

## Poor long-term patient and graft survival after primary percutaneous coronary intervention for acute myocardial infarction due to saphenous vein graft occlusion

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Brodie, B. R., VerSteege, D. S., Brodie, M. M., Hansen, C. J., Richter, S. J., Stuckey, T. D., Gupta, N, Pulsipher, M., Downey, W. (2005). Poor long term patient and graft survival after primary percutaneous coronary intervention for acute myocardial infarction due to saphenous vein graft occlusion. *Catheterization and Cardiovascular Interventions*, 65(4), 505-509.

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This is the peer reviewed version of the following article: Brodie, B. R., VerSteege, D. S., Brodie, M. M., Hansen, C. J., Richter, S. J., Stuckey, T. D., Gupta, N, Pulsipher, M., Downey, W. (2005). Poor long term patient and graft survival after primary percutaneous coronary intervention for acute myocardial infarction due to saphenous vein graft occlusion. *Catheterization and Cardiovascular Interventions*, 65(4), 505-509, which has been published in final form at <http://dx.doi.org/10.1002/ccd.20392>. This article may be used for non-commercial purposes in accordance with [Wiley Terms and Conditions for Self-Archiving](#).

### **Abstract:**

Primary percutaneous coronary intervention (PCI) for ST segment elevation myocardial infarction (STEMI) due to saphenous vein graft (SVG) occlusion has been associated with poor procedural results and poor short-term outcomes, but long-term graft patency and patient survival have not been evaluated. Consecutive patients (n = 2,240) with STEMI treated with primary PCI from 1984 to 2003 were followed for 6.6 years (median). Follow-up angiography was obtained in 80% of hospital survivors following primary PCI for SVG occlusion at 2.3 years (median). Patients with primary PCI for SVG occlusion (n = 57) vs. native artery occlusion had more prior MI, advanced Killip class, and three-vessel coronary disease and lower acute ejection fraction (EF). Patients with SVG occlusion had lower rates of TIMI 3 flow post-PCI (80.7% vs. 93.6%;  $P = 0.0001$ ), higher in-hospital mortality (21.1% vs. 8.0%;  $P = 0.0004$ ), and lower follow-up EF (49.3% vs. 54.7%;  $P = 0.055$ ). Culprit SVGs were patent in 64% of patients at 1 year and 56% at 5 years. Late survival was strikingly worse in patients with primary PCI for SVG occlusion vs. native vessel occlusion (49% vs. 76% at 10 years), and SVG occlusion was the second strongest predictor of late cardiac mortality by multivariate analysis (HR = 2.11; 95% CI = 1.38–3.23;  $P = 0.0006$ ). Patients with STEMI due to SVG occlusion treated with primary PCI have poor acute procedural results, frequent late reocclusion, and very high late mortality. The introduction of new adjunctive therapies (distal protection, thrombectomy, and drug-eluting stents) may improve short-term outcomes, but improved long-term outcomes may require new and more durable revascularization strategies.

**Keywords:** reperfusion | coronary bypass surgery | primary angioplasty

**Article:**

## **INTRODUCITON**

Patients with prior coronary bypass surgery represent an increasing proportion of patients with ST segment elevation acute myocardial infarction (STEMI) [1] Attempts at establishing reperfusion of occluded saphenous vein grafts (SVG) with thrombolytic therapy have not been very effective [2], and mechanical reperfusion with primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy. Despite potential advantages, mechanical reperfusion of occluded SVGs is frequently complicated by distal embolization and no-reflow, and procedural outcomes and short-term clinical outcomes have been much worse than for mechanical reperfusion of occluded native vessels [3–5]. Late outcomes following primary PCI for STEMI due to SVG occlusion have not been well defined. The purpose of this study is to examine our large database of patients with STEMI treated with primary PCI to compare late cardiac survival and late graft survival in patients with SVG occlusion vs. native vessel occlusion.

## **MATERIALS AND METHODS**

### **Study Population**

Our study population consists of 2,240 consecutive patients with STEMI treated with primary PCI without prior thrombolytic therapy at our institution from 1984 to 2003. Patients with chest pain of < 12 hr duration (> 12 hr for persistent pain or hemodynamic compromise), with electrocardiographic ST segment elevation  $\geq 1$  mm in  $\geq 2$  contiguous leads or left bundle branch block, and without severe comorbid disease were selected for intervention.

