Factors associated with the no-reflow phenomenon following percutaneous intervention of saphenous vein coronary bypass grafts

Mohammad Hashemi-Jazi[(1)], Sayed Mojtaba Hosseini[(2)], Ali Gholamrezaei[(3)]

Original Article

Abstract

BACKGROUND: We investigated clinical and procedural factors associated with the no-reflow phenomenon following percutaneous coronary intervention (PCI) of the saphenous-vein grafts (SVG).

METHODS: A cross-sectional study was done on patients who had undergone PCI of the SVG. Patients' medical documents were reviewed for demographic, clinical, laboratory, and procedural data. Slow/no-reflow was defined based on the thrombolysis in myocardial infarction (TIMI) grade (0 to 2). Univariate and multiple logistic regression analyses were performed to investigate factors associated with slow/no-reflow and $P < 0.050$ was considered as significant.

RESULTS: A total of 205 patients were studied (81% man, mean ± standard deviation of age was 66.8 ± 9.6 years). Slow/no-reflow was found in 38 (18.5%) patients. High diastolic blood pressure ($P = 0.010$), leukocytosis ($P = 0.017$), diffuse lesions ($P = 0.007$), degenerated SVG ($P < 0.001$), proximal lesions ($P < 0.001$), thrombosis ($P = 0.013$), and lower number of used stents during procedure ($P = 0.032$) were associated with slow/no-reflow in unadjusted analyses. Factors independently associated with slow/no-reflow were pre-procedural high diastolic blood pressure with odds ratio (OR) = 3.858 [95% confidence interval (95% CI), 1.157-12.860], degenerated SVG with OR = 5.901 (95% CI: 1.883-18.492), proximal lesions with OR = 5.070 (95% CI: 1.822-14.113), pre-intervention TIMI grade with OR = 0.618 (95% CI: 0.405-0.942), number of used stents for PCI with OR = 0.074 (95% CI: 0.011-0.481) for > 1 stent, and length of stents used for PCI with OR = 0.100 (95% CI: 0.019-0.529) for > 30 mm stents.

CONCLUSION: This study on the clinical and procedural factors associated with the slow/no-reflow phenomenon following PCI of the SVG can be used in risk estimation of this serious complication and tailoring preventive strategies to at-risk patients.

Keywords: Angioplasty, Coronary Artery Bypass, No-Reflow Phenomenon, Percutaneous Coronary Intervention, Saphenous Vein

Introduction

Coronary artery bypass grafting (CABG) is a common revascularization technique in patients with coronary artery disease.[1] Although CABG has more long-term benefits than percutaneous coronary intervention (PCI) for severe cases,[2] failure of the venous grafts limits the long-term efficacy of CABG.[3] Failure of the saphenous vein graft (SVG) is a common complication following CABG, which is associated with considerable morbidity and mortality.[3] Despite advances in surgical techniques and medical treatments, significant stenosis is seen in up to 60% of the venous grafts at 10 years following CABG.[3]

Depending on the time from surgery, various factors contribute to the development of the vein graft failure, from technical factors to the long-term atherosclerotic degeneration and hyperplasia of the graft intima. Patient-related risk factors have been reported as smoking, dyslipidemia and hypertension, and also genetic predisposition.[3]

Revascularization of the diseased SVG with PCI has been associated with better outcomes than repeated CABG and is the currently preferred method.[3] However, PCI of the SVG is not complication free. Distal embolization and slow or no-reflow after PCI of the SVG occurs more frequently than intervention on native coronary

1- Professor, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2- Professor, Hypertension Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
3- General Practitioner, Student Research Committee, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
Correspondence to: Sayed Mojtaba Hosseini, Email: smhcardio86@gmail.com

vessels.[4] The no-reflow phenomenon occurs in up to 15% of the SVG-PCI and is associated with high risk of major adverse cardiac events and mortality.[5] Yet, the pathophysiology of the no-reflow phenomenon is not clear. Some proposed mechanisms are distal embolization with thrombus and macro-debris, vasospasm, and leukocytes plugging.[6]

Current procedural and pharmacological strategies have limited success for the management of no-reflow phenomenon.[7] Accordingly, prevention is of great importance and is probably the only effective measure to approach this potentially serious complication.[8] For this aim, a systematic analysis of various possible clinical and angiographic predictors of no-reflow is required. A limited number of studies have been done in this regard so far. Current evidence has suggested a number of possible predictors such as clinical presentation, presence of thrombus, and degenerated SVG.[9-11] Considering the lack of data in this regard, we investigated the association of a number of clinical and procedural factors with slow/no-reflow (SNR) following PCI of the SVG.

