

นิพนธ์ต้นฉบับ

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Abstract

Drug-Coated Balloon in De Novo Coronary Lesions: The “Leaving Nothing Behind”
Strategy in Contemporary PCI

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Background: Drug-coated balloons (DCB) have emerged as an alternative revascularization strategy in percutaneous coronary intervention (PCI), aiming to deliver antiproliferative therapy without permanent metallic implantation. This “leave nothing behind” approach may mitigate long-term complications associated with drug-eluting stents (DES), including stent thrombosis, chronic inflammation, and neo atherosclerosis. **Objectives:** To provide a comprehensive review of the current evidence, clinical applications, technical considerations, and guideline perspectives regarding the use of DCB in de novo coronary artery lesions. **Methods:** A narrative review of randomized controlled trials, meta-analyses, and contemporary consensus documents was conducted, focusing on DCB use across key clinical scenarios including small vessel disease, diffuse coronary artery disease, bifurcation lesions, high bleeding risk (HBR) patients, and large vessel disease. **Results:** In small vessel disease, DCB has demonstrated non-inferiority to second-generation DES with reduced late lumen loss. In diffuse coronary disease, DCB-either alone or in combination with DES-achieves comparable rates of major adverse cardiovascular events (MACE), target lesion revascularization (TLR), and target vessel revascularization (TVR) to DES-only strategies. In bifurcation lesions, DCB is most effective inside branch treatment, reducing restenosis while minimizing metal implantation. In HBR patients, DCB allows shorter dual antiplatelet therapy duration while maintaining favorable clinical outcomes. Emerging evidence also supports the feasibility of DCB in selected large vessel lesions, particularly in strategies aimed at reducing total metal burden and preserving vascular physiology. However, outcomes remain highly dependent on optimal lesion preparation and device-specific characteristics. **Conclusions:** DCB represents a promising alternative or complementary strategy to DES in selected de novo coronary lesions. Its advantages in reducing metal burden and enabling shorter dual antiplatelet therapy to make it particularly attractive in specific patient populations. Nevertheless, wider adoption is currently limited by heterogeneity in available evidence, lack of a clear class effect, and insufficient large-scale randomized trials. Future studies are required to define its role in contemporary PCI practice and to harmonize international guideline recommendations.

Keywords: De novo coronary lesion; Drug-coated balloon; Leaving nothing behind; Percutaneous coronary intervention

