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Effect of Percutaneous Coronary Interventions for In-Stent Restenosis in Degenerated Saphenous Vein Grafts Without Distal Embolic Protection

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OBJECTIVES This study was designed to investigate the impact of percutaneous coronary interventions (PCIs) in degenerated saphenous vein grafts (SVGs) without distal embolic protection.

BACKGROUND Distal embolic protection devices have been shown to reduce the incidence of no reflow/slow flow during PCI of de novo lesions in degenerated SVGs. It is unclear whether PCI of in-stent restenosis (ISR) lesions in degenerated SVGs is associated with no reflow/slow flow and whether distal embolic protection is beneficial in these cases as well.

METHODS We studied 54 consecutive patients with treated ISR lesions in degenerated SVGs who underwent PCI without distal embolic protection in a single center. Procedural and in-hospital outcomes were examined.

RESULTS The average age was 71 ± 8 years; 32% of the patients had diabetes. The mean lesion length was 13 ± 6 mm and the procedural success rate was 98% (53/54). Cutting balloon angioplasty was used in 46% (25/54) of cases, and a new stent was inserted in 46% (25/54) of patients. Gamma brachytherapy was performed in 19% (10/54) of patients. During the procedure there were no episodes of no reflow/slow flow, and there were no patients with in-hospital Q-wave or non–Q-wave myocardial infarction. There was one in-hospital noncardiac death.

CONCLUSIONS In this consecutive series of patients with ISR of degenerated SVGs undergoing PCI without distal protection, there were no episodes of slow flow/no reflow and no procedure-related myocardial infarctions. It appears that distal embolic protection may not be necessary during PCI of ISR lesions in degenerated SVGs. (J Am Coll Cardiol 2003;41:749–52) © 2003 by the American College of Cardiology Foundation

The absence of blood flow or decreased blood flow (no flow/slow flow) is a serious complication of percutaneous revascularization strategies that may result in an increased incidence of morbidity and mortality (1). The risk of coronary no reflow/slow flow is markedly increased in interventions of degenerated saphenous vein grafts (SVGs) and occurs in up to 20% of cases (1,2). Distal embolic protection devices have been shown to reduce the incidence of no reflow/slow flow and procedure-related myocardial infarction (MI) in percutaneous coronary intervention (PCI) of de novo lesions in degenerated SVGs (3).

In-stent restenosis (ISR) has different tissue pathology compared to a de novo obstructive atherosclerotic lesion (4). The ISR lesion consists predominantly of neointimal smooth muscle cells (5,6) and may be less likely to result in distal embolization of debris during the PCI procedure. Given the potential decreased risk of distal embolization for PCI of ISR lesions, we hypothesized that distal protection might not be necessary in the treatment of ISR in degenerated SVGs. This study investigated the procedural and in-hospital outcomes of 54 consecutive patients who underwent PCI for ISR of 54 lesions in degenerated SVGs without distal protection.

METHODS

All 54 patients were treated at a single center between January 2000 and December 2001. Patients who had sustained an ST-segment elevation MI in the previous 72 h were excluded. Degenerated SVGs were defined as SVGs more than three years old with the presence of extensive luminal irregularities on the angiogram. Baseline patient characteristics and in-hospital events were recorded by independent hospital chart review.

All ISR lesions were classified according to Mehran et al. (7). Anginal symptoms were classified according to the Canadian Cardiovascular Society guidelines (8). The choice of PCI rather than medical or surgical revascularization was made by the attending cardiologist. Angiographic success was defined as a reduction of 20% and a <50% final residual diameter stenosis in the lesion. Procedural success was defined as angiographic success in the absence of major in-hospital complications (death, Q-wave MI, and emergent bypass surgery). Q-wave MI was defined as the presence of new Q waves on the postprocedure electrocar-

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Abbreviations and Acronyms

CK = creatinine kinase
ECG = electrocardiogram
ISR = in-stent restenosis
MI = myocardial infarction
PCI = percutaneous coronary intervention
SVG = saphenous vein graft
TIMI = Thrombolysis In Myocardial Infarction

diogram (ECG) and a corresponding rise by at least threefold above normal limits of the serum creatinine kinase (CK)-MB fraction. Non–Q-wave MI was defined as a rise by at least threefold above normal limits of the serum CK-MB fraction without the appearance of new Q waves on the post-procedure ECG. All patients had post-PCI and next-day ECGs, and cardiac enzyme determinations at 6 to 8 h and at 16 to 18 h post-PCI.

