

INVITED COMMENTARY

Are All DCBs Created Equal?

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The paper by Boitet et al.¹ is timely, given the problems with below knee (BTK) drug coated balloons (DCBs), and concerns over increased amputations in those patients treated with the Amphirion DCB (Medtronic Inc. Minneapolis, MN, USA) leading to device recall and stoppage of the IN.PACT DEEP trial,² though causal links could not be established. This study indicates the In.Pact balloon has the highest amounts of paclitaxel (PTX), but what that amounts to in this context remains unknown. Studies suggest that DCBs are superior to drug eluting stents (DESs) in terms of the primary objective, i.e. reducing neointimal hyperplasia,³ yet most of the positive results seem to come from studies that typically focus on the femoropopliteal segment. In fact, there are only marginally positive results for BTK DESs (including coronary DES usage) vs. plain old balloon angioplasty,⁴ though with little effect on overall survival in (diabetic) patients with critical limb ischaemia⁵ as might be expected.

Overall the paper is written very systematically, examining five typical DCBs providing comparable sizes against a standardised protocol, with nice graphics and acknowledged limitations, but there are indeed some points to ponder.

The authors have looked for deposition in muscle but concern has been raised regarding patients with ulcers and what happens if PTX is deposited in those tissues as well;³ that scenario has not really been factored in alongside the typical endpoints. This is not just because of arteriolar obstruction as the authors suggest but also potentially linked to the anti-mitotic effect of PTX itself. Setting that scenario up experimentally will be challenging and this may therefore need tissue sampling from actual patients. The next step will be to learn if the DCBs that result in higher PTX embolisation actually then result in delayed or indeed worsened ulcer healing.

While it would be acceptable to aim for consistency in the test material in an experimental scenario, i.e. a 4 × 40 mm balloon, there is no control for the real life scenario wherein much smaller DCBs are used in the crural vessels with the Ranger (Boston Scientific, Hemel Hempstead, UK) dropping down to a 2 mm diameter. Simplistic mathematical comparisons suggest a smaller amount of PTX would be lost as emboli, but there is a complex consideration of the interplay of PTX formulation/deposition, type of excipient, duration of inflation, base dose, and retained/delivered dose for instance,³ which is highlighted well by the authors. We therefore have no insights that a smaller balloon would result in less PTX embolisation, and lacking that as a control in their study is a missed opportunity.

Looking at the results, it would therefore seem that the most distal tissue concentrations were consistently lowest for the Ranger balloon, but there was no difference in the concentrations of PTX in

the muscular arterioles. There was little difference in PTX concentrations in the proximal muscles, suggesting that “leftover” particles then tend to migrate to the most distal arteriolar bed. The authors inform us that there was no real difference in the small arteriolar deposition between the DCBs and this might be somewhat reassuring, but conflicts with the result for the tibialis anterior.

There seemed to be PTX loss into the plasma with the Lutonix balloon (Bard Peripheral Vascular, Inc., Tempe, AZ, USA) without necessarily translating into distal embolisation, suggesting issues with the bonding and nature of the PTX nanocrystals, and the discrepancy against aortic levels may simply reflect the hepatobiliary clearance of PTX; this also suggests proportionately deficient PTX delivery to the vessel wall, again undesirable. Drug loss in such a fashion becomes relevant given the recent concerns with increased mortality relating to use of drug eluting technology in general.⁶ The higher concentration of PTX on the In.Pact balloon results in higher loss into the proximal muscles, with also higher remnant PTX on the DCB itself, neither of which is desirable. In terms of deposition rates, again the Ranger balloon seems to deposit maximum PTX into the target vessel wall.

This paper thus clearly highlights inconsistencies that suggest all DCBs are not created equal; most vascular interventionists tend to settle on a “DCB of choice” but as more of such data keeps coming in, hopefully with correlation from human data to support or refute such experiments, they will need to ponder their choices for the future.

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