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Prediction of No Reflow Phenomenon in Percutaneous Coronary Intervention with Optical Coherence Tomography and Analysis of Risk Factors

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ABSTRACT

Objective: To investigate the predictive value of no reflow phenomenon in interventional therapy by measuring plaque quantitatively with optical coherence tomography (OCT).

Methods: Our study involved 196 patients who visited the Department of Cardiology of the Second Affiliated Hospital of Zhengzhou University from January 2020 to January 2022. According to whether there was no reflow during the operation, they were divided into the A group (46 cases) and B group (150 cases). We systematically collected general clinical data and coronary angiography related data of patients through inpatient cases, measured fiber cap thickness and the lipid core angle of diseased vascular plaque through optical coherence tomography, and analyzed the relationship between fiber cap thickness and no reflow phenomenon.

Results: BMI, LDL, phospholipase A, proportion of family history of coronary heart disease, length of atherosclerotic plaque with thin fiber cap A group were higher than in the normal flow group ($P < 0.05$), while the thickness of the fibrous cap was lower than that B group ($P < 0.05$). Further multivariate logistic regression analysis showed that fiber cap thickness, and length of atherosclerotic plaque with thin fiber cap were independent risk factors for no reflow phenomenon ($P < 0.05$). Further ROC curve analysis found that the thickness of fiber cap had a high predictive value for no reflow phenomenon, and the best cutoff value for no reflow was 55, AUC: 0.985 (95% CI: 0.968-1.000, P<0.001).

Conclusions: Optical coherence tomography can predict the occurrence of no reflow phenomenon by quantitatively measuring the fiber cap thickness. The prediction effect is the best when the fiber cap thickness is 55.

INTRODUCTION

At present, percutaneous coronary intervention (PCI) is an effective treatment for acute ST segment elevation myocardial infarction (STEMI) [Guidelines for diagnosis and treatment of acute ST segment elevation myocardial infarction 2019]. However, after the criminal vessel is opened, some patients will have no reflow phenomenon. No reflow phenomenon refers to that after the criminal vessel is opened, dissection, embolism, spasm, endometrial tear, and other conditions are excluded, and the infarct related areas cannot obtain effective blood perfusion [Montone 2020]. Some studies [Fajar 2018] show that no reflow phenomenon is a predictor of adverse prognosis of STEMI patients after PCI, which increases the risk of adverse events, such as malignant arrhythmia and recurrent myocardial infarction, and reduces the prognosis of patients [Pantea-Roşan 2020; Tasar 2019].

There are many studies on no reflow phenomenon from the perspective of inflammatory reaction, but few studies on the characteristics of coronary plaque and no reflow phenomenon. In clinical work, with the development of endovascular imaging, some studies also have explored the characteristics of coronary artery plaque through intravascular ultrasound (IVUS) to reveal the relationship with no reflow phenomenon [Yajuan 2021]. However, due to the limitation of resolution, IVUS can only conduct qualitative analysis on plaque, but cannot conduct quantitative calculation. Optical coherence tomography (OCT) quantitatively can calculate plaque. Therefore, this study aims to explore the predictive research value of no reflow phenomenon in PCI through quantitative calculation of plaque by OCT, so as to make early discovery and treatment of no reflow phenomenon in PCI, and improve the prognosis of patients.

DATA AND METHODS

General information: We collected the relevant information from 196 patients, who were admitted to the Department of Cardiovascular Medicine of the Second Affiliated Hospital of Zhengzhou University for PCI, due to "acute myocardial infarction" from January 2020 to January 2022. Among 196 subjects, 46 patients with TIMI blood flow grade ≤ 2 were classified as A group [Huang 2020], and a total of 150 cases with TIMI3 was included in the B group. The research scheme was implemented after being approved by the Ethics Committee of the Second Affiliated Hospital of Zhengzhou University (ethical batch number: 2022379).

