

Stenting of Saphenous Vein Grafts with Drug Eluting Stents – Maybe Not as Good as in Native Vessels

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Since the introduction by Floyd Loop at the Cleveland Clinic of the internal mammary artery (IMA) as an arterial graft to bypass the left anterior descending artery (LAD), it has been the gold standard conduit for revascularization, principally because it demonstrated its potent survival benefit in the long term follow-up.¹ However, patients with multivessel coronary artery disease (CAD) undergoing coronary artery bypass graft (CABG) still required the saphenous vein grafts (SVG) as a bypass conduit to non-LAD coronary arteries and unlike the extremely high durability and patency rates for the LIMA graft, 50% of SVGs develop severe disease or occlusion at 10 years.

Over the last decades, percutaneous coronary intervention (PCI) has offered a less invasive revascularization alternative compared to CABG, particularly for patients with less extensive obstructive CAD. Interventional cardiology has rapidly progressed, with clear improvement of the technique that has permitted the widespread use of stents in more than 95% of interventional procedures, including the treatment of more complex stenosis such as long lesions, small vessels, multivessel disease, and SVGs.²⁻⁵

Currently, PCI of SVG comprise about 10% of all interventional procedures in many centers⁶ and is associated with a higher risk of both emboli-related myocardial infarction (MI) and restenosis, despite major advances in pharmacological and device therapy.⁷ Thus, although drug-eluting stents (DES) vs. bare metal stents (BMS) have shown better outcomes in the treatment of native coronary artery disease,⁵ most major studies excluded or had few patients with SVG lesions, and studies comparing DES vs. BMS in SVG interventions have yielded conflicting results, and most of them do not have long-term follow-up.^{2,7-10}

The article by Collet et al.¹¹ published in this issue of the **Revista Brasileira de Cardiologia Invasiva** provides additional insights into the comparison of DES vs. BMS for the treatment of SVGs, using data from a Registry that included consecutive patients enrolled and divided according to the type of stent deployed (209 with DES and 99 with BMS). The rationale of this study is this lack of large studies with long-term follow-up (> 1 year). The authors found that during hospitalization, there was a trend toward higher major adverse cardiac events (MACE) in the DES vs. BMS group (12% vs. 5.1%, respectively; $P = 0.06$). However, after up to 24 months of follow-up, MACE was equivalent between both groups (17.2% vs. 18.2%, respectively; $P = 0.87$), as was definite/probable stent thrombosis (2.3% vs. 2%, respectively; $P = 0.94$). In conclusion, in this real world series of complex patients, the authors found no long-term safety concerns related to the use of DES in the treatment of SVG lesions, with similar rates of cardiac death/MI/stent thrombosis in both cohorts, but no demonstrable benefit in reduction in subsequent revascularization. Based on the results of the present study and given the post-hoc nature of this paper and the small numbers of patients, firm conclusions may be difficult to draw from the present analysis and larger randomized studies addressing these issues are warranted.

Nevertheless, recent meta-analysis combining randomized and observational studies have suggested benefit from DES vs. BMS in the treatment of SVG lesions.^{2,7-10,12} Hakeem et al.⁹ showed a lower rate of MACE (19% vs. 28%, respectively; $P < 0.00001$), driven by lower rates of death ($P = 0.02$), MI ($P = 0.007$), and target vessel revascularization (TVR) ($P = 0.0002$). There were no differences in stent thrombosis (1% vs. 1.7%, respectively; $P = 0.08$). While a reduction in TVR is plausible, one might wonder how use of a DES instead of a BMS

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might reduce death and MI, leaving open the question as to whether the result was due to concomitant drug therapy or that DES were used in patients with fewer major comorbidities. On the other hand, Lee et al.¹² demonstrated that TVR was lower for SVG intervention with a DES [odds ratio (OR) 0.59, 95% confidence interval (CI) 0.49 to 0.72], with also lower rates of MI (OR 0.69, 95% CI 0.49 to 0.99), but no differences in stent thrombosis or death between both groups. Thus, both studies showed lower rates of TVR.

Another interesting phenomenon seen in some trials that pursued late follow-up is the so called "late catch-up phenomenon" in TVR. This because the initial benefit seen in the first years in TVR is not sustained with longer-term follow-up.¹⁰ TVR after SVG intervention occurs more commonly at untreated sites other than at the target lesion after the first year.⁸ This progression of disease at SVG sites other than the target lesion might account for most of the late TVR.

Another important reason for the lack of benefit of DES to treat SVG is that the pathophysiology of atherosclerosis is different among veins and arteries. Vein grafts are subjected to unique mechanisms of graft failure, such as anastomotic lesions, kinking, and entrapment, in which DES may offer no benefit over BMS. The lack of long-term benefit of DES in SVG lesions is also likely related to a progressive degenerative process that is not necessarily stopped by a very focal or segmental therapy such as stenting. Importantly, once SVGs begin to degenerate, there is a high rate of graft failure and much more rapid progression of disease than in native vessels.^{7,8}

The largest, most important randomized study in this topic is the recently presented ISAR-CABG trial that showed at one-year follow up, that DES group had a 35% lower incidence of the primary composite end point (death, MI, and TLR) compared to BMS group (16.5% vs. 22.1%; $P = 0.028$).¹³ Not surprisingly, this difference was mainly driven by the decrease in target lesion revascularization (7.2% vs. 12.9%; $P = 0.020$) with little difference in other factors comprising MACE. The longer term follow-up of this study should provide better answers to the question of the exact benefits of DES to treat SVGs.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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