### **Treatment Protocol**

Patients were treated with heparin and aspirin in the emergency department and transferred promptly to the catheterization laboratory for mechanical reperfusion. Stents were first used in 1995 and overall were used in 33% of patients. Platelet glycoprotein IIb/IIIa inhibitors were first used in 1996 and overall were used in 29% of patients. Ticlopidine or clopidogrel were used in stented patients and were continued for at least 1 month.  $\beta$ -adrenergic blocking agents and nitrates were initially used at the operator's discretion and became standard treatment in the later years of the study.

### **Clinical and Angiographic Follow-Up**

Clinical follow-up was obtained by hospital and office chart review and telephone contact in 96% of hospital survivors at a median follow-up time of 6.6 years. Follow-up angiography was performed routinely during the first 3 years of the study and during participation in several clinical trials, or for recurrent ischemic symptoms or after abnormal functional testing.

Follow-up angiography was obtained in 80% of hospital survivors with primary PCI for SVG occlusion at a median follow-up time of 2.3 years.

### **Definitions and Data Analysis**

Time to reperfusion was defined as the time from the onset of symptoms until balloon inflation. Coronary flow in the infarct artery was assessed visually by the operator and classified according to TIMI grading system on a scale of 0 to 3 [6]. Reinfarction was defined as recurrent chest pain associated with any secondary rise in the creatine kinase level and the MB fraction higher than the nadir, with or without diagnostic electrocardiographic changes. Urgent target vessel revascularization was defined as the need for repeat PCI or bypass surgery for recurrent ischemia or hemodynamic compromise.

Left ventricular ejection fractions were calculated from tracing contours of right anterior oblique cine angiograms using the area-length method with correction for the right anterior oblique projection [7].

### **Statistical Analysis**

Statistical comparisons of categorical variables were performed using the chi-square test or Fisher's exact test. Student's unpaired t-test was used for comparing continuous variables. Differences in late graft patency by type of graft and differences in late cardiac survival between patients with native artery vs. SVG occlusion were examined with Kaplan-Meier survival curves and their associated Wilcoxon statistics. Multivariable analyses of predictors of late cardiac survival were performed using Cox proportional hazards regression models. All clinical variables in Table I plus infarct artery type (SVG vs. native artery) were entered into the model. All analyses were performed with SAS (Cary, NC) and SPSS (Chicago, IL) software.

## **RESULTS**

### **Baseline Variables**

Of the 2,240 patients in our study cohort, 107 had prior coronary bypass surgery. The infarct vessel was a native coronary artery in 50 of these patients and an SVG in 57 patients (Table I). The median time from bypass surgery to the index myocardial infarction in patients with primary PCI for SVG occlusion was 9.8 years. Patients with primary PCI for SVG vs. native artery occlusion were slightly older, more often male, and had a higher frequency of prior infarction, Killip class 3–4, and three-vessel coronary artery disease and had lower acute left ventricular ejection fraction (Table I).

### **Procedural and In-Hospital Outcomes**

Patients with primary PCI for SVG vs. native vessel occlusion had a significantly lower frequency of TIMI 3 flow post-PCI and a significantly higher in-hospital mortality (Table II). There were no differences in reinfarction, urgent target vessel revascularization, or stroke, and no

differences in infarct size based on peak creatine kinase and the MB fraction. Left ventricular ejection fraction at follow-up angiography was lower in patients with PCI for SVG occlusion.

### Late Graft Patency

Graft survival following primary PCI for STEMI due to SVG occlusion was poor (Fig. 1). The culprit infarct SVG was patent in 64% of patients at 1 year and 56% at 5 years. Patency of the culprit SVG was better in stented (n = 19) vs. nonstented (n = 37) patients at 5 years (80% vs. 45%; P = 0.053).

Noninfarct SVGs (n = 75) were patent in 58% of patients at 1 year and 58% at 5 years (Fig. 1). Left internal mammary grafts (used in 26 patients) remained patent in 95% of patients at 5 years.