บทคัดย่อ

ภูมิหลัง: บอลลูนเคลือบยา (Drug-coated balloon; DCB) ได้กลายเป็นอีกหนึ่งทางเลือกของการรักษาหลอดเลือดหัวใจด้วยการขยายหลอดเลือดผ่านสายสวน (Percutaneous coronary intervention; PCI) โดยมีเป้าหมายเพื่อส่งยาต้านการเพิ่มจำนวนของเซลล์เข้าสู่ผนังหลอดเลือดโดยไม่ต้องมีการฝังอุปกรณ์โลหะแบบถาวร แนวคิด “ไม่ทิ้งสิ่งแปลกปลอมไว้ในหลอดเลือด” นี้จะช่วยลดภาวะแทรกซ้อนระยะยาวที่พบจากการใช้ขดลวดเคลือบยา (Drug-eluting stent; DES) เช่น การเกิดลิ่มเลือดในขดลวด การอักเสบเรื้อรังและการเกิดคราบไขมันใหม่ภายในขดลวด **วัตถุประสงค์:** เพื่อทบทวนหลักฐานปัจจุบัน การนำไปใช้ทางคลินิก ข้อพิจารณาทางเทคนิค และมุมมองจากแนวทางเวชปฏิบัติเกี่ยวกับการใช้ DCB ในรอยโรคหลอดเลือดหัวใจชนิดรอยโรคใหม่ **วิธีการศึกษา:** เป็นการทบทวนวรรณกรรมเชิงบรรยาย (narrative review) จากงานวิจัยแบบสุ่มมีกลุ่มควบคุม (randomized controlled trials) การวิเคราะห์อภิมาน (meta-analyses) และเอกสารฉันทามติสมัยใหม่ โดยเน้นการใช้ DCB ในสถานการณ์สำคัญ ได้แก่ โรคหลอดเลือดขนาดเล็ก โรคหลอดเลือดหัวใจแบบกระจายรอยโรคบริเวณแยกแขนงหลอดเลือด ผู้ป่วยที่มีความเสี่ยงต่อการเกิดเลือดออกสูง (high bleeding risk; HBR) และโรคหลอดเลือดขนาดใหญ่ **ผลการศึกษา:** ในโรคหลอดเลือดขนาดเล็ก DCB แสดงผลลัพธ์ไม่ด้อยกว่าขดลวดเคลือบยารุ่นที่สอง โดยมีการสูญเสียเส้นผ่านศูนย์กลางของหลอดเลือดในระยะยาว (late lumen loss) น้อยกว่าในโรคหลอดเลือดแบบกระจาย DCB ไม่ว่าจะใช้เดี่ยวหรือร่วมกับ DES ให้ผลลัพธ์ด้านเหตุการณ์หัวใจและหลอดเลือดไม่พึงประสงค์สำคัญ (MACE) การทำหัตถการซ้ำที่รอยโรคเดิม (TLR) และการทำหัตถการซ้ำที่หลอดเลือดเป้าหมาย (TVR) ไม่แตกต่างกับการใช้ DES เพียงอย่างเดียว สำหรับรอยโรคแบบแยกแขนง DCB มีประสิทธิภาพเด่นในกิ่งข้าง (side branch) โดยช่วยลดการตีบซ้ำและลดการใส่วัสดุโลหะในหลอดเลือดในผู้ป่วย HBR การใช้ DCB ช่วยให้สามารถลดระยะเวลาการใช้ยาต้านเกล็ดเลือดสองชนิด (dual antiplatelet therapy; DAPT) ได้ ขณะยังคงผลลัพธ์ทางคลินิกที่ดี นอกจากนี้ หลักฐานใหม่ยังสนับสนุนความเป็นไปได้ของการใช้ DCB ในหลอดเลือดขนาดใหญ่ในผู้ป่วยที่คัดเลือกอย่างเหมาะสม โดยเฉพาะในกลุ่มที่ต้องการลดปริมาณโลหะและคงสภาพการทำงานตามธรรมชาติของหลอดเลือด อย่างไรก็ตาม ผลลัพธ์ขึ้นอยู่กับความถี่ของการเตรียมรอยโรคที่เหมาะสมและคุณสมบัติเฉพาะของอุปกรณ์เป็นอย่างมาก **สรุป:** DCB เป็นทางเลือกที่มีศักยภาพทั้งในฐานะการรักษาหลักหรือเสริมร่วมกับ DES ในรอยโรคหลอดเลือดหัวใจชนิดรอยโรคใหม่ ในผู้ป่วยที่เหมาะสม ข้อดีของการลดการฝังโลหะและการใช้ DAPT ระยะสั้นทำให้ DCB น่าสนใจเป็นพิเศษในผู้ป่วยบางกลุ่ม อย่างไรก็ตาม การนำไปใช้ในวงกว้างยังถูกจำกัดด้วยความไม่สม่ำเสมอของหลักฐาน การขาดผลลัพธ์ที่เป็นผลลัพธ์แบบกลุ่มที่ชัดเจน และการขาดการศึกษาแบบสุ่มขนาดใหญ่เพิ่มเติม งานวิจัยในอนาคตจึงมีความจำเป็นเพื่อกำหนดบทบาทของ DCB ในการทำ PCI ยุคปัจจุบัน และเพื่อให้แนวทางเวชปฏิบัติระดับนานาชาติมีความสอดคล้องกันมากขึ้น

คำสำคัญ: รอยโรคหลอดเลือดหัวใจชนิดรอยโรคใหม่, บอลลูนเคลือบยา, ไม่ทิ้งสิ่งแปลกปลอมไว้ในหลอดเลือด, การขยายหลอดเลือดผ่านสายสวน

Introduction

Percutaneous coronary intervention (PCI) has evolved from plain balloon angioplasty to bare-metal stents (BMS) and subsequently drug-eluting stents (DES), significantly reducing restenosis rates. However, DES implantation remains associated with long-term complications such as stent thrombosis, delayed endothelial healing, and neo atherosclerosis¹. Drug-coated balloons (DCB) have been developed to overcome these limitations by delivering antiproliferative drugs without leaving a permanent implant, aligning with the concept of “leaving nothing behind”^{2,3}. This strategy aims to reduce chronic vessel injury and improve long-term vascular healing.

