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Drug-Coated Balloon (DCB) Angioplasty in Large Coronary Vessels: A Future Game Changer?

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Introduction

Take Home Messages

- DCB results are comparable to drug-eluting stents (DES) in most efficacy measures
- The philosophy of "leaving nothing behind" is tempting for specific lesions (e.g. diffuse disease, side branches, small arteries) and clinical circumstances (e.g. diabetes, multivessel disease, acute coronary syndromes, high bleeding risk individuals)
- Future well-designed clinical trials with strict inclusion criteria are needed

Since their introduction in 2004, drug-coated balloons (DCBs) have emerged as a novel technology for improving percutaneous coronary intervention (PCI) outcomes by mitigating revascularisation, in-stent restenosis, and associated major adverse cardiac events (MACE) (1). DCBs function by locally delivering antiproliferative drugs to the vessel wall during balloon inflation via semi-compliant balloon. An excipient on the DCB aids in retaining the drug on the balloon during transit, enhancing the drug's adherence to the vessel wall, and improves the deposition of the drug in the tissue. Paclitaxel and sirolimus are commonly used drugs that prevent smooth muscle proliferation, minimize endothelial dysfunction and neoatherosclerosis. Their lipophilic nature facilitates quick absorption by cells and homogenous distribution, resulting in a sustained impact on smooth muscle cells. (2-5)

Leaving Nothing Behind

The main downsides of balloon angioplasty were vessel-threatening dissections and significant restenosis. To overcome balloon angioplasty's limitations, bare metal and drug-eluting stents were developed. (6) New-generation drug eluting stents (DES) lowers restenosis and first-year in-stent thrombosis compared to bare metal stent. (6-8) However, very-late stent-related incidents remained at 2% per year without plateauing. (9,10) The concept of 'leaves nothing behind' was

born aiming to deliver an anti-restenotic agent to the vessel wall following optimal lesion preparation. DCB therapy is recommended for in-stent restenosis by the European Society of Cardiology (Class IA). (9,10) DCB is a viable alternative to standard stent implantation for in-stent restenosis and de novo coronary artery lesions of coronary vessel >2.5mm, as evidenced by emerging evidence. (11)

Drug-Coated Balloon Angioplasty in de novo Coronary Artery Lesions

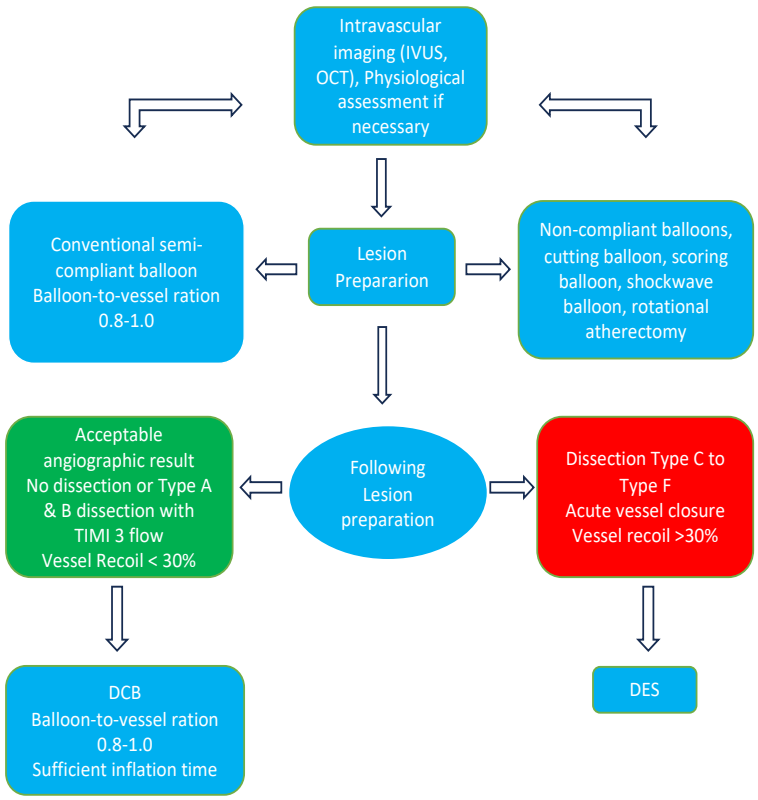
DCB angioplasty has no significant differences in the de novo coronary lesions with significantly lower incidences of target lesion revascularisation, MACE, and late lumen loss compared to uncoated devices and similar incidences compared to DESs. Comparable or superior efficacy of DCBs over other therapies for the treatment of de novo coronary lesions (**Table 1**) were demonstrated. DCB appears promising as an alternative to DESs in the de novo coronary lesions and their applicability **(Figure 1)** is outlined.

