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Absorb BRS for in-stent restenosis: the final bow before (scaffold) collapse?

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Restenosis in drug-eluting stents (DES) complicates 3%–8% of procedures at 1 year, 8%–15% at 2 years and 8%–31% at 10 years. [1 2] Restenosis after plain-old balloon angioplasty (POBA) is due to negative remodelling, while restenosis after bare metal stent (BMS) is mostly related to neointimal hyperplasia. However, restenosis after DES is due to the combination of neointimal hyperplasia and early neoatherosclerosis.[3] Putative causes for restenosis after DES include mechanical factors, such as miss, gap, polymer peeling, media barotrauma, stent underexpansion, platform fracture or inhomogeneous strut distribution, and biological factors, such as hypersensitivity reactions or drug resistance. DES restenosis is dynamic, spanning from focal (<2 years) to a diffuse pattern (>5 years). This differs from restenosis after BMS, and unfortunately, is more difficult to treat.

Treatment options include POBA with conventional balloon, scoring balloon, cutting balloon, paclitaxel (or sirolimus)-eluting balloon and placement of a new DES or coronary artery bypass graft surgery. Laser and intracoronary endobrachytherapy have gradually been abandoned. Current European guidelines favour the implantation of a new DES or the use of drug-eluting balloons.

In this issue of the journal, Madanchi *et al* present an alternative treatment: the implantation of a bioresorbable vascular scaffold (BRS).[4] BRS was designed to provide a temporary mechanical support, thought to increase lumen size and flow, while disappearing over time (around 3 years) in the hope of restoring vasomotor tone and normal coronary physiology. In theory, late lesion and metallic stent-related events should be mitigated. Eight years ago, the implantation of BRS in DES restenosis made sense since the platform guaranteed a good immediate angiographic result with no additional metallic layer on the long run. Several trials were initiated but, since the retrieval of BRS from the market, none have been published so far.

Indeed, despite reassuring initial reports and short-term outcomes, concerning issues rapidly emerged. In a combined analysis from the ABSORB trials with 3-year follow-up, significant increases in the risk of target vessel myocardial infarction and target lesion revascularisation (TLR), as well as early and late scaffold thrombosis (ST), were observed compared with contemporary DES.[5] Dedicated implantation protocols improved the risk of TLR,[6 7] but ST remained a concern, and no benefit, such as restored vasoreactivity, could be demonstrated.[8] Although BRS did not survive these disappointing results, long-term outcomes are paramount and still need to be analysed as potential positive effects would be expected once the platform is completely resorbed.

In the 5-year follow-up of the ABSORB III trial, target lesion failure was 17.5% vs 15.2% for DES (p=0.15). However, target vessel myocardial infarction (10.4% vs 7.5%; p=0.04) and ST rates (2.5% vs 1.1%; p=0.03) were higher. As suspected, a time dependency, from 3 years onwards, was observed where the Absorb BRS displayed similar outcomes to DES, and the ischaemic complications seemed to subside. An important caveat is that 42.8% of patients continued dual antiplatelet therapy until 5 years.[9]

Other trials with long-term follow-ups have reported acceptable outcomes such as the ABSORB JAPAN trial, in which TLR was 10.2%, TVR 15.0%, and no different to DES with no ST observed from 3 years onwards.[10] In the Everbio-2 trial, 5-year outcomes were similar between BRS and other DES with target vessel myocardial infarction rates of 4% and TLR rates of 19%.[11]

Linked

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Thus, the appealing concept of a dissolving device has invariably translated into disappointing clinical results up to 3 years, and unfortunately, no clear advantage beyond that.[12]

WHAT ABOUT BRS IN TREATING RESTENOSIS AFTER DES?

The evidence relies on the Lucerne experience,[4] and the authors should be congratulated for filling the gap and providing a rigorous, single-centre observation in 89 patients over a median of 5-year follow-up. Lesions were complex, as 73% had diffuse, proliferative and even occlusive restenosis making comparisons with contemporary trials very hazardous. Although the initial outcomes were encouraging, they observed a steep rise in target vessel revascularisation (TVR) and TLR from 1 year onwards, peaking at a staggering 48% and 44% at 5 years, respectively. The rates of ST were high and continued to increase over the follow-up period, peaking at a cumulative rate of 8.4%. These rates are significantly higher than other contemporary trials assessing in-stent restenosis treatment with either drug-coated balloons or DES.

Patients with restenosis are at higher risk of recurrent events, either from an inherently aggressive form of coronary artery disease, suboptimal cardiovascular risk factor management, or anatomical and procedural issues. That a high-risk patient population such as the one studied did poorly on the long term is no surprise. How much worse did they do because of BRS implantation is uncertain?

The study highlights the singularity of in-stent restenosis and hints once again towards different pathophysiological processes compared with de novo atherosclerotic coronary artery disease.

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