Mechanism of Action of Drug-Coated Balloons

DCBs are semi-compliant balloon catheters coated with antiproliferative agents such as paclitaxel, sirolimus or biolimus, combined with excipients that facilitate rapid drug transfer into the vessel wall⁴. Paclitaxel exerts a cytotoxic effect by inhibiting microtubule function during mitosis, whereas sirolimus and biolimus act through mTOR inhibition, leading to suppression of smooth muscle cell proliferation (cytostatic)². Compared with DES, DCB enables rapid drug delivery without polymer-related inflammation, potentially improving vascular healing^{1,5}. (Figure 1) In addition to the antiproliferative drug, the **excipient** is a key determinant of DCB performance, acting as a carrier that enhances drug adhesion, limits premature loss, and facilitates transfer to the vessel wall during inflation^{2, 6-7}. Excipients are broadly classified as **hydrophobic** or **hydrophilic**, each with distinct pharmacokinetic profiles. Hydrophobic excipients, typically used with lipophilic agents such as paclitaxel, improve drug retention and prolong tissue residence but may result in heterogeneous distribution and potential particulate embolization^{2,8}. In contrast, hydrophilic excipients, commonly used in limus-based platforms, enable more uniform drug transfer but may be associated with increased washout and lower tissue retention⁷. Overall, no strategy has demonstrated clear superiority, and DCB efficacy depends on balancing drug transfer, retention, and coating stability^{2, 6-7}.

