

Clinical Outcomes of Using Drug-Coated Balloons During Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction Patients – Insights from High-Risk Groups: A Single-Center Experience

ST Yükselmeli Miyokard Enfarktüsü Hastalarında Primer Perkütan Koroner Girişim Sırasında İlaç Kaplı Balonların Kullanımının Klinik Sonuçları – Yüksek Risk Gruplarından Elde Edilen Bulgular: Tek Merkez Deneyimi

ABSTRACT

Objective: ST-elevation myocardial infarction (STEMI) is one of the leading causes of mortality worldwide. Current guidelines recommend primary percutaneous coronary intervention (PPCI) using drug-eluting stents as the standard management for these patients. Stent-free percutaneous coronary intervention (PCI) using drug-coated balloons (DCB) has been suggested as a novel approach to avoid stent-related complications. This study aimed to assess the efficacy and safety of using DCB in STEMI patients.

Method: We compared STEMI patients who presented during the period between 2019 and 2023 and underwent primary PCI using DCB to those treated with drug-eluting stents (DES) in terms of in-hospital and six-month major adverse cardiac events (MACE).

Results: A total of 128 STEMI patients who underwent primary PCI using DCB were compared to 128 matched patients managed using DES. Small-vessel culprit lesions (< 3 mm) and distal lesions were significantly more frequent in the DCB group compared to the DES group. DCBs were used in major epicardial vessels in around 55% of patients and in side branches in almost 45% of cases. Regarding MACE, either in-hospital or within six months, there was no significant difference between the two groups. Moreover, at six-month follow-up, MACE, reinfarction, and repeat revascularization were numerically lower but statistically non-significant in the DCB group. Subgroup analysis showed that in-hospital MACE and reinfarction rates were statistically significantly higher when DCBs were applied to large vessels (> 3 mm) and in cases of in-stent thrombosis (P = 0.014 and 0.001, respectively).

Conclusion: Drug-coated balloons appear non-inferior to DES during primary PCI in terms of MACE, including mortality and reinfarction, even in major epicardial coronaries. However, it should be used cautiously in certain lesion subsets, especially large vessels (> 3 mm) and in-stent thrombosis.

Keywords: Drug-coated balloons, drug-eluting stents, primary percutaneous coronary intervention, ST-elevation myocardial infarction

ÖZET

Amaç: ST yükselmeli miyokard enfarktüsü (STEMI), dünya çapında önde gelen ölüm nedenlerinden biridir. Mevcut kılavuzlar, bu hastalar için standart tedavi olarak ilaç salımlı stentler kullanılarak yapılan primer perkütan koroner girişim (PPCI) önermektedir. İlaç kaplı balonlar (DCB) kullanılarak yapılan stent içermeyen PCI, stentle ilişkili komplikasyonları önlemek için yeni bir yaklaşım olarak önerilmektedir. Bu çalışma, STEMI hastalarında DCB kullanımının etkinliğini ve güvenliğini değerlendirmek amacıyla yapılmıştır.

Yöntem: 2019-2023 yılları arasında başvuran ve DCB kullanılarak primer PCI uygulanan STEMI hastalarını, DES ile tedavi edilen hastalarla hastane içi ve 6 aylık Majör Kardiyak Olaylar (MACE) açısından karşılaştırdık.

Bulgular: Toplam 128 STEMI hastası, DCB kullanılarak primer PCI uygulandı ve DES kullanılarak tedavi edilen 128 eşleştirilmiş hastayla karşılaştırıldı. 3 mm'den küçük damarlar ve distal lezyonlar, DES'e kıyasla DCB'de önemli ölçüde daha yüksekti. DCB, hastaların yaklaşık %55'inde

ORIGINAL ARTICLE

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majör epikardiyal damarlarda ve vakaların neredeyse %45'inde yan dallarda kullanıldı. Hastane içinde veya 6 ay içinde MACE açısından iki grup arasında anlamlı bir fark yoktu. Ayrıca, 6 aylık takipte, MACE, reinfarktüs ve tekrar revaskülarizasyon DCB grubunda sayısal olarak daha düşüktü, ancak istatistiksel olarak anlamlı değildi. Alt grup analizi, DCB'nin 3 mm'den büyük damarlara uygulandığı durumlarda ve stent içi trombozda hastane içi MACE ve reinfarktüs oranlarının istatistiksel olarak anlamlı şekilde daha yüksek olduğunu gösterdi (P değeri sırasıyla 0,014 ve 0,001).

Sonuç: DCB, mortalite ve reinfarktüs dahil MACE açısından, majör epikardiyal koroner arterlerde bile primer PCI sırasında DES'e göre daha düşük performans göstermiyor gibi görünmektedir. Ancak, belirli lezyon alt gruplarında, özellikle 3 mm'den büyük damarlarda ve stent içi trombozda dikkatli kullanılmalıdır.

