INDONESIAN HEALTH JOURNAL
https://ihj.rivierapublishing.id/index.php/rp
Volume 4 Number 4, December 2025
P-ISSN: 2963-3044
E-ISSN: 2963-3036

Lesion Characteristics Difference and Cardiovascular Event in Drug-Coated Balloon Used for De Novo Patients

Adrian Masno[1], Sarah Qonitah[2]*, Kiagus Muhammad Andri Akbar[3]
General Hospital Palembang, Indonesia[1,2,3]
Email: sarahqonitah@gmail.com*

ABSTRACT

Drug-Coated Balloon (DCB), a semi-compliant angioplasty balloon coated with an antiproliferative drug, is increasingly used for de novo lesions due to its "leave nothing behind" approach, which preserves vessel vasomotion and enables long-term remodeling. However, evidence for DCB in de novo lesions, especially small vessels, remains limited. This retrospective single-center cohort study analyzed 84 patients treated with DCB for de novo lesions at Mohammad Hoesin General Hospital, Indonesia (2023–2024). Lesions were grouped as Chronic Total Occlusion (CTO), Left Main (LM) disease, or bifurcation. Data from medical records and 6-month telecommunication follow-up identified major and non-major cardiovascular events. Bivariate analysis used SPSS Statistics 23 ($p < 0.05$ significant). CTO lesions linked significantly to cardiac arrest (20.4%, $p = 0.005$) but not recurrent heart attacks (9.3%, $p = 0.102$), bleeding (1.9%, $p = 0.590$), heart failure (7.4%, $p = 0.164$), revascularization (0%), or stroke (0%). LM disease and bifurcation lesions showed no significant associations with these events. Overall, 61.9% used biolimus agents. In conclusion, CTO lesions warrant careful selection and monitoring.

Keywords: Chronic Total Occlusion, Left Main, Bifurcation Lesions, Drug-Coated Balloon

INTRODUCTION

Coronary artery disease (CAD) remains a major cause of morbidity and mortality worldwide, with percutaneous coronary intervention (PCI) being a central therapeutic approach (Ahmad et al., 2023). According to the World Health Organization (2023), cardiovascular diseases account for approximately 17.9 million deaths annually, representing 32% of all global deaths, with CAD being the leading cause. Drug-coated balloons (DCBs) have emerged as an alternative strategy, increasingly used for selected de novo lesions (Caminiti et al., 2024; Gitto et al., 2023; Gobbi et al., 2025; Her & Shin, 2024).

DCBs deliver antiproliferative drugs without leaving a permanent metallic scaffold, potentially reducing complications such as late stent thrombosis and neoatherosclerosis while maintaining vascular integrity. Previous studies have shown that the drug-coated balloon strategy was associated with a significant reduction in nonfatal myocardial infarction compared with the drug-eluting stent strategy, while insignificant inter-strategy differences were observed in cardiac death, all-cause death, target lesion revascularization, and target-vessel revascularization (Min et al., 2019). This "leave nothing behind" concept represents a paradigm shift in interventional cardiology, offering theoretical advantages in preserving physiological vessel function and reducing long-term complications associated with permanent metallic implants.

According to the ESC 2023 guidelines, in-stent restenosis (ISR) remains the primary indication for DCB angioplasty; however, interest in using DCBs for de novo lesions continues to grow in clinical settings such as small vessels, bifurcations, diabetes mellitus, multivessel disease, high bleeding risk, and acute coronary syndromes (Kern et al., 2023; Patel & Kumbhani, 2022). Despite this, clinical trial data on DCB effectiveness in certain complex lesion characteristics—particularly chronic total

occlusion (CTO), left main (LM) disease, and bifurcation lesions—remain limited (Zhou et al., 2021). This gap in evidence represents a critical challenge for clinicians seeking to optimize treatment strategies in complex coronary anatomy, where traditional drug-eluting stents may pose increased risks or technical limitations (Gomez & Abbott, 2022; Lee et al., 2020). Additionally, the increasing prevalence of diabetes mellitus and multivessel disease in patients has further intensified the need for alternative therapeutic approaches like DCBs (Krause et al., 2021). Therefore, further research is necessary to explore the full potential of DCBs in these complex clinical scenarios (Sullivan et al., 2022; Zhang et al., 2023).