Materials and Methods

This cross-sectional study was conducted on patients who had undergone CABG between Mar 2011 and Feb 2015 in the Chamran and Sina Heart Centers of Isfahan, Iran. Patients for whom angioplasty of the coronary grafted saphenous vein has been done were included into the study. Patients for whom PCI has been done for more than one saphenous vein and those who had major complications during the procedure (e.g. myocardial infarction, cardiogenic shock) were not included into the study. The sample size was calculated as 200 patients using the G*Power software (version 3, University of Düsseldorf, Düsseldorf, Germany) and estimating 10 factors associated with SNR to be evaluated in the logistic regression model. The study was approved by the Ethics Committee of the Isfahan University of Medical Sciences (grant # 394095) and patients' data were used anonymously.

The following data were gathered by reviewing patients' medical documents retrospectively: age and gender, pre-procedural measured systolic and diastolic blood pressure (SBP and DBP, respectively), past medical history with regards to the coronary risk factors including smoking, hypertension, dyslipidemia, and diabetes mellitus. Laboratory data were reviewed for anemia (hemoglobin of < 13 g/dl in men and < 12 g/dl in women), high creatinine (> 1.3 mg/dl in men and > 1.1 mg/dl in women), leukocytosis (white blood cell > 10000 per mcl), and hyperglycemia (random blood glucose $\geq$ 200 mg/dl). Estimated glomerular filtration rate (eGFR) (ml/min/1.73m^2) was calculated by the chronic kidney disease epidemiology collaboration (CKD-EPI) formula.[12]

The following data were gathered regarding disease characteristics: length of the lesion (diffuse, tubular, or discrete with length of > 20, 10-20, and < 10 mm, respectively), degeneration score (0: $\leq$ 25%, 1: 26-50%, 2: 51-75%, 3: >75%), percentage of stenosis (categorized to 75-90%, 90-99%, or 100%), location of the stenosis (proximal, mid part, and/or distal),[13] and presence of thrombosis. Procedural data were reviewed for direct stenting, using a balloon (pre- or post-dilation), a number of the stents used, length of the stents (categorized to > 30, 25-30, 15-25, or < 15 mm),[13] and using distal embolic filters during angioplasty.

The study primary outcome was the occurrence of the SNR. The Slow- and no-reflow were defined as acute impairment of blood flow to thrombolysis in myocardial infarction (TIMI) grade of 2 and 0–1 respectively, despite successful treatment of the vessel obstruction.[14] Angioplasty procedures have been performed by two experienced interventional cardiologists using standard techniques.[13] In case of visible thromboses, longer stents were applied to cover them all.

Data were analyzed using the SPSS software (version 16, SPSS Inc., Chicago, IL, USA). Data are presented as the mean $\pm$ standard deviation (SD) for quantitative variables or number (valid percent) for categorical variables. Quantitative data were checked as with normal distribution using the Kolmogorov-Smirnov Test. Student's independent t-test (for quantitative data with normal distribution), Mann-Whitney Test (for quantitative data without normal distribution and for ordinal data) and chi-square or Fisher's exact tests (for categorical data) were applied for comparison of patients with SNR and those with normal reflow. Spearman and Pearson correlation were applied to check the correlations among the variables. A P of less than 0.050 was considered statistically significant in these analyses. Stepwise logistic regression analysis was performed to find possible independent predictors of SNR. Possible predictors were considered as those variables associated with the SNR in univariate analyses with P < 0.100. Odds ratios (OR) and 95% confidence intervals (95% CI) are mentioned wherever needed.

