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The Correlation between Left Ventricular Ejection Fraction and Peripheral Blood MCP-1 NT-Pro BNP in Patients with Acute Coronary Syndrome

Ma Chengtai*, Jiang Yanxia, Chen Xingjun, Tian Xintao and Shi Lei

Eastern emergency medicine, Affiliated Hospital of Qingdao, University Medical College, Shandong Province 266003, China

Abstract

Background: To analyse the correlation between left ventricular ejection fraction and Peripheral blood MCP-1 、NT-pro BNP in patients with acute coronary syndrome.

Hypothesis: The relationship between MCP-1 and NT-pro BNP.

Methods: Peripheral blood MCP-1 NT-pro BNP were examined in 89 patients with acute coronary syndrome, measured LVEF by Color Doppler ultrasound. The patients were divided into three groups according to LVEF and were analysed the correlation: group A composed of 28 patients with LVEF ≤ 40%, group B composed of 31 patients with LVEF between 41% and 55%, group C composed of 30 patients with LVEF>55%. The patients were further divided according to type of ACS patients with acute myocardial infarction (AMI) group and unstable angina (UA) group, comparing the index differences.

Results: Peripheral MCP-1, NT-pro BNP levels tend to increase gradually (C group <B group <A group) ($p < 0.001$) with reduced ejection fraction in groups divided according to LVEF. Further analyses showed that MCP-1 and NT-pro BNP was positively correlated ($r = 0.551$, $p < 0.05$), and both negatively correlated with LVEF ($r = -0.609$ and -0.636, $p < 0.05$). IN groups divided according to type of ACS patients, there was no significant difference between AMI group and UA group, while LVEF difference between the two groups was statistically significant ($p<0.05$).

Conclusions: There is a good correlation between left ventricular ejection fraction and MCP-1 and NT-pro BNP .MCP-1and NT-pro BNP were combine detected in the peripheral blood of patients with ACS, can provide more objective basis for risk stratification and prognosis.

Keywords: Acute coronary syndrome (ACS); Monocyte Chemo attractant protein-1(MCP-1); N terminal pro-brain natriuretic peptide (NT-pro BNP); Left ventricular ejection fraction (LVEF)

Introduction

Acute coronary syndrome (ACS) is acommon clinical type of coronary heart disease, including ST-elevation myocardial infarction, non-ST elevation myocardial infarction and unstable angina [1]. Imbalance between myocardial oxygen supply and demand, caused by coronary atherosclerotic plaque rupture, local thrombosis or Coronary artery spasm, was the common pathophysiological mechanisms of ACS. Inflammation and the immune response involved in the pathological process according to based experimental results, and inflammatory factors associated with the pathological process are the focus of research now. MCP-l is one of cytokines closely related with atherosclerosis (AS), by detecting serum levels of MCP-1, can be used to infer coronary atherosclerosis severity and prognosis assessment [2]. Brain natriuretic peptide (BNP), as the renin-angiotensin-aldosterone system natural antagonists, has been recognized for the diagnosis of heart failure, and plays an important guiding role on prognosis for ACS. There are studies that NT-pro BNP and BNP have similar clinical significance in the diagnosis and prognosis of cardiovascular diseases [3,4]. left ventricular ejection fraction (LVEF) ,measured by echocardiographic, is a reliable indicator used in the clinical evaluation of left ventricular systolic function, can objectively reflect the global left ventricular systolic function, and can be used to assess the condition and prognosis of acute coronary syndrome .This study was designed on measuring above indicators, and correlation analysis, to give reference for further assessing the risk stratification of patients and prognosis with ACS .

Subjects and Methods

Research objects

89 patients with ACS were selected in eastern emergency medicine affiliated Hospital of Qingdao University Medical College from December 2012 to May 2013.history taking, physical examination and peripheral blood collection were done when they came to Hospital ,including age, gender, medical history and other general information , conventional biochemical, myocardial enzymes , other test results immediate hospitalization, and ACS diagnosis standard compliant from the American Heart Association (ACC/AHA) . Simultaneously all enrolled patients were done functional class according to NYHA. All patients were done coronary angiography during hospitalization, were confirmed that at least one degree of stenosis ≥ 50%. Exclusion criteria include severe infections, liver and kidney dysfunction, immune system disorders, connective tissue diseases and malignant tumors.

Research methods

All patients were taken at the time of admission peripheral blood 5ml, supernatant after centrifugation, which stored at -80ºC for determination.MCP-1 concentrations were measured by enzyme-linked immunosorbent assay (ELISA), according to the kit instructions to operate. Other biochemical parameters, serum creatine kinase, NT-pro BNP, etc., were tested by the hospital laboratory when admission,

***Corresponding author:** Ma chengtai, Eastern emergency medicine, Affiliated Hospital of Qingdao, University Medical College, Shandong Province 266003, China, Tel: +86-532-291134; E-mail: machengtai@163.com

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and done cardiac Doppler ultrasound within 10 days after admission. Left ventricular ejection fraction (LVEF) was calculated by Biplane Simpson method, all patients were divided into three groups according LVEF: group A ≤ 40%, group B, 41% ~ 55%, group C>55%.