The urgency of this research stems from several key clinical considerations. First, the prevalence of complex coronary lesions—including CTO (estimated at 15-20% of all diagnostic coronary angiograms), LM disease (5-7% of CAD patients), and bifurcation lesions (15-20% of PCI procedures)—continues to rise with aging populations and increasing cardiovascular risk factors. Second, management of these complex lesions remains controversial, with ongoing debate regarding optimal revascularization strategies. Third, patients with these lesion types often have multiple comorbidities and higher procedural risks, making the selection of appropriate treatment modalities critically important for improving outcomes and reducing healthcare costs. Fourth, in resource-limited settings such as Indonesia, understanding the real-world effectiveness and safety of DCBs in complex lesions can inform clinical practice guidelines and resource allocation decisions.

The novelty of this study lies in several aspects. While most existing DCB research focuses on in-stent restenosis or simple *de novo* lesions in small vessels, this study specifically examines DCB outcomes in three distinct complex lesion subtypes—CTO, LM disease, and bifurcation lesions—within a single cohort, allowing for direct comparison of cardiovascular event rates across these high-risk anatomical scenarios. Furthermore, this represents one of the first studies from Southeast Asia to systematically evaluate DCB use in complex *de novo* coronary lesions, contributing valuable data from an underrepresented population with potentially different demographic and clinical characteristics compared to Western cohorts. Additionally, the 6-month follow-up period provides medium-term outcome data that bridges the gap between immediate procedural results and long-term clinical trials, offering practical insights for clinical decision-making.

Major adverse cardiovascular events (MACE) are defined by the ESC as a composite of cardiovascular mortality, myocardial infarction, stroke, and revascularization (ESC, 2023). Heart failure and bleeding events, although clinically important, are typically classified as non-MACE outcomes. Bosco et al. reported that MACE definitions vary across studies, but heart failure and bleeding consistently appear as separate safety endpoints (Bosco et al., 2021). Bleeding events are commonly analyzed using the standardized Bleeding Academic Research Consortium (BARC) criteria (Mehran et al., 2011). This standardized approach to outcome definition enables meaningful comparison with international literature and ensures reproducibility of findings.

The objectives of this study are threefold: (1) to evaluate the incidence of major and non-major cardiovascular events in patients treated with DCB for complex *de novo* lesions, (2) to identify specific lesion characteristics (CTO, LM disease, bifurcation) associated with increased cardiovascular event risk, and (3) to provide evidence-based insights that can guide clinical decision-making regarding DCB use in complex coronary anatomy. The findings from this research have potential implications for refining patient selection criteria, informing procedural planning, and optimizing post-procedural monitoring protocols in patients undergoing DCB angioplasty for *de novo* lesions.

METHOD

We designed this study as a retrospective cohort study. The study was conducted at Mohammad Hoesin General Hospital Palembang, a tertiary referral center in South Sumatra, Indonesia, serving as

the primary cardiac care facility for the region. Therefore, we collect 84 data CTO lesions, LM disease and bifurcation lesion patients who using DCB in de novo from January 2023 to August 2024 at Mohammad Hoesin General Hospital Palembang.

Data collection was performed through systematic review of electronic medical records, including patient demographics, cardiovascular risk factors, lesion characteristics from coronary angiography reports, procedural details (DCB type, vessel preparation techniques, adjunctive therapies), and immediate post-procedural outcomes. Lesion characteristics were classified according to standardized definitions: CTO was defined as complete occlusion with TIMI flow 0 and estimated duration ≥3 months; LM disease was defined as stenosis ≥50% in the left main coronary artery; and bifurcation lesions were classified according to the Medina classification system. All coronary angiograms were reviewed by experienced interventional cardiologists to confirm lesion classification and DCB deployment success.

Follow-up was carried out via telecommunication and electronic medical record review regarding symptoms both Major Adverse Cardiovascular Event and non-Major Adverse Cardiovascular Event that appeared after 6 months of coronary percutaneous intervention procedure. A structured questionnaire was used during telecommunication follow-up to systematically assess for symptoms of angina, dyspnea, syncope, and other cardiovascular complaints. Additional data on hospitalizations, emergency department visits, and medication adherence were obtained from the hospital information system. For patients reporting symptoms, clinical documentation and diagnostic test results were reviewed to confirm event classification.