Table 1. Demographic data, medical history, and laboratory data in all patients and comparison between patients with normal reflow and slow/no-reflow after procedure

Variables	All (n = 205)	Normal reflow (n = 167)	Slow/no-reflow (n = 38)	P
Age (year) (mean ± SD)	66.8 ± 9.6	67.0 ± 9.0	66.3 ± 11.8	0.681[*]
Man	166 (81.0)	136 (81.4)	30 (78.9)	0.819[**]
Coronary risk factors based on medical history [n (%)]				
Smoking	50 (24.4)	41 (24.6)	9 (23.7)	> 0.999[**]
Hypertension	122 (59.5)	99 (59.3)	23 (60.5)	> 0.999[**]
Dyslipidemia	57 (27.8)	46 (27.5)	11 (28.9)	0.843[**]
Diabetes	54 (26.3)	41 (24.6)	13 (34.2)	0.227[**]
Pre-procedural blood pressure				
Systolic blood pressure ≥ 140 mmHg [n (%)]	81 (39.5)	66 (39.5)	15 (39.5)	> 0.999[**]
Diastolic blood pressure ≥ 90 mmHg [n (%)]	30 (14.6)	19 (11.4)	11 (28.9)	0.010[**]
Laboratory data [n (%)]				
Anemia[£]	44 (21.5)	38 (22.8)	6 (15.8)	0.391[**]
High creatinine[¥]	35 (17.1)	24 (14.4)	11 (28.9)	0.053[**]
Leukocytosis[§]	13 (6.3)	7 (4.2)	6 (15.8)	0.017[**]
Hyperglycemia[‡]	19 (9.3)	15 (9.0)	4 (10.5)	0.759[**]
eGFR < 60 ml/min/1.73m^2	66 (32.1)	50 (29.9)	16 (42.1)	0.178[**]

[*] Student's independent t-test; [**] Fisher's exact test; [£] Hemoglobin < 13 g/dl in men and < 12 g/dl in women; [¥] Serum creatinine > 1.3 mg/dl in men and > 1.1 mg/dl in women; [§] White blood cell count > 10000 per mcl; [‡] Random blood sugar > 200 mg/dl
eGFR: Estimated glomerular filtration rate

Results

A total of 280 patients were evaluated during the study, among which 75 patients were not eligible for the study. Finally, data of 205 patients were included in the analyses showing that 81% are man, and mean ± SD of age was 66.8 ± 9.6 years. Thirty-eight (18.5%) of the patients had SNR after PCI including 23, 9, and 6 patients with post-PCI TIMI grade of 2, 1, and 0, respectively. Demographic data, medical history, and laboratory data with the comparisons between the two groups of patients with SNR and normal reflow are summarized in tables 1 and 2. There was no difference between the two groups regarding age, gender, or frequency of coronary risk factors (P > 0.050). Compared to those with normal reflow, patients with SNR had more frequent pre-procedural high DBP (28.9% vs. 11.4%, P = 0.010), high creatinine (28.9% vs. 14.4%, P = 0.053), and leukocytosis (15.8% vs. 4.2%, P = 0.017) (Table 3). There was also a non-significant difference between the two groups in kidney function (eGFR < 60: 42.1% in SNR vs. 29.9% in normal reflow, P = 0.178).

With regards to the disease and procedural characteristics, patients with SNR had longer lesion length (26.3% vs. 12.7% with diffuse lesions, P = 0.007), higher SVG degeneration scores (71.1% vs. 29.9% with scores of 2 or 3, P < 0.001), more frequent proximal lesions (76.3% vs. 35.9%,

P < 0.001) and less frequent mid part and distal lesions (25.9% vs. 66.4%, P < 0.050), more frequent thrombosis (42.1% vs. 21.6%, P = 0.013), and lower number of used stents during procedure (18.4% vs. 24.6% with more than one stent used, P = 0.032) (Table 2). There was a non-significant difference between the two groups in stenosis severity with 100% stenosis being more frequent in patients with SNR (28.9% vs. 9.6%, P = 0.105). Also, stent length tended to be shorter in these patients (P = 0.095)(Table 2). In total, distal embolic filters have been used in 19 (9.3%) patients with no difference between the two groups of patients with SNR and normal reflow (P = 0.759).

