



Treatment of in-Stent Restenosis - What is Important in the Interest of the Patient?

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Despite the very low restenosis rates of modern drug eluting stents (DES), interventions on narrowed coronary stents represent more than 10% of all percutaneous coronary interventions. These recurrences pose a challenge because primary stent therapy has failed in this situation. Accordingly, these lesions represent a distinct negative selection, especially when in-stent restenosis (ISR) after DES is involved. A network meta-analysis identified the implantation of an everolimus eluting stent (EES) or the use of a drug coated balloon (DCB) as the two most effective measures to reduce recurrence within the first year [1]. A patient level meta-analysis presented last year at EuroPCR reported a slightly higher target lesion revascularization rate (TLR) after DCB with concomitant reduction of hard clinical endpoints such as death and myocardial infarction by the use of paclitaxel coated balloons as compared to DES in ISR treatment [2].

The results of the meta-analysis presented here by Elgendy et al. basically confirm these findings. The authors focus on the comparison of DCB with EES in 5 randomized studies, and especially on the repeated revascularizations. After one year there was no significant difference in the frequency of target vessel revascularization (TVR). After 3 years, however, a significant advantage for EES is reported [3]. However, it must be critically noted that only the two studies that showed increased TVR rates in the DCB group even after one year were evaluated here (RIBS IV [4] and V [5]). Unfortunately, the already published 3-year data of the TIS study, in which higher TVR rates were found in the EES group (22% versus 13% after DCB), is not included [6]. The long-term data of the two other trials included have not yet been

published. Therefore, the main conclusion of the present analysis, that DCB are associated with a higher TVR after 3 years, is possibly based on a selection bias.

Another point of criticism relates to the underlying methodology. No analysis at patient level was performed. Instead, the published event rates were divided by the intention to treat number of patients, which does not sufficiently consider the influence of cross-over between groups and lost to follow up. In the past, such an approach has raised doubts about the safety of sirolimus DES [7,8] involving vigilance by regulatory authorities, which could not be reproduced in patient level analyses [9]. Analogous points of criticism (selection bias in longer follow-up, no patient level data, lack of attention to cross-over and lost to follow-up) also apply to the currently much discussed meta-analysis by Katsanos et al. about paclitaxel coated devices in the field of peripheral interventions [10].

An interesting finding from ISAR DESIRE III [11] as well as RIBS IV [4] and V [5] is the different handling of therapy failure after DES or DCB for ISR treatment. The willingness for reintervention appears to be significantly lower in the presence of several stent layers than after DCB angioplasty. This automatically leads to an overestimation of the clinical endpoint of revascularization, which at least partly explains the significant difference in the major adverse cardiac events in RIBS IV [12] after one year. On the other hand, this means that DCB leaves more therapeutic options open for ISR treatment. The disadvantage of DCB in the endpoint of repeated revascularization paradoxically means an advantage for the patient. Irrespective of this, the quality of lesion preparation in DCB angioplasty has a relevant influence on repeated revascularization [13]. The mechanical work including correction of a possibly incomplete stent deployment has to be done here. The criteria for an acceptable result of lesion preparation are the absence of flow limiting dissections and a maximum diameter stenosis of 30% [14].

There remains the question of the long-term outcome after ISR therapy. In this case, DCB therapy alone offers theoretical advantages by avoiding further stent layers and thus a reduced thrombotic risk [14]. In comparison to first-generation DES, there is also evidence of a reduction in the hard endpoints such as death and myocardial infarction [2,11]. Further long-term data in comparison to current generation DES remain to be awaited. The evaluation of the different therapy modalities in the long-term course should not be limited to the question of repeated revascularization but should include hard endpoints such

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as death, myocardial infarction or stent thrombosis. The patient's first interest is probably in having to undergo a new intervention as rarely as possible. However, the desire to survive without myocardial infarction or stent thrombosis is probably more fundamental. All arguments here are against several metal layers and clearly in favor of DCB.

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