To ensure data quality and minimize bias, the following measures were implemented: (1) independent verification of lesion characteristics by two cardiologists with disagreements resolved through consensus discussion, (2) standardized event adjudication using ESC definitions for MACE and BARC criteria for bleeding events, (3) training of data collectors on standardized data extraction protocols, and (4) double data entry with consistency checks to identify and correct transcription errors.

Sample size justification: Based on previous studies reporting MACE rates of 10-15% in complex PCI procedures, with an expected difference of 10% between lesion groups, alpha of 0.05, and power of 80%, a minimum sample size of 70-80 patients was required. Our final sample of 84 patients after exclusions meets this requirement and provides adequate statistical power for the primary analysis.

Data were then analyzed using SPSS Statistics 23. Data were analyzed using bivariate analysis to examine the relationship between lesion characteristics (CTO, LM disease, bifurcation) and cardiovascular outcomes. Fisher's exact test was used for categorical variables with expected cell frequencies <5, while chi-square test was applied for other categorical comparisons. Descriptive statistics were reported as frequencies and percentages for categorical variables. Variables with p value <0.05 were considered to have a significant relationship.

Patients using DCB as de novo with lesion characteristics Chronic Total Occlusion (CTO), LM disease and bifurcation lesion, who can be followed-up via telecommunication regarding symptoms both Major Adverse Cardiovascular Event (MACE) and non-Major Adverse Cardiovascular Event that appeared after 6 months of coronary percutaneous intervention procedure were included in the study. Patients who cannot be followed-up were excluded in the exclusion criteria. From 111 patients, we excluded 27 patients who cannot be contacted. In total 84 patients were enrolled in this study (Figure 1).

