The clinical prediction factors of nonculprit lesions progression in patients with acute ST elevation myocardial infarction after primary percutaneous coronary intervention

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Abstract

Objective :To investigate the relationship between the clinical features and progression of nonculprit lesions in patients with ST-elevation myocardial infarction (STEMI) after primary percutaneous coronary intervention (PPCI). Methods: A total of 192 patients (57.1 ± 9.2 years) with STEMI who underwent PPCI from January 2016 to December 2017 in Beijing Anzhen Hospital were enrolled in this study. All patients underwent PPCI as treatment for culprit lesions.Clinical and angiographic follow-up were performed in 12 months. All patients were divided into Nonculprit lesions(NCL) progression group (82 cases) and the control group (110 cases) according to angiographic follow-up outcome in 12 months. The clinical and angiographic features were analyzed.Results: Levels of body mass index（BMI）,serum creatinine （Scr）,fasting blood glucose（FBG）,glycated serum albumin（GSA）,glycated hemoglobin(GHb) and homocysteine (Hcy) in NCL progression group were significantly higher than those in the control group(P < 0. 05,respectively).Logistic regression showed that FBG(odds ratio = 1. 274,95% confidence interval: 1. 077-1. 505,P = 0. 005) and Scr (odds ratio =1. 020,95% confidence interval:1. 002-1. 038,P=0. 027) were independent predictors of NCL progression.Partial correlation analysis showed that FBG was positively correlated with NCL progression(r = 0. 231,P = 0. 001) .Receiver operating characteristic(ROC) curve showed that the boundary point of FBG to predict NCL progression was 5. 715 mmol /L, the sensitivity was 74. 4% and the specificity was 46. 4%.Conclusion: FBG is an valuable predictor for NCL progression in patients with STEMI after PPCI.

Background

Primary percutaneous coronary intervention (PPCI) can salvage dying myocardium, reduce cardiovascular events, and improve prognosis in patients with ST-elevation myocardial infarction (STEMI).However, recent clinical studies have shown that nonculprit lesions (NCL)may progress after PPCI and the progression of NCL could be the most significant factor that affects the prognosis after PPCI.[1-2] However, the clinical correlation factors of the progression of NCL were not clear. In this study, we investigate the relationship between the clinical features and the progression of NCL in patients with STEMI after PPCI.

Methods

All participants or their family members were informed about the potential publication of their identities and images, and all of them completed consent forms. All procedures and protocols were approved by the ethics committee of Capital Medical University, and the experiments were conducted according to the Helsinki declaration (1975 and subsequent revisions).

From January 2016 to December 2017, 192 patients (160 men and 32 women) with acute STEMI who underwent PPCI treatment were enrolled in this retrospective study Clinical and angiographic follow-up was performed in all patients for 12 months. The inclusion criteria were as follows. (1) Acute myocardial infarction lasted for < 12 h and only one nonculprit lesion was found in the setting of STEMI. Acute

myocardial infarction was defined as follows: evidence of ischemic chest pain lasting for > 30 min, and new ST segment elevation of ≥ 2 mm in two or more contiguous electrocardiographic leads; a de novo lesion; single vessel treatment in a native vessel ≥ 2.5 mm in diameter and occluded, thrombus containing; thrombolysis in myocardial infarction (TIMI) flow grade of 0 to 2 in the culprit artery; and the grade of stenosis of nonculprit lesions was < 70%. (2) There was no contraindication for anticoagulation and antiplatelet therapy.

The main exclusion criteria included the following: previous percutaneous coronary intervention (PCI) in an infarction related artery (IRA) (*n* =3), Killip class ≥ 3 (*n* =3), left or right bundle branch block (*n* =4), IRA with excessive proximal tortuosity or severe calcification (*n* =5), left ventricular ejection fraction < 35% (*n* =5), lack of clinical and angiographic follow-up (*n* =10), in-hospital death after PPCI (*n* =4), myocardial infarction within two weeks of PPCI to exclude potential subacute stent thrombosis of the intervened arterial segment (*n* =3), and repeated PCI of culprit coronary lesions for restenosis or progression (*n* =17).

Coronary angiography was performed using the Judkins method, and coronary artery lesion classification was based on the American College of Cardiology/American Heart Association guideline.[3] Thrombus aspiration catheters (DIVER CE, Invatec, Brescia, Italy) were used for thrombotic burden lesions. Stents were implanted using a routine method, and the procedure succeeded with residual stenosis < 20%, TIMI flow grade of 3 and no acute complications (death, myocardial infarction, emergency coronary artery bypass grafting (CABG)), and no major adverse cardiac events (cardiac death, myocardial infarction, target vessel revascularization) in hospital. Clinical and angiography follow-up was performed for 12 months.