Anahtar Kelimeler: ilaç kaplı balonlar, ilaç salımlı stentler, primer perkütan koroner girişim, ST yükselmeli miyokard enfarktüsü

ST-elevation myocardial infarction (STEMI) is one of the leading causes of mortality worldwide.¹ Currently, guidelines recommend primary percutaneous coronary intervention (PCI) using drug-eluting stents (DES) as the standard management for these patients.² DES have been shown to perform better compared to bare-metal stents (BMS) and percutaneous transluminal coronary angioplasty (PTCA) over the last decade. DES are made of a scaffold coated with an antiproliferative drug that reduces cell proliferation inside the stent and prevents early in-stent restenosis.³

On the other hand, several complications of DES, such as stent thrombosis, in-stent restenosis, stent fracture, and the need for long-term dual antiplatelet therapy, still exist.⁴ Moreover, the no-reflow phenomenon, which is a nightmare for interventional cardiologists inside the catheterization laboratory, commonly occurs after stent deployment, unfortunately leading to a greater area of myocardial scarring and reduced myocardial salvage.⁵

Accordingly, the stent-free PCI era started to emerge with bioresorbable vascular scaffolds (BVS), which were first proposed by Tamai in 1999.⁶ Initially, BVS showed favorable outcomes in early clinical trials for selected coronary lesions, comparable to second-generation DES.⁷ Later on, randomized trials involving larger numbers of patients revealed inferior long-term outcomes for BVS compared to DES, with higher rates of thrombotic events and myocardial infarction.^{8,9} As a consequence, Abbott withdrew the Absorb BVS from the market in 2017.¹⁰ Hence, drug-coated balloons (DCB) have been suggested as a novel approach to avoid stent-related complications and currently stand alone as the concept of metal-free PCI. Drug-coated balloons are semi-compliant angioplasty balloons covered with antiproliferative drugs, which are released immediately at the site of balloon inflation and diffuse into the subintimal space.¹¹

Drug-coated balloons stand for the concept of "leaving nothing behind," in which no permanent stent struts or vascular implants are left in the vessel wall. Hence, DCBs are expected to minimize stent-related complications such as in-stent restenosis and stent thrombosis. In addition, native vessels preserve normal vasomotion due to the lack of chronic inflammation caused by metallic struts and polymers.¹²

Currently, DCBs have been studied in clinical trials for various indications, but they have only been validated in the guidelines

ABBREVIATIONS

ACS	Acute coronary syndrome
BMS	Bare-metal stents
BVS	Bioresorbable vascular scaffolds
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CVA	Cerebrovascular accident
DAPT	Dual antiplatelet therapy
DCB	Drug-coated balloons
DES	Drug-eluting stents
DM	Diabetes mellitus
ECG	Electrocardiography
ECHO	Echocardiography
GP	Glycoprotein
HTN	Hypertension
IHD	Ischemic heart disease
ISR	In-stent restenosis
IV	Intravenous
IVUS	Intravascular ultrasound
LAD	Left anterior descending artery
LCX	Left circumflex artery
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiac events
NC	Non-complaint
PPCI	Primary percutaneous coronary intervention
PVD	Peripheral vascular disease
RCA	Right coronary artery
STEMI	ST-elevation myocardial infarction
TIMI	Thrombolysis in myocardial infarction
TLF	Target lesion failure
TLR	Target lesion revascularization
VIF	Variance inflation factor

for the treatment of in-stent restenosis (ISR).¹³ However, there is a paucity of data in the literature discussing the effects of DCBs on the entire acute coronary syndrome (ACS) population. This study aimed to assess the clinical outcomes of using DCBs in STEMI patients undergoing primary PCI.

Materials and Methods

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Ethics Committee

of King Abdullah Medical City (Approval Number: 24-1237, Date: 19.05.2024).

Study Design, Setting, and Duration

This was a single-center, retrospective cohort observational study conducted in the catheterization laboratory of the Cardiology Department during the period from February 2019 to December 2023. Written informed consent was obtained from every patient to review their medical records after an explanation of the medical research and publication process.

Study Population

The study included STEMI patients with diffuse long culprit segments (> 20 mm) who underwent primary PCI to the culprit lesion using either drug-eluting stents or a paclitaxel drug-coated balloon-only strategy, without the need to use a drug-eluting stent.

We excluded patients who developed significant flow-limiting dissection (type C-F) after using DCBs that necessitated crossover to DES, those who were non-compliant with or stopped dual antiplatelet therapy (DAPT) due to any medical issues, and patients with insufficient follow-up data.

Study Variables and Clinical Assessment

Baseline demographic and clinical data were obtained from all patients. Risk factors for coronary artery disease, including diabetes mellitus (DM), hypertension (HTN), smoking, dyslipidemia, previous cerebrovascular accident (CVA), peripheral vascular disease (PVD), ischemic heart disease (IHD), and previous PCI or coronary artery bypass grafting (CABG) due to coronary artery disease (CAD), were reviewed. Electrocardiography (ECG) was evaluated to confirm the diagnosis of STEMI and identify the expected culprit lesion. All patients were loaded before transfer to the catheterization laboratory with aspirin 300 mg, ticagrelor 180 mg or clopidogrel 600 mg, atorvastatin 80 mg, and unfractionated heparin (70-100 IU/kg intravenous (IV) bolus when glycoprotein IIb/IIIa inhibitors were not planned to be used, and 50-70 IU/kg when glycoprotein (GP) IIb/IIIa inhibitors were planned).

