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Long term outcomes of saphaneous vein graft intervention in elderly patients with prior coronary artery bypass graft

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Abstract

Objectives   To investigate the procedure characteristics and long term follow-up of percutaneous coronary intervention (PCI) for saphaneous vein graft (SVG) lesions in the elderly patients. **Methods**   From December 2005 to December 2011, 84 graft lesions were treated percutaneously. Seventeen were located at proximal anastomosis, 48 were located at SVG body, 19 were located at distal anastomosis. Primary endpoint was defined as major adverse cardiovascular events (MACE, composite of cardiac death, target vessel revascularization, acute myocardial infarction). **Results**   The graft age was 6.7 ± 4.0 years. Most anastomosis lesions (80.0%) presented within one year post coronary artery bypass grafting (CABG). Proximal anastomosis lesion had the lowest successful rate for PCI compared with graft body and distal anastomosis lesions (70.6% *vs.* 91.7%, 79.0%, $P < 0.05$). The distal embolic protection device was used in 19.1% of patients, most frequently used in body graft PCI (29.2%, $P < 0.01$). The diameter of the stent was smallest in distal anastomosis group (2.9 ± 0.4 mm, $P < 0.05$). The highest post dilatation pressure was required in the proximal anastomosis (17.8 ± 2.7 atm, $P < 0.05$). The patients were followed up for 24.3 ± 16.9 months. MACE occurred in 18.57% of patients. Incidence of MACE was highest among proximal anastomosis PCI (47.1% *vs.* body graft PCI 16.7%, distal anastomosis PCI 21.1%; $P < 0.05$). Old myocardial infarction was the predictive factor for the poor clinical outcomes ($P = 0.04$). **Conclusions**   PCI of SVG lesions is feasible with lower success rate. PCI of ostial graft anastomosis lesions had the lowest procedure success rate and highest MACE rate compared with graft body and distal anastomosis lesions. Old myocardial infarction was a predictive factor of poor outcomes.

1   Introduction

It was known that about 50% of vein grafts developed significant stenosis or occlusion within 10 years following coronary artery bypass grafting (CABG).[1] With the wide use of CABG over two decades in China, increasing number of patients with occluded graft revisited the hospital; a large proportion of them needs repeat revascularization. However, the treatment of saphenous vein graft (SVG) disease remains a major challenge. Repeated CABG carries a very high risk,[2] especially for the elderly patients. Percutaneous coronary intervention (PCI) of SVG lesions was unavoidable even though it was associated with high rates of periprocedural complications and restenosis at long-term fol-

low-up.[3,4] In this study, we summarized our experience and outcomes of SVG intervention for elderly patients in the drug eluting stent (DES) era.

2   Methods

2.1   Patients and invasive strategy

In our registry from Beijing An-Zhen Hospital, between December 2005 and December 2011, a total of 762 consecutive patients with previous CABG underwent PCI for the treatment of coronary artery disease. Seventy of them were performed PCI for SVG. Informed consent was obtained from patients prior to undergoing urgent or selective PCI. Percutaneous graft stenting was performed via the femoral (using 6F, 7F, sheaths) or the radial arterial route (using 6F sheaths). The decisions to treat native vessels, choice of stents, use of glycoprotein IIb/IIIa inhibitors, vascular access, use of distal embolic protection devices (EPD) in vein graft PCI cases, and the use of diagnostic devices during the procedures were all made the discretion of ex-

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perienced operators. All patients received dual antiplatelet therapy (aspirin and clopidogrel) and an intravenous bolus injection of heparin (70 IU/kg body weight) before the procedure. Aspirin 100 mg daily was continued indefinitely after the procedure. The patients who had bare metal stents (BMS) were given clopidogrel 75 mg daily for a total period of 6 months. The patients receiving DES were given clopidogrel 75 mg daily for 12 months.