The culprit coronary lesions were clearly identified by a combination of electrocardiography and coronary angiography. Nonculprit lesions were defined as those with a diameter of stenosis < 70%. All patients underwent PPCI for the culprit lesions.

Quantitative coronary angiography was performed in the first angiography. Follow-up angiography was performed by two independent investigators who were blinded to the results. We categorized the lesions according to the American College of Cardiology/American Heart Association. Classification on the basis of morphological characteristics of lesions that cause significant stenosis of the coronary arteries. [3] These included two categories of simple lesions (A or B1 lesions) and complex lesions (B2 or C).

Collected data included demographic information, medical history, coronary artery disease risk factor status, detailed coronary angiographic information, biomarkers associated with coronary atherosclerosis at the time of baseline PCI, and coronary angiographic information at the time of angiographic follow-up.

All clinical, laboratory, and coronary angiographic data were evaluated by two independent investigators who were not involved in the angiographic procedures.

Defination of NCL progression[3] : The stenosis degree of NCL was ≥50% at the time of baseline PCI and the degree of NCL progression ≥10% at the time of angiographic follow-up. The stenosis degree of

NCLwas <50% at the time of baseline PCI and the degree of NCL progression ≥30% at the time of angiographic follow-up. The degree of NCL progression ≥30% ,while there were no NCL at the time of baseline PCI . NCL progression to total occlusion.

Hypertension was defined as Systolic blood pressure 140 mmHg (1 mmHg = 0.133 kPa)/and/or diastolic blood pressure 90 mmHg or are taking antihypertensive drugs According to *2010 Chinese Hypertension Prevention Guide* revised *edition*.[4].

Diabetes is defined as a typical symptoms of diabetes (more drinks, polyphagia, polyuria, weight loss) and fasting plasma glucose tendency for 7.0 / L or 2 h after oral glucose tolerance test blood sugar 1 tendency for 1.1 ,according to the the China *Guideline* for the *Prevention* of *Type 2 Diabetes* (*2017 Edition*). [5]

SPSS20.0 software were used for all statistical analyses. Count data are expressed as cases and percentages, and the $\chi 2$ test was used for analysis. Numerical data are expressed as mean±SD and were compared using the Student's t test. Nonnormally distributed numerical data are expressed as the median and 25th–75th interquartile range and were compared using a rank-sum test. partial correlation analysis was used to evaluate the correlations between the FBG, and progression of NCL. binary Logistic regression analysis was performed to examine independent risk factors for progression of NCL. Receiver-operating characteristic (ROC) analysis and calculation of sensitivity and specificity were performed to test the ability of FBG to predictive the progression of NCL. A *P* value of less than 0.05 was considered statistically significant.

All patients were divided into the control group without NCL progression and the progression group (with NCL progression) according to the defination of NCL progression.

Results

There were 82 (71 men and 11 women) patients without NCL progression(the control group) and 110 (89 men and 21 women) patients with NCL progression (the progression groups).

There was no significant differences in age,sex,history of diabetes mellius,rates of ,hyperlipidemia, smoking, myocardial infarction, PCI, CABG, heart rate, systolic arterial pressure, left ventricular ejection fractions (LVEF), cardiac troponin I (cTnI) peak value,Triglyceride(TG),*total* cholesterol (TCHO),High density liptein cholesterol(HDL-C),low-density lipopro-tein cholesterol (LDL-C) ,*Total* three-triiodothyronine(TT3),*total* thyroxine(TT4),*free* triiodothyronine(FT3),C reactive protein (CRP),*urine* acid(UA), Time from attack to reperfusion,myocardial blush grade (MBG) of 0–1 in the culprit artery,Predilation rate,Thrombolic lesion rate,≥ 2 vessle lesion rate,collateral circulation rate,culprit lesion length,complex lesion rate,and degree of baseline stenosis between the two groups (all $P > 0.05$)(Table 1).

There were significant differences in body mass index(BMI),fasting blood glucose(FBG),glycated albumin(GA),hemoglobinA*1c*(HbA1c),homocysteine(Hcy),*serum* creatinine(Scr),and follow-up stenosis

degree between the two groups (*P* <0.05,P<001,P<0.0001,respectively)(Table1).

For medications, patients received a similar amount of β-blockers (62% *vs*. 65%), calcium antagonists (30% *vs*. 28%), ACEI/ARB(56% *vs*.54%),and statins (91% *vs*. 89%) in each group (all *P* < 0.05) (Table1).