Possible predictors of the SNR (with P < 0.100 in univariate analyses) were included into a stepwise logistic regression model. At first, the stenosis severity was negatively associated with SNR which was against the univariate analysis results, probably due to a high correlation with the pre-intervention TIMI grade (Spearman's rho coefficient = -0.620, P < 0.001). Accordingly, stenosis severity was excluded from the model. Possible predictors of SNR are summarized in table 3, and only factors with the significant association are presented. Positive factors independently associated with the SNR were pre-procedural DBP of ≥ 90 mmHg with OR = 3.858 (95% CI: 1.157-12.860), degenerated SVG with OR = 5.901 (95% CI: 1.883-18.492), and having proximal lesions with OR = 5.070 (95%

Table 2. Disease and procedure characteristics in all patients and comparison between patients with normal reflow and slow/no-reflow after procedure

Variables	All (n = 205)	Normal reflow (n = 167)	Slow/no-reflow (n = 38)	P
Length of lesion [n (%)]				0.007[*]
Diffuse > 20 mm	31 (15.1)	21 (12.7)	10 (26.3)	
Tubular 10-20 mm	34 (16.6)	25 (15.1)	9 (23.7)	
Discrete < 10 mm	139 (67.8)	120 (72.3)	19 (50.0)	
Degeneration score [n (%)]				< 0.001[*]
3 (>75%)	37 (18.0)	25 (15.0)	12 (31.6)	
2 (50-75%)	40 (19.5)	25 (15.0)	15 (39.5)	
0-1 (< 50%)	128 (62.4)	117 (70.0)	11 (28.9)	
Degree of stenosis [n (%)]				0.105[*]
100%	27 (13.2)	16 (9.6)	11 (28.9)	
90-99%	123 (60.0)	106 (63.5)	17 (44.7)	
75-90%	55 (26.8)	45 (26.9)	10 (26.3)	
Stenosis location [n (%)]				< 0.001[†]
Proximal	89 (43.4)	60 (35.9)	29 (76.3)	
Mid part	65 (31.7)	59 (35.3)	6 (15.8)	
Distal	56 (27.3)	52 (31.1)	4 (10.5)	
Thrombosis	52 (25.4)	36 (21.6)	16 (42.1)	0.013[†]
Direct stenting	74 (36.1)	62 (37.1)	12 (32.4)	0.706[†]
Using balloon (pre-/post dilation)	133 (64.9)	107 (64.1)	26 (68.4)	0.708[†]
No. of stents [n (%)]				0.032[*]
0	16 (7.8)	8 (4.8)	8 (21.1)	
1	141 (68.8)	118 (70.7)	23 (60.5)	
> 1	48 (23.4)	41 (24.6)	7 (18.4)	
Stent length [n (%)]				0.095[*]
> 30 mm	41 (20.0)	38 (23.0)	3 (9.1)	
25-30 mm	25 (12.2)	21 (12.7)	4 (12.1)	
15-25 mm	79 (38.5)	64 (38.8)	15 (45.5)	
< 15 mm	53 (25.9)	42 (25.5)	11 (33.3)	
Using distal embolic filters [n (%)]	19 (9.3)	15 (9.0)	4 (10.5)	0.759[†]
Baseline TIMI flow (mean ± SD)	2.33 ± 1.08	2.53 ± 0.94	1.42 ± 1.17	< 0.001[*]

The following variables were considered as ordinal variables: length of lesion, degeneration score, the degree of stenosis, number of stents, and stent length. The stenosis location and using balloon was considered as nominal variables. P represents the overall comparisons for these variables.
[*] Mann-Whitney test; [†] Fisher's exact test
TIMI: Thrombolysis in myocardial infarction

CI: 1.822-14.113). Negative factors associated with SNR were pre-intervention TIMI grade with OR = 0.618 (95% CI: 0.405-0.942) and the number of stents used for PCI with OR = 0.074 (95% CI: 0.011-0.481) for > 1 stent, and the length of stents used for PCI with OR = 0.100 (95% CI: 0.019-0.529) for stents > 30mm of the stents (Table 3). Because the decision on the number of stents used during PCI might have been affected by the presence of SNR, a second model was conducted without this factor, finding positive and negative factors similar to the previous model.

