STATE-OF-THE-ART PAPER

Saphenous Vein Graft Intervention

Michael S. Lee, MD,* Seung-Jung Park, MD,‡ David E. Kandzari, MD,§
Ajay J. Kirtane, MD, SM,‖ William F. Fearon, MD,† Emmanouil S. Brilakis, MD, PHD,¶
Paul Vermeersch, MD,# Young-Hak Kim, MD,‡ Ron Waksman, MD,**
Julinda Mehilli, MD,†† Laura Mauri, MD,‡‡ Gregg W. Stone, MD‖

*Los Angeles and Palo Alto, California; Seoul, South Korea; Atlanta, Georgia; New York, New York;
Dallas, Texas; Antwerp, Belgium; Washington, DC; Munich, Germany; and Boston, Massachusetts*

Saphenous vein grafts are commonly used conduits for surgical revascularization of coronary arteries but are associated with poor long-term patency rates. Percutaneous revascularization of saphenous vein grafts is associated with worse clinical outcomes including higher rates of in-stent restenosis, target vessel revascularization, myocardial infarction, and death compared with percutaneous coronary intervention of native coronary arteries. Use of embolic protection devices is a Class I indication according to the American College of Cardiology/American Heart Association guidelines to decrease the risk of distal embolization, no-reflow, and periprocedural myocardial infarction. Nonetheless, these devices are underused in clinical practice. Various pharmacological agents are available that may also reduce the risk of or mitigate the consequences of no-reflow. Covered stents do not decrease the rates of periprocedural myocardial infarction and restenosis. Most available evidence supports treatment with drug-eluting stents in this high-risk lesion subset to reduce angiographic and clinical restenosis, although large, randomized trials comparing drug-eluting stents and bare-metal stents are needed. (J Am Coll Cardiol Intv 2011;4:831–43) © 2011 by the American College of Cardiology Foundation

The long-term success of surgical coronary revascularization is limited by accelerated atherosclerosis and intimal fibrosis of the saphenous vein graft (SVG) after its use as a vascular conduit. At 1 year, the incidence of 1 or more total SVG occlusions has been reported to be as high as 41% after on-pump bypass surgery (Table 1) (1–8). Because of increased morbidity and mortality with repeat coronary artery bypass graft surgery, SVG intervention is considered by many to be the preferred revascularization modality in patients with diseased SVGs and accounts for approximately 5% to 10% of all percutaneous coronary interventions (PCI) (9–14).

In this review, we describe the risk factors for complications after SVG intervention and discuss the optimal procedural treatment strategies regarding periprocedural anticoagulation, choice of stent, and measures to mitigate the risks of distal embolization.

Pathobiology of SVG

SVG intervention remains technically challenging and is associated with higher rates of periprocedural myocardial infarction, in-hospital mortality, restenosis, and occlusion compared with PCI of native coronary arteries largely because of the friable, degenerated atheromatous and thrombotic debris that develop when SVGs deteriorate (15). Progression of disease outside the stented segment can also lead to high rates of target vessel revascularization. Therefore, treatment of native coronary artery lesions is preferred to treatment of degenerated SVG if feasible.

A recognized consequence of SVG intervention is distal embolization of atheroembolic debris with decreased epicardial and microvascular perfusion due to capillary plugging and vasospasm from the release of neurohumoral factors such as serotonin. Distal embolization may result in the slow or no-reflow phenomenon in approximately 10% to 15% of cases and is associated with periprocedural angina and ischemic ST-segment changes (16). In such instances, subsequent myocardial infarction occurs in 31% of patients and in-hospital mortality increases 10-fold (17). However, distal embolization remains difficult to predict (18).

Abbreviations and Acronyms

BMS = bare-metal stent(s)

CI = confidence interval

CK-MB = creatine kinase-myocardial band

DES = drug-eluting stent(s)

FDA = U.S. Food and Drug Administration

FFR = fractional flow reserve

HR = hazard ratio

MACE = major adverse cardiac event(s)

OR = odds ratio

PCI = percutaneous coronary intervention

PTFE = polytetrafluorethylene

SVG = saphenous vein graft

TIMI = Thrombolysis In Myocardial Infarction

Predictors of Adverse Clinical Events

Periprocedural creatine kinase-myocardial band (CK-MB) elevation after successful SVG intervention was common (ranging from 15% to 47%) (19,20). The use of embolic protection devices has been systematically associated with periprocedural myocardial infarction rates <10% (21,22). Differences in myocardial infarction rates between studies may also be explained by differences in myocardial infarction definitions, the sensitivity and frequency of biomarker measurement, and the complexity of SVG disease studied. Hong et al. (19) reported that 15% of patients experienced major CK-MB release exceeding 5× the upper limit of normal following SVG PCI. Although the association of

Table 1. Saphenous Vein Graft Occlusion Rates From Selected Studies

Study/First Author (Ref. #)	1 Year	5 Years	10 Years
PRAGUE-4 (1)	41 (per patient on-pump)	NA	NA
	51 (per patient off-pump)	NA	NA
PREVENT IV (2)	41.7 (per patient)	NA	NA
	26.6 (per SVG)	NA	NA
Fitzgibbon et al. (3)	19 (per SVG)	25 (per SVG)	40 (per SVG)
RIGOR (4)	31 (per patient)	NA	NA
	19 (per SVG)	NA	NA
Halabi et al. (5)	39.3 (per patient)	NA	NA
Khot et al. (6)	30.1 (SVG)	NA	NA
ROOBY (7)	28.7 (per patient on-pump)	NA	NA
	36.5 (per patient off-pump)	NA	NA
Goldman et al. (8)	20 (per patient)	31 (per patient)	39 (per patient)

Values are %.

NA = not available; PREVENT IV = Project of Ex Vivo Vein Graft Engineering via Transfection; RIGOR = Reduction in Graft Occlusion Rates; ROOBY = Veterans Affairs Randomized On/Off Bypass study.

periprocedural myonecrosis and late clinical outcomes is controversial among patients undergoing native vessel PCI, even minor elevations of CK-MB (1× to 5× normal) after SVG intervention have been associated with increased mortality at 1 year (6.5% vs. 4.8%, p < 0.05), with CK-MB release exceeding 5× the upper limit of normal increasing 1-year mortality by 144%. Multivariate analysis revealed that major CK-MB release after SVG intervention was a powerful independent predictor of late mortality (odds ratio [OR]: 3.3, 95% confidence interval [CI]: 1.7 to 6.2).

Lesion length, greater angiographic degeneration of SVGs, and larger estimated plaque volume have been identified as predictors of 30-day major adverse cardiac events (MACE) after SVG intervention (23–25). This may be explained by the fact that the greater the amount of plaque, the greater the likelihood of distal embolization after intervention, leading to myocardial infarction.

Patient sex also appears to be a significant predictor of outcomes after SVG intervention. Women had higher 30-day cumulative mortality rates (4.4% vs. 1.9%, p = 0.02) compared with men (26). Furthermore, women had a higher incidence of vascular complications (12% vs. 7.3%, p = 0.006) and post-procedural acute renal failure (8.1% vs. 4%, p = 0.02).

In a 172-patient study of SVG intervention with drug-eluting stents (DES), chronic renal insufficiency (serum creatinine ≥1.5 mg/dl) was the only significant predictor of 1-year MACE (hazard ratio [HR]: 2.2, 95% CI: 1.1 to 4.3, p = 0.03) (27). A trend was also present toward higher rates of target vessel revascularization in the renal insufficiency group (21.8% vs. 10.3%, HR: 2.42, 95% CI: 0.94 to 6.24, p = 0.059). Similar results were observed with bare-metal stents (BMS). Overall mortality rates were significantly higher in patients with renal insufficiency (p < 0.001) (28).

Decision to Perform SVG Percutaneous Intervention

The decision regarding whether or not to intervene in a diseased SVG should be guided by the patient's symptoms, angiographic evidence of a significant stenosis, and noninvasive evidence of myocardial ischemia in the region subtended by the SVG. Even though the role of intravascular ultrasound or fractional flow reserve (FFR) measurement in assessing the significance of SVG disease has not been well studied, FFR can be performed in an SVG in a similar fashion as in a native coronary vessel. The pressure sensor should be positioned in the distal two-thirds of the native vessel so the entire conduit can be interrogated. Intravenous adenosine should be administered to induce hyperemia and a slow pullback of the pressure wire can be performed to distinguish focal from diffuse disease. Prospective validation of an FFR cutoff value of 0.75 to 0.80 to detect hemodynamically significant SVG stenosis has not been performed. Nonetheless, this cutoff is generally used in clinical practice. Of note, however, SVG disease progresses more rapidly than native coronary artery disease, and the safety of deferring intervention on a diseased SVG with a nonischemic FFR has not been studied.