Table 1: Summary of Findings from Meta-analysis

Study	Patient Group	Studies included	Minimum Follow-up	Primary Outcomes	Findings
Elgendy et al. (11)	De novo coronary lesions	14 RCTs	12 months	TLR, MACE, Myocardial infarction, All-cause mortality	DCBs similar to drug-eluting stents in target lesion revascularization. Lower incidence of myocardial infarction and all-cause mortality with DCBs. No significant difference in MACE, vessel thrombosis, or cardiovascular mortality.
Wang et al. (12)	De novo coronary lesions	33 RCTs	6 months	LLL, TLR, MACE	DCBs show significantly lower incidences of TLR, MACE, and LLL compared to uncoated devices. Similar incidences compared to DESs.
Zhong et al (13)	De novo coronary lesions	26 RCTs,	6 months	MACE, In-segment LLL, TLR, MACE, Myocardial infarction, all-cause death	DCB only strategy comparable efficacy to DES for MACE and clinical outcomes. DCB only strategy better than 1st & 2nd generation DES for in-segment LLL DCB only strategy worse than DES for in-segment LLL in ACS

Abbreviations: TLR (Target lesion revascularisation), LLL (Late lumen loss), MACE (Major adverse cardiovascular event), DES (Drug eluting stent)

Figure 1: Drug-Coated Balloon Applicability to a Coronary de novo Lesion (14)



Abbreviation: IVUS = Intravascular ultrasound, OCT = Optical Coherence Tomography , Type A and type B dissections are characterized by a wide dissection lumen. The diameter of the dissection cap exceeds at least one quarter of the diameter of the apparent normal lumen. The outer edge of dissection cap is within the true lumen of the reference in type A dissection and beyond it in type B dissection. Type C and type D dissections are characterized by a thin dissection lumen. The diameter of dissection lumen is within one quarter of the reference diameter. Its outer edge is within the true lumen of the reference in type C dissection and beyond it in type D dissection. Type E dissection is characterized by the presence of a flap protruding into the true lumen or spiral appearance. (15)

Drug-Coated Balloon Angioplasty in Large Coronary Vessel Disease

Although DCB only angioplasty in large coronary vessels is not routine, it has shown to be comparable with decreased MACE rates and superior angiographic outcomes irrespective of anatomy. The evidence **(Table 2)** suggests DCB angioplasty is safe and efficacious for large vessel coronary artery disease with equivalent long-term mortality to DES. These findings make DCBs an attractive treatment for these lesions. Moreover, DES in elective PCI has significantly increased vessel inflammatory response for up to 2 months compared to DCB group (16) and it is convincing that more evidence is coming to DCB strategy as an alternative in large coronary vessel disease.

Table 2: Summary of Findings on DCBs for Large Vessel Disease

Study	Patient Group	Key Findings
Yu et al (17)	Retrospective study n = 527 Large vessel group (diameter > 2.8 mm)	Lower MACE and target lesion revascularization in large vessels with DCB compared to small vessels.
Shin et al (18)	Retrospective study n = 67 Macrovascular lesions (diameter 2.5 mm - 3.5 mm)	Lower late lumen loss in DCB-treated patients compared to DES during dual antiplatelet therapy for 6 weeks.
Merinopoulos et al (19)	Retrospective study n = 1237; 544 DCB and 693 DES predominantly large vessels (elective practice)	DCB-only angioplasty is safe compared to DES in routine clinical practice in terms of all-cause mortality and MACE, including unplanned target lesion revascularisation.
Merinopoulos et al (SPARTAN DCB Study) (20)	Retrospective study n = 1517; 429 with DCB and 1088 DES Stable, de novo coronary artery disease	No evidence of late mortality associated with DCB angioplasty compared with non-paclitaxel second-generation DES in up to 5 years of follow-up. DCB is a safe option for the treatment of de novo coronary artery disease.

