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Original Article

Changes in galectin-3 levels and left ventricular systolic function in patients with acute coronary syndrome after percutaneous coronary intervention

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Abstract: Purpose: This study aimed to explore the relevance of changes in Galectin-3 (Gal-3) levels and left ventricular systolic function of patients with acute coronary syndrome (ACS) after percutaneous coronary intervention (PCI). Methods: This study selected 82 ACS patients who were admitted into our hospital for PCI treatment from Aug 2018 to Aug 2019 as candidates. Also, this study chose 82 healthy people after their hospital physical examination as the normal group. The study utilized quantitative enzyme-linked immunosorbent assay (ELISA) to test the serum Gal-3 level of patients. The study also utilizes multiple logistic regression to analyze the Gal-3 relationship with the left ventricular function of ACS patients after PCI. Results: The univariate analysis revealed that gender, age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, cardiac function classification, total cholesterol amount, blood creatinine, triglyceride, fasting blood glucose, diabetes and hypertension between these two groups showed no statistically significant difference ($P > 0.05$). The Gal-3 level and NT-pro BNP levels of patients after PCI were lower than in patients before PCI, which had a statistically significant difference ($P < 0.05$). The comparison of hs-CRP levels in patients between both groups showed no statistical difference ($P > 0.05$). There was no statistically significant difference in the diameter of the left atrium, CO and SV before and after PCI ($P > 0.05$). The LVEDD and LVESD level of patients after PCI were lower than before PCI, with a statistically significant difference ($P < 0.05$). The results of Pearson correlation analysis revealed that Gal-3 level has a positive correlation with LVEDD ($r = 0.721$, $P < 0.05$) and a negative correlation with LVEF ($r = 0.607$, $P < 0.05$). Conclusion: There is a close relationship between the change of Gal-3 level and ventricular systolic function. Therefore this index can be clinically used for early diagnoses and disease treatment.

Keywords: Acute coronary syndrome, PCI, Gal-3 level, left ventricular systolic function

Introduction

Acute coronary syndrome (ACS) is a clinically common acute ischemic syndrome of small blood vessels. The clinical symptoms are mainly chest pain, chest tightness, sweating, dizziness and shortness of breath. Some patients do not have typical clinical symptoms, or may not have symptoms [1]. Currently, Tte commonly used clinical methods to treat ACS are PCI or thrombolytic therapy. A vascular stent is implanted to resolve lesions, coronary artery stenosis or occlusion, which helps restore perfusion to the heart muscle, preserve heart mechanisms and improve the prognosis [2]. However, blood vessels are often partially inflamed due to invasive intervention and damage of the vascular endothelium caused by medical devices [3]. Therefore, it is important to diagnose ACS in time and accurately determine the prognosis because taking reasonable clinical intervention measures prevent disease progression and improves the survival rate of patients. In recent years, biomarkers have become the basic tools for disease diagnosis, treatment and evaluation of prognosis. Heart failure, ventricular remodeling and left ventricular dysfunction are strong predictors of poor prognosis of ACS. Gal-3 has multiple biological functions. Gal-3 is gradually being used in the

clinic as a biomarker for ACS prognosis [4]. Related studies have indicated that the Gal-3 level can not only predict the risk of atrial fibrillation and heart failure of ACS patients, but also predict the left ventricular dilatation after cardiac infarction of ACS patients [5]. However, there are few reports about the correlation between serum Gal-3 level and left ventricular systolic function of ACS patients. Therefore, this study has selected 82 ACS patients who were admitted to our hospital for PCI treatment from August 2018 to August 2019 as research subjects. Our study reveals the usefulness of galectin-3 as a biomarker and suggests the potential of anti-galectin-3 therapy in treating heart failure.

Resources and methods

General resources

A total of 82 ACS patients who were admitted to our hospital for PCI treatment from August 2018 to August 2019 were selected as research subjects. There were 22 cases of unstable angina, 26 cases of acute non-ST segment elevation myocardial infarction and 34 cases of acute ST segment elevation myocardial infarction. Selection criteria: (1) Patients with ACS diagnosis [6]; (2) Patient's first diagnosis of ACS; (3) The clinical data of patients are complete; (4) Patients have given informed consent. Excludes criteria: (1) Patients who have server liver or kidney dysfunction; (2) Patients who have malignant tumors and autoimmune diseases; (3) Patients who have hematologic system issues or sever internal diseases. This study was approved by the ethics committee of our hospital.

Methods

Clinical data collection: This study has collected the clinical data regarding gender, age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, cardiac function classification, total cholesterol amount, blood creatinine, triglycerides, fasting blood glucose, diabetes and hypertension of ACS patients.

