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Commentary: Saphenous vein graft patency after coronary artery bypass grafting. It's all about getting the basics right

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CENTRAL MESSAGE

Lack of benefit of lipid-lowering agents on SVG patency in the first year S/P CABG is a reflection of basic mechanism of early graft failure, which is thrombosis rather than atherogenesis.

Optimal efficacy of coronary artery bypass grafting (CABG) remains compromised because of vein graft attrition and progression of native coronary artery disease. A total of 10% to 20% of vein grafts fail at 1 year and almost 50% at 10 years.^{1,2} Despite this dismal performance, the saphenous vein graft still remains the most commonly used conduit for CABG surgery.

Vein graft patency depends on modifiable and nonmodifiable factors, including native coronary artery disease burden, quality of vein, technique of vein harvest, surgical technique, on-pump versus off-pump, use of antiplatelet agents, cholesterol-lowering agents etc.^{3,4} However, it is key to appreciate that the pathogenesis of vein graft failure differs during the first year post-CABG, where it is mainly neointimal hyperplasia, as opposed to the subsequent years, where it is predominantly atherosclerosis.^{3,4}

Surgical harvesting of the saphenous vein results in a loss of continuity of the vasa vasorum that provides nutrition, oxygen, and removes waste products. This results in hypoxemia of the harvested vein and formation of free radicals, predisposing to early vein graft disease.⁵ Furthermore, post-systemic implantation, the vein graft is immediately subjected to the pulsatile arterial system, leading to longitudinal wall (shear) stress.⁶ This causes neointimal hyperplasia. However, this newly formed endothelium is functionally compromised and prone to thrombosis and stenosis.⁷

Beyond the first year of graft implantation, atherosclerosis rather than neointimal hyperplasia becomes the main culprit of vein graft attrition. Essentially, the predisposing factors as well as the process of atheroma formation are the same for vein grafts and native arteries and, like native atheromas, graft atheromas can rupture and cause thrombotic occlusion of the graft.^{8,9}

Based on these differing underlying pathogenic mechanisms for vein graft attrition, several strategies have been proposed to improve vein graft patency post-CABG from antiplatelet agents to lipid-lowering agents.^{10,11} In this issue of the *Journal*, Zhu and colleagues¹² have presented the post hoc analysis of the DACAB (Different Antiplatelet Therapy Strategy After Coronary Artery Bypass Graft Surgery) trial,¹³ in which they demonstrated the impact of baseline low-density lipoprotein cholesterol (LDL-C) levels on vein graft patency in patients on ticagrelor with or without aspirin 1 year after CABG and concluded that baseline LDL-C is not associated with 1-year vein graft patency after CABG and that regardless of the baseline LDL-C levels, ticagrelor + aspirin was superior to aspirin alone in maintaining vein graft patency. They further hypothesized that the primary factor causing early vein graft failure might not be atherosclerosis but thrombosis.

This study lends further credence to the fact that based on both experimental and clinical experience, early vein graft failure within a year is mainly due to thrombotic and technical events rather than atherogenesis, which takes longer to

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manifest. Thus, it comes as no surprise that the study by Zhu and colleagues¹² was not able to demonstrate any beneficial effect of aggressive lowering of LDL-C in the first year. It is plausible that the much-awaited long-term follow-up of the same study might show different results.

However, it is also important to appreciate that the study by Zhu and colleagues¹² is a post hoc analysis of the DACAB trial and was not designed to study the effect of LDL-C on vein patency. A very large percentage of patients (approximately 75%) underwent off-pump coronary artery bypass; thus, the results of this study cannot be generalized to the majority of on pump cases.

It is also very difficult to ascertain from this study or most other studies of this type whether the benefits of antiplatelet or lipid-lowering agent are due to prevention of native vessel disease, graft disease, or combination of the two. Also, the DACAB trial excluded patients older than 80 years. The exclusion of these older patients from clinical trials creates challenges in generalizing the results to the entire geriatric population.

In summary, dual-antiplatelet agents such as ticagrelor and aspirin show benefit over just aspirin alone in patients post CABG; however, the apparent lack of benefit of additional aggressive lipid lowering on vein graft patency in the first year is most likely a reflection of the differing basic pathogenic mechanism of early graft failure, mainly due to thrombosis as opposed to atherogenesis. Appropriately designed studies with long-term follow-up are needed to elucidate the impact of aggressive lipid-lowering agents on graft patency and major adverse cardiac events after CABG.

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