Abbreviations: MACE (Major adverse cardiovascular event), DES (Drug eluting stent)

Drug-Coated Balloon Angioplasty in ST elevation Myocardial Infarction (STEMI)

The studies (**Table 3**) demonstrate DCB angioplasty is safe and effective in STEMI patients. Early outcomes for DCB integration as primary reperfusion in these individuals are promising. DCB in STEMI provide potential advantages during high thrombus burden and inflammatory states. Local drug delivery by DCB during peak inflammatory states may preserve endothelial function. (21) However, DCB only angioplasty outcomes require larger long-term randomised control studies compared to conventional reperfusion strategy using DES in STEMI.

Table 3: Summary of findings on DCBs use in STEMI

Study	Patient Group	Key Findings
REVELATION Trial (22)	STEMI patients with large coronary artery disease (n=120)	No significant difference in LLL and clinical outcomes between DCB angioplasty and other methods at 9-month follow-up.
Gobic et al. (23)	STEMI patients (n=75)	Similar results between DCB angioplasty and other methods at 6-month follow-up.
Merinopoulos (24)	STEMI patients (n=1139)	Non-inferiority of DCB angioplasty to DES in terms of fractional flow reserve at 9 months. No significant difference in all-cause mortality between DCB and DES groups.

Abbreviations: MACE (Major adverse cardiovascular event), DES (Drug eluting stent), STEMI (ST elevation myocardial infarction), LLL (Late lumen loss)

Drug-Coated Balloon Angioplasty in Bifurcation Lesions

Current European Bifurcation Club recommend provisional single branch stenting as the first-line treatment for bifurcation lesions, but it may still change the vessel's anatomical structure and damage the side branches, resulting in limited collateral flow, myocardial ischemia, and complete side branch occlusion in severe cases. (25, 26) The prolonged operational duration also increases X-ray doses. (27)

DCB presents a potential alternative in treating bifurcation lesions, avoiding some downsides associated with conventional methods, by a simpler way to enlarge side branch arteries without affecting their anatomy. reducing restenosis without leaving metal implants in bifurcations. (28) Studies (**Table 4)** emphasize the safety and efficacy of DCB in bifurcation lesions, but further larger studies comparing DCB and DES are needed. Ongoing refinements in procedural technique and patient selection will help translate these findings into routine clinical application.

Table 4: Summary of findings on DCB use in bifurcation lesion.

Study	Patient Group	Intervention	Key Findings
DEBIUT Study (29)	Bifurcation Lesions (n = 20)	DCB coated with paclitaxel, provisional stenting of main branch with BMS	Successful operations, no acute or subacute branch occlusion, no MACE at 4-month follow-up.
PEPCAD V Study (30)	Bifurcation Lesions (n = 28)	DCB coated with paclitaxel provisional stenting of main branch with BMS	Low LLL of main and side branches at 9 months, low restenosis rates
Kleber et al. (31)	Bifurcation Lesions (n = 64)	DCB vs POBA	Lower rate of restenosis in the DCB group at 9 months.
Zheng et al. (32)	Bifurcation Lesions (n = 934)	DCB vs POBA	Better short-term efficacy in the DCB group for side branch treatment.
Schulz et al. (33)	Bifurcation Lesions (n = 39)	DCB alone	Low TLR and MACE rate indicating safety of using DCB alone.
PEPCAD-BIF Trial (34)	Bifurcation Lesions (n = 64)	DCB vs POBA	Reduced LLL in the DCB group compared to POBA

Abbreviations: TLR (Target lesion revascularisation), LLL (Late lumen loss), MACE (Major adverse cardiovascular event), DES (Drug eluting stent), POBA (Percutaneous balloon angioplasty), BMS (Bare metal stent)