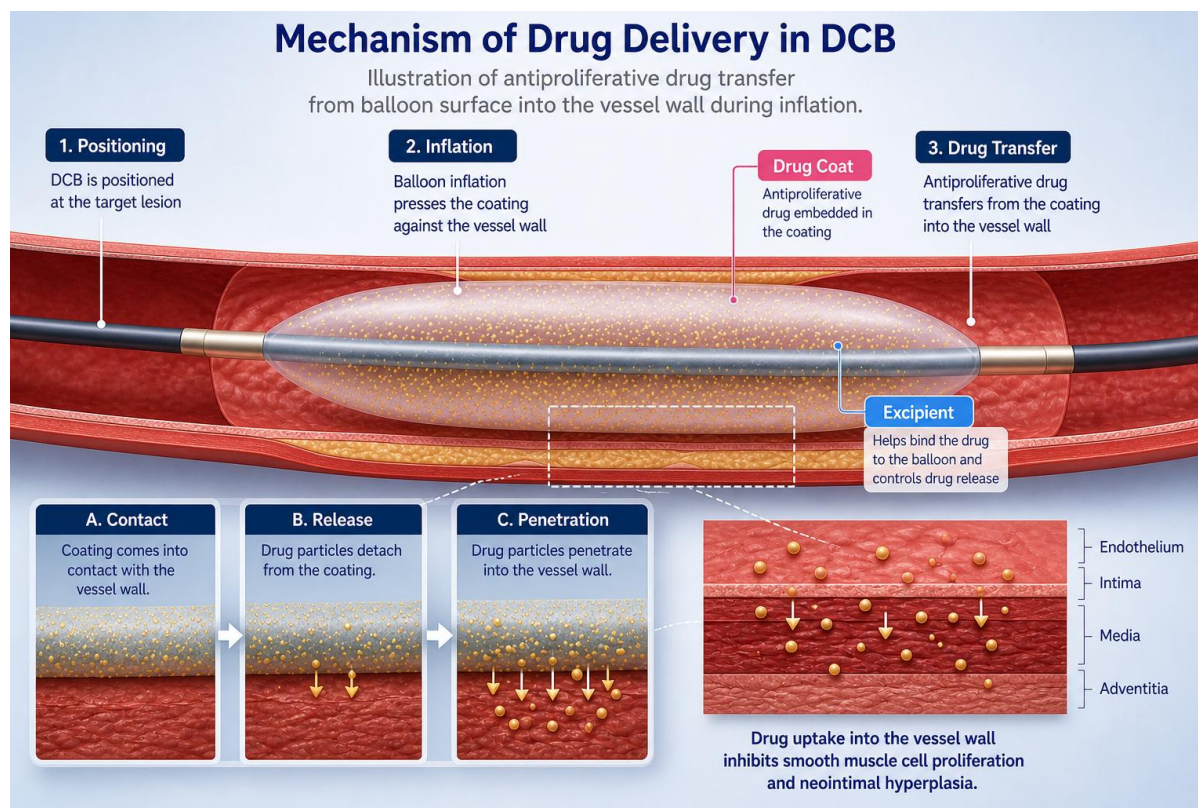


Figure 1. Mechanism of Drug Delivery in DCB

Clinical Applications in De Novo Lesions

1. Small Vessel Disease: Small coronary vessels (<3 mm) are associated with higher restenosis rates following stent implantation¹⁰. Multiple randomized trials have demonstrated that DCB is non-inferior to second-generation DES in terms of major adverse cardiovascular events (MACE), with significantly lower late lumen loss¹⁰⁻¹². However, interpretation of the available evidence remains challenging and is likely multifactorial. First, the absence of a class effect among DCB devices contributes to variability in clinical outcomes, as differences in drug type, excipients, coating technology, and catheter design may influence anti-restenotic efficacy^{2,3,13}. Some devices have demonstrated superior performance compared with others, highlighting the importance of device-specific characteristics. Second, procedural factors particularly lesion preparation play a critical role in determining outcomes. Inadequate or absent predilation has been associated with suboptimal results and may partly explain discrepancies across clinical trials. Notably, in the PICCOLETO trial, only 25% of patients assigned to the DCB arm underwent lesion predilation, which has been considered a major limitation affecting the study outcomes¹⁴. Recent meta-analyses incorporating large patient populations further support the overall non-inferiority of DCB compared with contemporary DES, while emphasizing the importance of optimal technique and appropriate device selection¹⁵.

2. Diffuse Coronary Artery Disease: Diffuse coronary artery disease does not have a universally accepted definition based on lesion length. In clinical practice, lesions exceeding 20–30 mm are often considered diffuse; however, the term more broadly reflects the extent of disease and the need for long or multiple stent implantation, which is associated with increased metal burden and adverse clinical outcomes. In diffuse coronary lesions, DCB (alone or in combination with DES) has demonstrated comparable outcomes to DES only strategies in terms of MACE, target lesion revascularization (TLR), and target vessel revascularization (TVR)¹⁶. Diffuse CAD remains a challenging subset for percutaneous coronary intervention (PCI), particularly in cases requiring long stent length, which is associated with increased risks of restenosis, stent thrombosis, and delayed vascular healing¹. DCB, either as a standalone strategy in smaller vessels or in combination with DES in long lesions, has emerged as a potential alternative approach. Evidence from clinical studies demonstrates that DCB-based strategies are associated with long-term clinical outcomes comparable to DES only approaches, with no significant differences in major adverse cardiovascular events (MACE), target vessel revascularization (TVR), or target lesion revascularization (TLR)¹⁶. These findings suggest that DCB may play an important role in the treatment of diffuse CAD, particularly by minimizing total stent length and avoiding excessive metal implantation. In very long lesions, a hybrid strategy combining DCB and DES may be advantageous, achieving acceptable long-term outcomes comparable to DES-only strategies. Overall, current evidence supports the feasibility and safety of DCB in diffuse coronary disease, although further randomized trials are warranted to confirm these findings and define optimal treatment strategies^{4,17}.

3. Bifurcation Lesions: Remain one of the most complex subsets in PCI, with higher risks of restenosis and procedural complications, particularly in the side branch (SB). DCB has emerged as a potential strategy to reduce metal burden while preserving vessel physiology. DCB has demonstrated superiority over plain balloon angioplasty (POBA) for side branch treatment, particularly in reducing late lumen loss¹⁸. However, its role compared with DES based strategies remains less clearly defined, and current evidence is still evolving⁴. A recent state-of-the-art review by Saad M. Ezad et al. summarized the evolving role of DCB in bifurcation

lesions, particularly emphasizing side branch treatment and hybrid DES-DCB strategies¹⁹. First, the most established role of DCB is in the treatment of the side branch following main vessel stenting, where DCB can reduce restenosis without additional metal implantation. This approach is particularly attractive in provisional stenting strategies, where minimizing SB stenting is desirable. Second, DCB only strategies for both main branch (MB) and SB may be feasible in selected cases with favorable lesion characteristics, provided that optimal lesion preparation is achieved and no flow-limiting dissection is present. However, this approach requires careful patient and lesion selection and remains supported primarily by small studies and observational data¹⁹. Third, lesion preparation is especially critical in bifurcation PCI. Adequate predilation of both MB and SB, appropriate balloon sizing, and optimization of flow are essential to achieve acceptable angiographic results prior to DCB use. Failure to achieve these conditions increases the likelihood of bailout stenting and suboptimal outcomes^{18,19}. Finally, hybrid strategies combining DES in the main vessel and DCB in the side branch represent a pragmatic and increasingly adopted approach, balancing scaffold support in the main vessel with a “leave nothing behind” strategy in the SB. Available data suggest that such strategies are associated with acceptable clinical outcomes, although large randomized trials are still lacking¹⁹. Overall, DCB offers a promising adjunctive tool in bifurcation PCI, particularly for side branch management, but further high-quality evidence is required to define its optimal role relative to contemporary DES strategies.

