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

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Introduction
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)

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

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.

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<th>Study</th>
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<th>Minimum Follow-up</th>
<th>Primary Outcomes</th>
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<tr>
<td>Elgendy et al. (11)</td>
<td>De novo coronary lesions</td>
<td>14 RCTs</td>
<td>12 months</td>
<td>TLR, MACE, Myocardial infarction, All-cause mortality</td>
<td>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.</td>
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<tr>
<td>Wang et al. (12)</td>
<td>De novo coronary lesions</td>
<td>33 RCTs</td>
<td>6 months</td>
<td>LLL, TLR, MACE</td>
<td>DCBs show significantly lower incidences of TLR, MACE, and LLL compared to uncoated devices. Similar incidences compared to DESs.</td>
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<tr>
<td>Zhong et al (13)</td>
<td>De novo coronary lesions</td>
<td>26 RCTs</td>
<td>6 months</td>
<td>MACE, In-segment LLL, TLR, MACE, Myocardial infarction, all-cause death</td>
<td>DCB only strategy comparable efficacy to DES for MACE and clinical outcomes. DCB only strategy better than 1st &amp; 2nd generation DES for in-segment LLL DCB only strategy worse than DES for in-segment LLL in ACS</td>
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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)

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.
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.

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<th>Table 3: Summary of findings on DCBs use in STEMI</th>
<th>Study</th>
<th>Patient Group</th>
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<tr>
<td>REVELATION Trial (22)</td>
<td>STEMI patients with large coronary artery disease (n=120)</td>
<td>No significant difference in LLL and clinical outcomes between DCB angioplasty and other methods at 9-month follow-up.</td>
<td></td>
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<tr>
<td>Gobic et al. (23)</td>
<td>STEMI patients (n=75)</td>
<td>Similar results between DCB angioplasty and other methods at 6-month follow-up.</td>
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<tr>
<td>Merinopoulos (24)</td>
<td>STEMI patients (n=1139)</td>
<td>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.</td>
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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.

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

**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