Conclusion

Recent evidence indicates the effectiveness of drug-coated balloon (DCB) angioplasty across coronary lesions and patient groups. DCBs, avoiding metallic implants and preserving vascular function, show promise in coronary artery disease. However, further optimization is necessary before widespread adoption as DCB only as routine in the large coronary vessels. A "hybrid

approach" using DCBs along limited stenting segments may be effective for severe diffuse disease. DCB-shortened dual antiplatelet therapy can benefit high-risk bleeding patients. (36)

In conclusion, DCB angioplasty proves safe and effective, offering advantages such as eliminating permanent metallic implants, accelerating patient recovery, improving side-branch access, and reducing complications and repeat revascularization rates. Ongoing trial such as SELUTION DeNovo, multi-centre international open-label randomized trial (37) will provide more insights into evidence-based practice of DCB only strategy. Future research should focus on optimizing DCB integration and exploring its full potential through procedural improvements and expanded applications in large de novo coronary artery lesions.

Disclosures

None

References

1. Belkacemi A, Agostoni P, Voskuil M, et al. Drug-Eluting Balloons In Coronary Artery Disease-Current And Future Perspectives. ICR. 2011; 6:157-260.
2. Bukka M, Rednam PJ, Sinha M. Drug-eluting balloon: design, technology and clinical aspects. Biomedical Materials. 2018; 13:032001.
3. Cortese B, Orrego PS, Agostoni P, Piraino D, Andolina G, Seregni RG. Effect of drug-coated balloons native coronary artery disease left with a dissection. JACC Cardiol Intv. 2015; 8:2003-2009.
4. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016; 4:1-12.
5. Axel DI, Kunert W, Goggelmann C, et al. Paclitaxel inhibits arterial smooth muscle cell proliferation and migration in vitro and in vivo using local drug delivery. Circulation. 1997;96(2):636-45. Lee SY, Hong MK, Shin DH, et al. Clinical outcomes of dual antiplatelet therapy after implantation of drug-eluting stents in patients with different cardiovascular risk factors. Clin Res Cardiol. 2017; 106:165–73.
6. Varenhorst C, Lindholm M, Sarno G, et al. Stent thrombosis rates the first year and beyond with new- and old-generation drug-eluting stents compared to bare metal stents. Clin Res Cardiol. 2018; 107:816–23.
7. Valgimigli M, Bueno H, Byrne RA, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Eur Heart J. 2018; 39:213–60.
8. Baan J Jr, Claessen BE, Dijk KB, et al. A randomized comparison of paclitaxel-eluting balloon versus everolimus-eluting stent for the treatment of any in-stent restenosis. JACC Cardiovasc Interv. 2018; 11:275–83.
9. Kolh P, Windecker S, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg. 2014; 46:517–92.