4. High Bleeding Risk (HBR) Patients: Recent contemporary reviews further support the role of DCB in patients at HBR, particularly due to the ability to shorten dual antiplatelet therapy duration while maintaining comparable clinical outcomes. Although DCB-based PCI may facilitate shorter DAPT duration due to the absence of a permanent implant, antiplatelet therapy should be individualized according to clinical presentation (e.g., ACS versus chronic coronary syndrome), bleeding risk, lesion complexity, procedural outcome, and the need for bailout stenting.^{3,5,20} The DEBUT trial demonstrated that DCB is non-inferior and superior to BMS in high bleeding risk patients, enabling shorter dual antiplatelet therapy duration (~1 month)²¹. This represents a major clinical advantage in patients at increased risk of bleeding.

5. Large Vessel Disease: The role of DCB in large coronary vessels (≥ 3.0 mm) has historically been limited, given the well-established efficacy of DES in this setting. However, emerging evidence suggests that a DCB based strategy may be feasible and beneficial in selected patients, particularly in the context of reducing metal burden and promoting physiological vessel healing¹⁷. A key conceptual advantage of DCB over DES lies in the avoidance of permanent metallic implantation. While DES provides immediate luminal scaffolding, it also introduces a persistent “metal burden,” which has been associated with chronic inflammation, impaired vasomotion, and late adverse events such as neoatherosclerosis and very late stent thrombosis¹. In contrast, DCB enables a “leave nothing behind” strategy, preserving native vessel architecture and potentially allowing restoration of endothelial function and vasoreactivity over time^{17,20}. This concept becomes particularly relevant in the treatment of long or complex lesions in large vessels, where extensive stenting may result in a “full metal jacket” (FMJ) configuration. Although FMJ stenting ensures complete lesion coverage, it has been associated with increased risks of restenosis, thrombosis, and impaired vessel adaptability due to extensive metallic burden. In this context, DCB—either as a standalone strategy or in combination with focal DES implantation—may offer a more physiologically favorable approach by minimizing total stent length while maintaining adequate revascularization¹⁷. Although early data are encouraging, the role of DCB in large vessel disease remains exploration and should currently be limited to carefully selected lesions and experienced

operators until robust randomized evidence becomes available¹⁷. Hybrid approaches, combining DES for focal scaffold-requiring segments and DCB for the remaining vessel, may further optimize outcomes by balancing mechanical support with preservation of vessel physiology. Intracoronary imaging, such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT), plays an important role in this setting by enabling precise lesion assessment, guiding lesion preparation, and identifying candidates suitable for a DCB-based strategy²². Despite these promising concepts, robust randomized evidence comparing DCB with contemporary DES in large vessel disease remains limited. Therefore, while DCB represents a compelling strategy to reduce metal burden and preserve vascular physiology, further large-scale trials are required before its routine adoption in this population^{5,17}.

Lesion Preparation for Drug-Coated Balloon Angioplasty²³ Optimal lesion preparation is a critical determinant of procedural success in DCB angioplasty and represents the cornerstone of the “DCB only” strategy^{4,18}. Current recommendations from the German and international DCB consensus groups emphasize that adequate lesion modification should be achieved prior to drug delivery to ensure optimal drug uptake and minimize acute complications. Lesion preparation should begin with predilation using a semi-compliant or non-compliant balloon, with a balloon-to-vessel ratio of approximately 0.8–1.0. In more complex lesions, specialty balloons such as scoring or cutting balloons may be required to achieve adequate plaque modification. Adjunctive techniques, including rotational atherectomy or intravascular lithotripsy, may be considered in heavily calcified lesions to optimize vessel compliance and luminal gain^{4,18}. An optimal angiographic result before DCB application is defined by the presence of TIMI 3 flow, absence of flow-limiting dissections, and residual stenosis $\leq 30\%$. Functional assessment (e.g., fractional flow reserve [FFR]) and intracoronary imaging modalities such as IVUS or OCT may further guide procedural optimization in selected cases²³. When these criteria are met, DCB can be safely applied using nominal pressure with an adequate balloon length extending beyond the lesion margins to ensure complete drug coverage. Inflation time should be maintained for at least 30–60 seconds to facilitate effective drug transfer¹⁸. Conversely, in cases of suboptimal lesion preparation-defined by residual stenosis $>30\%$, flow-limiting dissection, or impaired coronary flow-bailout stenting with DES is recommended to ensure procedural safety and durability of the result^{4,18}. Overall, these recommendations highlight that successful DCB therapy is highly dependent on meticulous lesion preparation, appropriate device selection, and careful procedural execution. (Figure 2)