Discussion

The aim of the present study was to investigate possible clinical and procedural factors associated with the SNR phenomenon following PCI of the SVG. The rate of SNR phenomenon after SVG-PCI in our study (18.5%) was similar to other reports (about 14%).[9,10] Success of the PCI for diseased SVG is limited by the no-reflow complication which is associated with about 15% increased risk of mortality and 30% increased risk of post-procedural acute myocardial infarction (AMI).[15] Accordingly, finding predictors of this serious complication would be helpful for promptly tailoring preventive strategies to at-risk patients. In our study, we found possible associations of a number of patients, lesions, and procedural characteristics with the occurrence of SNR after SVG-PCI. Pre-procedural high diastolic blood pressure, proximal location of the lesion, and

Table 3. Stepwise logistic regression analysis of predictors of slow/no-reflow after procedure

Variable	OD (95% CI)	P
Positive predictor		
Pre-procedural diastolic blood pressure ≥ 90 mmHg	3.858 (1.157-12.860)	0.028
Degenerated SVG (score of 2-3 vs. 0-1)	5.901 (1.883-18.492)	0.002
Lesion location (proximal vs. others)	5.070 (1.822-14.113)	0.002
Negative predictor		
Pre-intervention TIMI flow	0.618 (0.405-0.942)	0.025
No. of stents (indicator 0)		
1	0.223 (0.052-0.956)	0.001
> 1	0.074 (0.011-0.481)	0.006
Stent length (indicator < 15 mm)		
15-25 mm	1.122 (0.370-3.402)	0.839
25-30 mm	0.391 (0.087-1.756)	0.221
> 30 mm	0.100 (0.019-0.529)	0.007

Nagelkerke R square = 0.415
SVG: Saphenous-vein coronary bypass grafts; TIMI: Thrombolysis in myocardial infarction; OD: Odds ratio; CI: Confidence interval

degenerated SVG were found as independent positive predictors of SNR after SVG-PCI in our study. Also, pre-intervention TIMI grade and the number and length of the stents used for PCI were found as independent negative predictors.

A limited number of studies have systematically investigated possible predictors of no-reflow after PCI of SVG. Patients' characteristics and clinical presentation may provide valuable data in this regard. Similar to our results, two other studies found no association between patients' age and the risk of no-reflow.[9,10] Only one report by Liu et al. found older age associated with distal embolization after SVG-PCI.[11] However, studies on patients referring with AMI have reported an association between patient's age and risk of no-reflow after PCI.[16,17] Diabetes and hyperglycemia may be associated with the no-reflow phenomenon as a result of impaired microvascular function and/or worse functional recovery.[18] An association between hyperglycemia/diabetes and no-reflow is reported in patients who had AMI following PCI of the coronary vessels.[18,19] However, our study, as well as others,[9-11] found no such association in PCI of the SVG. With regards to the possible association between lipid profile and no-reflow, the results of previous studies on patients presenting with AMI have been controversial.[20,21] Our study, as well as others,[9,10] found no association in this regard for the SVG-PCI. Neither hypertension nor smoking is consistently reported as factors associated with no-reflow after PCI in patients with AMI,[22-24] or after SVG-PCI.[9-11] Although we found no association between history of hypertension and SNR, there was an association between pre-procedural high diastolic blood pressure (≥ 90 mmHg) and

occurrence of SNR in our study which was independent of other evaluated factors. High diastolic blood pressure can reflect an uncontrolled chronic hypertension which may increase the risk of no-reflow. On the other hand, hypotension at admission (systolic blood pressure < 100 mmHg) is reported as an independent predictor of no-reflow after PCI in patients with AMI.[17] This can be attributed to decreased blood flow in the lesion site and increased plugging of the leukocytes, another risk factor of the no-reflow phenomenon.[25] With regards to the patients' drug history, previous studies have failed to demonstrate association of no-reflow with specific medications (e.g. glycoprotein IIb/IIIa inhibitors).[9,26]