10. Elgendy IY, Gad MM, Elgendy AY, et al. Clinical and angiographic outcomes with drug-coated balloons for de novo coronary lesions: a meta-analysis of randomized clinical trials. J Am Heart Assoc. 2020;9: e016224.
11. Wang D, Wang X, Yang T, et al. Drug-Coated Balloons for De Novo Coronary Artery Lesions: A Meta-Analysis of Randomized Clinical Trials. Yonsei Med J. 2023;64(10):593-603.
12. Zhong PY, Ma Y, Shang YS, et al. Efficacy of Drug-Coated Balloon Approaches for de novo Coronary Artery Diseases: A Bayesian Network Meta-Analysis. Front Cardiovasc Med. 2022; 9:899701.
13. Jeger RV, Farah A, Ohlow MA, et al. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): 3-year follow-up of an open-label randomised non-inferiority trial. Lancet. 2020;396(10257):1027-1034. doi:10.1016/S0140-6736(20)31868-1
14. Shigeyama, Junsho, Shigenori Ito, Hiroaki Kondo, Osamu Ito, Toyoaki Matsushita, Mitsuhiro Okamoto, Junji Toyama, Yoshimitsu Ban, Tatsuya Fukutomi, and Makoto Itoh. "Angiographic Classification of Coronary Dissections after Plain Old Balloon Angioplasty for Prediction of Regression at Follow-up." Japanese Heart Journal 42 (2001): 393-408.
15. Merinopoulos, Ioannis, U Bhalraam, Terri Holmes, Vassiliki Tsampasian, Natasha Corballis, Tharusha Gunawardena, Chris Sawh, Clint Maart, Trevor Wistow, Alisdair Ryding, Simon C. Eccleshall, James Smith, and Vassilios S. Vassiliou. "Circulating Intermediate Monocytes CD14++CD16+ Are Increased After Elective Percutaneous Coronary Intervention." PLOS ONE, December 14, 2023. https://doi.org/10.1371/journal.pone.0294746.
16. Yu X, Ji F, Xu F, et al. Treatment of large de novo coronary lesions with paclitaxel-coated balloon only: results from a Chinese institute. Clin Res Cardiol. 2018;107(8):633-641. doi:10.1007/s00392-018-1346-8
17. Shin ES, Ann SH, Balbir SG, Lim KH, Kleber FX, Koo BK. Fractional flow reserve-guided paclitaxel-coated balloon treatment for de novo coronary lesions. Catheter Cardiovasc Interv. 2016;88(2):193-201. doi:10.1002/ccd.26257
18. Merinopoulos I, Gunawardena T, Corballis N, et al. Paclitaxel drug-coated balloon-only angioplasty for de novo coronary artery disease in elective clinical practice. Clin Res Cardiol. 2023;112(9):1186-1193. doi:10.1007/s00392-022-02106-y
19. Merinopoulos I, Gunawardena T, Wickramarachchi U, et al. Long-term safety of paclitaxel drug-coated balloon-only angioplasty for de novo coronary artery disease: the SPARTAN DCB study. Clin Res Cardiol. 2021;110(2):220-227. doi:10.1007/s00392-020-01734-6
20. Yerasi C, Case BC, Forrestal BJ, et al. Drug-Coated Balloon for De Novo Coronary Artery Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;75(9):1061-1073. https://doi.org/10.1016/j.jacc.2019.12.046
21. REVELATION Study Group. Two-Year Clinical Outcomes of the REVELATION Study: Sustained Safety and Feasibility of Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent in Acute Myocardial Infarction. EuroIntervention. 2022;34(1):E39-E42.
22. Gobić D, Tomulić V, Lulić D, et al. Drug-Coated Balloon Versus Drug-Eluting Stent in Primary Percutaneous Coronary Intervention: A Feasibility Study. Am J Med Sci. 2017;354(6):553-560.
23. Merinopoulos I, Gunawardena T, Corballis N, et al. Assessment of Paclitaxel Drug-Coated Balloon Only Angioplasty in STEMI. JACC Cardiovasc Interv. 2023;16(7):771-779.