A total of 256 STEMI cases underwent primary PCI to the culprit lesion and were stratified into a DCB-only strategy group consisting of 128 patients and a matched DES group consisting of 128 patients.

All cases were subjected to a conventional PPCI procedure, where a workhorse wire was used to cross the distal lesion, with or without aspiration thrombectomy according to the operator's decision. For the DCB group, balloon dilatation of the culprit lesion was performed using semi-compliant, non-compliant, cutting, or scoring balloons according to operator choice. If residual stenosis was less than 30% and dissection was less than type C, the DCB was inflated at nominal pressure (6-8 atm) at the lesion site for one minute. SeQuent Please Neo (B. Braun) and Prevail (Medtronic) were the only two DCB brands used in this study.

On the other hand, the DES group was managed by deploying a DES at the culprit lesion, with or without pre-stenting balloon dilatation according to the operator's choice.

Coronary angiographic findings were recorded, including access site, culprit vessel, native or in-stent culprit lesion, use of regular

balloons, non-complaint balloons (NC), cutting or scoring balloons, use of aspiration catheters, and tirofiban. Size, length, presence of calcification, bifurcation lesions, and the site of the treated culprit lesion (proximal, mid, or distal) were also recorded. Small-caliber vessels were defined as vessels less than 3 mm in diameter. Thrombolysis in myocardial infarction (TIMI) flow before and after the intervention was evaluated by two blinded interventional cardiologists.

During index hospitalization, bedside echocardiography (ECHO) was performed, with left ventricular ejection fraction (LVEF) measured using the Simpson method immediately after the procedure. All patients were followed in-hospital for major adverse cardiac events, including acute heart failure, stroke, reinfarction, repeat revascularization, and cardiac arrest.

Follow-up was performed by reviewing patients' medical records. Routinely in our center, patients are scheduled for a follow-up visit one month after discharge and then every three to six months as outpatient visits, according to clinical evaluation. Echocardiographic assessment is routinely performed three to six months after primary PCI and in the case of any new events.

At six-month follow-up, all patients were assessed for left ventricular systolic function and MACE, including hospitalization for heart failure, reinfarction, repeat revascularization, stroke, and cardiac arrest. During follow-up, compliance with DAPT for one year was reviewed for all patients, as non-compliance was one of the exclusion criteria.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS version 23.0) software produced by IBM (Chicago, Illinois, USA). Patients were classified into two groups: DCB and DES. Qualitative data were presented as numbers and percentages and compared using the chi-square test. Quantitative data were presented as mean \pm standard deviation and compared using the independent t-test. A p value < 0.05 was considered statistically significant. Regarding regression analysis, multicollinearity was assessed using variance inflation factors (VIFs). All variables included in the multivariable model had VIF values below the commonly accepted threshold (VIF < 5), indicating no significant multicollinearity. Furthermore, variables were first screened in univariable analyses, and those with P < 0.05 were considered candidates for inclusion in the multivariate analysis.

Results

Characteristics of the Study Population

This retrospective observational study included STEMI patients who underwent primary PCI using a drug-coated balloon at our institution between February 2019 and December 2023. A total of 128 patients met the inclusion criteria and were included in the DCB group. The sample size was determined by the total number of eligible cases available during the study period. A control group of 128 matched patients who underwent primary PCI with drug-eluting stents was selected based on key clinical and angiographic variables (e.g., age, gender, diabetes status, and lesion characteristics) to minimize selection bias. The matched design allowed for a balanced comparison of major adverse cardiac events between the two groups.

Table 1. Clinical profile of both study groups

Variables	DCB (n = 128) (%)	DES (n = 128) (%)	P
Diabetes	82 (64)	100 (78.1)	0.08
Hypertension	78 (61)	94 (73.4)	0.13
Smoking	52 (41)	48 (37.5)	0.71
Obesity	40 (31)	54 (42.2)	0.22
Dyslipidemia	38 (29.7)	46 (35.9)	0.48
Previous revascularization	30 (23)	44 (34.4)	0.17
Previous CVA	12 (9.4)	16 (12.5)	0.57
Killip class I	84 (65.6)	78 (61)	0.72
Killip class II	36 (28)	31 (24.2)	0.84
Killip class III	8 (6)	18 (14)	0.09
Killip class IV	0 (0)	1 (0.8)	0.96

DCB, Drug-coated balloons; DES, Drug-eluting stents; CVA, Cerebrovascular accident.

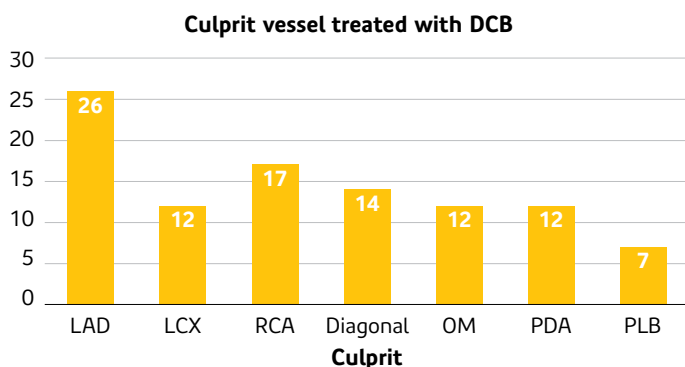


Figure 1. Culprit vessels treated with drug-coated balloons (DCB).