Angiographic analysis was performed by independent observers without knowledge of the clinical data using a validated, automated edge-detection algorithm (CMS, MEDIS, Leiden, Netherlands) as previously described (9). No reflow/slow flow conditions were defined using the Thrombolysis In Myocardial Infarction (TIMI) blood flow grades (10): no reflow was defined as TIMI 0 to 1 flow and slow flow as TIMI 2 flow. The use of online intravascular ultrasound imaging was at the operator's discretion. Intravascular ultrasound studies were performed with the Boston Scientific Corporation/Cardiovascular Imaging System as described previously (11). Vascular brachytherapy was indicated for diffuse ISR, but discouraged if a new stent was implanted. If a new stent was inserted, ticlopidine (250 mg twice daily) or clopidogrel (75 mg once daily) was given routinely for four weeks in addition to aspirin 325 mg, which was prescribed indefinitely.

Statistical analysis was performed using SAS software (SAS Institute Inc., Cary, North Carolina). Categorical data are presented as percent frequencies and compared by chi-square statistics. Continuous variables are presented as mean ± SD.

Table 1. Baseline Clinical Characteristics

Variables	Values
Age (yrs)	71 ± 8
Male gender	63% (34/54)
History of smoking	32% (17/54)
Systemic hypertension	59% (32/54)
Diabetes mellitus	32% (17/54)
Family history of CAD	30% (16/54)
Hypercholesterolemia	69% (37/54)
Prior myocardial infarction	43% (23/54)
Unstable angina	44% (24/54)
Prior coronary bypass	100% (54/54)
Prior coronary angioplasty	100% (54/54)
LVEF (%)	45 ± 14

CAD = coronary artery disease; LVEF = left venticula ejection fraction.

Table 2. Angiographic Characteristics

Variables	Values
ISR	100% (54/54)
Pattern of ISR (7)	
Focal (I)	56% (30/54)
Intrastent (II)	19% (10/54)
Proliferative (III)	22% (12/54)
Total occlusion (IV)	4% (2/54)
Lesion location within SVG	
Ostial	20% (11/54)
Within body	80% (43/54)
Distal anastomosis	0% (0/54)
Lesion length (mm)	13.4 ± 6.4
Pre-reference diameter (mm)	3.2 ± 0.6
Pre-diameter stenosis (%)	77 ± 15
Final diameter stenosis (%)	17 ± 18

ISR = in-stent restenosis; SVG = saphenous vein graft.

RESULTS

The average age was 71 ± 8 years and there were 63% men patients (Table 1). There were 32% of subjects with a smoking history, 59% with systemic hypertension, 32% with diabetes mellitus, and 69% with hypercholesterolemia. Unstable angina was present in 44%, and 43% had a history of prior MI. The mean left ventricular ejection fraction was decreased at 45± 14%.

Angiographic characteristics are shown in Table 2. All patients had ISR of a single lesion in one degenerated SVG. The classification of ISR lesions (7) was as follows: focal (class I) 56% (n = 30); intrastent (class II) 19% (n = 10); proliferative (class III) 22% (n = 12); total occlusion (class IV) 4% (n = 2). Lesions were located at the aorto-ostium in 20% and within the body of the SVG in 80% of patients; there were no lesions at the site of the distal anastomosis. The mean lesion length was 13 ± 6 mm and prediameter stenosis 77 ± 15%.

The angiographic success was 100%; 19% of the lesions were treated with balloon angioplasty alone (Table 3), the cutting balloon was used in 46%, and a new stent was required in 46% of cases. The rate of glycoprotein IIb/IIIa inhibitor use was 35%. Intravascular brachytherapy was used in 10 cases (19%); 8/10 in proliferative lesions (ISR class III) and 2/10 in the two total occlusions (ISR class IV).

The procedural outcomes and in-hospital events are shown in Table 4. Procedural success was 98%. There were no cases of no reflow or slow flow. On the final post-PCI

Table 3. Procedural Characteristics

Variables	Values
Angiographic success	100% (54/54)
Plain balloon angioplasty	19% (10/54)
Cutting balloon angioplasty	46% (25/54)
New stent inserted	46% (25/54)
Atherectomy/thrombectomy	0% (0/54)
Glycoprotein IIb/IIIa inhibitor use	35% (19/54)
Intravascular ultrasound guidance	43 (23/54)
Intravascular brachytherapy	19% (10/54)

