EuroIntervention 2023;19:e882-e883 published online e-edition December 2023

The longest way round is the shortest way home: drug-coated balloons for long lesions in large coronary arteries

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Despite the initial pivotal studies of percutaneous coronary intervention (PCI) with drug-coated balloons (DCB) 15 years ago, strong evidence for the use of DCB still remains limited to in-stent restenosis (ISR), for which PCI with DCB is a class Ia recommendation. Treatment of *de novo* disease with DCB could be advantageous in vessels with diffuse disease, high bleeding risk patients, and patients with acute coronary syndrome, yet evidence is scarce, and the use of DCB is mainly reserved for the treatment of lesions in small vessels[1]. The treatment of large vessels (≥3.0 mm in diameter) is distinct to that of small coronary arteries owing to a larger subtended myocardial territory, greater plaque volumes, calcification, and bifurcations. Evidence demonstrating the feasibility of performing angioplasty with DCB in such vessels is lacking.

In the current issue of EuroIntervention, Leone and colleagues report short- and medium-term follow-up of patients treated with DCB for long *de novo* coronary lesions in large vessels[2]. In this retrospective observational study from 2 recruiting centres in Italy, an analysis was conducted of 93 patients and 100 PCI with DCB in vessels ≥3.0 mm in diameter with a mean treated length of 45 mm. PCI with DCB alone was undertaken in 70% of lesions, DCB and bailout PCI with drug-eluting stents (DES) was performed in 6%, and a planned hybrid procedure of PCI with DCB and DES was performed in the remaining lesions. Within the mean follow-up of 350 days, an overall target lesion failure (TLF) rate of 5.1% was observed, with no cardiac death or target vessel myocardial infarction.

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This study highlights the feasibility and safety of performing PCI with DCB in large vessels with long lesions, albeit in a small and very select group of patients (100 lesions in 2 centres over 2 years). However, information pertaining to the types of lesions treated with DES at the 2 centres during the study period and the specific criteria that led to the choice of DCB treatment in this context would have been very relevant to better understand the scope of the data. Furthermore, no information was provided about the criteria for selecting full DCB versus the hybrid approach. The authors state that the lesions in the hybrid strategy group tended to be longer, but no information on vessel size or plaque composition was provided (i.e., was a hybrid approach with DES used in more proximal lesions in larger vessels?).

The primary finding was that PCI with DCB in large vessels with long lesions is feasible, with a low proportion of patients requiring bailout PCI with DES (6%). This is far lower than has been observed in previous studies. Potential explanations for this might be related to the different criteria used to determine if a stent was needed, as well as the use of intracoronary imaging and physiology to determine the need for stenting in non-flow-limiting type C-E dissections. The value of functional assessments in the acute context of dissections generated by balloon inflation requires further evaluation.

The second finding was the reported TLF rate of 5.1% at 12 months for the combined patient cohort. Whilst this overall event rate is similar to previous studies, the co-authors separated the TLF rate by treatment group, which revealed a TLF rate of 1.5% in those treated with DCB versus 10.7% in the hybrid DCB and DES group. As previously mentioned, there is a lack of information on the characteristics of the lesions selected for each strategy, but the groups might have been

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DOI: 10.4244/EIJ-E-23-00043

Table 1. Ongoing studies relating to DCB use in *de novo* CAD.

Study name	Completion	Population	n	Study type	Endpoints	Study aims
SELUTION DeNovo NCT04859985	2024 (Est.)	– *De novo* disease – CCS	3,326	Prospective, randomised, controlled trial	– TVF at 12 months	– 1:1 randomisation of SELUTION SLR (MedAlliance) DCB or DES. – Powered for 12-month TVF non-inferiority versus DES.
TRANSFORM II NCT04893291	2024 (Est.)	– *De novo* disease – CCS and ACS	1,820	Prospective, randomised, controlled trial	– TLF at 12 months	– 1:1 randomisation of sirolimus-coated DCB versus everolimus-eluting stent – Powered for 12-month TLF non-inferiority versus DES
CAGE-FREE III NCT05209412	2024 (Est.)	– *De novo* disease – CCS and ACS	370	Prospective, randomised, controlled trial	– FFR at 12 months	– 1:1 randomisation of paclitaxel-coated DCB versus zotarolimus-eluting stent
DCB-LVD NCT05550233	2024 (Est.)	– *De novo* disease – CCS and ACS	240	Prospective, randomised, controlled trial	– LLL at 12 months	– 1:1 randomisation of DCB versus DES – Reference vessel diameter ≥3.0 mm
UNIQUE-DCB-I NCT04104854	2024 (Est.)	– *De novo* disease – CCS and ACS	220	Prospective, randomised, controlled trial	– LLL at 12 months	– QFR-guided PCI with DCB or DES (1:1 randomisation)
LARGE-ONE NCT05961787	2025 (Est.)	– *De novo* disease – CCS and ACS	134	Prospective, randomised, controlled trial	– LLL at 13 months	– 1:1 randomisation of SeQuent Please (B. Braun) DCB versus Firehawk (MicroPort) DES – Reference vessel diameter ≥3.0 mm

ACS: acute coronary syndrome; CAD: coronary artery disease; CCS: chronic coronary syndrome; DCB: drug-coated balloon; DES: drug-eluting stent; Est: estimated; FFR: fractional flow reserve; LLL: late lumen loss; PCI: percutaneous coronary intervention; QFR: quantitative flow ratio; TLF: target lesion failure; TLR: target lesion revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation

significantly different (i.e., a longer lesion length in the hybrid group), therefore no conclusions can be derived from these data. The hybrid approach seems to be an attractive strategy in the context of diffuse disease, which includes patients with worse prognosis and for whom the optimal treatment options are not well established.

Another significant caveat of the present study is the use of different types of DCB, which are mainly -limus based. DCB efficacy is influenced by drug dose, formulation, and release kinetics, with comparative studies demonstrating the lack of a class effect. It is therefore difficult to draw any conclusions for such a small patient cohort.

In summary, in this small observational retrospective study, the use of DCB in large coronaries with long lesions, with or without hybrid PCI with DES, was feasible and appears to be safe. Ongoing randomised studies **(Table 1)** are eagerly awaited to determine the role of DCB for the treatment of *de novo* coronary disease and will address some of the criticisms highlighted herein.

Conflict of interest statement

N. Gonzalo has received research grants from Abbott; and speaker and consultancy fees from Abbott, Boston Scientific, Philips, Abiomed, and Shockwave Medical. A. Shabbir has received speaker fees and honoraria from Philips and iVascular.

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