Advantages of DCB

- Absence of permanent metallic scaffold, potentially reducing chronic vessel injury and preserving vascular physiology¹
- Elimination of device-related stent thrombosis associated with permanent metallic implants¹
- Potential for shorter dual antiplatelet therapy duration in selected patients²¹

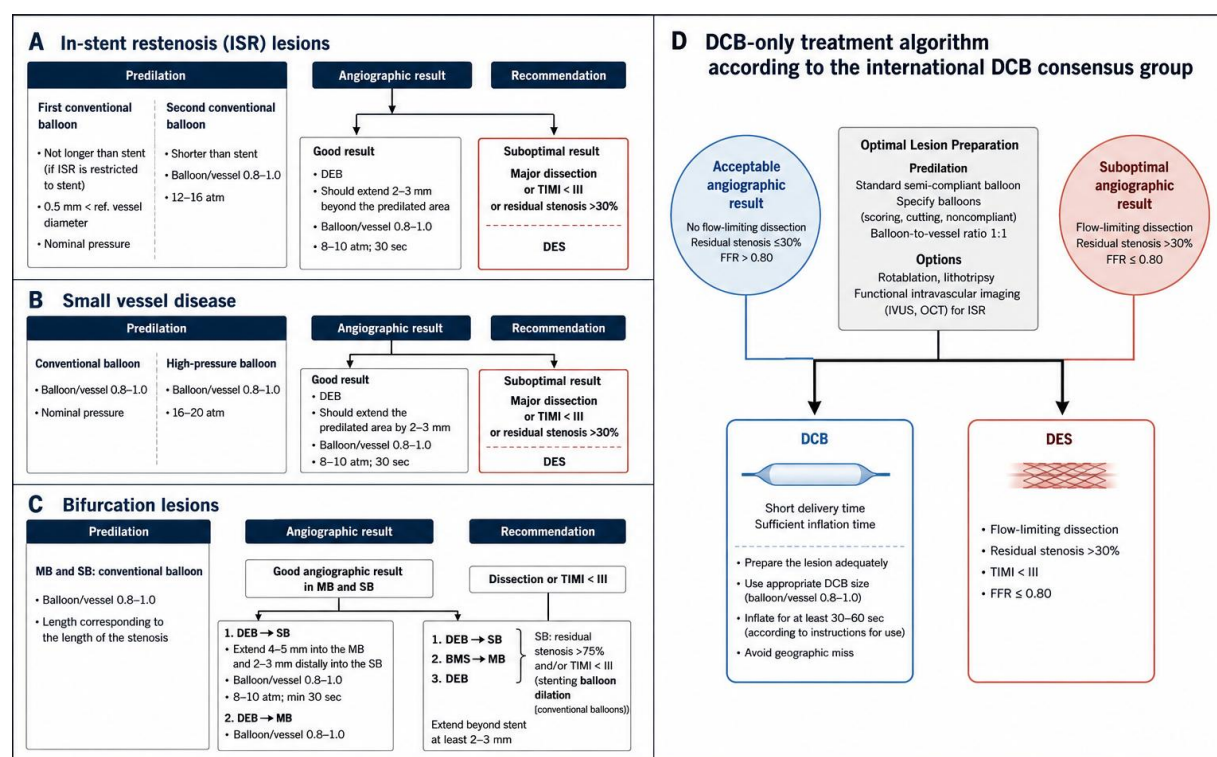
Potential for positive vessel remodeling and late lumen enlargement²⁴

Limitations Despite increasing evidence, several limitations should be considered. First, many studies are underpowered for hard clinical endpoints such as mortality and myocardial infarction²⁴. Second, heterogeneity among DCB devices-including differences in drug type, excipients, and coating technologies-limits generalizability and prevents a clear class effect^{2,3}. Third, outcomes are highly dependent on optimal lesion preparation, which is operator-dependent and not standardized across studies^{15,18}. Fourth, some studies have reported higher rates of restenosis or repeat revascularization in specific scenarios, particularly when lesion preparation

preparation is inadequate^{2,4}. Finally, long-term data in complex lesion subsets remain limited, and While DCB has an established role in coronary ISR and is endorsed by ESC guidelines, recommendations for de novo coronary lesions remain limited, reflecting the relative lack of adequately powered randomized trials and ongoing evolution of the evidence base²⁴.

