BASKET-SMALL 2: advancing DCB beyond in-stent restenosis

Drug-coated balloons (DCB) were first used as a new therapeutic option in the treatment of in-stent restenosis, with proven inhibition of restenosis in clinical studies.[1–3] DCB have received a class 1 indication in the 2014 European Society of Cardiology guidelines[4] for the treatment of both bare metal stent (BMS) and drug-eluting stent (DES) in-stent restenosis. The next question is whether DCB are effective in de-novo coronary lesions, specifically in small coronary vessels.

Percutaneous coronary intervention (PCI) in small coronary vessels (defined as <3·0 mm in diameter) is associated with an increased rate of restenosis and lesion failure[5] because PCI is less capable of accommodating neointimal growth after stenting in small vessels than it is in large vessels. Several studies (mostly registries)[6,7] have evaluated the use of DCB in small vessels, but there is a scarcity of robust data from randomised controlled trials.[8,9]

In *The Lancet*, Raban V Jeger and colleagues[10] present the results of the BASKET-SMALL 2 study. The investigators evaluated whether DCB were non-inferior to second-generation DES in an all-comer population with small coronary vessels and indication for PCI. Their primary endpoint was the 12-month composite clinical endpoint of major adverse cardiac events (MACE), consisting of cardiac death, non-fatal myocardial infarction, and target vessel revascularisation.

To our knowledge, this is the largest prospective study conducted to evaluate the use of DCB in small coronary vessels. The investigators should be commended for doing this study because, in daily practice, at least 30% of PCI involve small coronary vessels. It is also not easy to recruit patients for a trial like this one, especially when the interventional cardiology community's predominant practice is to stent.

Over 6 years (2012–17), 758 patients with small vessel disease were randomly allocated to receive treatment either with paclitaxel-coated balloon or one of two second-generation DES (paclitaxel-eluting stent in the initial phase, then everolimus-eluting stent). Lesion preparation was mandatory and randomisation was only possible if angiographic criteria were met (no high-grade dissection, no reduced blood flow, and residual stenosis ≤30%).

The rate of MACE after 12 months did not differ between the two groups (7·3% for DCB *vs* 7·5% for DES, p=0·9180). Further, the individual components of the primary endpoint did not differ between the two groups (DCB *vs* DES: cardiac death 3·1% *vs* 1·3%, p=0·1131; non-fatal myocardial infarction 1·6% *vs* 3·5%, p=0·1123; and target vessel revascularisation 3·4% *vs* 4·5%, p=0·4375).

In PCI, DCB is thought to have several advantages over DES because it inhibits excessive neointimal hyperplasia after balloon angioplasty without leaving a permanent metallic frame (thus there is potential for favourable vascular remodelling), eliminates the risk of stent thrombosis, and reduces the duration of dual antiplatelet therapy. Paclitaxel is the drug of choice for most of the available DCB because of its highly lipophilic properties and sustained antiproliferative effect, despite its short contact with the vessel wall.

Jeger and colleagues emphasise the need for optimal lesion preparation according to established consensus group recommendations[11] to obtain favourable outcomes from DCB. Flow-limiting coronary dissection can occur as a result of ballooning, and acute closure of the vessel remains one of the most dreaded complications. With sound knowledge on the different grades of coronary dissection,[12] one can carefully select patients that are suitable for DCB angioplasty. In the present study, no patients had acute closure of the target vessel after PCI.

The study has several limitations. Patients in the DES group had a mixture of paclitaxel and everolimus-based stents (ratio of 1:3), which might have affected clinical outcomes. The investigators adjusted for the change in DES by increasing the sample size. In addition, all patients in the study received treatment with paclitaxel and iopromide-coated DCB and their results could only be extrapolated to those who received similar therapy. There is also a scarcity of routine angiographic follow-up in the study, which might lead to an underestimation of event rates. Finally, there was no routine core-laboratory analysis of the angiographies at baseline and at follow-up.

In summary, the BASKET-SMALL 2 study found that paclitaxel and iopromide-coated DCB were non-inferior to second-generation DES, with similar MACE rates seen at 12 months for both groups. This finding supports the use of DCB beyond in-stent restenosis (ie, in small native coronary artery disease).

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We declare no competing interests.

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