

Analysis on correlation between blood stasis syndrome of coronary heart disease and coagulation function and blood platelet parameters.

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Abstract

Purpose: To discuss on the correlation between the blood stasis syndrome of coronary heart disease and coagulation function and blood platelet parameters.

Method: 74 cases of coronary heart disease patients are selected as the objectives of the research, including 50 patients with syndrome of blood stasis and 24 patients without syndrome of blood stasis. The Prothrombin Time (PT), the Activated Partial Thromboplastin Time (APTT), the Fibrinogen (FIB), the blood Platelet count (PLT), the Platelet Distribution Width (PDW), the Mean Platelet Volume (MPV), the large platelet ratio (PLCR) and the Thrombocytocrit (PCT) of patients of the two groups are inspected, and International Normalized Ratio (INR) is calculated, and the levels of various indexes are compared between the two groups. In addition, the Pearson correlation test is adopted to analyse the correlation between the blood stasis syndrome of coronary heart disease and various indexes. The binary logistic regression analysis is adopted to discuss on the influencing factors for the blood stasis syndrome of the coronary heart disease.

Results: The PT and INR of the group with the blood stasis syndrome are significantly lower than those of the group without the blood stasis syndrome ($P < 0.05$). The difference on various indexes related to blood platelet has no statistical significance ($P > 0.05$). There is correlation between the blood stasis syndrome of coronary heart disease and PT and INR ($P < 0.05$). INR is the influencing factor on the blood stasis syndrome of coronary heart disease.

Conclusion: There is a close correlation between the blood stasis syndrome of coronary heart disease and the coagulation function: INR reduces when PT shortens.

Keywords: Coronary heart disease, Blood stasis syndrome, Coagulation function, Blood platelet parameters, Analysis on correlation.

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Introduction

Patients of coronary heart disease have coagulation and fibrinolysis imbalance, presented as enhanced coagulation function and reduced fibrinolysis, leading to hypercoagulable blood state[1]. The correct understanding and treatment on changes on coagulation function of coronary heart disease patients plays a significant role in preventing adverse heart events. Therefore, the correlation between the coagulation function and blood platelet parameters and the disease state of patients of coronary heart disease with and without blood stasis syndrome is observed, so as to evaluate dangerous factors related to blood stasis syndrome of coronary heart disease patients, to provide basis for clinical prevention and treatment of blood stasis syndrome of coronary heart disease.

Clinical Data

General data

74 hospitalized patients of coronary heart disease in Cardiology Department of Guang'anmen Hospital during December 2013-August 2014 were adopted as the objectives of the research. According to the TCM syndrome scale [2] scoring based on two deputy director doctors of the hospital at the admittance of the hospital, the patients were divided into the group with the blood stasis syndrome of 50 cases and the group without the blood stasis syndrome of 24 cases. In which the group with the blood stasis syndrome included 21 males and 29 females, with ages of 57-84 y old, (70.0 ± 12.7) on average, and course of disease of 5-20 y, (13.0 ± 6.8) on average. They had cardiac functional grading [3] of grade I of 28 cases and grade II of 22 cases. 4 cases were conducted with Percutaneous Coronary Intervention (PCI) operation. The group without the blood stasis syndrome included 11 males and

13 females, with ages of 58-84 y old, 71.0 ± 12.1) on average, and course of disease of 5-18 y, (12.0 ± 5.9) on average. They had cardiac functional grading of grade I of 10 cases and grade II of 14 cases. 2 cases were conducted with Percutaneous Coronary Intervention (PCI) operation. There was no statistical significance on comparisons on age, gender and cardiac functional grading data ($P > 0.05$), with comparability.

Diagnostic criteria

The diagnostic criteria of ischemic heart disease [4] formulated by International Society of Cardiology and World Health Organization as well as the management guidance for stable type ischemic heart disease [5] formulated by American College of Cardiology (AHA) are taken as the western medicine diagnosis standard.

The "Research on Diagnostic Criteria on Coronary Heart Disease Blood Stasis Syndrome" [6] is taken as the traditional Chinese medicine diagnosis standard.