Adverse clinical events occurring >12 months after initial SVG intervention most frequently resulted from disease progression at untreated intermediate lesions (29). Because SVG disease can progress rapidly, some have advocated prophylactically stenting intermediate SVG lesions as opposed to continuing with medical therapy alone. In the small (57-patient) randomized VELETI (Treatment of Moderate Vein Graft Lesions With Paclitaxel Drug-Eluting Stents) trial, the 1- and 3-year MACE rates were significantly lower in patients in whom moderate (30% to 60%) SVG stenoses were treated with paclitaxel-eluting stents compared with patients who received medical treatment (3% vs. 19%, p = 0.09 at 1 year, and 3% vs. 26%, p = 0.02 at 3 years), thus supporting a strategy of plaque sealing with DES in moderate nonangiographically significant lesions in degenerated SVGs at increased risk for disease progression and adverse clinical events (30,31). However, this trial was an imaging study that was not powered for clinical endpoints. The 450-patient VELETI II (Sealing Moderate Coronary Saphenous Vein Graft Lesions With Paclitaxel-Eluting Stents) trial (NCT01223443) is currently randomizing patients with intermediate SVG lesions to either SVG intervention with paclitaxel-eluting stents versus medical therapy alone and has a primary clinical rather than angiographic endpoint.

Treatment of Occluded SVGs

In a study of 34 patients with chronic total SVG occlusion for which percutaneous revascularization was attempted, successful recanalization with stent implantation was low (68%) (32). At a median follow-up of 18 months, the rates of in-stent restenosis and target vessel revascularization were unacceptably high (68% and 61%, respectively) in patients who underwent successful stenting despite a high use of DES (95%). Given the poor short- and long-term outcomes of percutaneous revascularization in chronic total occlusion of SVGs, percutaneous revascularization should rarely be considered except for acute occlusion in the setting of myocardial infarction. Instead, attempts to recanalize the native coronary artery are preferred if feasible.

Antithrombin and Antiplatelet Therapy

The preferred parenteral antithrombotic therapy during SVG intervention has not been studied in a dedicated, prospective clinical trial. Several studies demonstrated that the role of glycoprotein IIb/IIIa antagonists in SVG intervention is limited given their failure to demonstrate a reduction in periprocedural myocardial infarction (33–35). However, 1 post hoc analysis demonstrated a trend toward improved procedural success when glycoprotein IIb/IIIa antagonists were used in conjunction with filter-based embolic protection (p = 0.058) but the MACE was not different at 30 days (36). In a single center, retrospective observational study, bivalirudin was associated with a significant reduction in major CK-MB elevation and a trend toward lower in-hospital non–Q-wave myocardial infarction, repeat revascularization, and vascular complications compared with unfractionated heparin (37). In the subset of 329 patients who underwent SVG intervention in ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy Trial) (38), the rates of ischemic bleeding and net clinical endpoints were similar with bivalirudin monotherapy, bivalirudin plus a glycoprotein IIb/IIIa antagonist, and heparin plus a glycoprotein IIb/IIIa antagonist. Minor bleeding complications were lower with bivalirudin alone compared with heparin plus a glycoprotein IIb/IIIa antagonist (26% vs. 38%, p = 0.05). Thus, bivalirudin may offer a safety advantage over other antithrombotic regimens, with equal or greater suppression of adverse ischemic events, although this conclusion is not definitive in the absence of an adequately powered randomized trial.

Stent Type Selection

Bare-metal stents. The SAVED (Saphenous Vein de Novo) trial reported that compared with balloon angioplasty, BMS were associated with higher procedural success (92% vs. 69%, p < 0.001), a trend toward a reduction in angiographic restenosis (36% vs. 47%, p = 0.11), and lower MACE through 240 days (26% vs. 38%, p = 0.04) (39). Since the SAVED report, the overwhelming majority of SVG intervention has been performed with stents, and subsequent

randomized trials have compared BMS with covered stents or DES (Table 2).

Covered stents. Stents covered with a mesh, most commonly polytetrafluorethylene (PTFE), have a theoretical advantage over conventional stents because they may "trap" friable atheroemboli and prevent distal embolization and serve as a smooth-muscle cell barrier and therefore decrease restenosis. However, 3 prospective randomized trials failed to demonstrate benefit with covered stents. SYMBIOT III (A Prospective, Randomized Trial of a Self-Expanding PTFE Stent Graft During SVG Intervention–Late Results) (40) compared the self-expandable PTFE-covered nitinol Symbiot stent (Boston Scientific Corp., Natick, Massachusetts) with BMS. At 8 months, the incidence of MACE between the Symbiot group and BMS was similar (30.6% vs., 26.6%, p = 0.43). A trend toward increased target lesion revascularization with the Symbiot stent was also observed (23.5% vs. 15.6%, p = 0.055). The RECOVERS (Randomized Evaluation of Polytetrafluoroethylene-Covered Stent in Saphenous Vein Grafts) trial (41) randomized 301 patients to treatment with either the PTFE-covered JoStent balloon-expandable stent (Jomed International AB, Helsingborg, Sweden) or BMS. The PTFE group had a higher incidence of 30-day MACE (10.9% vs. 4.1%, p = 0.047), mainly attributed to increased incidence of myocardial infarction (10.3% vs. 3.4%, p = 0.037). At 6 months, the restenosis rate was similar between the 2 groups (24.2% vs. 24.8%, p = 0.237), and the MACE rate was not different (23.1% vs. 15.9%, p = 0.153).

The BARRICADE (Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events) trial (42) also randomized 243 patients to treatment with either the PTFE-covered JoStent balloon-expandable stent (Jomed) or BMS. At 5-year follow-up, target vessel failure was higher in the JoStent group than in the BMS group (68.3% vs. 51.8%, p = 0.007), emphasizing the dismal long-term prognosis of SVG treatment with either BMS or covered stents.

Two other covered stents have shown promise in the treatment of degenerated SVGs although long-term head-to-head comparison data with BMS are lacking. In the SESAME first in human trial (43), 20 patients who underwent SVG intervention with a novel nanosynthesized, membrane-covered self-expanding superelastic all-metal endoprosthesis stent (SESAME stent, Advanced Bioprosthetic Surfaces, Ltd., San Antonio, Texas) had a 0% rate of MACE at 30 days. At 9 months, the MACE rate was 14% (3 patients underwent repeat intervention: 1 underwent target lesion revascularization for restenosis at the overlap of 2 stents and 2 underwent target vessel revascularization for lesions outside the stented segment). Preliminary results with the MGuard stent (InspireMD, Tel Aviv, Israel), a BMS with a polymeric net attached to its surface, demonstrated favorable early performance in a study that included 16 patients who underwent SVG intervention with no angiographic/procedural complications, and no adverse events up to 30 days (44).

Table 2. Clinical Outcomes of Randomized Stent Trials in Saphenous Vein Grafts

	SYMBIOT III			BARRICADE			RECOVERS			SOS			RRISC			ISAR-CABG		
	PTFE	BMS	p Value	PTFE	BMS	p Value	PTFE	BMS	p Value	PES	BMS	p Value	SES	BMS	p Value	DES	BMS	p Value
MACE																		
1 yr	30.6	26.6	0.43	39.2*	28.0*	0.07	23.1†	15.9†	0.15	37	49	0.20	15.8†	29.7†	0.15	15.4	22.1	0.03
3 yrs	NA	NA	NA	60.2	37.0	0.001	NA	NA	NA	54	77	0.49	58	41	0.13	NA	NA	NA
5 yrs	NA	NA	NA	68.3	51.8	0.007	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Death																		
1 yr	2.6‡	4.7‡	0.29	7.0	5.0	0.51	2.6†	2.8†	0.92	12	5	0.27	2.6†	0†	0.99	5.2	4.7	0.82
3 yrs	NA	NA	NA	18.8	11.2	0.13	NA	NA	NA	24	13	0.19	29	0	<0.001	NA	NA	NA
5 yrs	NA	NA	NA	29.8	22.3	0.20	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MI																		
1 yr	9.2	10.9	0.61	14.2	11.3	0.53	14.1†	5.5†	0.02	15	31	0.10	2.6†	0†	0.99	4.2	6.0	0.27
3 yrs	NA	NA	NA	21.0	14.1	0.21	NA	NA	NA	17	46	0.01	18	5	0.15	NA	NA	NA
5 yrs	NA	NA	NA	26.2	17.4	0.16	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TLR																		
1 yr	23.5	15.6	0.06	28.2	21.1	0.46	9.6†	8.3†	0.84	5	28	0.003	5.3†	21.6†	0.05	7.2	13.1	0.02
3 yrs	NA	NA	NA	37.4	21.8	0.02	NA	NA	NA	10	41	0.004	24	30	0.55	NA	NA	NA
5 yrs	NA	NA	NA	43.9	29.6	0.04	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

*Target vessel failure (composite of all-cause death, MI, or clinically driven target vessel revascularization). †6 months. ‡Cardiac death.

BARRICADE = Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events study; BMS = bare-metal stent(s); DES = drug-eluting stent(s); ISAR-CABG = Prospective, Randomized Trial of Drug-Eluting Stents Versus Bare Metal Stents for the Reduction of Restenosis in Bypass Grafts; MACE = major adverse cardiac event(s); MI = myocardial infarction; NA = not available; PTFE = polytetrafluoroethylene; RECOVERS = Randomized Evaluation of Polytetrafluoroethylene-Covered Stent in Saphenous Vein Grafts; RRISC = Reduction of Restenosis in Saphenous Vein Grafts With Cypher Sirolimus-Eluting Stent; SOS = Stenting of Saphenous Vein Grafts; SYMBIOT III = A Prospective, Randomized Trial of a Self-Expanding PTFE Stent Graft During SVG Intervention–Late Results; TLR = target lesion revascularization.