2.2 Definitions and clinical follow-up

The patients were followed up clinically or by telephone. The in-hospital mortality was defined as death during hospitalization associated with intervention. Following-up MACE composite of all-cause death, non-fatal myocardial infarction (MI), and target vessel revascularization (TVR). Acute myocardial infarction was defined as prescribed in ESC/ACC (European Society of Cardiology/American College of Cardiology) third universal guideline of myocardial infarction.[5] The significant stenosis was defined as any lesion of a major epicardial artery or branch vessel or graft (≥ 2.0 mm in diameter) which had a $\geq 50\%$ stenosis of the lumen on angiographic assessment. Immediate angiographic success was defined as $< 50\%$ stenosis in all lesions attempted. Procedure success was defined as angiographic success without the occurrence of any major immediate complications (death, Q-wave MI, emergency redo CABG). Major bleeding (not related to redo CABG) was defined as intra cranial bleeding, access site bleed resulting in a haematoma ≥ 5 cm or requiring intervention/surgery, haemoglobin decreased by ≥ 3 g/dL with an overt source or by ≥ 4 g/dL without an overt source, any blood product transfusion, or reoperation for bleeding. The patient's demographics, lesions treated, technical aspects of the procedure, procedure-related complications, adjunctive pharmacology, stent characteristics, and immediate procedure outcome were retrospectively studied. Cardiac enzymes following PCI were not routinely measured, except for patients with suspected perioperative infarction.

2.3 Statistics

Demographic, clinical, angiographic data were collected prospectively from the registry; continuous variables are expressed as mean ± SD and categorical variables as frequency (%). Previous report that clinical outcomes were different for vein graft lesion anatomies (anastomosis, body), we divided the patients into 3 groups according to anatomy (proximal, distal anastomosis, body graft). Continuous variables of procedure characteristics and clinical outcomes between different groups were compared by using the ANOVA test. Categorical variables were compared using

Chi-square test. Finally, baseline risk factors (e.g., age, diabetes mellitus (DM), dyslipidemia, old MI, hypertension, years of CABG and sex) were analyzed for poor clinical outcomes by using Cox regression analysis. $P < 0.05$ was considered statistically significant and all reported P values are two tailed. Statistical analysis was performed using the SPSS Version 16 for Windows version (SPSS, Chicago, IL)

3 Results

Between December 2005 and December 2011, 70 patients with prior CABG and 84 SVG lesions were treated percutaneously. Baseline characteristics of these patients were listed in Table 1. Patient's average age was 65.61 ± 8.70 years, 57.14% were male, 25.71% of them presented with acute myocardial infarction.

Table 1. Clinical characteristics of patients undergoing SVG-PCI, *n* =70.

Mean age, yrs	65.6 ± 8.7
Gender	
Male	40 (57.1%)
Graft age	6.7 ± 4.0
Diagnosis at admission	
Unstable Angina	42 (60.0%)
AMI	18 (25.7%)
Stable angina	10 (14.3%)
Hypertension	53 (75.7%)
Diabetes	40 (57.1%)
Previous stent	12 (17.1%)
Previous MI	18 (25.7%)

Data are presented as mean ± SD or *n* (%). AMI: acute myocardial infarction; MI: myocardial infarction; SVG: saphaneous vein graft; PCI: percutaneous coronary intervention..

Angiographic and intervention data were shown in Table 2. Totally, 84 SVG lesions were treated percutaneously. The intervened lesions located at aorta ostial anastomosis, graft body and distal anastomosis were 17, 48 and 19,respectively during the first year after CABG. Most anastomosis lesions (80.0%) presented within one year post CABG.

For lesions which were treated successfully, Judkins Right was the most common guide catheter (75.0%), followed by Amplatz left catheter (19.1%). BMW (Abbott Vascular; Abbott Park, Illinois) and super soft stabilizer (Cordis, Miami Lakes, FL) were the most commonly used workhorse guide wire in graft body lesions (60.4%), while Runthough wire (Terumo Medical Corporation) was mostly used in ostial graft lesion (41.2%). Hydrophic wire such as Whisper, Pilot wire series and chronic total occlusion (CTO)

Table 2.   Angiographic and procedure characteristics of SVG intervention.