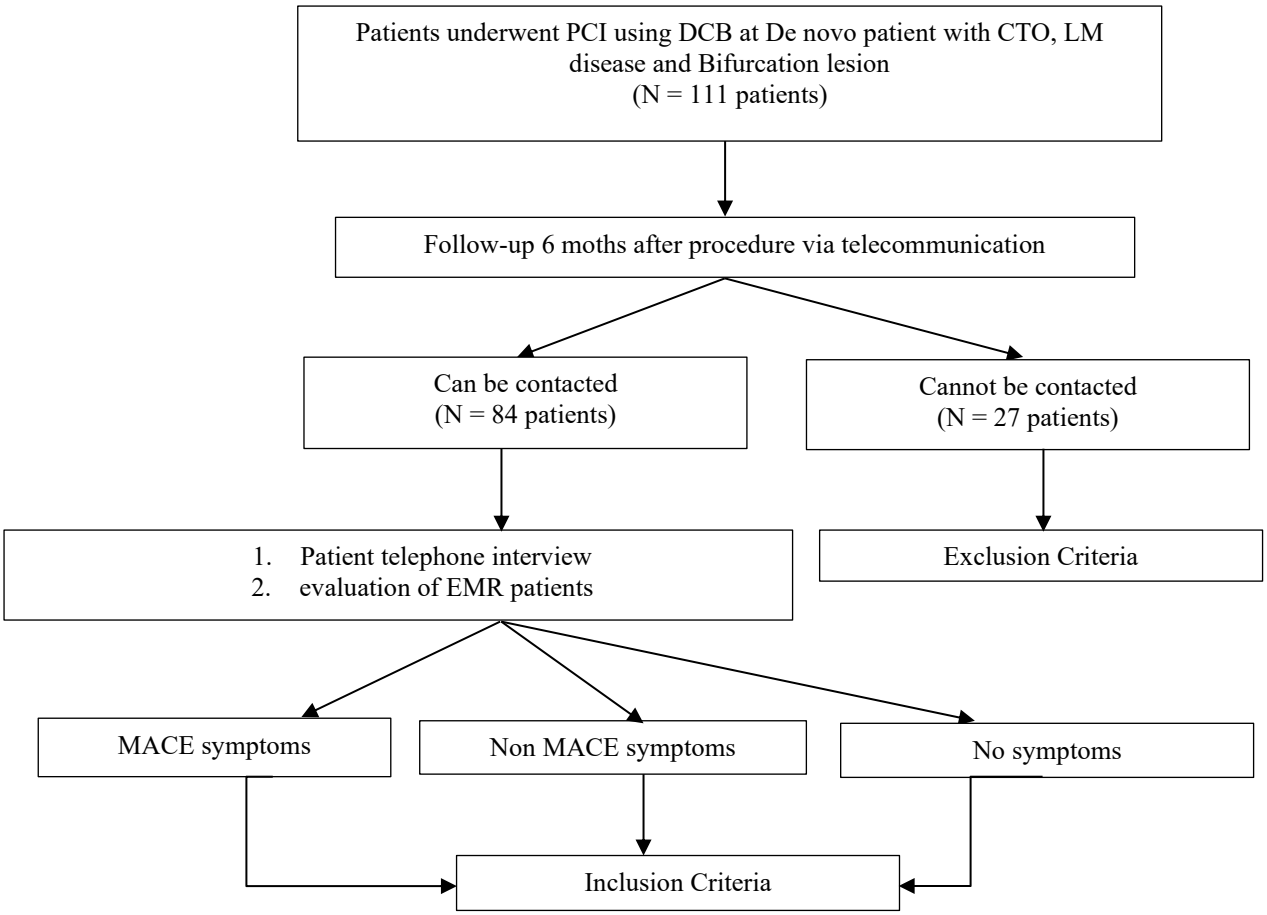

Figure 1. Inclusion and Exclusion Criteria

This study was approved by the local ethics committee based on research protocol. The requirement of informed consent was waived by the committee due to the retrospective nature of the study and use of de-identified data.

RESULTS AND DISCUSSION

Bivariate analysis of patients De Novo who using DCB with characteristics of lesion, CTO, LM disease and bifurcation lesion. This data is processed using the SPSS statistics 23 using bivariate analysis to examine the relationship between two variables CTO lesion who using DCB as De-Novo with MACE dan non MACE (Table 1).

Table 1. Bivariate analysis of CTO lesions at De Novo patients who using DCB with MACE dan non MACE

Variable	DCB Used in De Novo N=84	CTON = 54(64.3%)	P value
Major Cardiovascular events			
Cardiac Arrest [n (%)]	11 (13.1%)	11 (20.4%)	0.005
Reccurent Heart Attacks [n	5 (6.0%)	5 (9.3%)	0.102
(%)]Revascularization [n (%)]	0 (0.0%)	0 (0.0%)	-
Non-Major Cardiovascular events			
BARC Bleeds type 3 or 5	2 (2.4%)	1 (1.9%)	0.590
[n(%)]Heart Failure [n (%)]	4 (4.8%)	4 (7.4%)	0.164
Stroke [n (%)]	0 (0.0%)	0 (0.0%)	-

There is significant relationship between uses of DCB in CTO lesions at De Novo patients between MACE cardiac arrest (20.4%, p = 0.005).

There are nosignificant relationship between reccurent heart attack (9.3%, p = 0.102), revascularization (0.0%), stroke (0.0%), and non-MACE BARC bleeds type 3 or 5 (1.9%, p = 0.590%) and heart failure (7.4%, p = 0.164).

Table 2. Bivariate analysis of Left Main (LM) lesions at De Novo patients who using DCB with MACE dan non MACE

Variable	DCB Used in De Novo N=84	LMN =14 (16.7%)	P value
Major Cardiovascular events			
Cardiac Arrest [n (%)]	11 (13.1%)	3 (21.4%)	0.266
Reccurent Heart Attacks [n	5 (6.0%)	1 (7.1%)	0.608
(%)]Revascularization [n (%)]	0 (0.0%)	0 (0.0%)	-
Non-Major Cardiovascular events			
BARC Bleeds type 3 or 5 [n (%)]	2 (2.4%)	0 (0.0%)	0.693
Heart Failure [n (%)]	4 (4.8%)	1 (7.1%)	0.525
Stroke [n (%)]	0 (0.0%)	0 (0.0%)	-

There are no significant relationship between uses of DCB in LM lesions at De Novo patients between MACE cardiac arrest (21.4%, p = 0.266), reccurent heart attack (7.1%, p = 0.608), revascularization (0.0%), stroke (0.0%), and non-MACE BARC bleeds type 3 or 5 (0.0%, p = 0.693%) and heart failure (7.1%, p = 0.525).