Drug-eluting stents. The RRISC (Reduction of Restenosis in Saphenous Vein Grafts With Cypher Sirolimus-Eluting Stent) trial (21), which included 75 patients, reported that sirolimus-eluting stents (Cordis, Warren, New Jersey) reduced late loss, the binary restenosis rate, and target lesion and vessel revascularization compared with BMS at 6-month follow-up. However, the DELAYED RRISC (Death and Events at Long-Term Follow-Up Analysis: Extended Duration of the Reduction of Restenosis in Saphenous Vein Grafts With Cypher Stent) study (45), which was a post hoc analysis of RRISC trial at 3 years, reported similar rates of target vessel revascularization. Although statistically underpowered for clinical outcomes, significantly higher all-cause mortality at 3 years was reported with sirolimus-eluting stents compared with BMS. The SOS (Stenting of Saphenous Vein Grafts) trial (22), which included 80 patients randomized to either paclitaxel-eluting stents (Taxus, Boston Scientific Corp., Maple Grove, Minnesota) or BMS, demonstrated a significant reduction in MACE driven by lower target lesion revascularization rates with paclitaxel-eluting stents without increased death or myocardial infarction through nearly 3-year follow-up (46). The primary endpoint of these 2 small trials was angiographic restenosis, and the results showed similar angiographic restenosis rates at 6- (RRISC) and 12-month (SOS) follow-up but higher mortality at long-term follow-up in the RRISC trial. ISAR-CABG (Prospective, Randomized Trial of Drug-Eluting Stents Versus Bare Metal Stents for the Reduction of Restenosis in Bypass Grafts), which randomized 610 patients with diseased SVGs to DES and BMS, the primary endpoint of MACE at 1-year post index PCI was lower in the DES group than in the BMS group (15.4% vs. 22.1%, p = 0.03) and was mainly driven by a nearly 50% relative reduction in the risk of target lesion revascularization (7.2% vs. 13.1%, p = 0.02), with nonsignificant differences in mortality (47).

A meta-analysis comparing DES with BMS in SVG intervention (which also included nonrandomized studies) has also reported lower mortality, MACE, target lesion revascularization, and target vessel revascularization without increased risk of myocardial infarction or stent thrombosis (48). Eight other meta-analyses comparing DES with BMS in SVG intervention have demonstrated consistent results of improved efficacy with DES and no significant safety hazard (48–55).

Two ongoing trials are comparing DES with BMS in SVGs: 1) BASKETSAVAGE (Basel Stent Kosten Effektivitäts Trial–Saphenous Venous Graft Angioplasty Using Glycoprotein IIb/IIIa Receptor Inhibitors and Drug-Eluting Stents) (NCT00595647); and 2) the Veterans' Affairs Cooperative Study #571, DIVA (Drug Eluting Stents Versus Bare-Metal Stents in Saphenous Vein Graft Angioplasty) trials (NCT01121224).

Choice of DES in SVG. In a multicenter analysis of 172 real-world patients comparing first-generation DES, SVG intervention with sirolimus- and paclitaxel-eluting stents resulted in nonsignificant differences in survival (HR: 1.28, 95% CI: 0.39 to 4.25, p = 0.69) and target vessel revascularization (HR: 2.54, 95% CI: 0.84 to 7.72, p = 0.09) (56). Outcomes comparing second-generation stents in SVG intervention are not yet available; the SOS-Xience V (Prospective Evaluation of the Xience V Everolimus-Eluting Stent in Saphenous Vein Graft Atherosclerosis: The Stenting of Saphenous Vein Grafts Xience V Angiographic Study) (NCT00911976) will provide initial results with the everolimus-eluting stent in 2011.

SVG Intervention Technique

Pre-dilation versus direct stenting. As opposed to pre-dilation with balloon angioplasty, direct stenting has the potential benefit of trapping debris and decreasing distal embolization that may occur from repeated balloon inflations. In a registry of unselected patients who underwent SVG intervention, direct stenting was associated with a nearly 50% reduction in CK-MB elevations greater than 4× normal (13.6% vs. 23%, p < 0.12), overall lower maximum CK-MB release (9.5 vs. 19.6, p < 0.001), and fewer non–Q-wave myocardial infarctions (10.7% vs. 18.4%, p < 0.02) (57). A prospective randomized trial is needed to determine whether pre-dilation versus direct stenting is effective in reducing distal embolization.

Small stent diameter. In a study of 209 SVG lesions treated with DES, Hong et al. (58) examined the outcomes of 3 groups according to the ratio of the stent diameter to the average intravascular ultrasound reference lumen diameter (group I: <0.89, group II: 0.9 to 1.0, and group III: >1.0). Plaque intrusion volume as defined as the amount of tissue extrusion through the stent struts after SVG intervention was smallest in group I (group I: 0.25 ± 0.68 mm^3, group II: 0.40 ± 0.68 mm^3, and group III: 0.75 ± 1.34 mm^3; p = 0.007). The incidence of CK-MB elevation >3× normal was 6% in group I, 9% in group II, and 19% in group III (p = 0.03) without an increase in clinical events at 1 year. The incidence of 1-year target lesion revascularization (group I: 13%, group II: 9%, and group III: 15%; p = 0.5) and target vessel revascularization (group I: 13%, group II: 13%, and group III: 15%; p = 0.9) was similar. While the concept of undersized stent selection to reduce distal embolization is intriguing, such a method must be balanced by theoretically possibly higher rates of restenosis and stent thrombosis. Therefore, a prospective, randomized study is required to confirm the theoretical benefits of this technique.

Embolic protection devices. Distal embolization is common in SVG interventions. Particulate debris has been retrieved from as many as 91% of distal embolic protection devices (59). Despite the class I American College of Cardiology/

Table 3. Comparison of Different Embolic Protection Devices

	Distal Filter	Distal Balloon Occlusion	Proximal Balloon Occlusion
Complete occlusion	No	Yes	Yes
Allows perfusion	Yes	No	No
Ischemia	No	Yes	Yes
Maintenance of antegrade blood flow during intervention	Yes	No	No
Protects before crossing lesion	No	No	Yes
Crossing profile	High (3.2-F)*	Low (2.7)†	NA
Maneuverability	Reduced	Good	Good
Ease of use	Simple	Complex	Complex
Capture of smaller particles	No	Yes	Yes
Capture of neurohormonal substances	No	Yes	Yes

*FilterWire EZ (Boston Scientific). †PercuSurge GuardWire (Medtronic).
NA = not available.

American Heart Association PCI guidelines' recommendation for the use of embolic protection devices in SVG intervention, overall adoption remains low (60). In the American College of Cardiology National Cardiovascular Data CathPCI Registry, embolic protection was only used in 23% of patients (10). Currently available embolic protection devices include occlusion balloon plus aspiration systems, distal filter-based devices, and proximal flow interruption catheters (Table 3) (61).

Distal balloon occlusion devices. Distal balloon occlusion of the SVG beyond the lesion creates a stagnant column of blood that may prevent plaque embolization into the myocardial bed (Fig. 1). Upon the conclusion of the intervention, the blood with contained debris can be removed by an aspiration catheter before occlusion balloon deflation and restoration of antegrade blood flow. Several advantages are the low crossing profile and entrapment of debris of all sizes as well as neurohumoral mediators such as serotonin and thromboxane that may have an adverse effect on the distal microvasculature. Its disadvantages are: 1) the need to cross the lesion before adequate protection, possibly liberating friable material before balloon occlusion; 2) temporary cessation of blood flow leading to ischemia and possible hemodynamic instability, as well as limiting visualization making accurate stent placement difficult; 3) inability to obtain full evacuation, especially near the occlusion balloon; and 4) possible traumatic injury to the SVG during balloon occlusion. Distal lesions are not amenable to distal balloon occlusion devices because a relatively disease-free landing zone of approximately 3 cm distal to the lesion is required for placement of the occlusion balloon.

The Food and Drug Administration (FDA)–approved PercuSurge GuardWire (Medtronic, Minneapolis, Minnesota) consists of a 0.014-inch diameter wire with a central lumen affixed to an inflatable distal occlusion balloon (Fig. 2, Table 4). SAFER (Saphenous Vein Graft Angioplasty Free of Emboli, Randomized Trial) (20) demonstrated that it decreased the incidence of no-reflow (3.2% vs. 8.3%, p = 0.005) and 30-day MACE (9.6% vs. 16.5%, p = 0.004).

