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Drug-eluting stents for saphenous vein graft lesions: useful or harmful?

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Percutaneous treatment of atherosclerotic lesions in degenerated saphenous vein grafts (SVG) is an unresolved issue of growing importance and an ongoing challenge for interventional cardiologists. Given the demographic changes in Western societies with the estimated percutaneous coronary intervention (PCI) rate of 1 to 2% of patients per year within the first five years after coronary artery bypass graft surgery and 4% of patients per year subsequently[1], the number of patients undergoing SVG PCI might increase to as much as 15% of the work load in some centres[2]. Degenerated vein grafts have a specific pathophysiology with large, soft, friable plaques. These plaques are concentric and diffuse, contain inflammatory infiltrates but lack a fibrous cap, develop early after surgery due to surgical trauma, loss of intrinsic vascular supply and repetitive abrupt increases in wall stress, and are present in almost half of SVG after 11 years[1]. Current interventional treatment of SVG lesions includes the use of distal filter devices, while the role of bare metal stents (BMS) is less well defined due to their limited efficacy in preventing clinical endpoints[3]. Long-term outcome after interventional treatment of SVG lesions remains poor, primarily due to the high incidence of in-stent restenoses and atherosclerotic disease progression. These changes may respond favourably to the antiproliferative and immunosuppressive effects of drug-eluting stents (DES) because of their proven efficacy in reducing intimal hyperplasia and the incidence of in-stent restenoses for selected lesions. However, DES have not been tested for SVG lesions in major randomised controlled trials, since such lesions usually represent an exclusion criterion for enrolment. In this issue of EuroIntervention, Brilakis et al report a systematic review on the efficacy and safety of different stent types in SVG lesions[4]. In their overview, the authors compile data from 30 retrospective and three prospective studies that mainly compared DES vs. BMS regarding angiographic and clinical outcome. Most studies with data available reported smaller late lumen loss and a lower rate of target vessel or lesion revascularisation for DES compared with BMS, while rates of clinical endpoints usually were similar for both stent types. The authors conclude that DES decrease late loss and angiographic restenosis and appear to be safe in SVG PCI with similar rates of death, myocardial infarction, and stent thrombosis. Should we settle for this, or is there a reason for any justified doubts?

As reported by Brilakis et al, current knowledge on the interventional treatment of SVG lesions primarily is based on retrospective data with only short- to intermediate- term follow-up. In most of these studies, late lumen loss and rates of target vessel or lesion revascularisation were lower for DES than for BMS, while rates of clinical endpoints, such as death or myocardial infarction, were similar as this may have been expected. Only two small randomised controlled trials in the field have been performed so far, the Reduction of Restenosis In Saphenous vein grafts with Cypher sirolimus-eluting stent (RRISC) study[5] and the Stenting Of Saphenous vein grafts (SOS) trial.[6] The SOS trial enrolled 80 patients and showed that paclitaxel-eluting Taxus® stents compared with BMS had lower rates of target lesion revascularisation after a follow-up time of 1.5 years (5% vs. 28%; p=0.003) with similar rates of non-fatal myocardial infarction and death (15% vs. 31%; p=0.08 and 12% vs. 5%; p=0.27 respectively)[6]. The RRISC study[5] and its sequel, the observational DELAYED RRISC study[7], enrolled 75 patients and showed that sirolimus-eluting Cypher® stents compared with BMS were able to reduce late lumen loss

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(0.38±0.51 mm vs. 0.79±0.66 mm; p=0.001) with lower rates of target vessel revascularisation (5.3% vs. 27%; p=0.012) after six months. However, after a median of 32 months the difference in target vessel revascularisation had disappeared with rates that were similar in both stent groups (34% vs. 38%; p=0.74).[7] Of much more concern than this catch-up phenomenon is the fact that long-term all-cause mortality rates were much higher in DES than in BMS patients (29% vs. 0%; p<0.001); in other words, 11 of the 38 DES patients died during follow-up (seven due to cardiac causes, which included four due to definite or probable late stent thromboses), while all 37 BMS patients survived. Of course, this alarming finding could only be a play of chance since the trial was not powered for mortality, but it may just as well be due to a possible excess of late stent thromboses in patients treated with DES that might have contributed to this result.

Late stent thrombosis is a rather rare, but often disastrous event, specifically after DES implantation, that carries a mortality rate of up to 45% and a rate of non-fatal infarction of another 40%[8]. In native vessels, the primary pathophysiological mechanism related to late stent thrombosis is the lack of incomplete endothelial coverage of stent struts associated with persistence of fibrin deposits. Since endothelial healing after DES implantation might be even more delayed in SVG than in native vessels, the rate of late stent thrombosis could be higher in this type of lesion. While the annual event rate in native vessels has been estimated to be 0.6%[9], the actual numbers for SVG disease are not known due to limited data and rather short follow-up time in most registries.

Notwithstanding these relevant concerns, DES have a proven efficacy in preventing restenoses. Despite the hostile atherosclerotic milieu in degenerated SVG, DES are able to reduce clinical events, mainly repeated revascularisation, to the extent of those in native vessels[10]. This proven advantage must be counterbalanced against the potential harm of late stent thromboses. Based on current data, however, no recommendations regarding the use of DES in SVG PCI can be given. The balance between the prevention of in-stent restenosis and the risk of late stent thrombosis might be different in SVG than in native vessels, but only large-scale randomised controlled trials with an adequate long-term follow-up, such as the two ongoing randomised studies, the BAsel Stent Kosten Effektivitäts Trial – SAphenous Venous graft Angioplasty using Glycoprotein IIb/IIIa receptor inhibitors and drug-Eluting stents (BASKET-SAVAGE) and the Efficacy Study of Drug-Eluting and Bare Metal Stents in Bypass Graft Lesions (ISAR-CABG) patients undergoing SVG PCI will give us evidence where this line has to be drawn.

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