Blood sample collection and testing: The study collects 8 ml of blood from the elbow veins of patients in the morning when patients were fasted. Three ml of blood was taken and placed in an EDTA for 20 mins at the room temperature. Then, the serum was separated by centrifugation at 3000 r/min for 15 mins and stored in a freezer at -80°C. The quantitative enzyme-linked immunosorbent assay was used to test the levels of Gal-3 and NT-pro BNP. The concentration of Gal-3 was calculated by the standard curve and the kit was provided by Shanghai Yuanye Biotechnology Limited Company. Another 5 ml of blood sample was sent to the laboratory of our hospital to test total cholesterol level, blood creatinine, triglycerides and fasting blood glucose. Diabetes was diagnosed when the fasting blood glucose level ≥126 mg/dl or blood glucose level 2 hours after meals ≥200 mg/dl. Hypertension was diagnosed if the blood pressure was over 140/90 mmHg (1 mmHg = 0.133 kPa).

Heart function test: Patients underwent dynamic ultrasound imaging examination before and after PCI intervention. American Philips EPIQ 7 color Doppler ultrasound device was utilized. The device had a X5-1 probe and 2.0-5.0 MHz frequency. It was operated by fixed personnel. All the subjects were required to lay on their left, in a decubitus position and keep their breathing calm during the process. The transthoracic ultrasound was utilized to examine the heart and ECG was recorded simultaneously. The full volume mode was started with the four-chamber cardiac view. This mode collects the figures of the two apical chambers of the cardiac cycle, apical segment, middle segment and the left ventricular basal segment. It also obverses and measures the left atrium inner diameter, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic volume (LVESD), cardiac output (CO), stroke volume (SV) and left ventricular ejection fraction (LVEF).

Statistical methods: This study utilized SPSS 20.0 software to analyze and process data. The count data was described by n (%), which tests chi-square (x^2). The measurement data that conforms to a normal distribution was expressed as ($\overline{X} \pm sd$), which was tested by t test. The study analyzed variables with statistical significance based on multivariate unconditional logistic regression analysis. The correlation between the two variables was analyzed based on Pearson linear correlation analysis. The test level was $\alpha = 0.05$ and $P < 0.05$ indicated statistical significance.

Table 1. The comparison of clinical data of patients between two groups

Groups	PCI preoperative group (n = 82)	Normal group (n = 82)	t/χ^2	*P*
Gender			0.098	0.754
Male	43 (48.86)	45 (51.14)		
Female	39 (51.32)	37 (48.68)		
Age (sui)	55.26 ± 10.40	55.40 ± 10.55	0.086	0.932
Smoking history			0.098	0.754
Yes	36 (48.65)	38 (51.35)		
No	46 (51.11)	44 (48.89)		
Drinking history			0.025	0.874
Yes	34 (49.28)	35 (50.72)		
No	48 (50.53)	47 (49.47)		
Systolic Pressure (mmH/g)	124.26 ± 13.12	123.79 ± 12.98	0.231	0.818
Diastolic Pressure (mmH/g)	78.75 ± 9.66	78.30 ± 9.47	0.301	0.764
Heart Function Classification (level)			0.227	0.634
I~II	50 (51.55)	47 (48.45)		
III	32 (47.76)	35 (52.24)		
Total cholesterol (mmol/L)	3.89 ± 1.01	3.90 ± 1.03	0.063	0.950
Blood creatinine (mmol/L)	73.26 ± 12.15	73.40 ± 12.12	0.073	0.941
Triglyceride (μmol/L)	1.50 ± 0.42	1.52 ± 0.40	0.312	0.755
Fasting blood glucose (mmol/L)	6.90 ± 2.08	6.92 ± 2.04	0.062	0.950
Diabetes			0.026	0.871
Yes	52 (49.52)	53 (50.48)		
No	30 (50.85)	29 (49.15)		
Hypertension			0.098	0.754
Yes	43 (48.86)	45 (51.14)		
No	39 (51.32)	37 (48.68)		
Gal-3 (mg/mL)	4.97 ± 1.22	1.02 ± 0.30	28.470	< 0.001
NT-pro BNP (pg/mL)	612.97 ± 274.35	68.27 ± 59.34	17.820	< 0.001
hs-CRP (mg/L)	3.42 ± 1.20	1.35 ± 0.75	13.25	< 0.001

Results

The comparison of clinical data of patients between both groups

The univariate analysis revealed that the comparison of the clinical data of patients between two groups indicated no statistically significant difference ($P > 0.05$). The data showed that gender, age, smoking history, drinking history, systolic blood pressure, diastolic blood pressure, cardiac function classification, total cholesterol amount, blood creatinine, triglyceride, fasting blood glucose, diabetes and hypertension of patients were not different between groups. The levels of Gal-3, NT-pro BNP and hs-CRP in the PCI preoperative group were higher than these in the normal group, with a statistically significant difference ($P < 0.05$). See **Table 1**.