Inclusion and exclusion criteria: The clinical diagnosis is coronary heart disease., and there are symptoms related to myocardial ischemia, and PCI and OCT were performed in this hospital; Age 18-80; Preoperative blood flow of target

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Table 1. Comparison of baseline data between the two groups

	A group (*N* = 46)	B group (*N* = 150)	T/χ2	*P*
Age (years)	64.35±9.00	66.51±7.66	1.603	0.111
Male, n (%)	18 (39.1)	67 (44.7)	0.439	0.508
Heart rate	77.63±7.73	78.01±9.09	0.254	0.800
LVEF (%)	52.50±4.01	50.46±4.00	1.542	0.125
BMI (kg/m2)	26.73±4.30	25.23±4.34	2.052	0.042
Hypertension, n (%)	12 (26.1)	49 (32.7)	0.711	0.399
Diabetes	14 (30.4)	43 (28.7)	0.053	0.817
Smoking history, n (%)	7 (15.2)	20 (13.3)	0.105	0.746
Drinking history, n (%)	5 (10.9)	33 (22.0)	2.791	0.095
Family history, n (%)	14 (30.4)	25 (16.7)	4.187	0.041
Systolic pressure (mmHg)	123.54±10.58	124.93±13.73	0.631	0.529
Diastolic pressure (mmHg)	80.74±8.85	79.97±7.35	0.588	0.557

Table 2. Comparison of laboratory inspection data

	A group (*N* = 46)	B group (*N* = 150)	T/χ2	*P*
White blood cell count (109/L)	7.99±2.74	7.53±1.78	1.336	0.183
Red blood cell count (10^{12}/L)	4.62±0.50	4.78±0.56	1.793	0.075
Platelet count (109/L)	240.61±44.88	242.94±43.62	0.315	0.753
Hemoglobin (g/L)	132.59±12.37	133.46±12.81	0.408	0.684
Total cholesterol (mmol/L)	4.44±1.09	4.59±0.86	0.930	0.354
Triglyceride (mmol/L)	1.84±0.82	1.97±0.71	1.062	0.290
Low density lipoprotein (mmol/L)	2.75±0.90	2.27±0.73	3.691	0.000
High density lipoprotein (mmol/L)	0.97±0.26	1.03±0.35	1.166	0.245
Lp-PLA^2 (ng/ml)	282.63±76.79	237.48±75.40	3.538	0.000

Comparison of laboratory examination data between two groups: The levels of low density lipoprotein and phospholipase A2 in the A group were significantly higher than those in the B group, with a statistically significant difference (P<0.05). There was no significant difference in blood routine examination and blood lipid related indicators.

vessel TIMI3.Exclusion criteria: There are calcified lesions, bifurcation lesions, spasms and coronary self-hairpin layer in the target vessel; Coronary angiography showed thrombus in the target vessel; Within 14 days of acute myocardial infarction; Those with antiplatelet drugs and anticoagulant drugs contraindications (such as severe hemorrhagic disease history, obvious active bleeding, thrombocytopenia history, stroke history within 3 months, etc.);Severe or acute heart failure (NYHA grade IV or LVEF<30%);Complicated with uncontrollable malignant arrhythmia, serious valvular heart disease, aortic dissection, coronary artery fistula, congenital heart disease, etc; Combined with severe basic diseases (such as severe liver and kidney dysfunction, malignant tumor, severe infection, massive pleural effusion, high fever, etc.); There are contraindications to PCI such as contrast agent allergy, access vessel occlusion, etc; OCT data and related clinical data are incomplete and cannot be analyzed in one step.

Statistical analysis: Spss26.0 software was used for data analysis, and the collected data were divided into counting data and measuring data. The measurement data conforming to the normal distribution is expressed as "mean ± standard deviation (x ± u)". The independent sample t-test was used between groups. The counting data is expressed as absolute number (constituent ratio). The comparison between groups is based on χ2 Test, rank sum test was used to compare grade data. Multivariate logistic regression analysis was used to screen the independent risk factors of coronary non reflow. ROC curve was used to determine the predictive value of related variables for coronary no reflow phenomenon. The difference was statistically significant ($P < 0.05$).