Included patients were followed for major adverse cardiac events both in-hospital and for six months after the procedure.

Regarding demographic and clinical characteristics, there was no significant difference between the two groups in terms of age, diabetes, hypertension, smoking, previous revascularization, and Killip class at presentation (Table 1).

Several nationalities were identified in the study population, including patients from 13 countries. Around 62% were Saudi, 7% were Egyptian, 6% were from Bangladesh, and the remaining 25% represented ten other countries.

Regarding angiographic analysis, small-vessel culprit lesions (< 3 mm) and distal lesions were statistically significantly higher in the DCB group compared to the DES group. On the other hand, there was no significant difference between the two groups in terms of culprit vessel, native or in-stent culprit, lesion size and length, presence of calcification, bifurcation lesions, and TIMI flow before and after intervention. Furthermore, a high thrombus burden (\geq grade 4) was observed in 42.2% of the DCB groups versus 32.8% of the DES group, without a statistically significant difference (P = 0.27) (Table 2).

Table 2. Angiographic analysis of lesions treated with DCB versus DES

Variables	DCB (n = 128) (%)	DES (n = 128) (%)	P
LAD	34 (26.6)	48 (37.5)	0.19
LCX	16 (12.5)	30 (23.4)	0.11
RCA	22 (17.2)	28 (21.9)	0.5
Diagonal	18 (14.1)	12 (9.4)	0.41
Obtuse marginal (OM)	16 (12.5)	14 (10.9)	0.78
Posterior descending artery (PDA)	16 (12.5)	8 (6.3)	0.23
Posterolateral branch (PLB)	10 (7.8)	1 (1.6)	0.09
Native culprit lesion	104 (81.2)	108 (84.4)	0.63
In-stent culprit lesion	24 (18.8)	20 (15.6)	0.64
Proximal lesion	72 (56.3)	78 (60.9)	0.59
Mid lesion	18 (14.1)	34 (26.6)	0.08
Distal lesion	38 (29.7)	16 (12.5)	0.02
Small-caliber vessel (< 3 mm)	94 (73.4)	70 (54.7)	0.03
Large-caliber vessel (> 3 mm)	34 (26.6)	62 (48.4)	0.01
Regular balloon predilatation	86 (67.2)	94 (73.4)	0.44
NC balloon predilatation	36 (28.1)	46 (35.9)	0.33
Cutting balloon predilatation	6 (4.7)	8 (6.3)	0.69
Calcification	42 (33.3)	38 (29.7)	0.66
Bifurcation lesion	22 (17.2)	14 (10.9)	0.31
High thrombus burden	54 (42.2)	42 (32.8)	0.27
Aspiration catheter use	36 (28.1)	26 (20.3)	0.3
Tirofiban use	30 (23.4)	14 (10.9)	0.06
TIMI flow before intervention			
TIMI 0	102 (79.7)	95 (74.2)	0.29
TIMI I	16 (12.9)	21 (16.4)	0.43
TIMI II	7 (5.5)	8 (6.3)	0.79
TIMI III	3 (1.9)	4 (3.1)	0.53
TIMI flow after intervention			
TIMI I	4 (3.1)	9 (7)	0.15
TIMI II	13 (10.2)	17 (13.3)	0.44
TIMI III	111 (86.7)	102 (79.7)	0.13

DCB, Drug-coated balloons; DES, Drug-eluting stents; LAD, Left anterior descending artery; LCX, Left circumflex artery; RCA, Right coronary artery; NC, Non-complaint; TIMI, Thrombolysis in myocardial infarction.

Drug-coated balloons were used in both major epicardial vessels and side branches. They were used in 55% of cases in major epicardial coronaries, including the left anterior descending artery (26%), right coronary artery (17%), and left circumflex artery (12%). The remaining 45% were side branches, such as diagonal branches (14%), obtuse marginal branches (12%), posterior descending artery (12%), and posterolateral branches (7%) (Figure 1).

Drug-coated balloons were used to treat in-stent culprit lesions in 19% of patients and native coronary lesions in 81% of the study group. They were applied to proximal lesions in 56% of cases and to distal lesions in 30%. Regarding the treated culprit

Table 3. Comparison of MACE between STEMI patients treated with DCB and DES

Variables	DCB (%)	DES (%)	P
In-hospital MACE	12 (9.4)	6 (4.7)	0.30
Reinfarction	10 (7.8)	4 (3.1)	0.24
Repeat revascularization	10 (7.8)	4 (3.1)	0.24
Acute heart failure	4 (3.1)	2 (1.6)	0.56
Cardiac arrest	6 (4.7)	2 (1.6)	0.32
Stroke	0 (0)	2 (1.6)	0.83
Six-Month MACE	16 (12.5)	18 (14.1)	0.79
Reinfarction	4 (3.4)	6 (4.8)	0.7
Repeat revascularization	6 (5.1)	8 (6.3)	0.76
Hospitalization for heart failure	6 (5.1)	12 (9.5)	0.3
Cardiac arrest	4 (3.1)	2 (1.6)	0.56
Stroke	5 (3.9)	2 (1.6)	0.77

MACE, Major adverse cardiac events; STEMI, ST-elevation myocardial infarction; DCB, Drug-coated balloons; DES, Drug-eluting stents.

vessels where DCBs were used, 73% were small-caliber vessels (< 3 mm) (Figure 2). Most lesions were modified using regular balloons in around 67% of cases, while non-compliant balloons were used in 28%. Cutting and scoring balloons were used in a minority of cases, accounting for only 5% (Table 2).