Admission criteria

The patients in accordance with the above diagnostic standard: age of >50 y old; course of disease of 5-20 y; cardiac functional grading NYHA [2] \leq grade 2; with signed informed consent.

Exclusion criteria

The patients with acute coronary syndrome, hypertensive emergency, severe hypertension (systolic pressure ≥ 160 mmHg and/or diastolic pressure ≥ 100 mmHg) and other cardiac disease (valvular heart disease, pulmonary heart disease and cardiomyopathy); accompanied with malignant ventricular arrhythmias (frequent ventricular premature beat, grade II Type II atrioventricular block, grade III atrioventricular block); combined acute cerebrovascular disease, severe renal insufficiency, malignant tumor, blood system disease, immune system disease; combined with mental disorder; taking warfarin.

Methods

Observation indexes and method

Coagulation testing: The patients were conducted with venous blood collection with empty belly after 12h of ambrosia, to acquire peripheral venous blood of 2 ml, which was conducted with sufficient centrifugation with 3000 r/min for 10 min. 50 μ l of sample of PT, 50 μ l of sample of APTT and 10 μ l of sample of FIB were collected. The special calcium-containing thrombin activity enzyme kit (Japan Sysmex Company, with batch number of 567453), partial thromboplastin time test kit (Japan Sysmex Company, with batch number of 657666), fibrinogen determination kit (Japan Sysmex Company, with batch number of 567989) and automatic coagulation analyzer (Japan Sysmex Company, with model of CS-5100) were adopted to determine PT, APTT and FIB. The International Normalized Ratio (INR) was calculated

from PT and the International Sensitivity Index (ISI) for determination of reagent, with the formula of $INR = (PT_{test}/PT_{normal})^{ISI}$, in which PT_{test} is the PT result of the blood of thromboplastin of patients, and PT_{normal} is the PT result of the blood of thromboplastin of healthy people [7].

Detection on blood platelet parameters: The specialized blood reagent matching with Sysmex XE-2100 of the whole blood automatic blood analyzer (Japan Sysmex Company, with the batch number of 786578) was adopted for venous blood collection. The impedance method and the flow cytometry were adopted to determine the Platelet count PLT (PLT), the Platelet Distribution Width (PDW), the Mean Platelet Volume (MPV), the large platelet ratio (PLCR) and the Thrombocytocrit (PCT).

Statistical method

The SPSS 20.0 statistical software was adopted for data analysis, and the mean value \pm standard deviation ($\bar{x} \pm s$) was adopted to expression the measurement data; t-test was adopted; χ^2 was adopted for enumeration data; the Pearson correlation test was adopted for correlation analysis. The binary logistic regression analysis was adopted for analysis on influencing factors.

Results

Comparisons on blood coagulation function indexes between two groups

According to Table 1, the PT and INR values of the group with the blood stasis syndrome are significantly lower than that of the group without the blood stasis syndrome ($P < 0.05$).

Comparisons on blood platelet indexes between two groups

According to Table 2, the difference on various indexes of blood platelet between the two groups has no statistical significance ($P > 0.05$).

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Considering that the blood stasis syndrome of coronary heart disease and the patients without blood stasis syndrome are binary variables; the coronary heart disease with blood stasis syndrome is 0 and that without blood stasis syndrome is 1. According to the Pearson correlation analysis on the blood stasis syndrome of coronary heart disease and coagulation function (PT, INR, APTT, FIB) and blood platelet indexes (PLT, PDW, MPV, PLCR and PCT), as shown in Table 3, there was correlation between the blood stasis syndrome of coronary heart disease and PT and INR ($P < 0.05$), and there was no

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significant correlation with APTT, FIB and blood platelet indexes (PLT, PDW, MPV, PLCR and PCT).

Table 1. Comparisons on coagulation function between two groups ($\bar{x} \pm s$). Notes: PT: Prothrombin Time; INR: International Normalized Ratio; APTT: Activated Partial Thromboplastin Time; FIB: Fibrinogen.

