

Relationship between Intimal Hyperplasia and Saphenous Vein Graft Disease: Insights from the Cardiothoracic Surgical Trials Network VEST Trial

Objective

Diffuse intimal hyperplasia (IH) and graft irregularity adversely affect long-term patency of saphenous vein grafts (SVG), and the clinical outcomes of patients undergoing CABG. Mitigation of IH may, therefore, result in improved long-term success of CABG surgery. The VEST trial, which evaluated the efficacy of external graft support demonstrated a trend toward lower IH at one year in supported vs unsupported SVGs ($p=0.07$) in the primary analysis. Among the subgroup of patients for whom both randomized SVGs were evaluable at 1 year, IH area was reduced in supported SVGs ($p=0.04$). Here, we explore the relationship between IH and graft disease, and their associations with clinical events.

Methods

VEST is a randomized, multicenter, within-subject controlled trial in which one of two SVGs was randomized to external vein graft support or no support in patients undergoing multi-vessel CABG. The trial enrolled 224 patients of which 203 were evaluated at 12 months. The primary endpoint was IH area assessed by intravascular ultrasound at one-year post-randomization for each study graft. Secondary endpoints included degree of lumen irregularity (Fitzgibbon classification) and graft failure ($>50\%$ stenosis), assessed by invasive angiography and quantitative coronary angiography, respectively. Major cardiac and cerebrovascular events (MACCE, including death, MI, stroke and SVG or target vessel revascularization) are being collected as part of a 5- year follow-up. We conducted descriptive analyses of the associations among IH area, graft disease and MACCE.

Results

Over a median follow-up of 3 years, we observed 70 events in 46 of 224 patients (event rate 0.115/pt/year; 95%CI: [0.084, 0.156]). Patients with perfect SVG uniformity (Fitzgibbon I; $n=41/199$ with readable images) in both supported and unsupported SVGs had a lower incidence of MACCE compared to those with Fitzgibbon II or III in at least one graft (12% vs 20%). Analogously, SVG failure (87/202) or graft occlusion (74/203) of either or both randomized SVGs was associated with a higher incidence of MACCE (11% vs 30%; 14% vs 30%, respectively). Correspondingly, larger IH area was associated with greater lumen irregularity, a higher degree of SVG stenosis and higher incidence of MACCE (Table 1). Ischemia-driven revascularization of randomized SVGs or respective coronary targets was proportionally higher in unsupported grafts (4.0% vs 2.7%), confirming safety of the external support device.

Conclusions

In this sub-analysis of the VEST trial, the largest randomized evaluation of an external SVG support device intended to limit IH, we observed an association between IH area and presence of SVG disease at 1 year post surgery. Moreover, more severe SVG disease and larger IH areas were associated with an increased incidence of 3-year MACCE. Ongoing follow up to 5 years will further clarify the potential impact of IH area reduction by an external SVG support device on long-term clinical outcomes of CABG.

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Table 1. Relationship between IH and graft disease and clinical events		
		IH Area (mm²) Median
Fitzgibbon Classification	I	3.80
	II	5.59
	III	6.23
Visual Stenosis	No Stenosis	4.03
	<50% Stenosis	5.57
	≥50% Stenosis	6.09
Any Death, MI, Stroke, Revascularization	No	5.36
	Yes	5.61