Figure 2. Practical Algorithm for Drug-Coated Balloon (DCB) Angioplasty in Coronary Lesions

Proposed procedural workflow for lesion preparation, DCB application, and bailout stenting strategy in de novo coronary lesions. Conceptually adapted from the International DCB Consensus Group report by Jeger et al.²³.



DEB = drug-eluting balloon; DES = drug-eluting stent; BMS = bare-metal stent; MB = main branch; SB = side branch; ISR = in-stent restenosis; TIMI = Thrombolysis In Myocardial Infarction; FFR = fractional flow reserve; IVUS = intravascular ultrasound; OCT = optical coherence tomography.

Future Research Directions Future studies should focus on large, multicenter randomized controlled trials comparing DCB with contemporary DES across diverse lesion subsets, with adequate power to assess hard clinical endpoints^{5,15}. Standardization of lesion preparation techniques is essential to improve reproducibility and outcomes¹⁹. Further investigation into sirolimus-coated balloons is warranted due to their favorable safety profile^{3,5}. The integration of intracoronary imaging, such as IVUS and OCT, may further optimize procedural outcomes²¹. Additionally, emerging indications-including acute coronary syndrome, large vessel disease, and hybrid DCB-DES strategies-require further validation^{17,19}. Long-term follow-up studies are needed to evaluate durability, vascular remodeling, and clinical outcomes.

Guideline Perspective Current international guidelines provide limited but important recommendations regarding the use of drug-coated balloons (DCB), primarily in the setting of in-stent restenosis (ISR). The 2018 ESC/EACTS Guidelines recommend both DCB and drug-eluting stents (DES) as Class I, Level A therapies for ISR management²⁵. In contrast, the 2021 ACC/AHA/SCAI Guideline does not specifically include DCB, with DES

remaining the standard treatment strategy²⁴. This discrepancy reflects differences in regulatory approval, device availability, and the current evidence base between Europe and the United States. Although contemporary evidence increasingly supports the role of DCB beyond ISR-particularly in de novo coronary lesions-current guideline recommendations remain relatively conservative. Further large-scale randomized trials are needed to establish more consistent global recommendations.

Conclusions

Drug-coated balloon represents an important advancement in PCI, particularly in small vessel disease and high bleeding risk patients. The “leaving nothing behind” strategy offers potential long-term advantages by avoiding permanent implants. However, optimal lesion preparation, appropriate patient selection, and further high-quality evidence are essential before widespread adoption in routine clinical practice.

Table 1. Concept of “Leaving Nothing Behind” Strategy

Comparison between DES implantation and DCB angioplasty, highlighting absence of permanent scaffold and reduced chronic vessel injury.

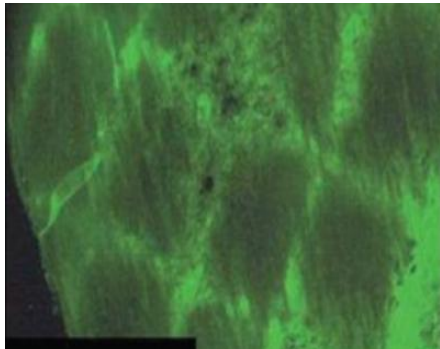
	DES	DCB
		
Stent	stent scaffold	no
Drug retention	polymer	carrier/embed imprint
Antiproliferative drug dose	low	high
Antiproliferative drug release	slow and control persistent drug exposure	fast release short lasting exposure
advantage	prevent recoil	leave nothing behind

Table 2. Current drug-coated balloons Thailand availability and manufacturer details(continued)

Device	Coating	Drug	Excipient	Attribute	Drug dose
Agent	Transpax	Paclitaxel	Acetyl-tri-butyl citrate (ATBC)	Hydrophobic	2 mcg/mm ²
Pantera Lux	Lux	Paclitaxel	Butyryl-Tri-Hexyl-citrate (BTHC)	Hydrophobic	3 mcg/mm ²
Prevail	FreePac	Paclitaxel	Urea	Hydrophilic	3.5 mcg/mm ²
Sequent please	Paccocath	Paclitaxel	iopromide	Hydrophilic	3 mcg/mm ²
MagicTouch	Nanolute	Sirolimus	Phospholipid based	Hydrophilic	1.27 mcg/mm ²
Selution	Micro-reservoir	Sirolimus	phospholipid encapsulation	Hydrophilic	1 mcg/mm ²
Bioascend	Reservoir-based systems	Biolimus A9	phospholipid	lipophilic	~1.0 – 1.5 mcg/mm ²