24. Kumsars I, Holm NR, Niemelä M, et al. Randomised comparison of provisional side branch stenting versus a two-stent strategy for treatment of true coronary bifurcation lesions involving a large side branch: the Nordic-Baltic bifurcation study IV. Open Heart. 2020;7: e000947.
25. Park TK, Lee JH, Song YB, et al. Impact of non-compliant balloons on long-term clinical outcomes in coronary bifurcation lesions: results from the COBIS (COronary BIfurcation stent) II registry. EuroIntervention. 2016; 12:456–4.
26. Jurado-Román A, Rubio-Alonso B, García-Tejada J, et al. Systematic isolated post-dilatation of the side branch as part of the provisional stent technique in the percutaneous treatment of coronary bifurcations. CR12 registry. Cardiovasc Revasc Med. 2018; 19:493–7.
27. Lassen JF, Burzotta F, Banning AP, et al. Percutaneous coronary intervention for the left main stem and other bifurcation lesions: 12th consensus document from the European bifurcation Club. EuroIntervention. 2018; 13:1540–53.
28. Belkacemi A, Agostoni P, Voskuil M, Stella PR. Coronary bifurcation lesions treated with the drug-eluting balloon: a preliminary insight from the DEBIUT study. EuroIntervention. 2011;7 Suppl K:K66-9.
29. Mathey DG, Wendig I, Boxberger M, et al. Treatment of bifurcation lesions with a drug-eluting balloon: the PEPCAD V (Paclitaxel Eluting PTCA Balloon in Coronary Artery Disease) trial. EuroIntervention. 2011;7 Suppl K: K61–5.
30. Kleber FX, Rittger H, Ludwig J, et al. Drug eluting balloons as stand-alone procedure for coronary bifurcational lesions: results of the randomized multicenter PEP-CAD-BIF trial. Clin Res Cardiol. 2016; 105:613–21.
31. Zheng Y, Li J, Wang L, et al. Effect of Drug-Coated Balloon in Side Branch Protection for de novo Coronary Bifurcation Lesions: A Systematic Review and Meta-Analysis. Front Cardiovasc Med. 2021; 8:758560.
32. Schulz A, Hauschild T, Kleber FX. Treatment of coronary de novo bifurcation lesions with DCB only strategy. Clin Res Cardiol. 2014; 103:451–6.
33. Kleber FX, Rittger H, Ludwig J, et al. Drug eluting balloons as stand-alone procedure for coronary bifurcational lesions: results of the randomized multicenter PEP-CAD-BIF trial. Clin Res Cardiol. 2016; 105:613–21.
34. Merinopoulos I, Gunawardena T, Corballis N, et al. Cost effectiveness analysis of drug-coated balloon only angioplasty for de novo coronary artery disease. Catheter Cardiovasc Interv. 2023;102(6):987-996.
35. Alfonso F. State of the art: balloon catheter technologies – drug-coated balloon. EuroIntervention. 2017; 13:680-695.
36. Wang L, Li X, Li T, Liu L, Wang H, Wang C. Novel application of drug-coated balloons in coronary heart disease: A narrative review. *Front Cardiovasc Med*. 2023; 10:1055274. doi:10.3389/fcvm.2023.1055274
37. Spaulding C, Krackhardt F, Bogaerts K, Urban P, Meis S, Morice MC, Eccleshall S. Comparing a strategy of sirolimus-eluting balloon treatment to drug-eluting stent implantation in de novo coronary lesions in all-comers: Design and rationale of the SELUTION DeNovo Trial. American Heart Journal. 2023 Apr; 258:77-84. doi: 10.1016/j.ahj.2023.01.007. Epub 2023 Jan 13. PMID: 36642225; PMCID: PMC1234567.
38. Corballis NH, Paddock S, Gunawardena T, Merinopoulos I, Vassiliou VS, Eccleshall SC. Drug-coated balloons for coronary artery bifurcation lesions: A systematic review and focused meta-analysis. *PLoS ONE*. 2021;16(7): e0251986. doi:10.1371/j

39. Merinopoulos, Ioannis, Tharusha Gunawardena, Natasha Corballis, Vassiliki Tsampasian, Simon C. Eccleshall, James Smith, and Vassilios S. Vassiliou. "The Role of Inflammation in Percutaneous Coronary Intervention, from Balloon Angioplasty to Drug Eluting Stents." Minerva Cardiology and Angiology 71, no. 6 (December 2023): 631-642.
40. Jeger RV, Farah A, Ohlow MA, et al. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial. Lancet. 2018;392(10150):849-856.
41. Latib A, Colombo A, Castriota F, et al. A Randomized Multicenter Study Comparing a Paclitaxel Drug-Eluting Balloon with a Paclitaxel-Eluting Stent in Small Coronary Vessels. J Am Coll Cardiol. 2012;60(24):2473-2480.
42. Tian J, Tang YD, Qiao S, et al. Two-year follow-up of a randomized multicenter study comparing a drug-coated balloon with a drug-eluting stent in native small coronary vessels. Catheter Cardiovasc Interv. 2020;95 Suppl 1:587-597.
43. Jeger RV, Farah A, Ohlow MA, et al. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): 3-year follow-up of an open-label randomised non-inferiority trial. Lancet. 2020;396(10257):1027-1034. doi:10.1016/S0140-6736(20)31868-1