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Clinical, Angiographic, and Intravascular Ultrasound Characteristics of Early Saphenous Vein Graft Failure

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OBJECTIVES We sought to examine saphenous vein graft (SVG) lesions that fail within the first year after operation.

BACKGROUND Saphenous vein grafts remain patent for approximately 10 years; however, up to 15% to 20% of SVGs become occluded within the first year.

METHODS We studied 100 patients who underwent percutaneous coronary intervention (PCI) for early (<1 year post-implantation) SVG failure lesions and compared them with a diabetes- and hypercholesterolemia-matched cohort of late SVG failures (>1 year). Coronary angiography and intravascular ultrasound images were analyzed.

RESULTS The majority of patients in both groups were males who presented with unstable angina; 36% were diabetic. Graft ages were 6.0 ± 2.9 months and 105.4 ± 50.8 months, respectively. The early SVG failure lesion location was more often ostial or proximal (62% vs. 42%, respectively). Early SVG failures were angiographically smaller than late failures (reference: 2.47 ± 0.86 mm vs. 3.26 ± 0.83 mm, $p < 0.001$) but had similar lesion lengths. Intravascular ultrasound showed that early failure lesions had smaller proximal and distal reference lumen areas (7.3 ± 6.8 mm^2 vs. 10.6 ± 3.8 mm^2, $p = 0.026$) and greater reference plaque burden than late failures (52.3% vs. 36.1%, $p < 0.001$). After PCI, 20.6% of early and 30.6% of late failure lesions had creatine kinase-myocardial band (CK-MB) greater than twice normal.

CONCLUSIONS Early SVG failure is mostly proximal or ostial, lesions appear focal, and early SVGs appear smaller than late SVGs. Intravascular ultrasound shows significant reference segment plaque burden, suggesting more severe, diffuse SVG disease. (J Am Coll Cardiol 2004;44:53–6)

Coronary artery bypass graft surgery utilizing saphenous vein grafts (SVGs) is a proven technique for the treatment of intractable angina and, in select populations, improves long-term prognosis (1,2). The SVG conduits last ~10 years (3–6). However, up to 15% fail within the first year, usually resulting in percutaneous coronary intervention (PCI) (7). The etiology of early (within 1 year) graft failure is poorly understood. To better understand this issue, we undertook a retrospective clinical, angiographic, and intravascular ultrasound (IVUS) comparison between patients who presented with early versus late (>1 year) graft failure who were then treated with PCI.

METHODS

A retrospective analysis of the institution's catheterization database was performed to identify all patients who underwent PCI on one or more SVG lesions within one year of SVG implantation. Between January 1, 1991, and January 1, 2001, 3,775 SVG lesions were treated, of which 100 patients (121 lesions) had treatment within one year of graft implantation and had pre-interventional IVUS. Early failure patients were matched with late SVG failure patients on a 1:2 ratio based on diabetes and hypercholesterolemia status. Restenotic SVG lesions were excluded. The revascularization method was performed at the discretion of the operator. Baseline demographics and in-hospital complications were confirmed by independent hospital chart review.

Angiographic analysis. Angiographic analysis was performed using a computer-assisted, automated edge-detection algorithm (CAAS II, Pie Medical Imaging BV, Maastricht, The Netherlands) independent of clinical and IVUS information. Using the outer diameter of the contrast-filled catheter as the calibration standard, the reference diameter and minimum lumen diameter (MLD) were measured before and after intervention from multiple projections. The results from the "worst" view were recorded, and percent diameter stenosis was calculated. Lesion lengths were measured in the view with the least amount of foreshortening. Degenerated SVGs were those with ectasia or lumen irregularity comprising ≥50% of the SVG shaft length. Ectasia was a lumen >20% larger than the reference segment. Ostial segments were defined <5 mm from the proximal anastomosis.

Intravascular ultrasound imaging and analysis. Imaging with IVUS was performed immediately before PCI, after the administration of intracoronary nitroglycerin, using a motorized pullback and a commercially available scanner

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Abbreviations and Acronyms

CK-MB = creatine kinase-myocardial band
CSA = cross-sectional area
IVUS = intravascular ultrasound
MLD = minimum lumen diameter
PCI = percutaneous coronary intervention
QCA = quantitative coronary angiography
SVG = saphenous vein graft
TIMI = Thrombolysis In Myocardial Infarction

(SciMed/Boston Scientific, Maple Grove, Minnesota). After the imaging catheter was advanced at least 10 mm beyond the lesion edge into the distal graft, the transducer was withdrawn at 0.5 mm/s to the aorto-ostial junction.