The TriActiv embolic protection system (Kensey Nash Corporation, Exton, Pennsylvania) differs from the GuardWire in that it has a flush catheter, which infuses heparinized saline, attached to the balloon guidewire. The mixture of saline, blood, and atheromatous debris is extracted through the guiding catheter. PRIDE (A Prospective, Randomized Controlled Trial of Distal Protection With the
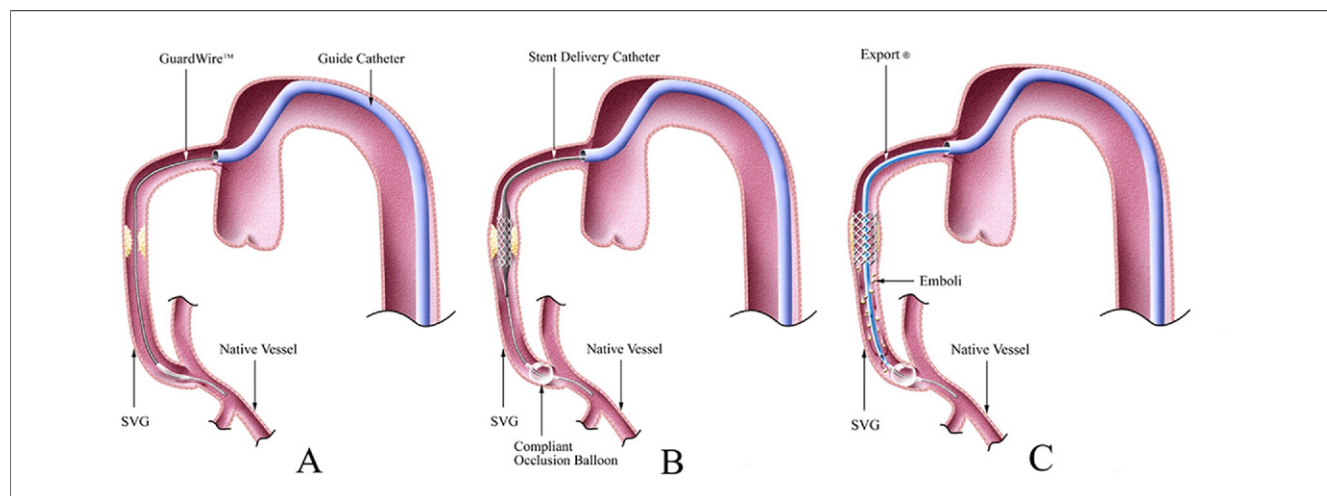
Figure 1. Distal Balloon Occlusion Device

(A) The lesion is crossed with the GuardWire. **(B)** GuardWire balloon inflated and percutaneous coronary intervention performed under distal protection. **(C)** Thereafter, the balloon is inflated until angiography shows no forward flow. Saphenous vein graft (SVG) intervention can be performed with complete distal protection. Image provided courtesy of Medtronic. ©2011 Medtronic or its affiliates. All rights reserved.
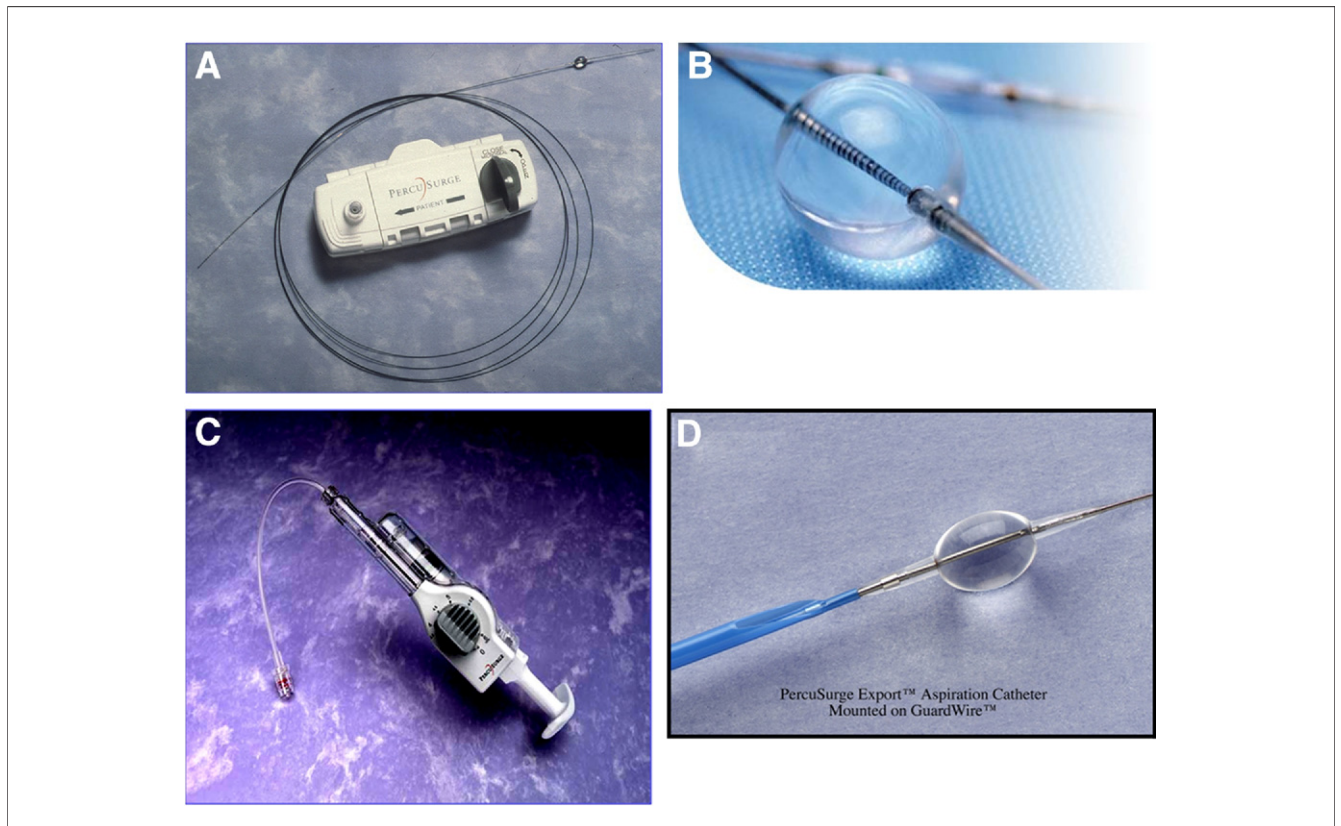
Figure 2. PercuSurge GuardWire Distal Protection System

(A) A Microseal adapter controls a miniature valve within the hypotube and keeps the occlusion balloon inflated while standard interventional devices such as balloons and stents are passed over the wire to perform percutaneous coronary intervention. A 0.014-inch nitinol-based hypotube guidewire inflates a **(B)** distal occlusion balloon, which stops blood flow to the distal microcirculation. **(C)** The EZ-Flator inflates the balloon to stop blood flow. **(D)** The Export aspiration catheter removes debris while the occlusion is inflated. Image provided courtesy of Medtronic. ©2011 Medtronic or its affiliates. All rights reserved.

Kensey-Nash TriActiv System Compared to the GuardWire or FilterWire) trial (62) reported that it was noninferior to a control group of patients treated with either the GuardWire and the FilterWire EZ (Boston Scientific) in terms of 30-day MACE (11.2% vs. 10.1%, p = 0.65; p = 0.02 for noninferiority). However, the TriActiv system was associated with more vascular complications (10.9% vs. 5.4%, p = 0.01) and the need for blood transfusion (7.7% vs. 3.5%, p = 0.02), perhaps in part because the procedure was performed with larger caliber (8-F) guiding catheters.

Distal embolic filters. A distal filter system is composed of a tightly wrapped filter attached to a guidewire and sheathed within a delivery catheter for placement distal to the target lesion (Fig. 3). It can trap debris that embolize while the intervention is performed over the guidewire. Upon completion, a retrieval catheter is advanced over the guidewire to collapse the filter and remove it along with retained contents.

Its advantages include the ease-of-use, maintenance of antegrade blood flow during intervention to avoid ischemia and the need for "hurried" PCI, and the ability to inject contrast media to facilitate accurate stent placement. It may be preferred in patients who are undergoing high-risk intervention and are at increased risk for hemodynamic instability in instances of temporary SVG occlusion, such as patients with severe left ventricular dysfunction, last remaining conduit, and need for multiple stents. Disadvantages include a high crossing profile (large diameter sheath approximately 3- to 4-F), poor maneuverability, inability to completely entrap microparticles and neurohumoral substances, possible occlusion of the filter due to large amounts of debris, possible incomplete apposition of the filter, and inability to use in very distal lesions because of the need for a landing zone to deploy the filter.

The first FDA-approved filter was the FilterWire EX (Boston Scientific). The FIRE (FilterWire EX Randomized Evaluation) trial (63) showed similar MACE rates at 30 days (9.9% vs. 11.6%, superiority p = 0.53, noninferiority p = 0.0008) and 6 months (19.3 vs. 21.9%, p = 0.44) (64) with the FilterWire EX and GuardWire plus system.