The only strong and consistent clinical characteristic predicting no-reflow in SVG-PCI is reported as presenting with AMI. Hong et al.[9] found no-reflow about two times more frequent in patients presenting with AMI compared to those referring with unstable/stable angina (24% vs. 13%). In another study, Sdringola et al.[10] found acute coronary syndrome (i.e. AMI and unstable angina) were significantly more frequent in patients with no-reflow than those with normal reflow (78% vs. 45%). Most of the patients in our study have been referred with stable/unstable angina. A number of patients with AMI had cardiogenic shock and were excluded from the study. Accordingly, we had limitations in this regard and were not able to evaluate the role of clinical presentation in development of SNR. Differences among the previous studies can be attributed to differences in defining the no-reflow phenomenon and more importantly to differences in patients' characteristics (e.g. clinical presentation). At this

time, the only clinical factor that can be considered as an independent predictor of no-reflow after SVG-PCI is AMI. Considering the limited number of reports on SVG-PCI, further investigation is necessary regarding patients medical history.

With regards to the laboratory findings, we found associations of leukocytosis and abnormal serum creatinine level with SNR after SVG-PCI. According to some evidence, white blood cell count[27] and neutrophil/lymphocyte ratio[28] can predict the occurrence of no-reflow after PCI and subsequent adverse cardiac events in patients referring with AMI. Our study is the first to report such an association in SVG-PCI. Possible mechanisms in this regard include mechanical plugging of leukocytes,[25] releasing oxygen free radicals leading to local edema,[29] and functional interactions between leukocytes and platelets in the microcirculation[30] which impair the flow upon reperfusion. Therefore, leukocytosis (and more precisely the neutrophil/lymphocyte ratio) can be considered as a predictor as well as a target for intervention in order to prevent no-reflow after SVG-PCI. The association between renal function impairment and incidence of and recovery from no-reflow after PCI in patients presenting with AMI is controversial.[26,31,32] Possible mechanisms include an association between renal function and coronary flow[33] and more severe renal function impairment in patients with the more severe illness. Other attractive laboratory data which is shown predictive for no-reflow after PCI in patients referring with AMI is the c-reactive protein (CRP).[34-36] Increased atherosclerosis associated with inflammation, promotion of microvascular thrombus formation and obstruction, and vasoconstriction via increased cyclo-oxygenase expression is suggested as possible mechanisms.[35,37] There is no data on the value of this laboratory test in predicting no-reflow after SVG-PCI and studies are warranted in this regard.

Characteristics of the lesions and angiographic findings during PCI on SVG may be helpful in estimating the risk of no-reflow and individualizing interventional approaches. We found an important association of having proximal stenosis and no-reflow after SVG-PCI. Proximal lesions in our study were accompanied with degenerated SVG, thrombosis, diffuse lesions, and complete stenosis more frequently than middle or distal lesions (data not shown). Such coexistence with other risk factors may explain, in part, the association between proximal lesions and no-reflow in our study. Also, proximal lesions may be more prone to disruption by interventional procedures resulting in distal

embolization, though there is no direct evidence in this regard. In Sdringola et al.[10] study, ostial lesions (within 3 mm of the proximal anastomosis) were less frequent in patients with no-reflow than those with normal reflow after SVG-PCI (13% vs. 35%). Hong et al.[9] also reported that no-reflow was less frequent in patients with lesions at ostium (8% vs. 22%); however, no difference was among proximal, middle, and distal lesions. It must be noted that distal protection devices which can decrease the risk of distal embolization have been used more frequently in the previous studies (about 40%) than ours (9%). Technically, these devices are more feasible for proximal lesions which may explain the differences among the different results of studies regarding the risk of no-reflow in proximal lesions.