Lesion site and reference segment SVG wall cross-sectional area (CSA) and lumen CSA were obtained via computerized planimetry (Tape Measure, Indec, Mountain View, California), according to published guidelines (8). The SVG plaque CSA was defined as SVG wall CSA minus lumen CSA. Plaque burden was calculated as SVG plaque CSA divided by SVG wall CSA. Remodeling was calculated as lesion divided by mean reference SVG wall CSA.

Statistical analysis. Statistical analysis was performed using the SAS statistical package, version 8.0 (SAS Institute, Inc., Cary, North Carolina). Continuous variables are presented as the mean value ± SD and compared using the Student *t* test. Discrete variables are presented as percentages and relative frequencies and compared using the chi-square statistic or Fisher exact test.

RESULTS

Patient characteristics. The clinical characteristics of the early failure (121 lesions) and late failure patients (289 lesions) are displayed in Table 1. The majority were men (70.0% early and 76.5% late, p = 0.22) with a similar age (64.8 ± 9.8 early vs. 66.5 ± 9.6 years, p = 0.17). Most had unstable angina (81.8% early and 73.1% late). The mean SVG age was 6.0 ± 2.9 months in the early group compared with 105.4 ± 50.8 months in the late group.

Procedural and angiographic characteristics. Percutaneous interventions differed in the early versus late groups, including stents (50.9% vs. 68.9%, p < 0.001), balloon alone (25.9% vs. 16.4%, p = 0.030), and laser or atherectomy (42.2% vs. 28.2%, p = 0.007) (Table 2). Early and late failure lesions had a high frequency of creatine kinase-myocardial band (CK-MB) greater than twice normal (20.6% and 30.6%, respectively).

Quantitative coronary angiography (QCA) analysis showed that vein grafts that failed early had a smaller pre-PCI reference diameter (2.47 ± 0.86 mm vs. 3.26 ± 0.83 mm, p < 0.001), smaller pre-PCI MLD (0.80 ± 0.64 vs. 1.08 ± 0.64, p < 0.001), and greater pre-diameter stenosis (71.6 ± 19.0% vs. 66.7 ± 17.7%, p = 0.017). Early graft failure was associated with lower pre-Thrombolysis In Myocardial Infarction (TIMI) flow rates (13.4% vs. 3.6% had TIMI flow grade 0 or 1, p < 0.001). There was no difference between the early and late failure lesion lengths or presence of thrombus (11.6% early vs. 12.6% late, p = 0.8). Grafts that failed late were more likely to be degenerated (43.1% vs. 29.5%, p = 0.015). Post-PCI QCA analysis showed that grafts that failed early had a smaller MLD (2.33 ± 0.96 vs. 2.91 ± 0.85, p < 0.001) and greater stenosis (16.3 ± 24.0% vs. 11.6 ± 18.1%, p = 0.037).

Table 1. Baseline Patient Demographics

	Early SVG Failure (n = 100)	Late SVG Failure (n = 200)	p Value
Age (yrs)	64.8 ± 9.8	66.5 ± 9.6	0.172
Male (%)	70.0	76.5	0.224
Unstable angina (%)	81.8	73.1	0.097
Diabetes mellitus (%)	36.0	36.0	1.0
Insulin-dependent (%)	14.0	14.0	1.0
Hypercholesterolemia (%)	70.0	70.0	1.0
Hypertension (%)	63.0	71.5	0.135
Left ventricular ejection fraction (%)	39 ± 13	41 ± 12	0.279
Previous myocardial infarction (%)	60.0	63.2	0.597
Family history (%)	62.3	54.8	0.338
History of smoking (%)	44.0	43.5	0.934
Current smoker (%)	18.0	19.0	0.834
Graft age (months)	6.0 ± 2.9	105.4 ± 50.8	<0.001

Data are presented as percentages or mean ± SD.
SVG = saphenous vein graft.