	Total (*n* = 84)	Aortal ostial (*n* = 17)	Body (*n* = 48)	Distal anastomosis (*n* = 19)	*P* value
Immediate failure	8 (9.5)	3 (17.6)	2 (4.2)	4 (21.1)	< 0.05
Procedure failure	13 (15.5)	5 (29.4)	4 (8.3)	4 (21.1)	
Target graft					
SVG-LAD	31 (36.9)	9 (52.9)	16 (33.3)	6 (31.6)	
SVG-LCX	23 (27.4)	4 (23.5)	13 (27.1)	6(31.6)	
SVG-RCA	30 (35.7)	4 (23.5)	19 (39.6)	7 (36.8)	
Jump graft	21 (25.0)	4 (23.5)	11 (22.9)	6 (31.6)	
Total occlusion	14 (16.7)	4 (23.5)	8 (16.7)	2 (10.5)	
Thrombus	12 (14.3)	2 (11.8)	8 (16.7)	2 (10.5)	
Distal protection device	16(19.1)	2 (11.8)	14 (29.2)	0	< 0.01
Aspiration	8 (9.5)	1 (5.9)	6 (12.5)	1 (5.3)	
Guide					
AL	16 (19.1)	4 (23.5)	8 (16.7)	4 (21.1)	
JR	63 (75.0)	11 (64.7)	39 (81.3)	13 (68.4)	
Guidewire					
BMW/Supersoft	37 (44.1)	5 (29.4)	29 (60.4)	3 (15.8)	
Runthrough	20 (23.8)	7 (41.2)	9 (18.8)	4 (21.1)	
Pilot/Whisper	25 (29.8)	5 (29.4)	10 (20.8)	10 (52.6)	< 0.05
Miracle/Cross IT	2 (2.4)	0	0	2 (10.5)	
Post dilatation	19 (22.6)	5 (29.4)	12 (25.0)	2 (10.5)	
Pre dilatation	64 (76.2)	12 (70.6)	36 (75.0)	16 (84.2)	
Direct stent	16 (19.1)	4 (23.5)	11 (22.9)	1 (5.3)	
Stent diameter (mm)	3.4 ± 0.6	3.3 ± 0.6	3.5 ± 0.5	2.9 ± 0.4	< 0.05
Maximum pressure (atm)	15.2 ± 2.6	17.8 ± 2.7	14.4 ± 2.1	14.8 ± 3.2	< 0.01
Stent length (mm)	25.6 ± 17.2	19.3 ± 8.1	30.2 ± 19.5	17.0 ± 6.0	< 0.05
Average number	1.1 ± 0.6	0.9 ± 0.3	1.4 ± 0.6	0.6 ± 0.5	< 0.01

Data are presented as mean ± SD or *n* (%). AL: Amplatz Left; JR: Judkins Left; LAD: left descending artery; LCX: left circumflex; RCA: right coronary artery; SVG: saphaneous vein graft.

wires such as miracle series (Abott vascular) and Choice PT (Boston Scientific; Natick, Massachusetts) were most mainly used in distal anastomosis lesions. A distal protection device was used in 19.1% of treated SVGs, generally used in graft body lesions (29.2%). No distal protection device was used in distal anastomosis lesions. A Filterwire (Boston Scientific) was used in 60% of distal EPD-treated lesions, Spider (ev3, Plymouth, Minnesota) in 40% of the patients. Eighty-four drug eluting stents were implanted in the SVG lesions. Sirolimus drug eluting stent were most frequently used DES. Direct stenting was performed in 19.0% of patients, and rarely used in distal anastomosis. More stents were implanted in body graft lesions. Average stent diameter was 3.4 ± 0.6 mm. Average post stent dilataion pressure was 15.2 ± 2.6 atm, with ostial anastomosis lesions needing the highest dilatation pressure (17.8 ± 2.7, *P*

< 0.01). Immediate angiographic success was 90.5%. The osital graft lesions had the highest failure rate (21.1%). Four patients died in hospital (5.7%) during the index hospitalization. The course of death in the four patients was severe cardiogenic shock, non-reflow after stent deployment, cerebral stroke and gastric bleeding, respectively.