Group with blood stasis syndrome	50	10.45 ± 1.66	0.977 ± 0.16	25.42 ± 5.65	2.87 ± 0.82
Group without blood stasis syndrome	24	11.56 ± 2.38	1.078 ± 0.21	27.38 ± 4.67	3.05 ± 0.57
t value		-2.313	-2.323	-1.475	-0.955
P value		0.024	0.023	0.144	0.343

Group	Number of cases	PT (s)	INR	APTT (s)	FIB (g/L)
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Table 2. Comparisons on blood platelet indexes between the two groups ($\bar{x} \pm s$).

Group	Number of cases	PLT ($\times 10^9/L$)	PDW (fL)	MPV (fL)	PLCR (%)	PCT (%)
Group with blood stasis syndrome	50	213.62 ± 62.06	11.84 ± 2.05	10.52 ± 0.93	28.44 ± 7.6	0.22 ± 0.06
Group without blood stasis syndrome	24	192.21 ± 63.68	11.76 ± 1.48	10.31 ± 0.74	27.17 ± 6.22	0.21 ± 0.05
t value		-1.378	-0.157	-0.960	-0.712	-1.160
P value		0.173	0.876	0.340	0.479	0.250

Notes: PLT: Blood Platelet Count; PWD: Platelet Distribution Width; MPV: Mean Platelet Volume; PLCR: Large Platelet Ratio; PCT: Thrombocytocrit.

Table 3. Correlation on blood stasis syndrome of coronary heart disease and coagulation function and blood platelet indexes. Notes: PT: Prothrombin Time; INR: International Normalized Ratio; APTT: Activated Partial Thromboplastin Time; FIB: Fibrinogen; PLT: Blood Platelet Count; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; PLCR: Large Platelet Ratio; PCT: Thrombocytocrit.

Indexes	Item	PT	INR	APTT	FIB	PLT	PDW	MPV	PLCR	PCT
Group with blood stasis syndrome	t value	-0.263	-0.264	-0.171	-0.112	0.139	-0.050	0.103	0.072	0.110
	P value	0.024	0.023	0.144	0.343	0.237	0.672	0.368	0.540	0.352

Binary logistic regression analysis on influencing factors of blood stasis syndrome of coronary heart disease

According to Table 4, the blood stasis syndrome of coronary heart disease is taken as the dependent variable, and PT, INR,

APTT, FIB, PLT, PDW, MPV, PLCR and PCT are taken as the independent variables, to conduct the binary Logistic regression analysis. According to the result, INR is the influencing factor of the blood stasis syndrome of coronary heart disease.

Table 4. Binary logistic regression analysis results of influencing factors of blood stasis syndrome of coronary heart disease. Notes: INR: International Normalized Ratio; PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time; FIB: Fibrinogen; PLT: Blood Platelet Count; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; PLCR: Large Platelet Ratio; PCT: Thrombocytocrit.

Variable	Regression coefficient	Standard deviation	χ^2 value	Degree of freedom	P value	OR value
Blood stasis syndrome	5.754	0.519	5.220	1	0.022	315.555
INR	-4.912	2.456	4.000	1	0.045	0.007
PT	-	-	-	1	0.972	-
APTT	-	-	-	1	0.879	-
FIB	-	-	-	1	0.722	-
PLT	-	-	-	1	0.200	-
PDW	-	-	-	1	0.507	-

MPV	-	-	-	1	0.186	-
FLCR	-	-	-	1	0.245	-
PCT	-	-	-	1	0.309	-

Discussion

In traditional Chinese medicine, coronary heart disease is within the range of “chest apoplexy and cardiodynia”, with pathogenesis of weakened body resistance, cold coagulation, phlegm damp and extravasated blood, but with the basic pathogenesis of heart arteries and veins stasis resistance. Blood stasis syndrome is one of the common syndrome types of coronary heart disease. According to modern medicine, the formation of blood stasis syndrome of coronary heart disease has similar pathology with lipid metabolism disorder in body, vascular endothelial injury and coagulation mechanism disorder, which leads to high coagulation state before thrombus in blood [8].

