CARDIOVASCULAR

Impact of Saphenous Vein Graft Radiographic Markers on Clinical Events and Angiographic Parameters

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Background. **Use of saphenous vein graft (SVG) radiographic markers has been associated with shorter cardiac catheterization procedure times and reduced contrast agent volume for postoperative coronary artery bypass graft (CABG) catheterizations. Use of such markers is varied and often operator-dependent, as the effect of SVG markers has not been fully evaluated. The goal of the present analysis was to evaluate the association of SVG markers with clinical outcomes and graft patency.**

Methods. **Data were drawn from the Project of Ex-vivo Vein Graft Engineering via Transfection (PREVENT) IV trial of patients undergoing CABG at 107 hospitals across the United States. Repeat angiography was performed within 12 to 18 months after CABG. The SVG markers were used at the discretion of the surgeon and were identified on the follow-up angiogram as any device used to mark the ostium, regardless of shape.**

Results. **The SVG markers were present in 51.2% of evaluable patients (910 of 1,778) and 52.3% of SVGs (2,228 of 4,240). Among patients with totally occluded SVGs (n = 911), visual identification of the SVG was obtained more frequently in those with an SVG marker (90.7% vs 72.1%, $p < 0.001$). The SVG stenosis 70% or greater at follow-up did not differ by use of markers (25.8% with marker vs 24.4% without marker, p = not significant). These findings were also consistent in ostial lesions (n = 942). Long-term death or myocardial infarction (MI) was similar by use of marker. The perioperative CABG MI was higher in patients with SVG markers (10.1% vs 5.5%, odds ratio adjusted 1.86, $p = 0.021$).**

Conclusions. **Saphenous vein graft radiographic markers were associated with higher rates of direct visualization of totally occluded SVGs without an adverse effect on graft patency or long-term clinical outcomes, but the association of SVG markers with increased perioperative CABG MI warrants further examination.**

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Use of saphenous vein graft (SVG) radiographic markers has been associated with shorter cardiac catheterization procedure times as well as a reduced volume of contrast agent for postoperative coronary artery bypass graft (CABG) catheterizations [1, 2]. It has been demonstrated that shorter catheterization times benefit the patient through reduced exposure to fluoroscopy-related radiation as well as the avoidance of overexposure to potentially toxic contrast agents [1, 3–6]. Use of such markers is varied and often operator-dependent [7] as the effect of SVG markers on clinical outcomes and subsequent graft patency has not been fully evaluated. Additionally, the association of SVG radiographic markers with postoperative complications and long-term survival is not well-characterized.

Given the uncertainty of the relationship of SVG radiographic markers with clinical outcomes and subsequent graft patency, the present analysis sought to evaluate the association of use of SVG markers with intermediate-term graft patency and angiographic outcomes at 12 to 18 months postsurgery, as well as postoperative and long-term clinical morbidity and mortality.

Patients and Methods

Patient Population

Data were drawn from the Project of Ex-vivo Vein Graft Engineering via Transfection (PREVENT) IV trial, the

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design of which has been described in detail elsewhere [8, 9]. In brief, the PREVENT IV trial was a phase III, multicenter, randomized, double-blind, placebo-controlled trial in which autologous vein grafts were treated ex vivo with edifoligide for patients undergoing primary CABG surgery (n = 3,014). Patients, age 18 to 80 years old, undergoing a first, isolated CABG surgery for atherosclerotic coronary artery disease with at least two planned vein grafts, were eligible. For the purpose of eligibility, grafts with multiple distal anastomoses were counted as single grafts. The first 2,400 patients enrolled were assigned to an angiography cohort and scheduled to return for angiography 12 to 18 months after surgery. Institutional Review Board approval was obtained at all sites and all patients gave written informed consent prior to participation. The present analysis includes the 1,778 patients who were assigned to the angiography cohort, who survived to 12 to 18 months, and who underwent the protocol angiography.