The BLAZE (Embolic Protection Transluminally with the FilterWire EZ Device in Saphenous Vein Grafts) registry reported on the outcomes of the second-generation FilterWire EZ, which has a lower crossing profile compared

Table 4. 30-Day Outcomes of Selected Trials of Embolic Protection Devices

	MACE	Death	MI	No-Reflow
SAFER				
GuardWire	9.6	1.0	8.6	3
Control	16.5	2.3	14.7	9
p value	0.004	0.17	0.008	0.001
FIRE				
FilterWire EX	9.9	0.9	9.0	NA
GuardWire	11.6	0.9	10.0	NA
p value	0.53	0.99	0.69	NA
BLAZE				
FilterWire EZ	6.7	0	6.7	NA
PRIDE				
TriActiv	11.2	1.3	9.9	NA
GuardWire/FilterWire EZ	10.1	0.6	8.8	NA
p value	0.65	0.45	0.64	NA
SPIDER				
Spider	9.1	0.3	7.7*	NA
GuardWire/FilterWire EZ	8.4	0.6	7.0*	NA
p value	0.79	NS	NS	NA
PROXIMAL				
Proxis	9.2	0.7	6.4*	NA
Control	10.0	1.0	7.9*	NA
p value	0.78	1.0	0.52	NA

Values are percentages. FilterWire is a product of Boston Scientific. GuardWire is a product of Medtronic Inc. Proxis is a product of St. Jude Medical. Spider is a product of ev3. TriActiv is a product of Kensey Nash. *Non–Q-wave MI.

BLAZE = Embolic Protection Transluminally with the FilterWire EZ Device in Saphenous Vein Grafts; FIRE = FilterWire EX Randomized Evaluation; NS = nonsignificant; PRIDE = A Prospective, Randomized Controlled Trial of Distal Protection With the Kensey-Nash TriActiv System Compared to the GuardWire or FilterWire; PROXIMAL = Proximal Protection During Saphenous Vein Graft Intervention; SAFER = Saphenous Vein Graft Angioplasty Free of Emboli, Randomized Trial; SPIDER = Saphenous Vein Graft Protection in a Distal Embolic Protection Randomized; other abbreviations as in Tables 1 and 2.

with the FilterWire EX (3.2-F vs. 3.9-F), an improved delivery system with a retooled nose cone, greater filter apposition of bends, and a smaller pore size (100 μm vs. 110 μm) (65). The device success rate was 97.8%, and 30-day MACE was 6.7%, all due to non–Q-wave myocardial infarction.

The SpideRx embolic protection device (ev3, Plymouth, Minnesota) is also FDA-approved for SVG intervention. It can cross the lesion using a conventional 0.014-inch guidewire, which may be beneficial in tortuous vessels. It is subsequently inserted through a delivery sheath over the guidewire. In the SPIDER (Saphenous Vein Graft Protection in a Distal Embolic Protection Randomized) trial, the SpideRx nitinol filter was noninferior to the FilterWire and the GuardWire (MACE: 9.1% vs. 8.4%, p = 0.001 for noninferiority) (66).

Another filter-based distal protection device, CardioShield (MedNova Ltd., Galway, Ireland), did not demonstrate noninferiority to the GuardWire. In the CAPTIVE (A Prospective, Randomized, Controlled Trial of Distal Pro-

tection With the Third-Generation Mednova Emboshield Compared to the GuardWire or FilterWire) (67), when analyzing the data on a modified intention-to-treat, in the noninferiority analysis, the 30-day MACE rate was significantly lower in patients treated with the GuardWire than in patients treated with the CardioShield group (8.8 vs. 10.1%, p = 0.022).

Proximal balloon occlusion device. The FDA-approved Proxis embolic protection system (St. Jude Medical, Maple Groves, Minnesota) employs a distal balloon that seals the inner sheath to the SVG while the proximal balloon seals the inner sheath to the inside of the guiding catheter (Figs. 4 and 5). Proximal balloon occlusion creates a stagnant column of blood suspending debris from embolizing downstream into the microvasculature. After completion of the intervention, the blood containing the debris can be aspirated with a suction catheter before deflating the balloon and restoring blood flow. The advantages are that the operator can use the guidewire of choice, protection from distal embolization of atheromatous debris can be established before crossing the lesion, both particles and vasoactive substances can be retrieved downstream, side branches can be protected, and distal lesions that are not amenable to distal embolic protection because of lack of a landing zone can be treated. The disadvantages are the inability to use the device in ostial or very proximal lesions as approximately 15 mm of disease-free segment proximal to the target lesion is required, and the cessation of antegrade perfusion resulting in myocardial ischemia.

In the PROXIMAL (Proximal Protection During Saphenous Vein Graft Intervention) trial (68), the Proxis device demonstrated noninferiority to the FilterWire or GuardWire. At 30 days, MACE occurred in 10.0% of control and 9.2% of test patients; difference = −0.8% (95% CI: −5.5% to 4.0%); p for noninferiority = 0.006.

Pharmacological Treatment of Slow or No-Reflow

Compromise of the integrity of the microvascular flow can lead to slow or no-reflow. Independent predictors for slow or no-reflow in SVG intervention include probable thrombus (OR: 6.9; 95% CI: 2.1 to 23.9; p = 0.001), acute coronary syndromes (OR: 6.4; 95% CI: 2.0 to 25.3; p = 0.003), degenerated SVG (OR: 5.2; 95% CI: 1.7 to 16.6; p = 0.003), and lesion ulceration (OR: 3.4; 95% CI: 0.99 to 11.6; p = 0.04) (16). Although convincing clinical trial data are lacking, pharmacotherapy targeted at microvascular flow with intragraft administration of vasodilators is the mainstay of treatment for slow or no-reflow. Delivery of pharmacotherapy to the distal microvasculature can be maximized with a microcatheter like an aspiration thrombectomy catheter.

Adenosine. Adenosine is an endogenous purine nucleoside, a vasodilator of arteries and arterioles, and inhibits platelet
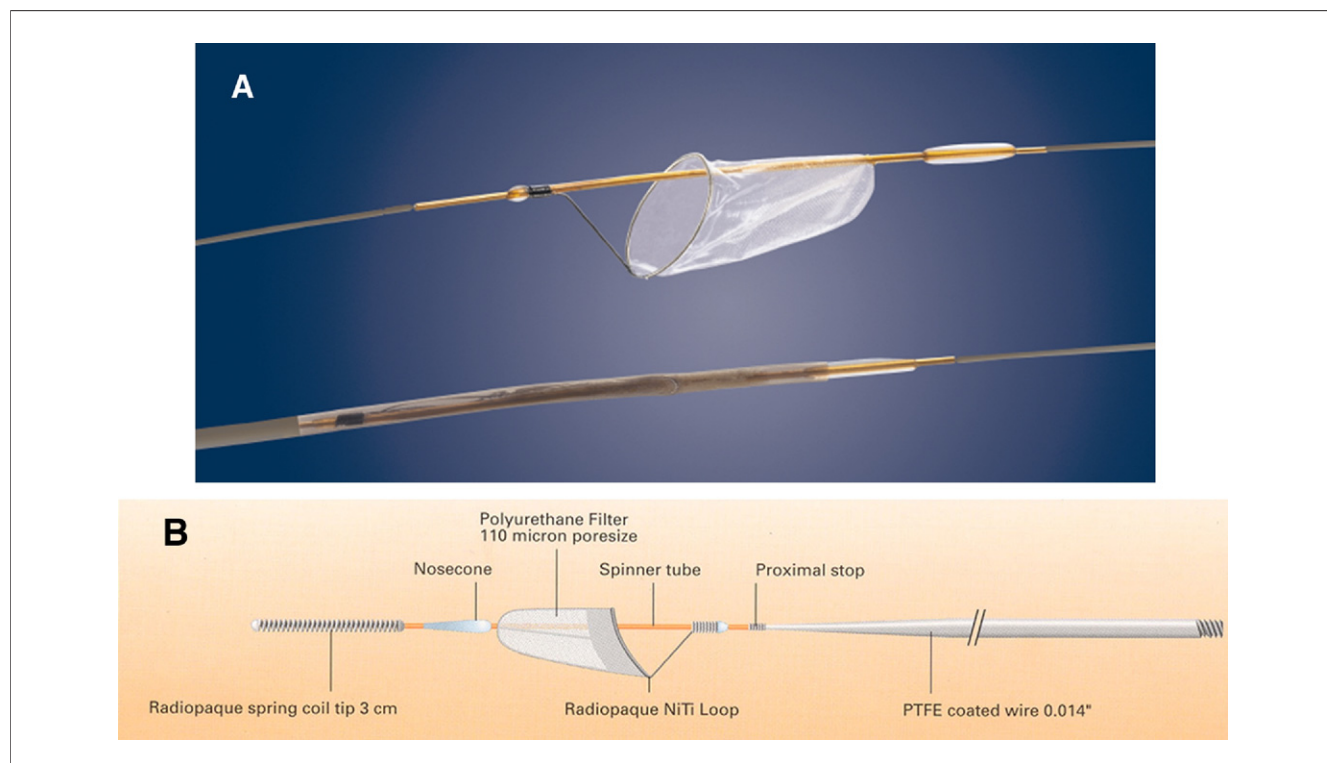
Figure 3. FilterWire EZ

(A) The FilterWire is composed of a polyurethane filter basket pre-mounted on a 0.014-inch guidewire and pre-loaded on a delivery sheath. The pore size is 100 μm. **(B)** The FilterWire is compatible with a 6-F guiding catheter, has a crossing profile of 3.2-F, can protect saphenous vein grafts 3.5 to 5.5 mm in diameter, and is available in wire lengths of 190 and 300 cm. A landing zone of >30 mm is required and a retrieval sheath is required for capture and removal of the filter. Image provided courtesy of Boston Scientific. ©2011 Boston Scientific Corporation or its affiliates. All rights reserved. PTFE = polytetrafluorethylene.