Graft survival free of target vessel revascularization (TVR) was also very poor for both culprit and nonculprit SVGs (Fig. 2). The culprit infarct SVG was free of occlusion or TVR in 38% of patients at 1 year and 17% at 5 years. Noninfarct SVGs were free of occlusion or TVR in 45% of patients at 1 year and 33% at 5 years. Left internal mammary grafts were free of occlusion or TVR in 95% of patients at 5 years.

**TABLE I. Baseline Clinical and Angiographic Variables Stratified by Infarct Artery Type**

	Infarct artery		P
	Saphenous vein graft (n = 57)	Native artery (n = 2,183)	
<b>Clinical variables</b>			
Age (years)	62.8 ± 10.5	59.7 ± 12.3	0.064
Age > 70 years	17 (29.8%)	510 (23.4%)	NS
Women	11 (19.3%)	679 (31.1%)	0.056
Diabetes mellitus	6 (10.5%)	326 (14.9%)	NS
Hypertension	32 (56.1%)	1023 (47.4%)	NS
Prior myocardial infarction	28 (49.1%)	353 (16.2%)	< 0.0001
Prior bypass surgery	57 (100%)	50 (2.3%)	< 0.0001
Current smoker	33 (57.9%)	1151 (53.1%)	NS
Anterior infarction	16 (28.1%)	847 (38.8%)	NS
Killip class 3–4	15 (26.3%)	357 (16.4%)	0.046
Time to reperfusion (hr)	5.1 ± 4.5	5.4 ± 4.9	NS
<b>Angiographic variables</b>			
TIMI 2–3 flow pre-PCI	9 (15.8%)	460 (21.1%)	NS
Three-vessel coronary artery disease	48 (84.2%)	475 (21.8%)	< 0.0001
Acute ejection fraction	46.1 ± 13.8 (n = 47)	50.8 ± 12.8 (n = 2024)	0.026

**TABLE II. TIMI Flow, In-Hospital Outcomes, Infarct Size, and Left Ventricular Ejection Fraction Stratified by Infarct Artery Type**

	Infarct vessel		<i>P</i>
	Saphenous vein graft (n = 57)	Native artery (n = 2,183)	
TIMI flow and in-hospital outcomes			
TIMI 3 flow post-PCI	46 (80.7%)	2043 (93.6%)	0.0001
Mortality	12 (21.1%)	175 (8.0%)	0.0004
Reinfarction	2 (3.5%)	58 (2.7%)	NS
Urgent target vessel revascularization	3 (5.3%)	106 (4.9%)	NS
Stroke	2 (3.5%)	27 (1.2%)	NS
Infarct size and ejection fraction			
Peak creatine kinase	2391 ± 2842	2424 ± 2561	NS
Peak MB fraction	176 ± 191	193 ± 178	NS
Follow-up ejection fraction	49.3 ± 13.7 (n = 27)	54.7 ± 13.4 (n = 834)	0.055