All patients were followed during their hospital stay and for six months after discharge for major adverse cardiac events, including reinfarction, repeat revascularization, stroke, heart failure, and cardiac arrest. There was no significant difference in MACE either in-hospital or within six months between patients treated with DCB and those treated with DES during primary PCI. Moreover, at six-month follow-up, MACE, reinfarction, and repeat revascularization were numerically lower but statistically non-significant in the DCB group. Kaplan-Meier curves showed no significant difference between DCB and DES regarding cumulative MACE hazard and MACE-free survival during the six months following primary PCI (P = 0.77) (Figure 3).

Among patients treated with a DCB-only strategy, MACE was observed in 9.4% during index hospitalization and in 12.4% during the six-month follow-up after discharge. Regarding in-hospital MACE, reinfarction and repeat revascularization occurred in 7.8% of patients, and 4.7% developed cardiac arrest. During the six months after discharge, the reinfarction rate was approximately 3.4%, repeat revascularization occurred in 5.1%, and cardiac arrest occurred in 3.1% of patients (Table 3, Figure 4).

Subgroup analysis of clinical outcomes was performed among different interventional strategies in which DCBs were used and showed that in-hospital MACE and reinfarction were statistically significantly higher when DCBs were used to treat large vessels (> 3 mm) (P = 0.014 and 0.005, respectively) and in cases of in-stent thrombosis (P = 0.001 and <0.001, respectively). Regarding lesion preparation, in-hospital MACE and reinfarction were numerically higher but statistically non-significant when regular balloon dilatation was used compared to specialized balloons (NC and cutting balloons) before DCB application (Table 4).

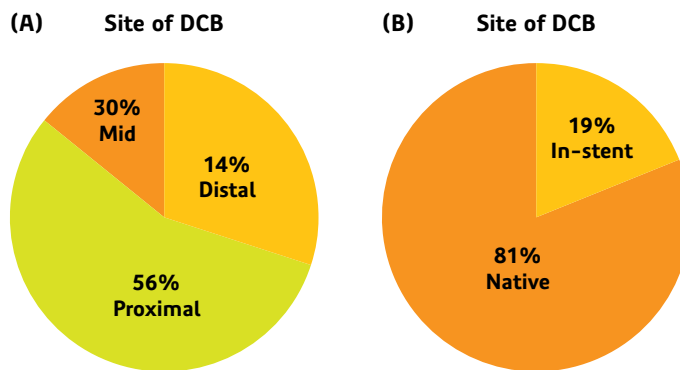


Figure 2. Coronary lesion sites where drug-coated balloons (DCB) were used. (A) Site where DCBs were used, either proximal, mid, or distal. (B) Site where DCBs were used, either in native lesions or in-stent.