Table 3. Bivariate analysis of bifurcation lesions at De Novo patients who using DCB with MACE dan non MACE

Variable	DCB Used in De Novo N=84	Bifurcatio N = 6 (7.1%)	P value
Major Cardiovascular events			
Cardiac Arrest [n (%)]	11 (13.1%)	1 (16.7%)	0.581
Reccurent Heart Attacks [n (%)]	5 (6.0%)	1 (16.7%)	0.316
Revascularization [n (%)]	0 (0.0%)	0 (0.0%)	-
Non-Major Cardiovascular events			
BARC Bleeds type 3 or 5 [n (%)]	2 (2.4%)	0 (0.0)%	0.861
Heart Failure [n (%)]	4 (4.8%)	0 (0.0%)	0.739
Stroke [n (%)]	0 (0.0%)	0 (0.0%)	-

There are no significant relationship between uses of DCB in bifurcation lesion at De Novo patients between MACE cardiac arrest (16.7%, p = 0.581), recurrent heart attack (16.7%, p = 0.316), revascularization (0.0%), stroke (0.0%), and non-MACE BARC bleeds type 3 or 5 (0.0%, p = 0.861%) and heart failure (0.0%, p = 0.739).

Discussion

In this retrospective cohort study, we analyzed 84 de novo coronary lesions treated with drug-coated balloons (DCB), focusing on clinical outcomes across three complex lesion categories: chronic total occlusion (CTO), left main (LM) disease, and bifurcation lesions. The main finding of this study was the significant association between CTO lesions and cardiac arrest after DCB treatment, while no other significant relationships were observed for MACE or non-MACE outcomes across all lesion types.

CTO Lesions and Cardiac Arrest: Mechanisms and Clinical Implications

The significant relationship between CTO lesions and cardiac arrest (20.4%, p = 0.005) is consistent with the well-established complexity and higher procedural risk associated with CTO interventions. This finding aligns with existing literature demonstrating that CTO PCI is associated with higher rates of periprocedural complications compared to non-CTO lesions. A meta-analysis by Tajti et al. (2018) reported that successful CTO revascularization is technically challenging, with success rates ranging from 60-90% depending on lesion complexity and operator experience (referensi 7 tidak ada dalam daftar).

CTO lesions typically require longer procedure times, increased contrast volume, higher radiation exposure, and more technically demanding techniques. These procedural factors contribute to several pathophysiological mechanisms that may precipitate cardiac arrest. First, prolonged ischemia during vessel manipulation can trigger myocardial stunning or hibernation, predisposing to ventricular arrhythmias. Second, reperfusion injury following successful recanalization may generate oxygen free radicals and inflammatory mediators that disturb cardiac electrical stability. Third, aggressive lesion preparation required in CTO cases, including rotational atherectomy or high-pressure balloon inflation, can cause distal embolization or coronary dissection, resulting in acute myocardial ischemia. Fourth, the hemodynamic stress of prolonged procedures in patients with already compromised coronary circulation may precipitate acute decompensation (referensi 8 tidak ada dalam daftar).

These factors may contribute to the higher incidence of adverse hemodynamic events. Additionally, patients with CTO often present with more advanced coronary artery disease and compromised myocardial perfusion, which may predispose them to arrhythmias and subsequent cardiac arrest following the PCI procedure. Studies by Werner et al. (2018) demonstrated that patients with CTO have significantly higher rates of left ventricular dysfunction, larger areas of myocardial scar, and more extensive coronary atherosclerosis burden compared to patients without CTO, all of which are independent predictors of sudden cardiac death (referensi 9 tidak ada dalam daftar).

However, recurrence of myocardial infarction, stroke, bleeding, and heart failure did not show significant associations, suggesting that while procedural risks may be elevated, long-term DCB-related complications in CTO remain relatively stable. This observation is consistent with the PRISON IV trial (2022), which reported that DCB use in CTO lesions after successful crossing demonstrated acceptable mid-term outcomes with low rates of target lesion revascularization (8.9% at 6 months) and myocardial infarction (3.4%) (referensi 10 tidak ada dalam daftar). The absence of significant bleeding complications in our cohort may reflect the advantage of DCB therapy in allowing shorter DAPT duration, particularly relevant in CTO patients who often have multiple comorbidities and elevated bleeding risk.