Multivariate logistic regression analysis indicated that fasting blood glucose(FBG)(*OR*: 1.274, 95%*CI*: 1.077-1.505,p=0.005) and serum creatinine(Scr) (*OR*: 1.020, 95%*CI*: 1.002-1.038,p=0.027) were independent predictor of the progress of NCL after primary PCI in patients with STEMI (*P*< 0.05)(Table2).

Partial correlation analysis showed that fasting blood glucose level was positively correlated with NCL progression (*r*= 0.231, *P*= 0.001)Table 3.

ROC analysis for the predictors of NCL progression indicated that a FBG level ≥5.715 mmol/L may predict the NCL progression, the sensitivity was 74.4% and the specificity was 76.6% (*AUC*: 0.613,*CI*:0.532-0.693,*P* 0.008)(Table 4).

Table1. Baseline clinical and angiographic characterisitcs

	The control group (*n*=110)	The progression group (*n*=82)	*P* value
Age(y)	56±9	58±10	NS
Male（%）	89（80.9%）	71（86.6%）	NS
BMI（kg/m^2）	25.5±2.9	26.7±3.6	<0.05
Diabetes mellius（%）	28（25.5%）	31（37.8%）	NS
FBG(mmol/L)	6.4±1.6	7.2±2.2	<0.01
GA(%)	15±3	16±4	<0.05
HbAlc/%	6.3±1.4	6.7±1.3	<0.05
Hypertension（%）	60(54.5%)	52(63.4%)	NS
Hyperlipidemia（%）	30(27.3%)	23(28.0%)	NS
Current somking（%）	71(64.5%)	52(63.4%)	NS
Prior myocardium infarction（%）	6(5.5%)	8(9.8%)	NS
Prior PCI（%）	10(9.1%)	10(12.2%)	NS
Prior CABG（%）	0	0	——
β-blockers（%）	68(62%)	53(65%)	NS
Calcium antagonists（%）	33(30%)	23(28%)	NS
ACEI/ARB（%）	61(56%)	44(54%)	NS
Statins（%）	100(91%)	73(89%)	NS
Heart rate, beats/min	82±13	83±12	NS
Systolic arterial pressure(mmHg)	133±23	131±21	NS
LVEF(%)	53±11	53±10	NS
cTnI peak value(ng/ml)	21.76±3.55	22.12±3.61	NS
TG(mmol/L)	1.9±1.3	2.0±1.2	NS
TCHO(mmol/L)	4.3±1.1	4.3±1.1	NS
HDL-C(mmol/L)	1.00±0.23	0.98±0.20	NS
LDL-C(mmol/L)	2.6±0.9	2.6±0.9	NS
Hcy((umol/L)	15±8	18±11	<0.05
TT3(nmol/L)	1.39±0.34	1.38±0.26	NS

TT4(nmol/L)	109±24	109±16	NS
FT3(pmol/L)	4.9±0.7	4.8±0.6	NS
CRP(mg/L)	3.36±1.01	5.55±1.93	NS
Scr （umol/L)	71±16	77±21	<0.05
UA(umol/L)	346±90	348±97	NS
Time from attack to reperfusion (min)	371±172	373±178	NS
MBG 0-1	45(40.91%)	34(41.46%)	NS
Predilation rate	34(30.91%)	27(32.53%)	NS
Thrombolic lesion rate(%)	27(24.55%)	21(25.61%)	NS
≥ 2 vessle lesion rate(%)	52(47.27%)	41(50.00%)	NS
Collateral circulation rate(%)	28（25.45%）	21（25.61%）	NS
Culprit lesion length(mm）	29.3±13.1	29.7±13.5	NS
Complex lesion rate（%）	44（40.00%）	32(39.02%)	NS
Baseline stenosis degree（%）	32.1±13.1	34.4±13.6	NS
Follow-up stenosis degree（%)	60.2±14.3	78.3±15.4	<0.0001

Data are presented as n(%) or mean ±SD unless other indicated .BMI:body mass index; FBG:fasting blood glucose; GA：glycated albumin; HbA1c：hemoglobin A*1c;* PCI:percutaneous coronary intervention; CABG:coronary artery bypass grafting; ACEI / ARB：angiotensin-converting enzyme inhibitor/angiotensin Ⅱ receptor blocker; LVEF:left ventricular ejection; TG：Triglyceride; TCHO：*total* cholesterol; HDL-C:High density liptein cholesterol; LDL-C：low-density lipoprotein cholesterol;Hcy:homocysteine; Scr:*serum* creatinine;TT3: *Total* three-triiodothyronine;TT4:*total* thyroxine;FT3:*free* triiodothyronine ; CRP：C-reactive protein;Scr：creatinine; UA：*urine* acid; MBG:myocardial blush grade.

