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Debate. Drug-coated balloons for de novo coronary artery lesions. Still not enough evidence, and the new drug-eluting stents are still better

A debate. Balones liberadores de fármaco para lesiones coronarias de novo. *Todavía no hay suficiente evidencia y lo mejor son los nuevos* stents *farmacoactivos*

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Question: What is the evidence available on the use of drug-coated balloons (DCB) in the de novo lesion setting?

Answer: Currently, the evidence on the use of DCB to treat de novo coronary artery lesions is limited. I'll be focusing on the following randomized clinical trials that compared the use of iopromide-based paclitaxel-coated balloons with second-generations stents in the novo coronary artery lesions. The BASKET-SMALL trial 2[1] included 758 patients with de novo stenosis in vessels with diameters < 3 mm. The study primary endpoint was a composite of major adverse cardiovascular events (MACE) at 12 months. Patients were randomized to receive a DCB or a drug-eluting stent (DES); 25% were first-generation (TAXUS, Boston Scientific, United States) and 75% second-generation stents (Xience, Abbott, United States). The rates of MACE were similar in both groups at 12 months (7.5% for the DCB vs 7.3% for the DES; HR, 0.97; 95%CI, 0.58-1.64; *P* = .9180). These results still stand at 3-year follow-up (a 15% rate of MACE for both DCB and DES; HR, 0.99; 95%CI, 0.68-1.45; *P* = .5).[2] Similarly, this trial found no differences in MACE among the following clinical settings: diabetes,[3] chronic kidney disease,[4] high risk of bleeding,[5] and acute coronary syndrome.[6] Clinical benefits can be described in very small caliber vessels (< 2.5 mm) according to 1 of the substudies.[7] The PEPCADN-STEMI trial[8] included 210 patients with non-ST-segment elevation acute coronary syndrome and 1 culprit lesions without evidence of thrombus. Patients were randomized to receive DCB (N = 104) or stent (N = 106; 56% of them were treated with conventional stents vs 44% who were treated with DES). A total of 15% of the patients from the DCB group received a bailout stent. At 9 months, the rate of target lesion failure was similar in both groups (3.8% for the DCB vs 6.6% for the DES; intention-to-treat analysis, *P* = .53). The REVELATION trial[9] randomized 120 patients with ST-segment elevation acute myocardial infarction with not heavily calcified de novo coronary artery lesions and residual stenosis < 50% after predilatation to receive DCB or DES. The study main primary endpoint was fractional flow reserve at 9 months in the infarct-related artery. A total of 11 patients (18%) from the DCB group required stenting. Fractional flow reserve estimated at follow-up was similar between both groups: 0.92 ± 0.05 in the DCB group and 0.91 ± 0.06 in the DES group; *P* = .27.

Recently, other DCBs with formulations from limus-type drugs—sirolimus and biolimus—have been assessed. Therefore, the BIO-RISE trial[10] included 206 patients with de novo lesions in small vessels (between 2.0 mm and 2.75 mm) who were randomized on a 1:1 ratio to receive a conventional balloon or a biolimus-coated balloon. At 9 months, late lumen loss was significantly lower in the DCB group (0.16 mm ± 0.29 mm vs 0.30 mm ± 0.35 mm; *P* = .001). Similarly, positive remodeling was described in 29.7% of the patients from the DCB group vs 9.8% of the patients from the conventional balloon group; *P* = .007). Finally, the randomized clinical trial SCBDNMAL[11] compared a crystalline sirolimus-based DCB with a iopromide-based paclitaxel-coated balloon (SeQuent SCB, B. Braun Melsungen, Germany [4 µg/ mm^2] vs DCB SeQuent Please, B. Braun Melsungen, Germany [3 µg/ mm^2]) in 70 patients with de novo lesions. At 6 months, late lumen loss was 0.01 mm ± 0.33 mm in the paclitaxel group vs 0.10 mm ± 0.32 mm in the sirolimus group (95%CI, from -0.07 to 0.24). Negative late lumen loss was described indicative of positive remodeling with a greater frequency in the paclitaxel based DCB group (60% vs 32%; *P* = .019).

Q.: Do you think there is enough evidence to recommend their use in the routine clinical practice?

A.: At this point, evidence indicates that DCB can play a role to treat de novo lesions in small vessels. However, several premises should be taken into consideration. The landmark studies upon

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which this indication should stand are those where the comparison stent should be a latest generation stent. Therefore, evidence from trials that compared the use of DCB vs conventional stents or first-generation DES should not be extrapolated to the current situation. Secondly, when the DCB strategy is analyzed in the de novo lesion setting, optimal lesion preparation should precede without flow-limiting dissections and residual stenosis of 30% at most.[12] Only then the use of DCB is advised. We should remember that stents were designed to solve the potential risk of acute vessel occlusion after balloon predilatation and that, incidentally, it also reduced the rate of restenosis. In this sense, like we have already seen in former studies, there will always be a percentage of lesions that will eventually need stenting as a bailout strategy after predilatation. Thirdly, the type of balloon, type of drug used, formulation, and release are much more relevant when treatment with DCB is planned. Obviously, not all DCBs are the same in this setting, which means that the results from 1 study with a certain type of DCB shouldn't be extrapolated to another DCB with a different formulation or drug release system. Finally, when dealing with de novo lesions the characteristics of these should be known such as calcifications, thrombus, size of the vessel, length, clinical syndrome, etc.

Therefore, while we await the results of the ongoing clinical trials[13] we can use iopromide-based paclitaxel-coated balloons to treat de novo stenoses in small vessels after optimal lesion preparation for the lack of significant traits of risk of acute vessel thrombosis (lack of significant residual dissection, flow-limiting, etc.).

Q.: Do you think that there are differences in the results obtained from the studies and in the level of evidence according to the size of the target vessel?

A.: To know the exact role of sirolimus-based DCBs in the management of de novo coronary lesions is still premature.[14] In such a hydrophilic drug, dose, formulation, and release are crucial to define its potential. Therefore, results can vary tremendously based on whether we're dealing with phospholipid encapsulated sirolimus or a crystalline coating, for instance. Regarding the size of the vessel, the use of the DCB is spared for small caliber vessels (< 3 mm), and, among them, it seems like very small caliber vessels (< 2.5 mm) are the ones that can benefit the most from its use.[7]

Q.: In which cases would you consider using DCBs to treat de novo coronary artery lesions?

A.: Like I said before, the current evidence available supports its use to treat small caliber coronary vessels, and with a certain type of DCB only (iopromide-based paclitaxel-coated balloons, 3 µg/mm^2).

Q.: What is the predilatation protocol, cross-over criteria, and specific DCB treatment technique in this setting?

A.: I use the DCB-only strategy, which involves good target vessel preparation, obtaining good angiographic results without clinically relevant residual dissections, and residual stenosis < 30%. It is in this setting where the bailout stent is not necessary that I use the DCB.

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CONFLICTS OF INTEREST

M. Sabaté is a consultant for Abbott Vascular and iVascular.

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