Clinical follow-up was available for 90% of patients either by face to face or telephone, the median period of follow up was 25 months. Results were listed in Table 3. Incidence of death, MI (including major periprocedural myocardial infarction), TVR were 7.1%, 2.9% and 8.6%, respectively during follow-up. Ostial anastomosis intervention had the highest rate of MACE (47.1%, *vs.* distal anastomosis 21.1%, graft body 16.67%, *P* < 0.05). TVR was performed in 6 patients, with the indication of myocardial infarction in 2 cases and angina in 4 other cases.

Table 3.   Clinical outcomes of patient undergoing SVG-PCI.

	Total (*n* = 70)	Ostial (*n* = 17)	Body (*n* = 48)	Distal (*n* = 19)	*P* value
MACE	13 (18.6)	8 (47.1)	8 (16.7)	4 (21.1)	< 0.05
TVR	6 (8.6)	3 (17.7)	3 (6.3)	2 (10.5)	
AMI	2 (2.9)	1 (5.9)	1 (2.1)	2 (10.5)	
Death	5 (7.1)	4 (23.5)	4 (8.3)	0	

Data are presented as *n* (%). AMI: acute myocardial infarction; MACE: major adverse cardiac event, which includes death, non-fatal myocardial infarction and target vessel revascularization; SVG: saphaneous vein graft; PCI: percutaneous coronary intervention; TVR: Target vascular revascularization.

Table 4.   Baseline risk factors for poor outcomes.

Factors	B	SE	Wald	Sig.	Exp (B)	95.0% CI Exp(B)	
						Lower	Upper
Diabetes mellitus	0.992	0.646	2.359	0.125	2.696	0.760	9.560
Dyslipidemia	−0.315	0.638	0.244	0.622	0.730	0.209	2.550
Sex	0.541	0.933	0.336	0.562	1.717	0.276	10.693
Previous history of PCI	−1.065	0.643	2.746	0.097	0.345	0.098	1.215
Old myocardial infarction	1.723	0.839	4.214	0.040	5.602	1.081	29.029
Hypertension	0.251	0.586	0.183	0.669	1.285	0.407	4.052
Years after CABG	0.111	0.077	2.063	0.151	1.117	0.960	1.299
Age	−0.004	0.034	0.016	0.898	0.996	0.932	1.064

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention.

The follwing baseline risk factors were entered as Cox regression models for poor clinical outcomes included age, sex, diabetes mellitus, dyslipidemia, hypertension, previous history of PCI, old myocardial infarction, years after CABG, the results were shown in Table 4. Old myocardial infarction was associated with higher MACE occurred ($P = 0.04$).

4   Discussion

Our results showed that PCI of SVG disease was feasible in elderly patients with a procedure which had a successful rate of 84.5%, MACE of 18.6% in a median in 2 year follow-up. SVG disease at anastomosis, especially aorta graft ostial anastomosis carried the worst clinical outcomes. The poor outcome of the percutaneous intervention of SVG ostial lesions could be explained by its pathophysiology. Anastomosis lesions usually happened within one year following CABG, probably due to thrombotic closure as a result of endothelial injury and the release of inflammatory cytokines during surgery. Technical factors, such as poor distal runoff, graft kinking, and small target vessel diameter, predisposed grafts to early occlusion.[6] After the first month, exposure of the vein grafts to arterial pressure resulted in neointimal hyperplasia. This pathophysiologic process caused intimal damage, fibrosis, platelet aggregation, the release of growth factors, and smooth muscle cell prolifera-