activation and aggregation. Although severe bradycardia may occur due to its effect on sinoatrial and atrioventricular nodal conduction, the half-life of adenosine is very short and these effects rarely last more than a few seconds. Prophylactic administration of intragraft adenosine does not appear to decrease the risk of slow or no-reflow, but it can reverse slow or no-reflow with multiple boluses (69). In a retrospective study of 143 patients, the incidence of slow or no-reflow was similar in patients who received pre-procedural administration of intragraft adenosine and those who did not (14.2% vs. 13.6%, p = 0.9). In patients who developed slow or no-reflow, high doses of intragraft adenosine (≥5 boluses of 24 μg each) resulted in reversal of slow or no-reflow compared with low doses (<5 boluses) (91% vs. 33%, p = 0.02), and final Thrombolysis In Myocardial Infarction (TIMI) flow grade was significantly improved (2.7 ± 0.6 vs. 2.0 ± 0.8, p = 0.04). Rapid, high-velocity injections of intragraft adenosine to reverse slow or no-reflow resulted in TIMI flow grade 3 in 91% of cases (70). **Nitroprusside.** Nitroprusside is a direct donor of nitric oxide. In a study of 20 patients, 9 (45%) developed slow or no-reflow after SVG intervention, intracoronary administration of nitroprusside (median dose: 200 μg) resulted in

significant and rapid improvement in both angiographic flow (p < 0.01 compared with pre-treatment angiogram) and blood flow velocity (p < 0.01 compared with pre-treatment angiogram) (71). Nitroprusside was not associated with significant hypotension or other adverse clinical events in this study, but can cause profound hypotension in patients who are volume depleted or hypotensive at baseline.

Verapamil. Prophylactic intragraft administration of verapamil before SVG intervention tended to reduce the occurrence of no-reflow compared with placebo (0% vs. 33.3%, p = 0.10), increased the TIMI frame count (53.3 ± 22.4% faster vs. 11.5 ± 38.9%, p = 0.016), and resulted in a trend toward improved TIMI myocardial perfusion grade (72). Intragraft verapamil (100 to 500 μg) improved the flow in all 32 episodes of no-flow (TIMI flow grade 1.4 ± 0.8 pre-, to 2.8 ± 0.5 post-intragraft verapamil, p < 0.001) and reestablished TIMI flow grade 3 in 88% of cases (73).

Nicardipine. Prophylactic intragraft administration of nicardipine, a potent arteriolar vasodilator, was followed by direct stenting for degenerated SVG without the use of a distal protection device in 83 patients and resulted in a total creatine phosphokinase >3× the upper limit of normal and CK-MB >3× the upper limit of normal in 1.5% and 4.4%
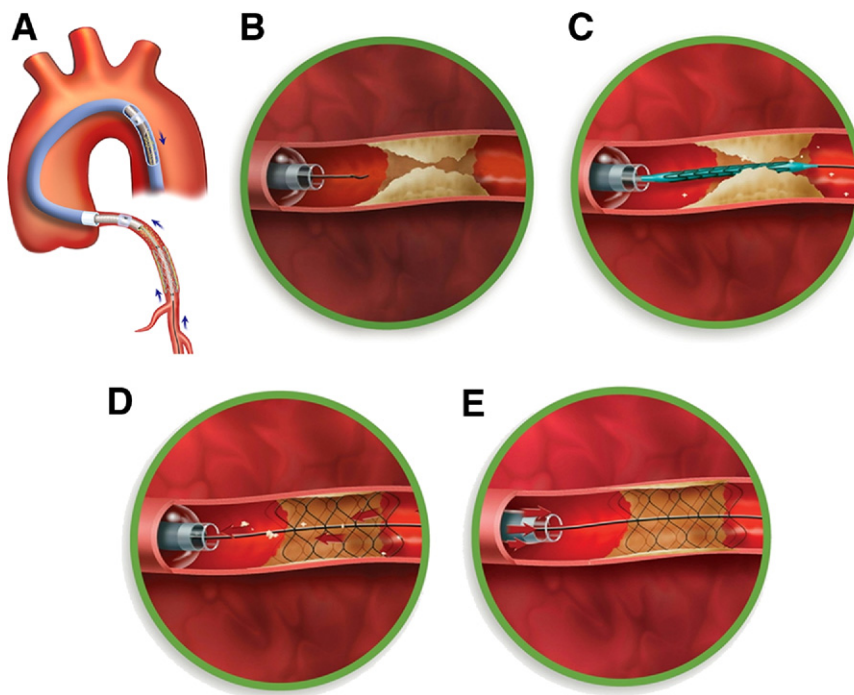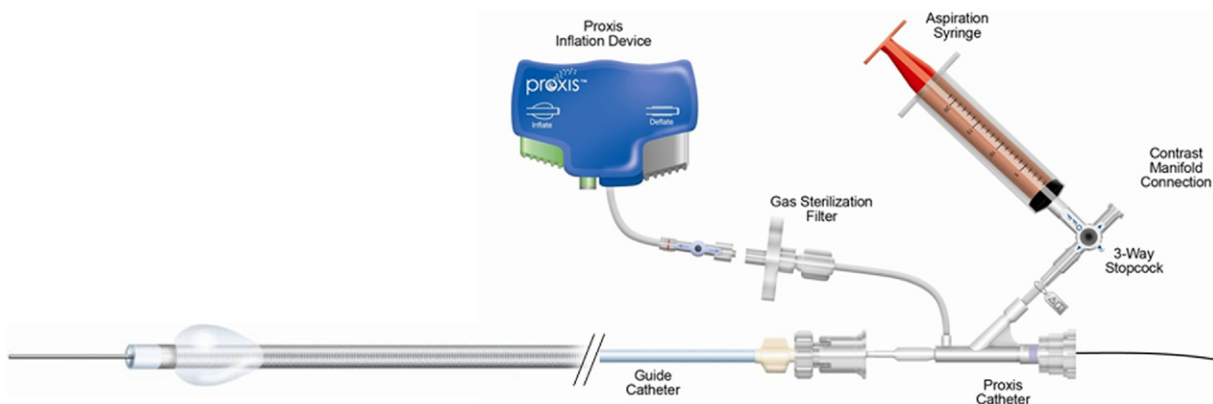
Figure 4. Proxis Proximal Embolic Protection Device

(A) Proximal embolic protection device can provide protection before crossing the lesion with a guidewire. **(B)** After the Proxis is advanced into the target vessel proximal to the lesion, the balloon is inflated to suspend blood flow in the SVG. **(C)** SVG intervention can be performed after a guidewire is advanced across the lesion. **(D)** Embolic debris is aspirated from the SVG after stenting. **(E)** The balloon is deflated, restoring blood flow in the SVG. Image provided courtesy of St. Jude Medical. ©2011 St. Jude Medical or its affiliates. All rights reserved. SVG = saphenous vein graft.

or patients, respectively (74). Slow or no-reflow occurred transiently in 2.4% of patients. In-hospital MACE occurred in 4.4%, and no additional MACE occurred from hospital discharge to 30 days.

Conclusions

Long-term event-free survival after coronary artery bypass surgery will continue to be limited as long as SVGs are used

Figure 5. Proxis Proximal Embolic Protection Device

The CO_2 inflation device is attached to the catheter and automatically inflates the Proxis sealing balloon. Another button deflates the balloon. An aspiration syringe removes liberated debris before balloon deflation. Image provided courtesy of St. Jude Medical. ©2011 St. Jude Medical or its affiliates. All rights reserved.

as conduits for surgical revascularization. Percutaneous SVG revascularization is a feasible treatment strategy, but success is limited by high rates of periprocedural adverse events (e.g., no-reflow, periprocedural myocardial infarction), intermediate-term restenosis, and SVG progression outside of the treated segments. Embolic protection devices are recommended by the American College of Cardiology/ American Heart Association guidelines to reduce periprocedural complications during SVG intervention and should be used whenever feasible to decrease the risk of distal embolization. Pre-dilation with an undersized balloon may improve procedural success by facilitating the delivery and deployment of the embolic protection device. The optimal pharmacological treatment for slow or no-reflow is unclear, although a variety of vasodilators have shown promise. Covered stents have failed to demonstrate clinical benefit in reducing periprocedural myocardial infarction and restenosis rates. Restenosis after SVG intervention is high with BMS. Use of DES may decrease restenosis compared with use of BMS, but confirmation from the ongoing large, randomized, controlled clinical trials are necessary to demonstrate the safety and efficacy of DES in SVGs. In general, patient outcomes are optimized when coronary artery bypass graft procedures are done without SVGs, although pan-arterial revascularization is still the exception rather than the rule. When diseased SVGs cause progressive ischemic syndromes, PCI of the native coronary arteries should be considered whenever possible.

Reprint requests and correspondence: Dr. Michael S. Lee, UCLA Medical Center, Adult Cardiac Catheterization Laboratory, 10833 Le Conte Avenue, Room A2-237 CHS, Los Angeles, California 90095-171715. E-mail: mslee@mednet.ucla.edu.

