effect or superiority over routine guideline-directed care.

Favorable changes from baseline were documented in self-reported lifestyle behaviors, including a high smoking cessation rate, increased physical activity, and greater engagement with dietitian follow-up. The accompanying reduction in self-reported PSQI scores is less frequently reported but clinically relevant, as poor and short sleep are recognized cardiovascular risk factors in patients with coronary disease.[21] Whether the improvement in sleep reflects lifestyle modification, weight loss, improved symptom control, or a combination of these factors cannot be determined from the present data and warrants dedicated objective investigation.

BIO-PCI does not replace guideline-directed secondary prevention or introduce different pharmacological, behavioral, or risk-factor targets. Rather, guideline-directed medical therapy and lifestyle measures constitute the residual-risk management component of the framework.[1,10] Its proposed distinction lies in integrating, from the index procedure onward, a DCB-first, implant-avoiding revascularization strategy with longitudinal patient-physician-team engagement and lifetime coronary risk management. The conceptual contribution therefore lies in the combined clinical framework rather than in the novelty of its individual components. Because the present study lacked a comparator undergoing conventional PCI followed by routine secondary prevention, it cannot determine whether implementing this approach as BIO-PCI provides incremental benefit beyond guideline-directed care. This question requires prospective controlled evaluation. The findings are consistent with the rationale for integrating implant-avoiding revascularization with sustained secondary prevention; however, the uncontrolled observational design does not permit the longitudinal changes to be causally attributed to BIO-PCI framework or distinguished from the effects of medication optimization, lifestyle modification, patient engagement, selection, regression to the mean, or other temporal factors.

Study Limitations

Body composition and sleep were assessed using bioelectrical impedance analysis and a self-reported questionnaire, respectively, both of which are subject to measurement variability. Finally, incomplete retrospective data and unquantified adherence to individual risk-factor interventions may have influenced the findings. As DCB treatment was not routinely reimbursed, treatment selection may also have been influenced by patients' willingness and ability to pay out-of-pocket costs, limiting generalizability to unselected all-comers undergoing PCI.

This study has several limitations. Its retrospective, single-center, single-arm design without a contemporaneous comparator precludes causal or comparative inference: the longitudinal changes cannot be attributed to DCB treatment or the BIO-PCI framework or distinguished from the effects of guideline-directed lipid-lowering, glucose-lowering, and antihypertensive therapy, dietary counseling, lifestyle modification, patient engagement, regression to the mean, or secular trends. The contribution of individual drug classes could not be quantified because treatment was clinically indicated rather than assigned. Follow-up medication dose changes, persistence, and adherence were not captured uniformly, so residual confounding remains substantial. Selection bias is likely: inclusion required acceptance of the DCB-first strategy and adequate follow-up data, so the paired analyses represent a selected per-protocol DCB-only cohort of 46 patients rather than an intention-to-treat evaluation

of the 48-patient procedural cohort, and reimbursement status may have further influenced treatment selection. The modest cohort size, the number of outcomes evaluated, and the absence of adjustment for multiple comparisons limit precision and render all nominal *P* values descriptive. Smoking, physical activity, diet, and sleep were self-reported without biochemical or device-based verification, and body composition was assessed by bioelectrical impedance, so measurement error and social desirability bias cannot be excluded. The paired assessment interval varied from 12 to 21 months, and clinical events were ascertained from institutional records without independent adjudication or registry linkage. Finally, the longitudinal component was not delivered as a prospectively standardized intervention, and its incremental value over usual post-PCI care cannot be determined.

CONCLUSION

In selected young patients with *de novo* CAD, DCB-first PCI was technically successful in most procedures. In the selected DCB-only longitudinal cohort, few clinical events and favorable changes from baseline in cardiometabolic, behavioral, and sleep-related measures were documented during multidisciplinary secondary prevention follow-up. Given the uncontrolled retrospective design, selected analytical population, small sample size, few events, and wide CIs, these observations neither establish clinical efficacy or safety nor permit causal attribution to DCB treatment or the BIO-PCI framework. Prospective controlled studies are required to determine whether this integrated approach provides incremental clinical value beyond usual guideline-directed care.

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Informed Consent: Given the retrospective nature of the study, written informed consent was not required and was waived.

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