According to research findings, the formation of thrombus is the main pathological process of coronary heart disease [9], and it is the dangerous factor leading to acute coronary artery syndrome. In order to reduce or eliminate the occurrence of adverse cardiovascular events of coronary heart disease and conduct secondary level prevention, it is necessary to conduct active treatment on controllable dangerous factors [10,11]. It is the hot spot on clinical research to select an appropriate drug for coagulation resistance and blood platelet resistance as the optimal treatment scheme for coronary heart disease patients so as to balance the risks on bleeding and thrombus.

Blood coagulation is the process of generating of thrombin by coagulation factor as per certain sequence, which changes fibrinogen into fibrous protein. Therefore, the coagulation process can be divided into the formation of the prothrombin complex, the activation of the prothrombin and the generation of the fibrous protein. As an important index [12] to evaluate the exogenous coagulation function of bodies, PT is utilized to evaluate the contents of fibrinogen, prothrombin and coagulation factors V, VII and X in human bodies. The shortening of the PT value indicates that the body is in a high-coagulation state or combined with a thrombus related disease. Due to INR, the PT of different laboratories and different reagents can be compared with each other. And both of them are important parameters reflecting the body blood coagulation functions, which can be utilized to evaluate the functions of the coagulation system of patients as well as guide for use of drugs for coagulation and thrombus resistance.

According to research findings, PT and INR values of blood stasis syndrome of coronary heart disease are lower than that without blood stasis syndrome ($P < 0.05$), indicating that the coagulation factors of the patients of coronary heart disease with blood stasis syndrome are over activated, with less time needed for blood coagulation. The blood is in a high coagulation state, with higher thrombus formation risks when compared with the patients without blood stasis syndrome. It is

consistent with the research finding in recent years; i.e., patients of coronary heart disease with blood stasis syndrome have high blood coagulation and low fibrinolytic status [13]. According to the statement on blood stasis syndrome in traditional Chinese medicine such as “no flowing of blood due to stasis” or “blocked blood due to stasis” indicate that the blood cannot “flow smoothly as water” in veins, with abnormality of blood rheology behavior [14]; it is speculated that the patients of coronary heart disease with blood stasis syndrome have serious injury in endothelial cells due to blood circulation and microcirculation obstacles [15], which activates the coagulation system because of naked intermediate collagen fiber tracts endothelium, generating large amount of coagulation factors. As the strong inducer of blood platelet, coagulation factors can give rise to aggregative response independent to blood platelet particle secretion [16], which enhances the risks of thrombus of patients of coronary heart disease with blood stasis syndrome. Based on Pearson correlation inspection, the risks on formation of thrombus of patients with blood stasis syndrome have significant correlation with PT and INR. It further illustrates that the formation of thrombus of patients with blood stasis syndrome is closely related to the pathological process of increased blood platelet aggregative ability due to generation of large amount of coagulation factors. Based on the binary Logistics regression analysis, INR is the independent influencing factor for thrombus formation risk of coronary heart disease with blood stasis syndrome, and it indicates that increased INR can be taken as one of the referencing basis for coronary heart disease with blood stasis syndrome. Mao et al. [17] take the increased activity of the coagulation factor VII as the referencing basis of the blood stasis syndrome of coronary heart disease. Both of them are combined, to provide wider and more accurate basis for traditional Chinese medical clinical diagnosis and treatment on system, cells and molecule aspects. In addition, due to insignificant difference between the two groups on blood platelet indexes, it indicates that there are increased prothrombin and other coagulation factors of coronary heart disease and blood stasis syndrome, and the increased blood platelet aggregative ability may be the main reason for thrombus formation. The increased amount of blood platelet does not play a very significant role in thrombus formation. Therefore, during the thrombus resistance treatment on coronary heart disease with blood stasis syndrome, it is necessary to lay emphasis on hindering the occurrence of the blood platelet aggregation response, to select the effect target of drugs restraining the blood platelet aggregation response process.

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