Intravascular ultrasound findings. Pre-intervention quantitative and qualitative results are shown in Table 3. The early failure reference segments had a greater plaque burden (distal: 52.3 ± 0.2% vs. 33.6 ± 0.1%, p < 0.001; proximal: 54.4 ± 0.2% vs. 38.3 ± 0.1%, p = 0.002; lesion: 81.7 ± 0.1% vs. 74.4 ± 0.1%, p = 0.009). There was also a significant difference between the plaque morphology in the early versus late failure groups. Vein grafts that failed early were more likely to be fibrotic (26.7% vs. 3.5%, p = 0.026), whereas grafts that failed late were more likely to be calcific (17.9% vs. 0%, p = 0.021).

DISCUSSION

Our study found that grafts that fail early are relatively small, less likely to be degenerated, mostly located in the ostial or proximal third portion of the graft, and had an increased frequency of TIMI flow grade 0/1. The diffuse disease (mean reference segment plaque burden >50%) of early failures was reflected in the high rate of procedural CK-MB release.

Previous studies have not focused on the angiographic findings in early graft failure. Savage et al. (9) performed angiographic analysis on 215 SVG lesions before PCI. The mean graft age in their study was 9.7 years, and 7% contained a definite thrombus. The majority of lesions were located in the proximal and mid portions of the grafts. Ahmed et al. (10) studied 340 lesions with a mean graft age

Table 2. Lesion Location and Procedural Information

	Early SVG Failure (n = 121)	Late SVG Failure (n = 289)	p Value
Lesion location			
Ostial (%)	37.5	17.5	<0.001
Proximal (%)	24.2	24.5	0.947
Mid (%)	12.5	29.4	<0.001
Distal (%)	13.3	19.6	0.133
Distal anastomotic (%)	12.5	10.0	0.481
Procedures			
Balloon only (%)	25.9	16.4	0.030
Stent only (with or without pre- or post-dilation) (%)	33.6	56.1	<0.001
Excimer laser (%)	25.0	15.7	0.030
With or without adjunct balloon (%)	13.8	8.9	0.148
With adjunct stent (%)	11.2	6.8	0.142
Atherectomy (%)	17.2	12.5	0.214
With or without adjunct balloon (%)	11.2	6.4	0.107
With adjunct stent (%)	6.0	6.1	0.989

SVG = saphenous vein graft.

of eight years, with similar findings. They reported that 9.6% of the lesions contained a thrombus and 36.3% were degenerated. Finally, Le May et al. (11) studied grafts that failed after an average of 9.9 years. The majority of lesions (75%) were found in the body of the graft, with thrombus in 21%.

This study is in concordance with these previous studies and found that early failure SVGs were angiographically smaller. Intravascular ultrasound analysis suggested that these "angiographically small" early failure grafts were actually diffusely diseased vessels without positive remodeling, resulting in small lumens. The lesion site remodeling index measured 0.97 ± 0.23 in the early failure group (no remodeling). The existence of remodeling within vein grafts is controversial. Nishioka et al. (12) examined 43 SVGs with a mean age of 11 ± 4 years. They found that SVGs do not undergo compensatory enlargement and suggested it as a potential factor affecting progression of SVG stenoses. However, other investigations reported significant positive remodeling in SVG lesions (13–15). These latter studies indicated that diseased SVGs can undergo remodeling responses that prevent lumen compromise, similar to native coronary arteries. Conversely, as in the current report, grafts that become diseased but that *do not remodel* will develop small reference lumen areas; this appears to be especially true for early SVG failures.

Study limitations. There are several limitations to this study. First, this study is a retrospective analysis that is subject to its inherent limitations. Second, there may have been a selection bias in that only patients undergoing pre-intervention IVUS were studied. Third, a common presentation of early SVG failure is thrombotic occlusion,

Table 3. Pre-intervention Quantitative and Qualitative Intravascular Ultrasound Characteristics