Each patient's harvested vein was treated ex vivo with either edifoligide, formulated as double-stranded oligonucleotide at a concentration of 40 μmol/L or 0.38 mg/mL, or an identical appearing buffered normal saline placebo. The study drug was administered using a pressure-mediated delivery system (Corgentech Inc, South San Francisco, CA); a trough inserted in a fluorinated ethylene polypropylene tube attached to a pressure syringe. The vein was harvested in the usual manner, placed on the trough, and inserted into the tube which was then filled with either edifoligide or placebo solution. Six pounds per square inch of nondistending pressure was applied to the tube for 10 minutes. The treated vein was then removed from the device, divided into appropriate lengths for grafting, and grafted into the patient using standard surgical techniques. Other than administration of the study drug, all graft handling, surgical, and medical interventions were left to the discretion of the operating surgeon, including the use of SVG markers.

Angiographic Evaluation

The SVG radiographic markers were identified on the follow-up angiogram as any device used to mark the ostium, regardless of shape. In the absence of visualization on the angiogram, total occlusions were assessed by aortogram study, retrograde filling at the distal anastomosis, lack of competitive flow, or clinical documentation. Number and location of SVGs placed during surgery was known by the angiographic core laboratory, so all SVGs were accounted for on the follow-up angiogram during the assessment of patency and percent stenosis.

The primary endpoint of the PREVENT IV trial was vein graft failure (≥75% vein graft stenosis) occurring 12 to 18 months after CABG surgery. Percent stenosis was measured by quantitative coronary angiography. Other angiographic endpoints included the thrombolysis in myocardial infarction (TIMI) frame count [10, 11] and the TIMI myocardial perfusion grade [12]. All angiograms were interpreted at the PERFUSE Angiographic Core Laboratory in Boston, MA.

Patients were contacted at 6 and 9 months and at 1 year after surgery for assessment of clinical events. Annual follow-up is ongoing and planned at 2, 3, 4, and 5 years. Median follow-up at the time of the present analysis was 3.1 years (interquartile range [IQR] 3.1 to 4.0 years). All suspected MIs and revascularization procedures were adjudicated by a blinded, independent clinical events committee using prespecified criteria. Perioperative in-

Table 1. Baseline and Surgical Characteristics by Use of Saphenous Vein Graft Radiographic Markers

Characteristic	SVG Marker (n = 910)	No SVG Marker (n = 868)	*p* Value
Age, Median (IQR) (Years)	64 (55, 70)	62 (55, 69)	0.23
Men	80.0%	82.5%	0.18
Weight median (IQR), kg	88 (77, 101)	88 (79, 100)	0.66
Hypertension	73.0%	73.0%	0.99
Hypercholesterolemia	76.1%	77.9%	0.38
Diabetes	37.8%	34.3%	0.12
Smoking (current)	24.7%	19.2%	0.005
Chronic lung disease	15.3%	12.0%	0.04
Atrial fibrillation	5.3%	7.2%	0.10
Renal failure	1.7%	0.7%	0.06
Myocardial infarction	41.3%	42.8%	0.52
Percutaneous coronary intervention	26.2%	28.7%	0.24
Congestive heart failure	5.8%	7.5%	0.16
Peripheral vascular disease	11.6%	10.3%	0.38
Cerebrovascular disease	10.4%	9.6%	0.58
Preoperative NYHA classification:			<0.001
I	45.3%	36.8%	
II	34.0%	34.8%	
III	15.1%	19.4%	
IV	5.5%	9.1%	
Left main disease ≥50% stenosis at baseline	25.1%	29.0%	0.066
Number of vessels with disease ≥50% stenosis at baseline			0.143
1	27.0%	29.9%	
2	15.2%	17.0%	
3	57.8%	53.1%	
Left ventricular ejection fraction, median (IQR)	52 (45, 60)	50 (40, 60)	0.06
Urgent surgery	49.0%	42.8%	0.009
Surgery duration, median (IQR), min	233 (196, 275)	225 (191, 266)	0.02
Cardiopulmonary bypass	80.6%	76.2%	0.025
Duration, median (IQR), min	102 (81, 124)	99 (80, 121)	0.13

SVG = saphenous vein graft; IQR = interquartile range; NYHA = New York Heart Association.