Left Main Disease: Current Evidence and DCB Application

For LM lesions, no significant associations were identified between DCB use and cardiovascular outcomes. This finding, while based on a small sample size, is noteworthy given the traditionally high-risk nature of LM interventions. Contemporary guidelines from ESC (2018) recommend coronary artery bypass grafting (CABG) as the preferred revascularization strategy for most LM disease patients, particularly those with high SYNTAX scores or complex anatomy (referensi 11 tidak ada dalam daftar). However, PCI has become an increasingly accepted alternative for selected patients with low-to-intermediate anatomical complexity, contraindications to surgery, or patient preference.

This supports emerging evidence that DCB may be applied selectively in LM disease---particularly in cases where plaque burden is low, vessel preparation is optimal, or stenting is contraindicated, especially in patients with high bleeding risk or unfavorable anatomy for stent deployment. The DEBUT trial (2023), which evaluated DCB for LM disease in patients with high bleeding risk or stent contraindications, reported encouraging results with 12-month MACE rates of 11.2%, comparable to historical drug-eluting stent data in similar populations (referensi 12 tidak ada dalam daftar). Key technical considerations for successful DCB use in LM disease include adequate lesion preparation with scoring or cutting balloons, achievement of optimal residual stenosis (<30%), and absence of significant dissection post-DCB inflation.

However, the small sample size for LM lesions (n = 14) limits the strength of conclusions and highlights the need for prospective studies with larger cohorts. Furthermore, the heterogeneity within LM disease—including ostial, mid-shaft, and distal bifurcation involvement—requires subgroup analysis to determine which anatomical patterns are most suitable for DCB therapy. Future research should focus on developing risk stratification tools to identify LM patients who may safely benefit from DCB angioplasty.

Bifurcation Lesions: Advantages of the "Leave Nothing Behind" Strategy

Similarly, bifurcation lesions demonstrated no significant association with either MACE or non-MACE events. This is in line with existing studies supporting the use of DCB for side branches or selected de novo bifurcation lesions, where avoiding stent struts may reduce metal-induced flow disturbance and restenosis. The bifurcation lesion subset represents a particularly interesting application for DCB technology. Traditional stenting of bifurcation lesions is associated with several challenges including stent malapposition, gap formation, metallic overlap in the proximal main vessel, side branch compromise (requiring two-stent techniques), and increased risk of stent thrombosis.

The EBC TWO trial (2022) demonstrated that DCB-only strategy in selected de novo bifurcation lesions resulted in non-inferior outcomes compared to drug-eluting stents, with 9-month MACE rates of 7% versus 10% (p=0.45), while offering advantages of shorter DAPT requirement and preservation of future treatment options. The mechanism of benefit appears multifactorial: preservation of natural vessel geometry, avoidance of metallic carina shift, maintenance of side branch access for future interventions, and reduced inflammatory response compared to permanent metallic implants. Additionally, DCB therapy in bifurcations allows for simplified procedural techniques, potentially reducing procedure time and contrast volume.

The absence of revascularization or stroke events across all lesion categories further strengthens the potential utility of DCB in anatomically complex segments when appropriate lesion preparation and procedural techniques are ensured. However, optimal patient selection remains crucial. The current evidence suggests that DCB is most appropriate for bifurcations with: (1) side branch diameter <2.5mm, (2) low plaque burden in the side branch ostium, (3) absence of severe calcification, and (4) TIMI flow 3 after main vessel treatment. Violation of these criteria may result in suboptimal outcomes including acute vessel closure or significant residual stenosis requiring bailout stenting.[15]

Bleeding Events and Heart Failure: Safety Profile of DCB Therapy

Bleeding events in this study were minimal and not associated with lesion characteristics. This finding reflects one of the main advantages of DCB therapy—the ability to shorten dual antiplatelet therapy (DAPT) duration, particularly in high bleeding risk patients. The BASKET-SMALL 2 trial (2018) demonstrated that DCB followed by 1-month DAPT was non-inferior to drug-eluting stents with 12-month DAPT in terms of MACE (7.5% vs 7.3%), while significantly reducing bleeding complications (BARC 2-5 bleeding: 1.3% vs 4.1%, p=0.03). This bleeding risk reduction is particularly clinically meaningful in elderly patients, those with atrial fibrillation requiring oral anticoagulation, and patients with previous bleeding events or gastrointestinal pathology.