Similar to our results, Hong et al. also reported a higher risk of no-reflow after SVG-PCI in longer lesions,[9] but Sdringola et al. found no association.[10] Liu et al. reported larger plaque volume as an important independent predictor of distal coronary embolization (evaluated by a rise in serum creatine kinase) after SVG-PCI.[11] Lesion length is reported to be associated with no-reflow after PCI on coronary vessels of patients with the acute coronary syndrome.[17,38] Longer target lesion is associated with the larger amount of thrombus and plaque burden. Vessels with a larger diameter can contain larger plaques or thrombus but have slower flow velocity which may describe the association between lesion length and risk of no-reflow. Moreover, compared with the native coronary vessel, the larger, less calcified, and thus more friable plaques of the SVG are more prone to disruption by balloon angioplasty resulting in embolization in the smaller distal native arteries. Similar to our results, previous studies have reported a higher frequency of thrombus in no-reflow than normal reflow (35-41% vs. 7-21%).[9,10] In addition to the above-proposed mechanism, it must be noted that risk of thrombus formation from plaque ulceration is higher in a diffusely diseased SVG. This can explain why thrombus was more frequently observed with a degenerated SVG in our study (41.5% vs. 15.6%), which is an important and independent predictor of no-reflow. Similar to our results, Hong et al. found a higher rate of degenerated SVG in patients with no-reflow compared with those with normal reflow after PCI (62% vs. 36%),[9] and the same result was reported by Sdringola et al. (56% vs. 16%).[10] Therefore, in a degenerated SVG, distal embolization by thrombus or macro-debris from a large plaque after

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intervention may play a major role in the no-reflow phenomenon. Another important predictor of the no-reflow phenomenon is the baseline TIMI grade.[17,26,31] Indeed, a less patent vessel prior to PCI can indicate a higher thrombus burden and more probable vasospasm. All of the above, the presentation of a case with degenerated SVG, thrombus, and large plaque or long lesion who had a baseline TIMI grade of less than 3 should be considered highly suspicious for the occurrence of no-reflow after SVG-PCI.

Interventional techniques may affect the risk of no-reflow after SVG-PCI. We found an inverse association between the number of stents used during PCI and the risk of SNR. In the study by Zhou et al. on patients with AMI, using more than one stent was associated with lower risk of no-reflow after PCI (16.7% vs. 27.8%).[17] However, it must be noted that the occurrence of no-reflow itself may affect the decision on the number of the stents being used during PCI. Also, stent length was inversely associated with the risk of SNR in our study. Hong et al. found a similar association after PCI in patients with AMI,[38] but not after SVG-PCI.[9] Shorter stents may be associated with higher risk of dissection and longer stents may better be able to cover unseen thrombi at the edges of the lesions. Unless more data are available, a clear conclusion cannot be made in these regards.

Few reports are available on the possible role of direct stenting in reducing the risk of no-reflow. In patients with AMI, Antoniucci et al.[39] found a lower risk of no-reflow with direct stenting compared with conventional stenting (5.5% vs. 12%). But, Sabatier et al. found no difference in this regard in a randomized trial.[40] We found no association between direct stenting and risk of no-reflow in SVG-PCI which was similar to other reports.[9] Although using distal protection devices has decreased the risk of no-reflow after SVG-PCI [41] and are shown to be cost-effective in this regard,[42] we found no association between distal embolic filters and the risk of no-reflow. It must be noted that distal embolic filters have been used in only 10% of our patients probably due to high costs of such devices. Hong et al. also found no association of using distal protection devices with post-intervention TIMI.[9] Differences among the studies may be related to interventional cardiologists' expertise and technical difficulties with these devices.[41]

Our study had a number of limitations to be mentioned. The study had limited sample size to precisely investigate a large number of factors that might predict SNR. Data were gathered retrospectively which might increase the risk of information bias. Also, the diagnosis of no-reflow in our study was only based on the TIMI grading. Intravascular ultrasound imaging and post-procedural electrocardiography and cardiac enzymes can provide more valuable data. Moreover, we could not gather data on the timing of the SVG disease which is important regarding the possible predictors.

Conclusion

We found possible associations of a number of patients, lesions, and procedural characteristics with the occurrence of slow/no-reflow after PCI of SVG. The pre-procedural high diastolic blood pressure ($\geq$ 90 mmHg), proximal lesion location, and degenerated SVG were positive independent predictors, and pre-intervention TIMI grade and the number and length of the stents used for PCI were negative independent predictors of slow/no-reflow after SVG-PCI in our study. Such data can be used in risk estimation of the no-reflow phenomenon and tailoring preventive strategies promptly to at-risk patients.

Acknowledgments

Conflict of Interests

Authors have no conflict of interests.

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