Table 2.Multivariate Logistic regression *analysis*

Factor	*B* value	*SE* value	*OR* value	95%CI	*P* value
Scr	0.20	0.009	1.020	1.002-1.03	0.027
FBG	0.242	0.085	1.274	1.077-1.50	0.005
BMI	0.089	0.049	1.093	0.992-1.203	0.071

OR：odds ratio；CI：confidence interval;Scr:*serum* creatinine; FBG:fasting blood glucose;BMI:body mass index.

Table 3.Partial correlation analysis between FBG and NCL progression

Factor	Partial correlation coefficient	*P* value
FBG	0.231	0.001

Table 4.ROC analysis for the predictors of NCL progression

the area under the ROC curve	SEM	95% CI	*P* value
0.613	0.041	0.532-0.693	0.008

Discussion

PPCI in a culprit artery is the preferred strategy for treating patients with acute STEMI. However, approximately 40%–65% of patients with STEMI present with three-vessel lesions. A clinical follow-up study of patients with three-vessel lesions after successful PCI suggested that nonculprit lesions may be progressing.[1] This may be the most important factor that affects the prognosis of patients with acute myocardial infarction after successful PCI.

However, there have been few studies on the clinical predictor for progression of nonculprit lesions. Tsiamis, *et al*.[6] performed follow-up angiography for 117 patients with acute coronary syndrome. These authors suggested that nonculprit lesions may have progressed, and acute myocardial infarction may be an independent predictive factor for progression of nonculprit lesions.

Our follow-up study on progression of nonculprit lesions suggested that this progression may be the most important prognostic factor in patients with STEMI after successful PCI.[7] Our data suggested that progression of nonculprit lesions could involve inflammation and a stress mechanism, and a high dosage of ramipril may inhibit progression of non-culprit lesions, which could be the main cause of revascularization after PPCI for patients with STEMI.

In the present study, we investigated the clinical prediction factors of NCL progression in patients with STEMI after PPCI. We carried out a 12-month clinical and angiographic follow-up in 192 patients, and found that there were significant differences in BMI,FBG,GA,HbA1c, and Hcy between the control group and the progression group ,it indicated that BMI,FBG,GA,HbA1c, and Hcy may be clinical correlation factors of nonculprit lesions progression in patients with STEMI after PPCI..

In our study, there were no significant differences in the patients' other characteristics and medical history between the control group and the progression groups. Additionally, all patients received comparable medication.

Multivariate logistic regression analysis indicated that FBG and Scr were independent predictor of the progress of NCL after primary PCI in patients with STEMI .Partial correlation analysis showed that FBG level was positively correlated with NCL progression. ROC analysis for the predictors of NCL progression indicated that a fasting glucose level ≥5.715 mmol/L may predict the NCL progression, the sensitivity was 74.4% and the specificity was 76.6%. It indicated that elevated FBG may be a independent predictor of NCL progression in STEMI patients underwent primary PCI.

Diabetes is an independent risk factor for coronary artery disease (CAD). Compared to the nondiabetic population, diabetes is associated with a 2-3-fold increase in the risk of cardiovascular disease and mortality due to cardiovascular disease[6].Previous studies have shown that glucose metabolism plays a role in the development and development of coronary heart disease and is closely related to the prognosis of coronary heart disease.even patients with mildly elevated blood glucose levels are more prone to AMI than patients with normal blood glucose levels[7]. Berry et al[8] found that FBG, HbA1c and the hsitory of diabetes are associated with the severity and progression of coronary atherosclerosis .In our study, fasting glucose and creatinine levels were found to be independent predicters of NCL progression, and fasting glucose was positively correlated with NCL progression in partial correlation analysis. Increased secretion of high levels of catecholamine, glucocorticoids and other hormones in acute myocardial infarction can enhance liver glycogen decomposition and inhibit glycogen production[9]. In addition to upregulating glucose production, insulin resistance and impaired glucose uptake mechanism during critical disease jointly lead to the occurrence of hyperglycemia[10-11]. Hyperglycemia leads to plaque progression may be related to the following mechanisms [12] :□non-enzymatic glycation of proteins and lipids increases, and the formation of reactive higher glycation end products, resulting in mechanical dysfunction of the vascular wall □It obstructs and makes circulating blood cells adhere to the blood vessel wall, and also interferes with cell function by binding to a variety of receptors on macrophages, endothelial cells and other cells, increasing pro-inflammatory signal transduction and promoting inflammation of the blood vessel wall. □During hyperglycemia, insulin receptor substrate 1 is down-regulated and the cells become resistant to insulin. Insulin-like growth factor 1 receptor sends signals through other alternative scaffold proteins to induce vascular smooth muscle cells to dedifferentiate, leading to migration and proliferation of vascular smooth muscle cells. □by activating protein kinase C, hyperglycemia causes many abnormal changes related to atherosclerosis, such as increased vascular permeability, endothelial dysfunction and reduced production of nitric oxide, resulting in impaired vasodilation, increased apoptosis, and increased production of extracellular matrix.