Logistics regression analysis

The result of multivariate logistic analysis revealed that Gal-3, NT-pro BNP and hs-CRP are risk factors for ACS patients ($P < 0.05$). See **Table 2**.

The comparison of Gal-3, NT-pro BNP and hs-CRP levels of patients before and after PCI

The Gal-3 and NT-pro BNP levels after PCI were lower than these before PCI, with a statistically significant difference ($P < 0.05$). The comparison of the hs-CRP level of patients in both groups indicated no statistically significant difference ($P > 0.05$). See **Table 3**.

Table 2. The result of multivariate analysis

Independent Variation	β	Wald χ^2	*P*	OR (95% CI)
Gal-3	0.829	3.360	0.009	2.292 (1.513~3.862)
NT-pro BNP	0.956	3.117	0.018	2.602 (1.440~3.960)
hs-CRP	0.997	4.882	0.001	2.709 (1.457~4.577)

Table 3. The comparison of Gal-3, NT-pro BNP and hs-CRP levels of patients before and after PCI

Groups	Gal-3 (mg/mL)	NT-pro BNP (pg/mL)	hs-CRP (mg/L)
Before PCI (n=82)	4.97 ± 1.22	612.97 ± 274.35	3.42 ± 0.78
After PCI (n=82)	3.05 ± 0.89	321.97 ± 102.95	3.30 ± 0.74
t	11.510	8.993	0.771
P	< 0.001	< 0.001	0.442

Table 4. The comparison of cardiac result of echocardiography of patients before and after PCI

Groups	Before surgery (n=82)	After surgery (n=82)	*t*	*P*
left atrium diameter (mm)	34.46 ± 3.17	35.03 ± 3.56	1.083	0.281
LVEDD (mm)	60.45 ± 7.40	57.27 ± 5.29	3.166	0.002
LVESD (mm)	34.23 ± 4.02	31.11 ± 3.67	5.190	< 0.001
CO (L/ml)	4.98 ± 1.20	5.01 ± 1.23	0.158	0.874
SV (ml)	78.90 ± 17.53	78.92 ± 17.45	0.007	0.994
LVEF (%)	41.15 ± 5.24	47.97 ± 7.22	6.923	< 0.001

Table 5. Correlation analysis of Gal-3 and NT-proBNT levels with LVEDD, LVESD and LVEF

Items	Gal-3		NT-pro BNP	
	r	P	r	P
LVEDD	0.721	< 0.001	0.197	0.183
LVESD	0.243	0.209	0.172	0.336
LVEF	-0.607	< 0.001	-0.168	0.387

The comparison of results of the cardiac echocardiography in patients before and after PCI

The comparison of the left atrium diameter, CO and SV before and after PCI revealed no significant difference (P > 0.05). The LVEDD and LVESD level before PCI were lower than after PCI while the LVEF level before PCI was lower than that after PCI, with a significant difference (P < 0.05). See **Table 4**.

The correlation between Gal-3 and left ventricular systolic function of patients in two groups

The result of Pearson analysis revealed that the Gal-3 level is positively correlated with LVEDD (r = 0.721, P < 0.05) and negatively correlated with LVEF (r = 0.607, P < 0.05). See **Table 5** and **Figure 1**.

Discussion

Acute coronary syndrome (ACS) occurs when the coronary atherosclerotic plague ruptures under the stimulation of the external environment, thus circulating to coronary arteries with the blood and further blocks the coronary artery lumen. This causes myocardial ischemia, hypoxia and myocardial necrosis [7]. The research data has indicated that the annual incidence of ACS in China is 5/10,000. There are about 500,000 patients dying of a new myocardial infarction each year, which severely affects the life and health of people. Currently, PCI is one of the commonly used methods to treat ACS, which can effectively reduce the mortality rate of ACS. However, some patients still suffer from impaired cardiac functions due to the lack of effective monitoring indicators after PCI [9]. The value of some biomarkers such as C-reactive protein, creatine kinase isoenzyme and myoglobin for evaluation of the prognosis of ACS patients is limited [10]. Therefore, it has a great significance to explore biomarkers for prognostic monitoring of ACS patients after PCI.