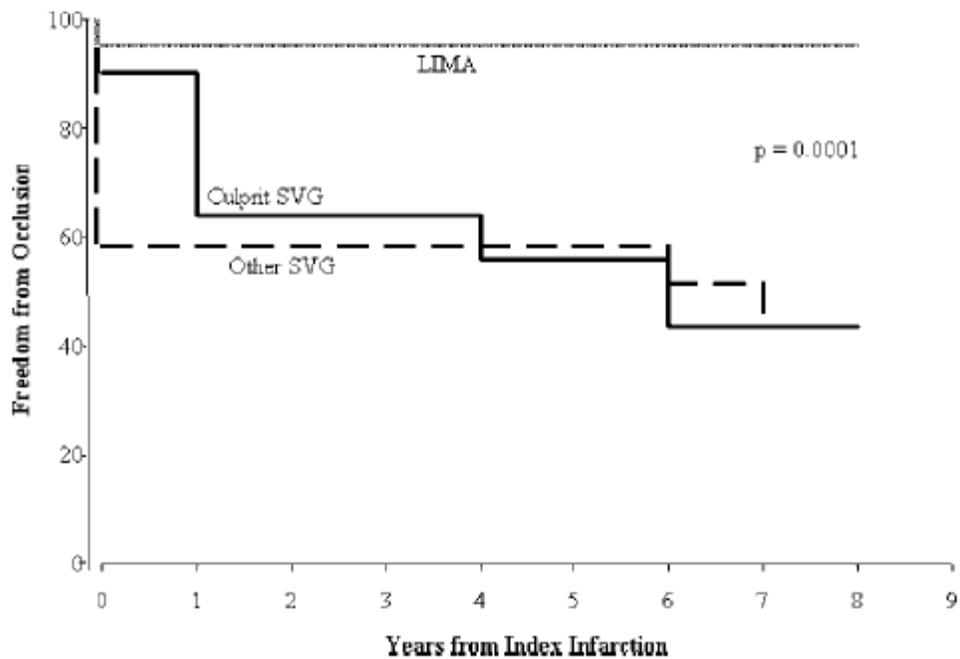
### Late Cardiac Survival

Late cardiac survival was significantly and strikingly worse in patients whose infarct artery was an SVG vs. a native coronary artery (49% vs. 76% at 10 years) with survival curves that diverged over time (Fig. 3). After adjusting for differences in baseline variables, primary PCI for SVG occlusion (vs. native artery occlusion) was the second strongest predictor of late cardiac mortality (Table III). After further adjusting for procedural outcomes (TIMI flow post-PCI), SVG occlusion remained a significant predictor of late cardiac mortality (hazard ratio ¼ 2.01; 95% CI ¼ 1.32–3.08; P ¼ 0.001).

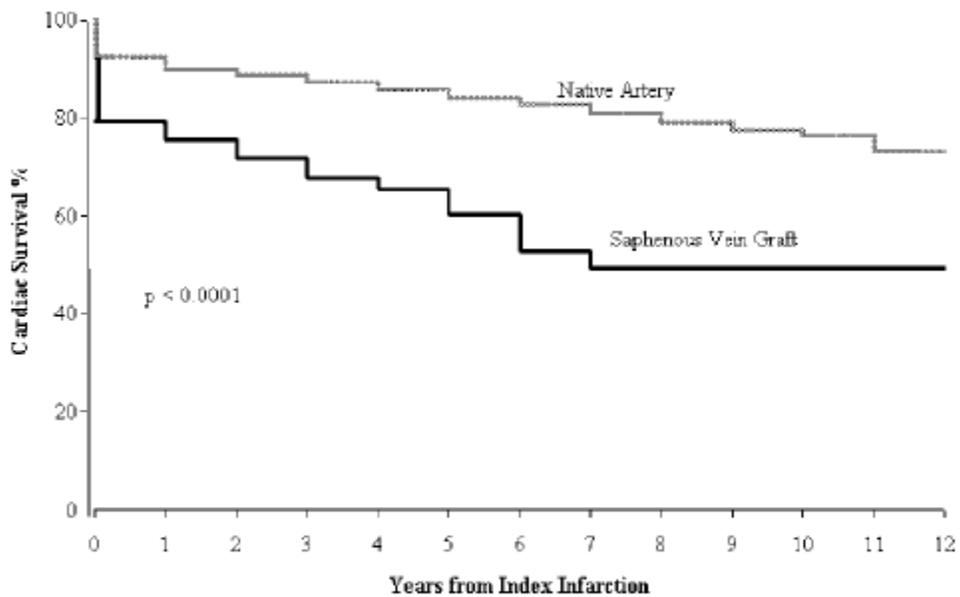
Seven of the 57 patients with primary PCI for SVG occlusion underwent repeat bypass surgery during their hospital stay. There were no differences in late cardiac survival between patients who underwent repeat bypass surgery and those who did not.

### DISCUSSION

Patients with prior coronary bypass surgery who present with STEMI due to SVG occlusion offer a than the progression of disease in patients following bypass surgery who have not suffered an acute myocardial infarction. In prior studies, SVG patency following coronary bypass surgery has been estimated at 88% at 1 year, followed by an occlusion rate of 2.1% per year [8,9].



**Fig. 1.** Kaplan-Meier estimates of freedom from occlusion comparing culprit SVGs, other SVGs, and left internal mammary grafts (LIMAs).



**Fig. 3.** Kaplan-Meier estimates of late cardiac survival in patients with primary PCI for SVG occlusion vs. native artery occlusion.