Table 4. Procedural Outcomes and In-Hospital Events

Variables	Values
Procedural outcomes	
Procedural success	98.1% (53/54)
No reflow /slow flow*	0% (0/54)
Dissection	1.9% (1/54)
Threatened/abrupt closure	0% (0/54)
Final ACT (s)	283 ± 76
CK-MB fraction 1–3 times upper limit of normal	3.7% (2/54)
CK-MB fraction >3 times upper limit of normal	0% (0/54)
In-hospital events	
MACE	2% (1/54)
Death	2% (1/54)
Cardiac death	0% (0/54)
Q-wave MI	0% (0/54)
Non–Q-wave MI	0% (0/54)
Repeat target lesion PCI	0% (0/54)
Length of stay in-hospital	2.2 ± 2.3 days (range 1–11 days)

*No reflow = TIMI 0–1 flow; slow flow = TIMI 2 flow.
ACT = activated clotting time; CK = creatinine kinase; MACE = Death, MI, repeat target lesion PCI; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

angiogram, TIMI 3 flow was present in all cases. There was one dissection, which was treated with deployment of a new stent. There were no cases of threatened or abrupt closure and no perforations. The final mean activated clotting time value was 283 ± 76 s. There was only one major in-hospital event in the 54 patients studied: a patient had a noncardiac death due to respiratory failure secondary to chronic obstructive pulmonary disease and pneumonia. There were no cases of non–Q-wave or Q-wave MI or repeat revascularization.

DISCUSSION

The no reflow/slow flow phenomenon has been described as the persistence of abnormally slow myocardial blood flow in an epicardial coronary artery or vein graft in the absence of evident vessel dissection, obstruction, or distal vessel cutoff (1). Patients who experience this complication following PCI have increased risk of MI and death and morbidity during the procedure (1,12). The exact mechanism of the no reflow/slow flow phenomenon is not known, but it is thought to stem from dysfunction or obstruction of the microcirculation at the level of the resistance arterioles (13). After PCI of the culprit lesion, no reflow/slow flow may occur through spasm of the distal microcirculation, platelet clumping, and the distal embolization of pieces of friable lipid-rich plaque (14). No reflow/slow flow phenomenon has been reported after rotablator for de novo and stent restenotic lesions in patients on beta-blockers, suggesting the contribution of microvascular unopposed alpha-agonism in this abnormal phenomenon (15).

Many proposed treatments have been published for the no reflow/slow flow phenomenon, including intracoronary injections of verapamil, diltiazem, nitroglycerin, nitroprusside, nicorandil, urokinase, abciximab, adenosine, papaverine, and intra-aortic balloon counterpulsation (12,16–22). Despite many of these treatments proving successful, no reflow/slow flow remains a problem, especially in degenerated SVGs in which no reflow/slow flow can occur in up to 20% of interventions, with unfavorable clinical outcome (12). Hong et al. (23) observed that distal embolization with associated no reflow/slow flow was an independent predictor of late mortality and in-hospital major CK-MB elevation (odds ratio 4.4; 95% confidence interval 1.9 to 10.1) in patients undergoing PCI for lesions in degenerated SVGs.

A marked reduction in major adverse cardiac events (post-PCI myocardial infarction and "no reflow" phenomenon) was observed in PCI of degenerated SVGs with distal protection in a recent prospective, randomized multicenter study (3). However, ISR lesions in SVGs were excluded from this trial.

In the present study of ISR lesions in degenerated SVGs, we found no episodes of no reflow/slow flow and no in-hospital MIs after PCI. The likely explanation for these favorable results without distal embolic protection is that the ISR lesions are pathologically distinct from de novo lesions. De novo lesions in degenerated SVGs consist of friable, atherothrombotic material with a high propensity to embolize when manipulated during PCI, with ensuing release of vasoactive substances (14,24). In sharp contrast, ISR lesions are the result of neointimal formation alone (7,25). Neointima is composed principally of proliferating smooth muscle cells (5,6) and extracellular matrix (26). Mural thrombus and soft lipid-rich elements have not been found in neointimal formation in the pig model (27) or in humans (28).

In the present study we indeed found the peri-PCI risk of distal embolization and ischemic events to be rare after PCI of ISR lesions in degenerated SVG without distal embolic protection.

Study limitations. This study has several limitations. It is a retrospective study from a single center. The study group may have been subject to selection bias. The decision not to use distal embolic protection was at the discretion of the interventional cardiologist. Focal type I ISR lesions were treated in over 50% of cases, although this is representative of the proportion of focal ISR lesions treated in other ISR treatment series. Diffuse ISR lesions made up 46% of cases in our series. Lastly, the number of patients in our series is relatively small.

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