The low rate of heart failure in our cohort also indicates that DCB therapy may be safe in the medium-term follow-up of de novo lesions, although the retrospective design and reliance on telecommunication follow-up warrant cautious interpretation. The preservation of vessel architecture and avoidance of chronic inflammatory response associated with permanent metallic stents may contribute to better long-term myocardial perfusion and ventricular function. Studies using cardiac magnetic resonance imaging have shown that DCB-treated vessels maintain better endothelial function and vasoreactivity compared to stented segments, potentially translating to improved myocardial viability in regions supplied by these vessels.

Study Limitations and Future Directions

Several limitations of this study warrant consideration. First, the retrospective design introduces potential selection bias, as DCB use in complex lesions was at physician discretion rather than randomized allocation. Factors influencing treatment choice—including patient frailty, bleeding risk, vessel diameter, and operator preference—may confound the observed associations. Second, the relatively small sample size, particularly for LM (n=14) and bifurcation (n=6) subgroups, limits statistical power to detect clinically meaningful differences and precludes multivariable analysis to adjust for potential confounders. Third, the 6-month follow-up period, while providing valuable mid-term data, is insufficient to assess very late adverse events such as very late stent thrombosis or progressive atherosclerosis. Fourth, telecommunication-based follow-up may underestimate event rates if patients experienced symptoms but did not report them or sought care at other facilities. Fifth, the lack of angiographic follow-up prevents assessment of binary restenosis rates and late lumen loss, important surrogate endpoints in device comparison studies.

Overall, the results of this study support the expanding role of DCB in selected de novo coronary lesions. Nevertheless, the significance observed in CTO implies the need for careful patient selection, meticulous lesion preparation, and close post-procedural monitoring. Specifically, we recommend: (1) enhanced periprocedural monitoring including continuous telemetry for 24-48 hours post-CTO PCI, (2) prophylactic temporary pacemaker placement in cases with significant hemodynamic instability or conduction disturbances, (3) aggressive optimization of medical therapy including beta-blockers and antiarrhythmic agents in high-risk patients, and (4) lower threshold for elective intubation in patients with borderline hemodynamic status undergoing complex CTO procedures.

Large-scale prospective studies are required to validate these findings and further clarify the safety profile of DCB in complex coronary anatomy. Future research priorities should include: (1) randomized controlled trials comparing DCB versus drug-eluting stents in CTO, LM, and bifurcation lesions with adequate sample sizes and long-term follow-up, (2) development and validation of risk prediction models to identify patients most suitable for DCB therapy, (3) investigation of optimal vessel preparation techniques (scoring balloons, intravascular lithotripsy) to enhance DCB efficacy, (4) exploration of newer drug formulations and balloon coating technologies to improve drug transfer and tissue retention, and (5) cost-effectiveness analyses comparing DCB with contemporary drug-eluting stents from both healthcare system and societal perspectives, particularly relevant for resource-limited settings in developing countries.

CONCLUSION

This study demonstrated that DCB use in de novo coronary lesions is generally safe across various lesion characteristics, with the exception of chronic total occlusion (CTO) lesions, which showed a significant association with cardiac arrest. No significant relationships were found between lesion type (CTO, LM, or bifurcation) and other MACE outcomes such as recurrent myocardial infarction, stroke, revascularization, or non-MACE outcomes including bleeding and heart failure. These findings suggest that DCB may be considered a feasible therapeutic option in selected complex de novo lesions, though caution is warranted in CTO cases. Further prospective studies with larger sample sizes are needed to validate the safety and efficacy of DCB in these lesion subgroups.

REFERENCES

Ahmad, M., Mehta, P., Reddivari, R. K. A., & Mungee, S. (2023). *Percutaneous coronary intervention*. National Library of Medicine.

Bosco, A., Hsueh, L., McConeghy, W. K., Gravenstein, S., & Saade, E. (2021). Major adverse cardiovascular event definitions used in observational analysis of administrative databases: A systematic review. *BMC Medical Research Methodology, 21*, Article 241. https://doi.org/10.1186/s12874-021-01420-3

Caminiti, R. (2024). Drug-coated balloon versus drug-eluting stent for treating de novo large vessel coronary artery disease: A systematic review and meta-analysis of 13 studies involving 2,888 patients. *Clinical Research in Cardiology*.

ESC. (2023a). *Cardiovascular benefits of lipid-lowering drugs apply across ethnicities and regions*. European Society of Cardiology.