REFERENCES

1. Widimsky P, Straka Z, Stros P, et al. One-year coronary bypass graft patency: a randomized comparison between off-pump and on-pump surgery angiographic results of the PRAGUE-4 trial. Circulation 2004;110:3418–23.
2. Alexander JH, Hafley G, Harrington RA, et al., for the PREVENT IV Investigators. Efficacy and safety of edifoligide, an E2F transcription factor decoy, for prevention of vein graft failure following coronary artery bypass graft surgery: PREVENT IV: a randomized controlled trial. JAMA 2005;294:2446–54.
3. Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper GD, 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.
4. Gluckman TJ, McLean RC, Schulman SP, et al. Effects of aspirin responsiveness and platelet reactivity on early vein graft thrombosis after coronary artery bypass graft surgery. J Am Coll Cardiol 2011;57:1069–77.
5. Halabi AR, Alexander JH, Shaw LK, et al. Relation of early saphenous vein graft failure to outcomes following coronary artery bypass surgery. Am J Cardiol 2005;96:1254–9.
6. Khot UN, Friedman DT, Pettersson G, Smedira NG, Li J, Ellis SG. Radial artery bypass grafts gave an increased occurrence of angiographically

7. severe stenosis and occlusion compared with left internal mammary arteries and saphenous vein grafts. Circulation 2004;109:2086–91.
7. Shroyer AL, Grover FL, Hattler B, et al., for the ROOBY Study Group. On-pump versus off-pump coronary-artery bypass surgery. N Engl J Med 2009;361:1827–37.
8. Goldman S, Zadina K, Moritz T, et al., for the VA Cooperative Study Group #207/297/364. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. J Am Coll Cardiol 2004;44:2149–56.
9. Brodie BR, Wilson H, Stuckey T, et al. Outcomes with drug-eluting versus bare-metal stents in saphenous vein graft intervention: results from the STENT (Strategic Transcatheter Evaluation of New Therapies) Group. J Am Coll Cardiol Intv 2009;2:1105–12.
10. Brilakis ES, Wang TY, Rao SV, et al. Frequency and predictors of drug-eluting stent use in saphenous vein bypass graft percutaneous coronary interventions: a report from the American College of Cardiology National Cardiovascular Data CathPCI Registry. J Am Coll Cardiol Intv 2010;3:1068–73.
11. Morrison DA, Sethi G, Sacks J, et al., for the VA Cooperative Study Group #385. Percutaneous coronary intervention versus repeat bypass surgery for patients with medically refractory myocardial ischemia: AWESOME randomized trial and registry experience with post-CABG patients. J Am Coll Cardiol 2002;40:1951–4.
12. Loop FD. A 20-year experience in coronary artery reoperations. Eur Heart J 1989;10 Suppl M:78–84.
13. Foster ED, Fisher LD, Kaiser GC, Myers WO. Comparison of operative mortality and morbidity for initial and repeat coronary artery bypass grafting: the Coronary Artery Surgery Study (CASS) registry experience. Ann Thorac Surg 1984;38:563–70.
14. Lytle BW, Loop FD, Cosgrove DM, et al. Fifteen hundred coronary reoperations: results and determinants of early and late survival. J Thorac Cardiovasc Surg 1987;93:847–59.
15. O'Connor GT, Malenka DJ, Quinton H, et al., for the Northern New England Cardiovascular Disease Study Group. Multivariate prediction of in-hospital mortality after percutaneous coronary interventions in 1994–1996. J Am Coll Cardiol 1999;34:681–91.
16. Sdringola S, Assali AR, Ghani M, et al. Risk assessment of slow or no-reflow phenomenon in aortocoronary vein graft percutaneous intervention. Catheter Cardiovasc Interv 2001;54:318–24.
17. Abbo KM, Dooris M, Glazier S, et al. Features and outcomes of no-reflow after percutaneous coronary intervention. Am J Cardiol 1995;75:778–82.
18. Carter LI, Golzar JA, Cavendish JJ, Dixon S. Embolic protection of saphenous vein graft percutaneous interventions. J Interv Cardiol 2007;20:351–8.
19. Hong MK, Mehran R, Dangas G, et al. Creatine kinase-MB enzyme elevation following successful saphenous vein graft intervention is associated with late mortality. Circulation 1999;100:2400–5.
20. Baim DS, Wahr D, George B, et al., for the SAFER Trial Investigators. Randomized trial of a distal embolic protection device during percutaneous intervention of saphenous vein aorto-coronary bypass grafts. Circulation 2002;105:1285–90.
21. Vermeersch P, Agostoni P, Verheye S, et al. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC Trial. J Am Coll Cardiol 2006;48:2423–31.
22. Brilakis ES, Lichtenwalter C, de Lemos JA, et al. A randomized controlled trial of a paclitaxel-eluting stent versus a similar bare-metal stent in saphenous vein graft lesions: the SOS (Stenting of Saphenous Vein Grafts) trial. J Am Coll Cardiol 2009;53:919–28.
23. Coolong A, Baim DS, Kuntz RE, et al. Saphenous vein graft stenting and major adverse cardiac events: a predictive model derived from a pooled analysis of 3958 patients. Circulation 2008;117:790–7.
24. Kirtane AJ, Heyman ER, Metzger C, Breall JA, Carrozza JP Jr. Correlates of adverse events during saphenous vein graft intervention with distal embolic protection: a PRIDE substudy. J Am Coll Cardiol Intv 2008;1:186–91.
25. Giugliano GR, Kuntz RE, Popma JJ, et al., for the SAFER Trial Investigators. Determinants of 30-day adverse events following saphe-

nous vein graft intervention with and without a distal occlusion embolic protection device. Am J Cardiol 2005;95:173–7.

26. Ahmed JM, Dangas G, Lansky AJ, et al. Influence of gender on early and one-year clinical outcomes after saphenous vein graft stenting. Am J Cardiol 2001;87:401–5.

27. Lee MS, Hu PP, Aragon J, et al. Impact of chronic renal insufficiency on clinical outcomes in patients undergoing saphenous vein graft intervention with drug-eluting stents: a multicenter Southern Californian Registry. Catheter Cardiovasc Interv 2010;76:272–8.

28. Gruberg L, Weissman NJ, Pichard AD, et al. Impact of renal function on morbidity and mortality after percutaneous aortocoronary saphenous vein graft intervention. Am Heart J 2003;145:529–34.

29. Ellis SG, Brener SJ, DeLuca S, et al. Late myocardial ischemic events after saphenous vein graft intervention—importance of initially "nonsignificant" vein graft lesions. Am J Cardiol 1997;79:1460–4.

30. Rodés-Cabau J, Bertrand OF, Larose E, et al. Comparison of plaque sealing with paclitaxel-eluting stents versus medical therapy for the treatment of moderate nonsignificant saphenous vein graft lesions: the moderate vein graft lesion stenting with the Taxus stent and intravascular ultrasound (VELETI) pilot trial. Circulation 2009;2:1978–86.

31. Rodés-Cabau J. Plaque sealing with paclitaxel-eluting stents for the treatment of moderate non-significant saphenous vein graft lesions. Three-year follow-up of the VELETI (Moderate Vein Graft Lesion Stenting With the Taxus Stent and Intravascular Ultrasound) trial. Paper presented at: i2 Summit 2010; March 14, 2010; Atlanta, GA.

32. Al-Lamee R, Ielasi A, Latib A, et al. Clinical and angiographic outcomes after percutaneous recanalization of chronic total saphenous vein graft occlusion using modern techniques. Am J Cardiol 2010;106:1721–7.

33. Mak KH, Challapalli R, Eisenberg MJ, Anderson KM, Califf RM, Topol EJ. Effect of platelet glycoprotein IIb/IIIa receptor inhibition on distal embolization during percutaneous revascularization of aortocoronary saphenous vein grafts. EPIC Investigators. Evaluation of IIb/IIIa platelet receptor antagonist 7E3 in Preventing ischemic Complications. Am J Cardiol 1997;80:985–8.

34. Roffi M, Mukherjee D, Chew DP, et al. Lack of benefit from intravenous platelet glycoprotein IIb/IIIa receptor inhibition as adjunctive treatment for percutaneous interventions of aortocoronary bypass grafts: a pooled analysis of five randomized clinical trials. Circulation 2002;106:3063–7.

35. Ellis SG, Lincoff AM, Miller D, et al. Reduction in complications of angioplasty with abciximab occurs largely independently of baseline lesion morphology. EPIC and EPILOG Investigators. Evaluation of 7E3 for the Prevention of Ischemic Complications. Evaluation of PTCA to Improve Long-Term Outcome With Abciximab GPIIb/IIIa Receptor Blockade. J Am Coll Cardiol 1998;32:1619 –23.

36. Jonas M, Stone GW, Mehran R, et al. Platelet glycoprotein IIb/IIIa receptor inhibition as adjunctive treatment during saphenous vein graft stenting: differential effects after randomization to occlusion or filter-based embolic protection. Eur Heart J 2006;27:920–8.

37. Rha SW, Kuchulakanti PK, Pakala R, et al. Bivalirudin versus heparin as an antithrombotic agent in patients who undergo percutaneous saphenous vein graft intervention with a distal protection device. Am J Cardiol 2005;96:67–70.