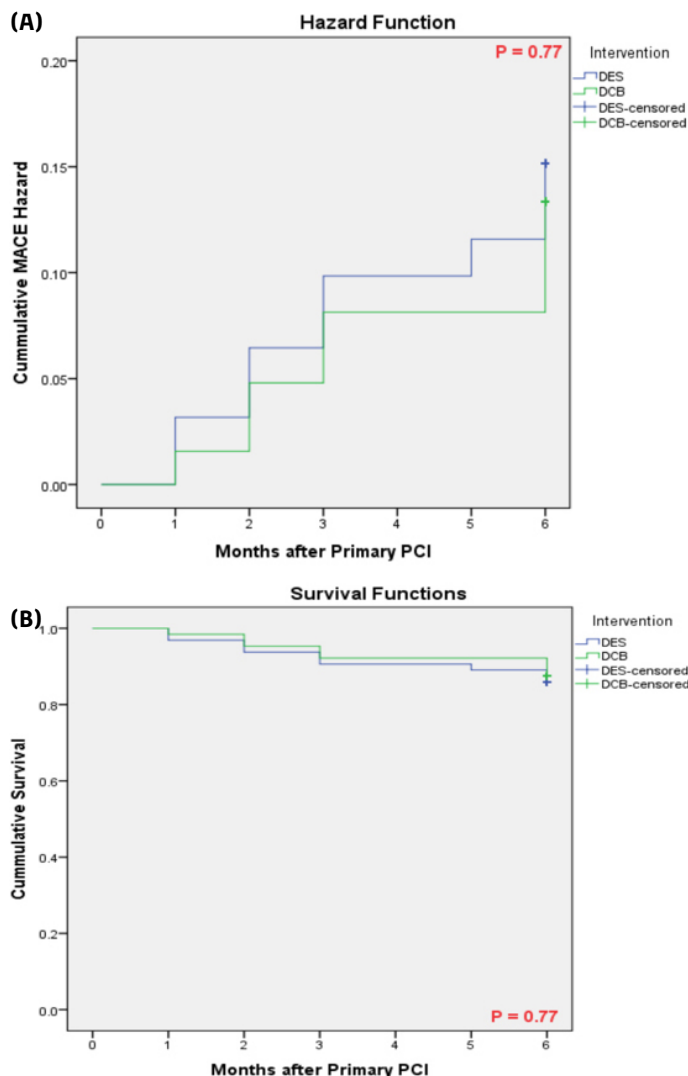


Figure 3. Kaplan-Meier curves comparing drug-coated balloons (DCB) versus drug-eluting stents (DES). (A) Cumulative major adverse cardiac event (MACE) hazard within six months after primary percutaneous coronary intervention (PCI). (B) MACE-free survival over six months after primary PCI.

Table 4. Subgroup analysis of clinical outcomes among different angiographic interventional strategies in patients treated with DCB

Variables	Small vessel (n = 94)	Large vessel (n = 34)	P	Native culprit (n = 104)	In-stent culprit (n = 24)	P	Regular balloons (n = 100)	Specialized balloons (n = 28)	P
In-hospital outcomes, %									
MACE	6 (6.4)	10 (29.4)	0.014*	6 (5.8)	10 (41.7)	0.001*	12 (12)	4 (4.3)	0.82
Reinfarction	2 (2.1)	8 (23.5)	0.005*	2 (1.9)	8 (33.3)	<0.001*	8 (8)	2 (7.1)	0.92
Repeat revascularization	2 (2.1)	8 (23.5)	0.005*	2 (1.9)	8 (33.3)	<0.001*	8 (8)	2 (7.1)	0.92
Cardiogenic shock	2 (2.1)	2 (5.9)	0.45	2 (1.9)	2 (8.3)	0.25	4 (4)	0 (0)	0.447
Cardiac arrest	4 (4.3)	2 (5.9)	0.79	4 (3.8)	2 (8.3)	0.51	4 (4)	2 (7.1)	0.62
Six-month outcomes, %									
MACE	12 (35.3)	10 (10.6)	0.12	12 (11.5)	10 (41.7)	0.16	16 (16)	6 (21.4)	0.964
Reinfarction	4 (4.7)	0 (0)	0.38	4 (4.2)	0 (0)	0.49	4 (4.4)	0 (0)	0.42
Repeat revascularization	4 (4.7)	2 (3.6)	0.8	4 (4.2)	2 (9.1)	0.5	4 (4.4)	2 (7.1)	0.69
Hospitalization for heart failure	0 (0)	6 (18.8)	<0.05*	0 (0)	6 (27.3)	<0.001*	5 (5)	2 (7.1)	0.83
Cardiac arrest	4 (4.8)	2 (6.3)	0.82	4 (3.8)	2 (8.3)	0.51	4 (4.4)	2 (7.1)	0.69

*Statistically significant. DCB, Drug-coated balloons; MACE, Major adverse cardiac events.

Multivariate binary logistic regression analysis showed that treating in-stent culprit lesion was an independent predictor of in-hospital MACE in PPCI cases managed using DCBs (odds ratio [OR] = 1.22, P = 0.041) (Table 5).

Regarding left ventricular ejection fraction at follow-up, there was no statistically significant difference between the two groups six months after the procedure (21.4% ± 23.2 vs. 28.3% ± 24.4; P = 0.48).

Discussion

In the present observational study, we evaluated the use of a drug-coated balloon-only strategy during primary PCI for ST-elevation myocardial infarction in a diverse and clinically complex patient population. Our results demonstrate that this approach is technically feasible and associated with acceptable short-term outcomes. The in-hospital MACE rate was 9.4%, increasing to 12.4% at six months, while reinfarction occurred in 7.8% of patients during the index hospitalization and in 3.4% during follow-up. DCBs were used not only in small coronary vessels but also in large epicardial arteries and proximal segments—55% and 56% of cases, respectively. In addition, vessel diameter > 3 mm and in-stent restenosis as the culprit lesion emerged as key angiographic predictors of adverse in-hospital outcomes. To our knowledge, our study represents one of the largest real-world assessments of a DCB-only PPCI strategy in a multinational cohort, offering new insights into clinical and procedural factors that may influence outcomes.

Moreover, this study aimed to identify high-risk groups and angiographic criteria that are more susceptible to complications and adverse events following the use of DCBs during PPCI.