Table 3. Comparison of clinical data during PCI

	A group (*N* = 46)	B group (*N* = 150)	T/χ2	*P*
Degree of vessel stenosis	83.54±6.45	82.70±8.11	0.645	0.520
Radial artery approach	40	138	0.554	0.457
Average length of implanted stent	26.70±6.75	24.91±7.50	1.447	0.149
Average diameter of implanted stent	3.01±0.58	2.99±0.54	0.219	0.827
Lenght of atherosclerotic plaque with thin fiber cap	11.15±1.98	8.45±0.98	12.518	0.000
Anterior descending branch	22	68	0.088	0.767
Left circumflex branch	8	30	0.153	0.695
Right coronary artery	16	52	0.000	0.989
Thin fiber cap thickness	66.52±29.08	171.00±62.72	10.929	0.000
Lipid core angle (quadrant)	1.80±0.72	1.69±0.70	0.931	0.353

Comparison of clinical data between two groups during PCI: Compared with the B group, the thickness of fibrous cap in the diseased area of the A group was significantly lower than that of B group ($P < 0.05$). There was no significant difference between the two groups in the degree of vascular stenosis, radial artery approach, average length of implanted stent, average diameter of implanted stent, location of diseased vessels, and angle of lipid core (quadrant) ($P > 0.05$).

Table 4. Multivariate logistic regression analysis of no reflow phenomenon

	B	S.E	Wald	OR	95% CI	*P*
Thin fiber cap thickness	-0.134	0.037	13.339	0.874	0.814-0.940	0.000
Lenght of atherosclerotic plaque with thin fiber cap	1.211	0.412	8.629	3.356	1.496-7.526	0.003

Multivariate logistic regression analysis of no reflow phenomenon: The multivariate logistic regression analysis was carried out with the no reflow phenomenon in patients undergoing PCI as the dependent variable (0=none, 1=yes), and the statistically significant indicators in the above table as the independent variables. The results showed that fiber cap thickness, and length of atherosclerotic plaque with thin fiber cap were independent risk factors for no reflow phenomenon ($P < 0.05$)

RESULTS

Comparison of baseline data between two groups: There was no significant difference between the two groups in age, sex, heart rate, smoking history, drinking history, diabetes history, hypertension history, diastolic blood pressure, systolic blood pressure and LVEF ($P > 0.05$). The BMI of A group was higher than that of B group, and the positive proportion of family history was higher than that of B group, the difference was statistically significant ($P < 0.05$). (Table 1)

DISCUSSION

At present, most studies [Wang 2018; Shihang 2021] believe that the pathophysiological mechanisms of no reflow are inflammatory reaction, oxidative stress, microcirculation embolism, endothelial dysfunction, etc. Previous studies [Libby 2021] have shown there is a strong inflammatory reaction in the ruptured plaque, which is an important link in the occurrence and development of coronary plaque. Inflammatory factors will promote the high expression of angiogenic factors and promote the formation of new blood vessels in the plaque. Among them, immature blood vessels will cause bleeding in the plaque and promote the exudation of red blood cells. The red blood cell membrane is rich in lipids, becoming the main source of free cholesterol in the plaque. At the same time, the activation of multiple pro-inflammatory genes in vascular smooth muscle cells will lead to the transformation obstacle of their phenotypes and ultimately lead to the reduction of extracellular matrix involved in the formation of fiber caps, resulting in the reduction of fiber cap thickness.

Table 5. ROC Curve of TCFA and lp-PLA2

	AUC	Cut-off	*P*	95% CI	Sensitivity	Specificity
Thin fiber cap thickness	0.985	55	0.000	0.968-1.000	0.935	0.967
Length of atherosclerotic plaque with thin fiber cap	0.875	9.5	0.000	0.800-0.949	0.804	0.873

ROC curve for prediction of fiber cap thickness: The ROC curve shows that the best critical point of fiber cap thickness is 55, AUC: 0.985 95% CI: 0.968-1.000 $P < 0.001$. The optimal critical point of length of atherosclerotic plaque with thin fiber cap was 9.5, AUC: 0.875,95% CI: 0.800-0.949, $P < 0.001$.

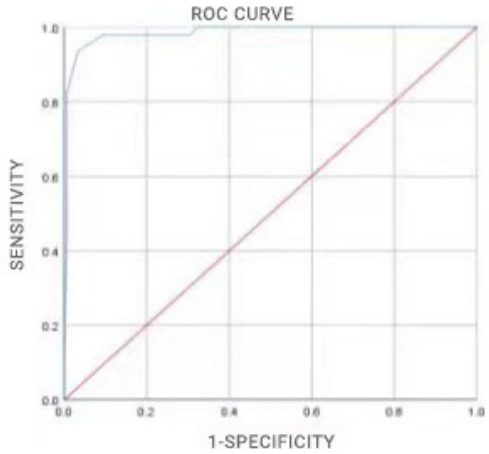

Figure 1. ROC curve of no reflow phenomenon predicted by TCFA

The above may be the mechanism of plaque characteristics leading to no reflow [de 2019; Parma 2020; Wolf 2020; Bennett 2016]. OCT [Spaide 2017] is a new imaging technology applied to coronary artery. Its axial resolution is 10 times that of IVUS, and its lateral resolution is three times that of IVUS. It can accurately and quantitatively measure plaque fiber cap.