38. Kumar D, Dangas G, Mehran R, et al. Comparison of bivalirudin versus bivalirudin plus glycoprotein IIb/IIIa inhibitor versus heparin plus glycoprotein IIb/IIIa inhibitor in patients with acute coronary syndromes having percutaneous intervention for narrowed saphenous vein aorto-coronary grafts (the ACUITY Trial Investigators). Am J Cardiol 2010;106:941–5.

39. Savage MP, Douglas JS, Fischman DL, et al., for the Saphenous Vein De Novo Trial Investigators. Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. N Engl J Med 1997;337:740–7.

40. Turco MA, Buchbinder M, Popma JJ, et al. Pivotal, randomized U.S. study of the Symbiot covered stent system in patients with saphenous vein graft disease: eight-month angiographic and clinical results from the Symbiot III trial. Catheter Cardiovasc Interv 2006;68:379–88.

41. Stankovic G, Colombo A, Presbitero P, et al., for the RECOVERS Trial Investigators. Randomized evaluation of polytetrafluoroethylene-covered stent in saphenous vein grafts: the Randomized Evaluation of polytetrafluoroethylene COVERed stent in Saphenous vein grafts (RECOVERS) trial. Circulation 2003;108:37–42.

42. Stone GW, Goldberg S, O'Shaughnessy C, et al. Five-year follow-up of polytetrafluoroethylene-covered stents compared with bare-metal stents in aortocoronary saphenous vein graft: the randomized BARRICADE (Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events) Trial. J Am Coll Cardiol Intv 2011;4:300–9.

43. Abizaid A, Weiner B, Bailey SR, Londero H. Use of a self-expanding super-elastic all-metal endoprosthesis; to treat degenerated SVG lesions: the SESAME first in man trial. Catheter Cardiovasc Interv 2010;76:781–6.

44. Maia F, Costa JR Jr., Abizaid A, et al. Preliminary results of the INSPIRE trial with the novel MGuard stent system containing a protection net to prevent distal embolization. Catheter Cardiovasc Interv 2010;76:86–92.

45. Vermeersch P, Agostoni P, Verheye S, et al., for the DELAYED RRISC Investigators. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC Trial. J Am Coll Cardiol 2007;50:261–7.

46. Brilakis ES, Lichtenwalter C, Abdel-karim AR, et al. Continued benefit from paclitaxel-eluting compared to bare-metal stent implantation in saphenous vein graft lesions during long-term follow-up of the SOS (Stenting of Saphenous Vein Grafts) trial. J Am Coll Cardiol Intv 2011;4:176–82.

47. Mehilli J. ISAR-CABG: randomized, superiority trial of drug-eluting-stent and bare metal stent in saphenous vein graft lesions. Paper presented at: American College of Cardiology 2011 Scientific Session; April 4, 2011; New Orleans, LA.

48. Wiisanen ME, Abdel-Latif A, Mukherjee D, Ziada KM. Drug-eluting stents versus bare-metal stents in saphenous vein graft interventions: a systematic review and meta-analysis. J Am Coll Cardiol Intv 2010;3: 1262–73.

49. Lee MS, Yang T, Kandzari DE, Tobis JM, Liao H, Mahmud E. Comparison by meta-analysis of drug-eluting stents and bare metal stents for saphenous vein graft intervention. Am J Cardiol 2010;105: 1076–82.

50. Meier P, Brilakis ES, Corti R, Knapp G, Shishehbor MH, Gurm HS. Drug-eluting versus bare-metal stent for treatment of saphenous vein grafts: a meta-analysis. PLoS ONE 2010;5:e11040.

51. Joyal D, Filion KB, Eisenberg MJ. Effectiveness and safety of drug-eluting stents in vein grafts: a meta-analysis. Am Heart J 2010;159: 159–69.e4.

52. Sanchez-Recalde A, Jiménez Valero SJ, Moreno R, et al. Safety and efficacy of drug-eluting stents versus bare-metal stents in saphenous vein grafts lesions: a meta-analysis. EuroIntervention 2010;6:149–60.

53. Testa L, Agostoni P, Vermeersch P, et al. Drug eluting stent versus bare metal stent in the treatment of saphenous vein graft disease: a systematic review and meta-analysis. EuroIntervention 2010;6:527–36.

54. Paradis J-M, Bélisle P, Joseph L, et al. Drug-eluting or bare metal stents for the treatment of saphenous vein graft disease: a Bayesian meta-analysis. Circ Cardiovasc Interv 2010;3:565–76.

55. Hakeem A, Helmy T, Munsif S, et al. Safety and efficacy of drug eluting stents compared with bare metal stents for saphenous vein graft interventions: a comprehensive meta-analysis of randomized trials and observational studies comprising 7,994 patients. Catheter Cardiovasc Interv 2011;77:343–55.

56. Lee MS, Hu PP, Aragon J, et al. Comparison of sirolimus-eluting stents with paclitaxel-eluting stents in saphenous vein graft intervention (from a multicenter Southern California Registry). Am J Cardiol 2010;106:337–41.

57. Leborgne L, Cheneau E, Pichard A, et al. Effect of direct stenting on clinical outcome in patients treated with percutaneous coronary intervention on saphenous vein graft. Am Heart J 2003;146:501–6.

58. Hong YJ, Pichard AD, Mintz GS, et al. Outcome of undersized drug-eluting stents for percutaneous coronary intervention of saphenous vein graft lesions. Am J Cardiol 2010;105:179–85.

59. Grube E, Schofer J, Webb J, et al., for SAFE Trial Study Group. Evaluation of a balloon occlusion and aspiration system for protection from distal embolization during stenting and saphenous vein grafts. Am J Cardiol 2002;89:941–5.

60. Smith SC Jr., Feldman TE, Hirshfeld JW Jr., et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). J Am Coll Cardiol 2006;47:216–35.

61. Mauri L, Rogers C, Baim DS. Devices for distal protection during percutaneous coronary revascularization. Circulation 2006;113:2651–6.

62. Carrozza JP, Mumma M, Breall JA, et al., for the PRIDE Study Investigators. Randomized evaluation of the TriActiv balloon-protection flush and extraction system for the treatment of saphenous vein graft disease. J Am Coll Cardiol 2005;46:1677–83.

63. Stone GW, Rogers C, Hermiller J, et al., for the FilterWire EX Randomized Evaluation Investigators. Randomized comparison of distal protection with a filter-based catheter and a balloon occlusion and aspiration system during percutaneous intervention of diseased saphenous vein aortocoronary bypass grafts. Circulation 2003;108:548–53.

64. Halkin A, Masud Z, Rogers C, et al. Six-month outcomes after percutaneous intervention for lesions in aortocoronary saphenous vein grafts using distal protection devices: results from the FIRE trial. Am Heart J 2006;151:915.e1–7.

65. Cox D, Masud A, Myers F, et al. Stenting in saphenous vein grafts with distal protection using the second generation FilterWire EZ: the BLAZE registry (abstr). Am J Cardiol 2003;92 Suppl 6:33L.

66. Dixon SR. Saphenous vein graft protection in a distal embolic protection randomized trial. Paper presented at: Transcatheter Cardiovascular Therapeutics 2005; October 18, 2005; Washington, DC.

67. Holmes DR, Coolong A, O'Shaughnessy C, et al. Comparison of the CardioShield filter with the GuardWire balloon in the prevention of embolisation during vein graft intervention: results from the CAPTIVE randomised trial. EuroIntervention 2006;2:161–8.

68. Mauri L, Cox D, Hermiller J, et al. THE PROXIMAL trial: proximal protection during saphenous vein graft intervention using the Proxis Embolic Protection System: a randomized, prospective, multicenter clinical trial. J Am Coll Cardiol 2007;50:1442–9.

69. Sdringola S, Assali A, Ghani M, et al. Adenosine use during aortocoronary vein graft interventions reverses but does not prevent the slow-no reflow phenomenon. Catheter Cardiovasc Interv 2000;51:394–9.

70. Fischell TA, Carter AJ, Foster MT, et al. Reversal of "no reflow" during vein graft stenting using high velocity boluses of intracoronary adenosine. Cathet Cardiovasc Diagn 1998;45:360–5.

71. Hillegass WB, Dean NA, Liao L, Rhinehart RG, Myers PR. Treatment of no-reflow and impaired flow with the nitric oxide donor nitroprusside following percutaneous coronary interventions: initial human clinical experience. J Am Coll Cardiol 2001;37:1335–43.

72. Michaels AD, Appleby M, Otten MH, et al. Pretreatment with intragraft verapamil prior to percutaneous coronary intervention of saphenous vein graft lesions: results of the randomized, controlled vasodilator prevention on no-reflow (VAPOR) trial. J Invasive Cardiol 2002;14:299–302.

73. Kaplan BM, Benzuly KH, Kinn JW, et al. Treatment of no-reflow in degenerated saphenous vein graft interventions: comparison of intracoronary verapamil and nitroglycerin. Cathet Cardiovasc Diagn 1996; 39:113–8.

74. Fischell TA, Subraya RG, Ashraf K, Perry B, Haller S. "Pharmacologic" distal protection using prophylactic, intragraft nicardipine to prevent no-reflow and non–Q-wave myocardial infarction during elective saphenous vein graft intervention. J Invasive Cardiol 2007;19:58–62.

Key Words: percutaneous coronary intervention ■ saphenous vein graft ■ stent.