In 2001, the basic concept of a drug-coated balloon providing a short-lasting application was proposed, and the first experimental studies were performed.^{14,15} Scheller et al.¹⁵ suggested delivering anti-cell proliferation drugs to the target diseased blood vessel through balloon expansion, thereby inhibiting intimal proliferative inflammation.¹⁶

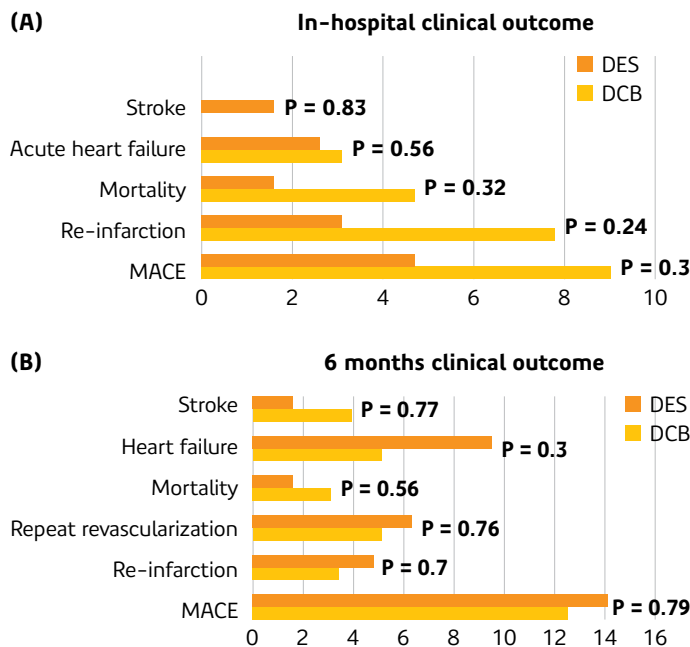


Figure 4. Comparison of clinical outcomes between drug-coated balloons (DCB) and drug-eluting stent (DES) groups. (A) In-hospital clinical outcomes. (B) Six-month clinical outcomes.

Several advantages and disadvantages have been proposed for using a DCB-only strategy during PPCI. On the one hand, it may overcome stent undersizing that occurs due to spastic condition during acute myocardial infarction. In addition, it may simplify complex lesions, especially in critically ill patients, and avoid the strict need for long-term antiplatelet therapy.^{13,17} On the other hand, in cases with a high thrombus burden, large thrombi may hinder adequate drug delivery to the vessel wall.^{13,18} Moreover, to achieve maximum benefit, DCBs require adequate and aggressive lesion preparation, which may result in significant coronary dissection.

Table 5. Independent predictors of in-hospital MACE in the DCB group

Variables	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
Diabetes	0.29	0.7-1.16	0.08			
Killip class	1.62	1.11-2.37	0.013*	1.14	0.9-1.43	0.27
In-stent culprit	1.85	1.07-2.45	0.02*	1.22	1.01-1.48	0.041*
Regular balloon use	1.21	1.03-1.51	0.96			
Large vessel	1.42	1.16-1.81	0.003*	1.03	0.92-1.15	0.62
Proximal lesion	1.34	0.86-1.67	0.74			
Distal lesion	0.31	0.18-1.19	0.28			

*Statistically significant. MACE, Major adverse cardiac events; DCB, Drug-coated balloon; OR, Odd ratios; CI, Confidence interval.

To our knowledge, this is the first study to evaluate the use of DCBs during PPCI in a heterogeneous patient population, including up to 13 nationalities. This was facilitated by the unique location and role of our institute in treating Hajj and Umrah patients while they are performing their religious activities in Makkah.

Despite the general concept that DCBs are mainly designed for treating small vessels and side branches, they were used in major epicardial coronaries, including the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA), in up to 55% of cases in the present study. In addition, DCBs were applied to proximal lesions in 56% of cases during PPCI.

The present study showed that in-hospital MACE was 9.4%, increasing to 12.4% at six-month follow-up. These results are concordant with Hao et al.,¹⁶ who reported that in PPCI cases treated with DCBs, MACE at one year was observed in 11% of cases, with no significant difference compared to the DES group.¹⁹

In addition, the REVELATION trial (Randomized Evaluation of paclitaxEL-coated balloon Versus drug-eluting stent In Acute ST-elevation myocardial infarction), published in 2017, evaluated the use of DCB versus DES during primary PCI in STEMI patients. At two-year follow-up, MACE was observed in only four out of 60 patients in the DCB arm, with no significant difference compared to the DES arm.²⁰ The higher MACE rate observed in our study may be explained by differences in the demographic data of the study groups and by different definitions of MACE between the two studies. In the present study, 64% of patients in the DCB arm were diabetic and 30% had dyslipidemia, compared to 13% and 17%, respectively, in the REVELATION trial. In addition, hospitalization due to heart failure was included as a component of MACE in the present study, which may have influenced the results.

More recently, Merinopoulos et al.²¹ published a large study conducted on 1,139 patients over four years, of whom 452 cases were managed using DCBs during PPCI. According to their results, all-cause mortality was observed in 10.8% of the DCB arm versus 9% in the DES group, without a statistically significant difference.

On the other hand, the present study showed that reinfarction in PPCI cases treated with DCB was observed in ten cases, with rates of 7.8% in-hospital and 3.4% at six-month follow-up. In this regard, the study by Gobić et al.²² reported a reinfarction rate in the DCB arm during PPCI of 5.3% at one-month follow-up and 0% during the subsequent six months. This relatively different result could be attributed to the smaller sample size of their study, as

they included 38 patients in the DCB group, whereas the present study analyzed 128 patients treated with DCB.