tion. Due to the surgical technique and severe fibrosis of the anastomosis site, compared with body graft lesions, the PCI of anastomosis lesions might be technically more difficult, and needed more hydrophilic and stiff wires. Post stent dilation was always performed and needed more pressure to achieve a better stent expansion. Sometimes, due to the smaller vessel volume in anastomosis lesions, the stent could not be totally deployed and the stent size was relatively smaller. All these factors contributed to a high rate of restenosis and MACE.

After the first year, the main cause for graft failure was aggressive atherosclerotic narrowing which occurred over the already injured endothelium was. PCI of SVG carried a high risk of non-reflow phenomena. An early study showed that long- term survival after SVG intervention was poor, with one fourth of patients dying at median follow-up of 4 years. However, this happened in the early period when the DES and EPD were not commonly used.[3] A more recent study indicated that the patients with SVG lesions remained a high-risk subgroup even in the era of drug-eluting stents, the mortality was 8.0% and MACE was 31.70% during follow-up of one year.[7]

Some studies had revealed the benefit of the use of EPD in lowering in-hospital cardiovascular event rate and improving long-term outcomes.[8] The AHA/ACC guidelines suggested mandatory use of EPD in SVG graft PCI.[9]

However, the embolic device was not commonly used in our study (only constituted 13% of the study group). In some cases, lesion location was not favorable for EPD such as distal anastomosis. However, in other cases, the operators with the perception that some SVGs (e.g., those with relative focal or smooth lesions) have low enough risks to using of an EPD unnecessarily. A recent pool analysis of 3,958 graft intervention patients also showed that estimates of plaque volume and SVG degeneration could be a predictor of 30-day MACE in SVG percutaneous coronary intervention.[10] Therefore, the recognition of the predictor was very important in developing countries like China where cost-effectiveness is still an issue.[11]

In this study, we indentified that old MI was associated with higher MACE rate, which could be possibly due to large size of ischemic or unviable myocardium. This indicated PCI of SVG in such patients should be taken with precaution. Previous study also indicated PCI of SVG graft CTO had a less successful procedure rate, more follow up event and higher restenosis rate even with modern technique.[12] Therefore, PCI of SVG-CTO was not recommended. In this study, 16.7% of patients with occluded grafts were included. CTO lesions were common in aorta ositial lesions (23.5%), which might further decrease the successful rate of aorta ostial lesion PCI.

In this study, all stented patients were implanted with DES. Although it is still controversial, most studies favor DES over BMS in lowering the rate of restenosis and TVR.[13–15] In a pool analysis of the patient using DES, the MACE was 19.0%, mortality rate was 7.8%, and TVR was 12.0%, which are very similar to our results.[14]

Platelet glycoprotein IIb/IIIa receptor was rarely used in this study. Previous pooled analysis showed the lack of benefit from GP IIb/IIIa receptor inhibition as adjunctive treatment for SVG-PCI.[16] To date, there are no prospective randomized trials clearly demonstrating the benefits of GP IIb/IIIa inhibitors in SVG-PCI. However, there may be a role in their usage as adjuncts with certain embolic protection devices, such as the distal filtration devices.

Our study presented some limitations. First, the study was not randomized and prospective, the operator selection and inclusion criteria might have influenced the final results. Moreover, the sample size was relatively small. However, the clinical outcomes of PCI for anastomosis lesions in comparison with body graft lesions were rarely discussed previously, especially for the elderly patients.

Our study showed that PCI of SVG lesions was feasible with lower successful rate. PCI of ostial graft anastomosis lesions had the lowest successful rate and highest MACE rate in compared with graft body and distal anastomosis lesions. Old myocardial infarction was a predictive factor of poor outcomes.

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