Table 3. Landmark Trials of DCB in Coronary Artery Disease²⁶⁻²⁸

Trial	Year	Lesion Type	Comparison	Main Findings
PACCOCATH ISR I	2006	ISR	DCB vs POBA	First trial demonstrating significant reduction in restenosis with paclitaxel-coated balloon.
PEPCAD II	2009	BMS-ISR	DCB vs Paclitaxel-DES	DCB showed lower late lumen loss and comparable clinical outcomes.
PEPCAD-DES	2009	DES-ISR	DCB vs POBA	DCB superior to balloon angioplasty for DES restenosis.
ISAR-DESIRE 3	2013	DES-ISR	DCB vs DES vs POBA	DCB non-inferior to DES and superior to POBA.
RIBS IV	2015	DES-ISR	DCB vs Everolimus-DES	DES achieved larger lumen gain, but DCB remained effective.
RIBS V	2014	BMS-ISR	DCB vs Everolimus-DES	Comparable angiographic and clinical outcomes.
BASKET-SMALL 2	2018	De novo small vessel disease	DCB vs DES	DCB non-inferior to second-generation DES for MACE.
BELLO	2012	Small vessel de novo lesions	DCB vs Paclitaxel-DES	Reduced late lumen loss with DCB.
RESTORE SVD China	2018	Small vessel disease	DCB vs DES	DCB non-inferior to DES for angiographic outcomes.

Table 3. Landmark Trials of DCB in Coronary Artery Disease²⁶⁻²⁸ (continued)

Trial	Year	Lesion Type	Comparison	Main Findings
PICCOLETO II	2020	Small vessel disease	DCB vs DES	New-generation DCB superior to DES for late lumen loss.
DEBUT	2019	HBR	DCB vs BMS	DCB reduced MACE compared with BMS in HBR patients.
PEPCAD-BIF	2011	Bifurcation side branch	DCB vs POBA	DCB reduced restenosis in side-branch treatment.
DCB-BIF	2012	Coronary bifurcation	DCB + provisional stenting	Demonstrated feasibility of DCB in bifurcation lesions.
REVELATION	2019	STEMI	DCB vs DES	Similar fractional flow reserve and clinical outcomes.
TRANSFORM I	2023	Large vessel	Sirolimus-DCB vs DES	Demonstrated feasibility of sirolimus-coated balloon strategy.

Table 4. Current Guideline / Consensus Recommendations for Coronary DCB Use by Region^{2,29-31}

Region / Country	Guideline / Consensus	Main DCB Recommendation	Clinical Scenarios Supported
Europe	European Society of Cardiology (ESC) Guidelines & International DCB Consensus	Strongest evidence for ISR; expanding role in de novo lesions	ISR (Class I), small vessel disease, bifurcation side branch, selected HBR and de novo lesions
Germany/ International Europe	International DCB Consensus Group	Supports DCB as alternative to DES in selected de novo lesions with optimal lesion preparation	ISR, SVD, bifurcation, diffuse disease, HBR
Asia-Pacific	Asia-Pacific Consensus Group	Recommends broader DCB application beyond ISR	SVD, bifurcation, CTO, selected large vessels
Thailand	Cardiovascular Intervention Association of Thailand (CIAT) Consensus Statement	Endorses DCB for ISR and selected de novo lesions small vessel (<2.5 mm) with emphasis on lesion preparation and DAPT tailoring	ISR, SVD, bifurcation lesions, HBR patients

Table 4. Current Guideline / Consensus Recommendations for Coronary DCB Use by Region^{2,29-31}
(continued)

Region / Country	Guideline / Consensus	Main DCB Recommendation	Clinical Scenarios Supported
Japan	Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) Expert Practice	Widely adopts DCB in routine PCI practice, especially small vessels(<3mm) and bifurcation lesions	ISR, SVD, bifurcation, diffuse CAD
South Korea	Korean Society of Interventional Cardiology Review & Expert Recommendations	Supports DCB-based PCI in selected de novo CAD with imaging-guided optimization	SVD, bifurcation, selected de novo lesions
China	Chinese expert consensus and contemporary RCT-driven practice	Increasing adoption of DCB- first strategies in de novo disease	SVD, STEMI, diffuse disease, large vessels
United States	FDA approval + limited consensus statements	Coronary DCB currently mainly approved for ISR; de novo use remains limited/off label	ISR predominantly; de novo use investigational or selective

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