Discordant with the present study, the REVELATION trial showed a zero reinfarction rate and a 3% target lesion revascularization (TLR) rate at nine-month follow-up, and rates of 1.8% and 5.4%, respectively, at two-year follow-up.²³ The higher reinfarction rate observed in our study may be explained by differences in lesion modification methods used prior to DCB application. In the present study, 67% of lesions were predilated using semi-compliant balloons, 28% using NC balloons, and 5% using cutting or scoring balloons. Previous studies have shown that modified balloons (specifically cutting and scoring balloons) were associated with significantly lower rates of major dissection and a reduced need for crossover to DES compared to conventional balloons in small-vessel lesions.^{24,25}

A few months ago, Sanz-Sánchez et al.²⁶ published an observational study evaluating the use of DCB-only therapy during PPCI and demonstrated low rates of target lesion failure (TLF) (3.4%). A target lesion revascularization rate of 1.8% was observed, with no reported cases of target vessel myocardial infarction. This discrepancy between their results and ours may be related to differences in patient population, as diabetic patients constituted 67% of our study group compared to only 32% in their study. In addition, stent thrombosis accounted for approximately 28% of patients treated with DCB in their study versus 19% in our cohort. Furthermore, only two DCB brands were used in the present study, whereas six different DCBs were used in the study by Sanz-Sánchez et al.,²⁷ which may have influenced the results. These promising findings by Sanz-Sánchez et al.²⁷ prompted the initiation of the COPERNICAN trial (Comparison Of Paclitaxel-Eluting Balloon versus Drug-Eluting Stent in ST-Elevation Myocardial Infarction), a randomized study comparing clinical outcomes of DCB versus DES in STEMI patients, with results anticipated soon.

Finally, subgroup analysis of the present study showed that in-hospital MACE and reinfarction rates were significantly higher in large vessels (> 3 mm) and in patients with in-stent culprit. Moreover, treatment of an in-stent culprit was identified as an independent predictor of in-hospital MACE following DCB use during PPCI. This finding may be explained by the higher thrombus burden in primary PCI cases, which could hinder adequate drug delivery to the vessel wall. In addition, semi-compliant balloons were used in more than 60% of our patients, which may have resulted in inadequate vessel preparation. Emerging published

evidence has shown that TLR rates are significantly higher in the semi-compliant balloon group compared to scoring and non-compliant balloons used prior to DCB therapy.²⁸

Theoretically, the routine use of scoring or cutting balloons before DCB deployment has been proposed to create cracks and dissections in the vessel wall, thereby facilitating drug transfer and penetration into the vessel wall and potentially enhancing the anti-restenosis efficacy of DCBs.²⁹ In this regard, the randomized NATURE trial (Non-compliant or cUtting balloon for lesion pReparaTion bEfore drug-coated balloon angioplasty) is currently ongoing to evaluate the safety and efficacy of cutting balloons compared to standard balloons (semi-compliant or non-compliant balloons) for lesion preparation prior to DCB treatment in normal-sized vessels.³⁰

Overall, our study provides one of the most detailed assessments to date of angiographic subgroups and procedural characteristics associated with outcomes following DCB-only PPCI in STEMI patients. The results underscore the importance of careful lesion assessment, meticulous vessel preparation, and individualized procedural planning.

In summary, DCB-only PPCI represents a viable alternative to DES in selected STEMI cases—particularly when long-term DAPT is undesirable, vessel dimensions are uncertain, or a metal-free PCI is preferred.³¹ However, heightened caution is warranted in lesions with a high thrombus burden, inadequate preparation, large-caliber vessels, or in-stent restenosis, where the risk of adverse events is increased. Optimal balloon preparation—preferably using scoring or cutting devices—and thoughtful angiographic evaluation remain central to the successful implementation of this strategy. As evidence from ongoing randomized trials becomes available, the role of DCBs in acute STEMI management is expected to become more clearly defined.

Limitation

The present study is a retrospective observational study and, consequently, is subject to multiple confounding factors. Therefore, large randomized, double-blinded clinical trials are recommended to compare DCB and DES during primary PCI. Although the relatively large sample size improves sensitivity compared to smaller cohorts, this study was powered only to detect relatively large absolute differences. Smaller but potentially clinically meaningful differences—particularly subgroup effects—may not have been detected. Accordingly, subgroup analyses should be considered exploratory and interpreted with caution. We also recommend greater use of intravascular ultrasound (IVUS) during the index procedure to adequately evaluate for and exclude major dissection after lesion preparation. Moreover, IVUS-guided angiographic follow-up is recommended to measure minimal lumen area and assess late lumen enlargement.

Conclusion

Drug-coated balloons appear to be non-inferior to DES during primary PCI in terms of MACE, including mortality, reinfarction, and repeat revascularization, even in major epicardial coronary arteries. However, DCB use should be approached cautiously in certain lesion subsets, particularly large vessels (> 3 mm) and cases of in-stent thrombosis. These findings are still exploratory and should be interpreted with caution until confirmed by large, IVUS-guided, randomized double-blinded clinical trials.

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