Conclusions

The results of this study suggest that BMI,FBG,GA,HbA1c, and Hcy may be clinical correlation factors of NCL progression in patients with STEMI after PPCI．FBG and Scr were independent predictor of the progress of NCL after primary PCI in patients with STEMI. This study is a single-center retrospective analysis, with a relatively small sample size and lack of detailed intravascular imaging data, which still needs to be improved by further randomized prospective controlled studies.

Abbreviations

STEMI:ST-segment elevation myocardial infarction;PCI:primary percutaneous coronary intervention;BMI:body mass index; FBG:fasting blood glucose; GA．glycated albumin; HbA1c．hemoglobin A*1c;* PCI:percutaneous coronary intervention; CABG:coronary artery bypass grafting; ACEI / ARB． angiotensin-converting enzyme inhibitor/angiotensin ． receptor blocker; LVEF:left ventricular ejection; TG． Triglyceride; TCHO．*total* cholesterol; HDL-C:High density liptein cholesterol; LDL-C．low-density lipoprotein cholesterol;Hcy:homocysteine;Scr:*serum* creatinine;TT3: *Total* three-triiodothyronine;TT4:*total* thyroxine;FT3:*free* triiodothyronine ; CRP．C-reactive protein;Scr．creatinine; UA．*urine* acid; MBG:myocardial blush grade.

Declarations

Ethics approval and consent to participate

This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in apriori approval by the Ethics Committee *of* Peking University. Informed consent was exempted by the board for this study.

Consent for publication

Not applicable

Availability of data and material

Please contact author for data requests.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

J.W. designed and coordinated the study, J.W.wrote the main manuscript text. X.-J.W.collected samples. All authors reviewed the manuscript.

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Figures

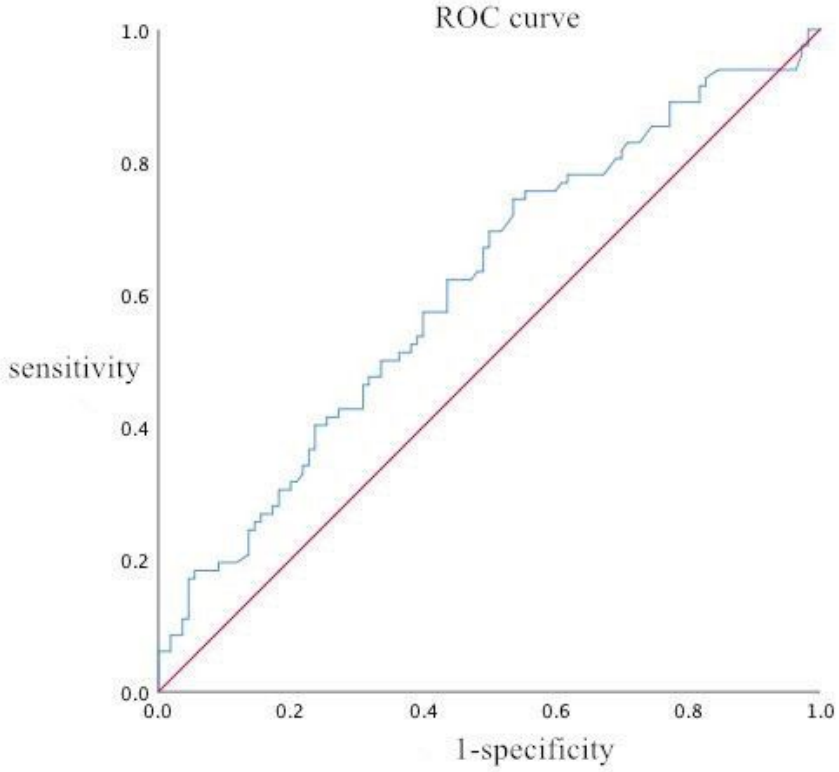

Figure 2

ROC curve for the predictors of NCL progression