Our study shows that late cardiac survival following primary PCI for STEMI due to SVG occlusion is strikingly worse compared with primary PCI for native coronary artery occlusion

with survival curves that diverge over time. There appear to be several reasons for this. First, patients with SVG occlusion have a higher baseline risk profile with more advanced age, more prior infarction, more frequent advanced Killip class, more three-vessel coronary disease, and lower acute ejection fraction. Second, procedural outcomes are worse with lower rates of TIMI 3 flow following PCI. Finally, long-term graft survival is very poor following primary PCI for SVG occlusion. This is likely related to both reocclusion at the PCI site and progression of disease at other sites in the SVG. After adjusting for differences in baseline variables, SVG occlusion was the second strongest independent predictor of late cardiac mortality. After further adjusting for procedural outcomes (TIMI flow), SVG occlusion remained an independent predictor of late cardiac mortality. This suggests that poor graft survival contributes to the high late cardiac mortality. Previous studies evaluating outcomes following elective PCI for SVG obstruction have shown a high frequency of late adverse events [10]. Our study indicates that late events following emergent PCI for STEMI due to SVG occlusion are substantially worse than after elective PCI.

### Study Limitations

Although all data were collected prospectively, our study is single-center and observational. Follow-up angiography was not prespecified and was obtained primarily for clinical indications. Our study spans almost 20 years; consequently, most of our patients did not have the latest adjunctive therapy used with primary PCI. Stents were used in 33% of patients, distal protection in three patients, thrombectomy in two patients, and drug-eluting stents were not used.

**TABLE III. Multivariate Predictors of Late Cardiac Mortality**

Variable	Hazard ratio	95% CI	<i>P</i>
Killip class 3–4	2.96	2.44–3.60	< 0.0001
Infarct artery SVG	2.11	1.38–3.23	0.0006
Age > 70 years	1.83	1.51–2.23	< 0.0001
Diabetes	1.79	1.45–2.20	< 0.0001
Anterior MI	1.61	1.35–1.93	< 0.0001
Reperfusion time > 2 hr	1.58	1.12–2.21	0.009
Three-vessel CAD	1.43	1.16–1.76	0.0006
Prior MI	1.27	1.02–1.57	0.02
Women	1.18	0.97–1.43	0.09

### Clinical Implications

The very poor procedural outcomes and poor short and long-term clinical outcomes should stimulate new therapies for patients with STEMI due to SVG occlusion. Already, there have been a number of new interventional therapies introduced to help improve procedural outcomes. Distal protection devices (PercuSurge GuardWire, Medtronic, and FilterWire, Boston Scientific) have been shown to be effective in elective PCI in SVGs and may also improve outcomes with primary PCI of occluded SVGs [11,12]. Short-term and possibly long-term outcomes in our patients may have been improved if distal protection devices had been available and were able to

be used more frequently. Thrombectomy (Possis Angiojet; Possis) has been shown to be effective as adjunctive therapy with PCI in thrombus containing lesions and may help in patients with STEMI due to SVG occlusion [13]. Drug-eluting stents reduce restenosis and TVR after elective PCI in native vessels and may be useful with primary PCI for occluded SVGs. More frequent use of stents and the use of drug-eluting stents would likely have improved late outcomes in our study cohort. Platelet glycoprotein IIb/IIIa inhibitors may offer some benefit in these patients with thrombus containing lesions, although there appears to be no benefit when used with elective PCI for SVG occlusion [14].

The poor late outcomes in patients treated with percutaneous intervention for SVG occlusion might encourage a more aggressive approach with surgical revascularization prior to hospital discharge. Unfortunately, this approach is often limited by comorbidities preventing repeat operation; in our limited experience, we were not able to document any improvement in outcomes with this approach.

More aggressive treatment with secondary prevention after the initial bypass procedure may help prevent or delay the occurrence of acute infarction, and aggressive secondary prevention after acute infarction may help improve subsequent outcomes. In addition to aspirin, b-blockers, and angiotensin-converting enzyme inhibitors, cholesterol-lowering therapy with statin medications and platelet inhibition with clopidogrel have been shown to be especially beneficial in patients with prior bypass surgery [15,16].

Despite these advances in therapy, once SVG disease becomes evident, usually there is accelerated progression of disease. This is likely a major factor, along with higher baseline risk profile and worse procedural outcomes, that contributes to poor long-term survival. Although we may achieve some improvement in outcomes with new procedural techniques and more aggressive secondary prevention, major improvements in outcomes will require more durable revascularization strategies.

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