Gal-3 is a β-galactosidase-binding lectin with various biological effects. It participates in cell growth, proliferation, inflammation, immune regulation, apoptosis and tumor metastasis through binding to cell surface receptors or extracellular receptors. It is a biomarker that can evaluate the severity of cardiac fibrosis and the prognosis of heart failure [11, 12]. Research has shown that the elevated Gal-3 level in the

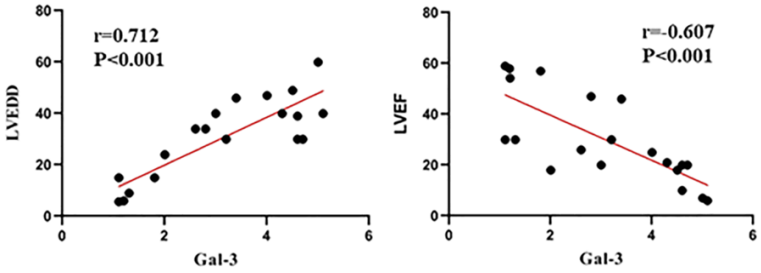

Figure 1. Correlation analysis of Gal-3 level with LVEDD and LVEF after PCI in ACS patients.

plasma of patients with heart failure is related to the poor prognosis of the disease. Also, Gal-3 mechanism of action may be related to its involvement in inflammation, immune response, and the promotion of myocardial restoration [13, 14]. However, there are still few reports about the evaluation of Gal-3 on the left ventricular systolic function. The study has shown that the Gal-3, NT-pro BNP and hs-CRP levels before PCI are higher than in a normal group. This indicates that Gal-3, NT-pro BNP and hs-CRP may participate in the formation of ACS by accelerating inflammation. Also, Gal-3, NT-pro BNP and hs-CRP have a high expression in the serum of ACS patients. Our study results have shown that the Gal-3 and NT-pro BNP levels of ACS patients after PCI are lower than these before surgery, which indicates the effectiveness of PCI in the treatment of ACS patients. The result of multivariate logistic analysis has shown that Gal-3, NT-pro BNP and hs-CRP are risk factors of ACS patients. Gal-3 can reflect the severity of myocardial fibrosis in heart failure. As a polypeptide form of B-type natriuretic peptide, NT-pro BNP has no biological activity. It cannot easily be degraded *in vitro* or *in vivo* and it has a high stability. These test results can directly reflect the condition of heart function [15]. As an inflammatory marker, hs-CRP can participate in multiple processes of atherosclerosis and thrombosis, which is closely related to the occurrence of cardiovascular disease [16]. The related studies have shown that ACS patients after PCI have improved left ventricular pump functions, reduced adverse remodeling and improved survival rates [17]. In this research, the result of echocardiography revealed that the left ventricular systolic function index decreased in patients before PCI, which indicates the presence of necrosis and damage of some of the cardiomyocytes. However, the LVEDD and LVESD after PCI have been significantly improved to a normal level, which indicates that PCI can significantly improve the left ventricular systolic function of patients. Currently, LVEF is a commonly used indicator to evaluate left ventricular systolic function in clinical practice. Also, LVEF is a powerful indicator to predict the clinical prognosis of patients with systolic heart insufficiency [18]. The result of Pearson analysis in this study has shown that Gal-3 level was positively correlated with LVEDD ($r = 0.721$, $P < 0.05$) and negatively corrected with LVEF ($r = -0.607$, $P < 0.05$), which indicates a close relation between Gal-3 and the left ventricular contraction function. Lok *et al.* [19] used the cardiac color ultrasound to monitor Gal-3 and NT-pro BNP levels of 240 patients with systolic heart failure and followed them for 8.5 years, the results revealed a close relation between Gal-3 level and the left ventricular systolic function, which is in line with our study. Chen's study about the Gal-3's relationship to the prognosis of heart failure patients has revealed that the mortality rate of patients with chronic and acute heart failure is related to the elevated Gal-3 level [20]. These previous studies suggested that Gal-3 is associated with activation of fibroblasts and macrophages, which are a hallmark of cardiac remodeling.

However, there is no current evidence indicating Gal-3 alone is correlated to the prognosis of heart failure patients. This study utilized a single hospital as the research unit. There is certain limitation due to the small sample size. Subsequent larger-scale studies are needed for further confirmation. In summary, the change of Gal-3 level is closely related to the left ventricular systolic function. Early diagnosis and treatment can be based on this index in clinical practice.

Disclosure of conflict of interest

None.

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