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EDITORIAL

Drug-Eluting Balloon: The Achilles' Heel of Interventional Cardiology.

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Interventional cardiology has witnessed a remarkable technological evolution, progressing from plain old balloon angioplasty (POBA) to bare-metal stents (BMS), and ultimately to contemporary drug-eluting stents (DES), which remain the cornerstone of percutaneous coronary intervention (PCI). Amidst these advancements, drug-eluting balloons/drug coated balloons (DEB/DCB) have emerged with the compelling concept of "leave nothing behind." Despite their theoretical advantages, DEBs continue to occupy a paradoxical position in modern practice-highly effective in selected scenarios yet limited in broader applicability. This duality renders DEB the "Achilles' heel" of interventional cardiology: a technology with undeniable strengths but critical vulnerabilities.

DEBs are designed to deliver antiproliferative agents i.e.; paclitaxel or sirolimus directly to the vessel wall during balloon inflation, without leaving a permanent metallic scaffold or polymer. This offers several advantages:

- Elimination of chronic foreign body reaction
- Reduced risk of late and very late stent thrombosis
- Shorter duration of dual antiplatelet therapy
- Preservation of vascular physiology

However, the absence of a scaffold also represents the principal limitation of DEBs lack of mechanical support, predisposing to acute recoil and flow-limiting dissections, especially in de novo lesions. It has been shown that a nonflow-limiting dissection after DCB treatment tends to heal during the first few months, with both the paclitaxel and sirolimus technologies, without leading to acute or subacute vessel closure[1,2]. The most compelling evidence for DEB use exists in in-stent restenosis (ISR), where additional stent layers are often undesirable. The PACCOCATH ISR trials first demonstrated the superiority of DEB over POBA, with significant reductions in late lumen loss (LLL) and restenosis rates[3]. These findings were sustained in long-term follow-up.

Subsequently, the PEPCAD II trial showed that DEB was comparable and in some endpoints superior to paclitaxel-eluting stents in BMS-ISR[4]. Further trials such as ISAR-DESIRE 3, RIBS V, and BELLO reinforced the role of DEB as a viable alternative to DES in ISR management[5,6].

Contemporary meta-analyses continue to support DEB as an effective treatment modality in ISR, particularly when avoidance of additional stent layers is desirable.

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Importantly, our recent study published in Cureus further contributes to this evidence base. In this study, we evaluated the clinical outcomes of DEB angioplasty in a real-world cohort and demonstrated favorable procedural success with acceptable short-term outcomes, reinforcing the utility of DEB in carefully selected patients[7].

The application of DEB in de novo coronary lesions has yielded inconsistent results. The PEPCAD III trial, which evaluated DEB combined with BMS, failed to demonstrate superiority over sirolimus-eluting stents, highlighting higher rates of restenosis and target lesion revascularization (TLR)[8]. However, subgroup analyses particularly in small vessel disease suggest a potential role for DEB where stent implantation is less favorable. Nonetheless, modern DES with improved polymer technology and thinner struts continue to outperform DEB in most de novo settings. Bifurcation lesions remain among the most complex subsets in PCI, accounting for nearly 15–20% of cases. The provisional stenting strategy is widely accepted, with increasing emphasis on minimizing unnecessary stent implantation. DEBs offer a theoretical advantage in side branch treatment, where stent placement may be avoided. The PEPCAD V study demonstrated the feasibility of DEB use in bifurcation lesions, although concerns regarding late thrombosis particularly with adjunctive BMS were noted[9]. The BEYOND trial further suggested improved angiographic outcomes when DEB was used in the side branch compared to conventional balloon angioplasty[10]. Despite these encouraging findings, DEB remains an adjunctive tool rather than a primary strategy in bifurcation PCI. The role of DEB in acute coronary syndrome (ACS) is limited and remains inadequately defined.

ACS lesions are characterized by:

- High thrombus burden
- Plaque instability
- Need for immediate and sustained luminal gain

In such settings, the absence of a scaffold becomes a critical limitation. Unlike DES, DEBs do not provide structural support or plaque sealing, increasing the risk of acute vessel closure. Current evidence does not support routine DEB use in ACS, although it may be considered in selected cases, particularly ISR presenting as ACS. The utilization of DEBs in CTO-PCI have substantially increased, benefiting the CTO PCI mainly due to absence of vessel scaffolding. However, there are limitations to its usage such as the risk of recoil due to the high plaque burden of CTO lesions, flow-limiting dissections after preparation, and lack of standardized sizing criteria for DEBs. Besides the theoretical advantage of DEBs in CTO-PCI, the current evidence is inadequate, with no large-scale randomized controlled trials directly comparing DEBs with DES in CTO PCI[11, 12].

Few retrospective and prospective studies done comparing DEBs and DES in CTO-PCI demonstrating no clear differences between DEBs and DES in terms of TLR, MACE, cardiovascular mortality and ischemic endpoints, signifying that DEB-based revascularization strategy may be an acceptable alternative in meticulously prepared CTO lesions in order to combat stent related complications. Keeping in mind the diversity of CTO lesions, a hybrid revascularization strategy with DES and DEB is the best approach to optimize the outcomes in selected patients. To establish the definite role of DEB in CTO PCI a large randomized trials are warranted[13-17].

Despite its advantages, several limitations hinder the widespread adoption of DEB:

- Lack of scaffolding leading to recoil and dissections
- Operator dependence, requiring meticulous lesion preparation
- Heterogeneity in drug delivery and balloon technology
- Limited efficacy in complex lesions (calcified, long, thrombotic)
- Continued reliance on paclitaxel, with ongoing debate regarding safety in peripheral interventions

These limitations prevent DEB from replacing DES as the default PCI strategy. Emerging technologies may redefine the role of DEB:

- Sirolimus-coated balloons, offering improved pharmacokinetics
- Enhanced drug delivery systems and excipients
- Hybrid PCI strategies combining DES and DEB

With these advancements, DEB may evolve from a niche therapy into a broader therapeutic option. Drug-eluting balloons represent one of the most conceptually elegant innovations in interventional cardiology. Their ability to deliver effective antiproliferative therapy without leaving a permanent implant aligns with the ideal of vascular restoration. However, until their inherent limitations are addressed, DEBs will remain confined to selected indications most notably ISR. Thus, they continue to embody a paradox within contemporary PCI: a powerful yet imperfect technology the Achilles' heel of interventional cardiology.

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