Plaque rupture, plaque erosion, and calcified nodules are common mechanisms of acute coronary syndrome (ACS) in OCT imaging [Yonetsu 2018]. Some studies [Gupta 2016] reported that 10%-30% of patients with acute STEMI will have no reflow after PCI, and the incidence of this phenomenon is higher in patients with acute STEMI. A total of 196 subjects were included in this study, 46 of whom had no reflow with an incidence of 23.5%, which is consistent with previous studies. Amano et al. [Amano 2016] studied 106 lesions in 93 ACS patients through IVUS and found that no reflow phenomenon is more likely to occur when thin fibrous cap atherosclerotic plaque exists. Zhen et al. [Zhen 2020] believed that thin fibrous cap atheromatous plaque was a predictor of no reflow in non STEMI patients. However, there are few studies on the prediction of no reflow phenomenon through OCT detection of thin fibrous cap atheromatous plaque. This study further found that the thickness of fibrous cap of criminal vascular plaque in STEMI patients was thinner in the no reflow group than in the normal blood flow group. Further logistic regression analysis found that the thickness of the thinnest fiber cap was an independent risk factor for no reflow. The ROC curve showed that the best cutoff value for predicting no reflow was 55, AUC: 0.985 95% CI: 0.968-1.000 $P < 0.001$. However, in this study, the lipid core angle between the two groups has no significant difference, which is inconsistent with the previous study [Hibi 2015] and may be related to the measurement unit (the lipid core angle in this study is in quadrant). In this study, compared with the normal blood flow group, the no reflow group has a higher proportion of severe thrombosis load, which is consistent with the previous study [Fajar 2018]. Severe thrombotic load increases the complexity of interventional operation, and the probability of damage to target vessels by guide wire and balloon greatly increases. Fractured fragments during operation can induce microcirculation obstruction, further aggravate myocardial reperfusion injury, thus leading to no reflow phenomenon. LDL migrates to the endothelium with the participation of chemokines and eventually forms oxidized low density lipoprotein (ox LDL), which can reduce plaque stability by promoting the formation of foam cells, inducing apoptosis of smooth muscle cells [Weidong 2018]. Song et al. [Song 2020] included 176 subjects in the study and found that LDL is a predictor of coronary no reflow phenomenon. In this study, LDL is not an independent risk factor for no reflow phenomenon. One of the reasons may be that multiple factors without reflow phenomenon participate in the process, and the weight of fiber cap thickness and LP-PLA2 in no reflow event is greater than LDL. Second, the sample size of this study may be small. LP-PLA2 can decompose OX-LDL into lysophosphatidylcholine and oxidized fatty acids, which can further accelerate vascular endothelial damage, ultimately leading to the occurrence of vascular inflammatory reaction under the mediation of viscous factors, inflammatory factors, etc., and further accelerate atherosclerosis [Mengqi 2021]. Bonnefont et al. [Bonnefont 2016] believed that LP-PLA2 is a predictor of cardiovascular events and coronary plaque instability and plays an important role in the evolution of thin fibrous cap atherosclerotic plaque. In this study, the LP-PLA2 level in the no reflow A group was higher than that in the B group normal flow group. Which was consistent with previous studies. The

deficiency of this study is that the sample size of this study is small, and it is a single-center retrospective study.

CONCLUSIONS

Optical coherence tomography can predict the occurrence of no reflow phenomenon by quantitatively measuring the fiber cap thickness. The fiber cap thickness is an independent risk factor for no reflow phenomenon, and the best cutoff value for predicting no reflow is 55, AUC: 0.985 95% CI: 0.968-1.000 $P < 0.001$. In clinical work, accurate prediction of no reflow phenomenon of coronary artery by optical coherence tomography is expected to greatly improve the prognosis of patients.

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