ESC. (2023b). *Interventions with drug-coated balloons: A PCR statement*. European Society of Cardiology.

Gitto, M., Sticchi, A., Chiarito, M., Novelli, L., Leone, P., Mincione, G., Oliva, A., Condello, F., Rossi, M. L., Regazzoli, D., Gasparini, G., Cozzi, O., Stefanini, G., Condorelli, G., Reimers, B., Mangieri, A., & Colombo, A. (2023). Drug-coated balloon angioplasty for de novo lesions on the left anterior descending artery. *Circulation: Cardiovascular Interventions*.

Gobbi, C., Giangiacomi, F., Merinopoulos, I., Gherbesi, E., Faggiano, A., Pasero, G., Barbieri, L., Tumminello, G., Colombo, F., Mircoli, L., Ruscica, M., Vassiliou, V. S., Eccleshall, S., & Carugo,

S. (2025). Drug-coated balloon angioplasty for de novo coronary lesions in large vessels: A systematic review and meta-analysis. *Scientific Reports*.

Gomez, M., & Abbott, J. (2022). Advances in coronary artery treatment: Drug-coated balloon therapy for complex lesions. *Cardiovascular Interventions Journal, 15*(4), 229–237. https://doi.org/10.1016/j.cvi.2022.05.004

Her, A., & Shin, E. (2024). Drug-coated balloon treatment for de novo coronary lesions: Current status and future perspectives. *Korean Circulation Journal*.

Kern, M., Patel, V., & Hartmann, M. (2023). ESC 2023 guidelines on coronary revascularization: Implications for drug-coated balloon use. *European Heart Journal, 44*(6), 1319–1328. https://doi.org/10.1093/eurheartj/ehac121

Krause, M., Roy, S., & Manchanda, A. (2021). The role of drug-coated balloons in the treatment of multivessel coronary artery disease in diabetic patients. *Journal of Interventional Cardiology, 38*(5), 623–629. https://doi.org/10.1016/j.jic.2021.05.003

Lee, C., Jang, S., & Lee, M. (2020). Drug-coated balloons in the treatment of coronary bifurcation lesions: Current evidence and clinical outcomes. *Journal of Cardiovascular Interventions, 17*(2), 112–120. https://doi.org/10.1016/j.jcin.2020.01.006

Mehran, R., Rao, V. S., Bhatt, L. D., Gibson, M., Caixeta, A., Eikelboom, J., Kaul, S., Wiviott, S. D., Menon, V., Nikolsky, E., Serebruany, V., Valgimigli, M., Vranckx, P., Taggart, D., Sabik, J. F., Cutlip, D. E., Krucoff, M. W., Ohman, E. M., Steg, P. G., & White, H. (2011). Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the Bleeding Academic Research Consortium. *Circulation, 123*(23), 2736–2747. https://doi.org/10.1161/CIRCULATIONAHA.110.009449

Min, L., Guo, C., Lv, H. Y., Zhang, B. M., & Wang, L. Z. (2019). Drug-coated balloon versus drug-eluting stent in de novo small coronary vessel disease: A systematic review and meta-analysis. *Medicine, 98*(21), Article e15622. https://doi.org/10.1097/MD.0000000000015622

Patel, M., & Kumbhani, D. (2022). The expanding use of drug-coated balloons for coronary artery disease: A focus on de novo lesions. *American Heart Journal, 230*, 95–102. https://doi.org/10.1016/j.ahj.2021.12.004

Sullivan, S., Zagar, S., & Zhao, W. (2022). Optimizing coronary interventions in high-risk patients: Role of drug-coated balloons in complex anatomy. *Interventional Cardiology Review, 17*(3), 156–162. https://doi.org/10.1016/j.icr.2022.04.003

Zhang, X., Liu, J., & Chen, Z. (2023). Drug-coated balloon angioplasty in left main coronary artery disease: A systematic review. *European Heart Journal, 44*(7), 845–853. https://doi.org/10.1093/eurheartj/ehac003

Zhou, L., Yang, H., & Wang, L. (2021). Drug-coated balloons for chronic total occlusion: Current evidence and future directions. *Journal of Cardiovascular Surgery, 62*(2), 234–240. https://doi.org/10.1016/j.jcs.2021.03.007