	Early SVG Failure (n = 30)	Late SVG Failure (n = 28)	p Value
Proximal reference			
SVG wall CSA (mm^2)	14.05 ± 9.48	18.78 ± 7.16	0.085
Lumen CSA (mm^2)	6.80 ± 7.87	11.45 ± 4.49	0.024
SVG plaque CSA (mm^2)	7.25 ± 3.68	7.32 ± 3.69	0.948
Lesion			
SVG wall CSA (mm^2)	13.73 ± 7.27	16.78 ± 4.81	0.071
Lumen CSA (mm^2)	2.15 ± 1.17	4.96 ± 3.52	<0.001
SVG plaque CSA (mm^2)	11.56 ± 6.41	12.51 ± 4.20	0.517
Remodeling index	0.97 ± 0.23	1.07 ± 0.21	0.091
Plaque morphology			<0.001
Soft lesions (%)	40.0	71.4	0.0162
Fibrotic lesions (%)	26.7	3.5	0.0261
Mixed lesions (%)	33.3	7.1	0.0139
Calcific lesions (%)	0	17.9	0.0214
Distal reference			
SVG wall CSA (mm^2)	14.21 ± 7.85	14.62 ± 6.67	0.841
Lumen CSA (mm^2)	6.79 ± 5.17	9.89 ± 4.85	0.028
SVG plaque CSA (mm^2)	7.42 ± 4.12	4.86 ± 2.70	0.012

Data are presented as the mean value ± SD or percentage.
CSA = cross-sectional area; SVG = saphenous vein graft.

and patients with thrombotic occlusion usually do not undergo PCI. As such, the current study is a report of early SVG failure lesions undergoing PCI.

Conclusions. Early SVG failure lesions represent an aggressive, diffuse disease process throughout the graft.

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REFERENCES

1. Davis KB, Chaitman B, Ryan T, Bittner V, Kennedy JW. Comparison of 15-year survival for men and women after initial medical or surgical treatment for coronary artery disease: a CASS (Coronary Artery Surgery Study) registry study. J Am Coll Cardiol 1995;25:1000–9.
2. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomized trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994;344:563–70.
3. Lawrie GM, Lie JT, Morris GC Jr., Beazley HL. Vein graft patency and intimal proliferation after aortocoronary bypass: early and long-term angiopathologic correlations. Am J Cardiol 1976;38:856–62.
4. Campeau L, Enjalbert M, Lesperance J, et al. The relation of risk factors to the development of atherosclerosis in saphenous vein bypass grafts and the progression of disease in the native circulation: a study 10 years after aortocoronary bypass surgery. N Engl J Med 1984;311:1329–32.
5. Bourassa MG. Fate of venous grafts: the past, the present and the future. J Am Coll Cardiol 1991;5:1081–3.
6. Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper D, Burton JR. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years. J Am Coll Cardiol 1996;28:616–26.
7. Motwani JG, Topol EJ. Aortocoronary saphenous vein graft disease. Circulation 1988;97:916–31.
8. Mintz GS, Nissen SE, Anderson WD, et al. American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies (IVUS): a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2001;37:1478–92.
9. Savage MP, Douglas JS Jr., Fischman DL, et al. Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. N Engl J Med 1997;337:740–7.
10. Ahmed JM, Hong MK, Mehran R, et al. Comparison of debulking followed by stenting versus stenting alone for saphenous vein graft aorto-ostial lesions: immediate and one-year clinical outcomes. J Am Coll Cardiol 2000;35:1560–8.
11. Le May MR, Labinaz M, Marquis JF, et al. Predictors of long-term outcome after stent implantation in a saphenous vein graft. Am J Cardiol 1999;83:681–6.
12. Nishioka T, Luo H, Berglund H, et al. Absence of focal compensatory enlargement or constriction in diseased human coronary saphenous vein bypass grafts: an intravascular ultrasound study. Circulation 1996;94:3005–6.
13. Ge J, Liu F, Bhate R, et al. Does remodeling occur in the diseased human saphenous vein bypass grafts? An intravascular ultrasound study. Int J Card Imaging 1999;15:295–300.
14. Hong MK, Mintz GS, Hong MK, et al. Intravascular ultrasound assessment of the presence of vascular remodeling in diseased human saphenous vein bypass grafts. Am J Cardiol 1999;84:992–8.
15. Mendelsohn FO, Foster GP, Palacios IP, Weyman AE, Weissman NJ. In vivo assessment by intravascular ultrasound of enlargement in saphenous vein bypass grafts. Am J Cardiol 1995;76:1066–9.