Statistical

Data analyses were done by SPSS19.0 statistical software, M ± DS represent normally distributed measurement data, the two groups were compared using test, multiple groups were compared using analysis of variance; Non-normal distribution of measurement data are used median (minimum - maximum); within the group was compared by Kruskal-Wallis H rank sum test NT-pro BNP was normally distributed after logarithmic transformation; correlation between the data using Pearson correlation analysis. statistically significant was P <0.05

The study met the standard of medical ethics, it was approved by the hospital ethics committee. All treatments were obtaining informed consent of patients and their families.

Results

1. Enrolled patients' general condition and related laboratory findings (Table 1).

2.With ejection fraction elevated ,peripheral MCP-1 and NT-pro BNP levels have gradual downward trend ,results of MCP-1 ANOVA :F=26.574, P<0.001; results of NT-pro BNP Kruskal-Wallis H rank sum test, X^2=38.549, P<0.001further comparisons between groups ,MCP-1 and NT-pro BNP differences among the three groups were statistically significant(P<0.05). In addition, hs-cTNT in three groups seems to have a downward trend, but there was no statistically significant (X^2=0.134, P=0.935) (Table 2).

3. NT-pro BNP was normally distributed after logarithmic transformation. EF was negatively correlated with the LogNT-pro BNP and MCP-1 .Correlation coefficients were -0.636 and -0.609, both P<0.01 (Figure 1A, 1B). LogNT-pro BNP was positively correlated with MCP-1, and coefficients was0.551, P<0.01 (Figure 1C).

4. According to ACS clinical Group, MCP-1 and LogNT-pro BNP in the AMI group and UA group difference was not statistically significant (p>0.05) and the two groups LVEF difference was statistically significant (p<0.05) (Table 3).

Discussion

Chemokines are a class of small molecules secreted protein, divided into four families: C-X-C, CC, C and CX3C,its specific function is Leukocyte recruitment and activation.MCP-1 is one of CC chemokine subfamily. Studies have shown that MCP-1 make the vascular endothelial cell damage and lipid infiltration, promote monocytes to invade endothelial phagocytosis lipoprotein and become foam cells. It can produce large amounts radicals, bring about the blood vessel spasm, abnormal lipid metabolism. It is an important mechanism of constituting atherosclerosis (AS) [5]. In recent years, there are research data show that MCP-1 was significantly higher in ACS patients serum concentrations, and relevant with infarction mortality and recurrence of major adverse cardiovascular events in patients with acute myocardial [6,7]. Tip MCP-1 have an important role in atherosclerosis pathogenesis and development [8,9], and in the occurrence of ACS .MCP-1 can play be an important role in various stages of AS, and is closely related with coronary ischemic events, reported in the literature [10]. Now, there are rarely reported correlation between MCP-1 and LVEF, NT-pro BNP. The results of this study show that MCP-1 have gradually increased tendency with reduced ejection fraction. Pearson correlation analysis showed a negative correlation (r=-0.609 p<0.01). The decrease in LVEF closely related with prognosis of ACS, especially

Term	Data
Age (years)	63 ± 11
Sex (M / F)	52/37
Systolic blood pressure (mmHg)	127 ± 19
Total cholesterol (mmol / L)	4.07 ± 0.98
Total bilirubin (umol / L)	16.25 ± 7.41
Glucose (mmol / L)	6.14 ± 1.77
NT-ProBNP (pg/ml)	827 (27,19927)
Hs-cTNT (ng/ml)	0.132 (0.006,13.27)
(CK-MB (IU/L)	22 (4,265)
Cr(umol/L)	84 ± 18
Urea nitrogen (mmol / L)	5.80 ± 1.45
LVEF (%)	51 ± 12
LVIDd (cm)	5.12 ± 0.59
MCP-1 (pg/ml)	160.95 ± 47.39
WBC (×10^9/L)	7.11 ± 1.79
NYHA Classification	
1	48 (53.9%)
2	29 (32.6%)
3	10 (11.2%)
4	2 (2.2%)

Table 1: Enrolled patient's general condition and related laboratory findings (n=89). Note: Hs-Ctnt: High-Sensitivity Troponin T; CK-MB: Creatine Kinase Isoenzyme; Lvidd: Left Ventricular End-Diastolic Diameter.

	A组 (n=28)	B组 (n=31)	C组 (n=30)
Age (years)	66 ± 9	63 ± 10	60 ± 14
Male (%)	17 (60.7)	17 (54.9)	18 (60.0)
Systolic pressure (mmHg)	128 ± 21	127 ± 14	129 ± 21
Total cholesterol(mmol/L)	4.45 ± 1.13	4.01 ± 0.85	3.78 ± 0.85*
Total bilirubin (umol/L)	13.90 ± 6.99	17.90 ± 8.89	16.73 ± 5.58
Blood glucose (mmol/L)	6.22 ± 1.88	6.34 ± 2.20	5.85 ± 1.05
NT-ProBNP (pg/ml)	6049.5(140,19927)	1769.0(38,18793)	224(27,3892)*#
Hs-cTNT (ng/ml)	0.136 (0.007,1.59)	0.132 (0.006,3.76)	0.132 (0.007,13.27)
CK-MB (IU/L)	32 (7,265)	26 (4,165)	16 (5,79)
Cr(umol/L)	86.61 ± 19.89	86.08 ± 19.64	80.15 ± 14.63
Urea nitrogen (mmol/L)	6.48 ± 1.67	5.73 ± 1.30*	5.23 ± 1.12*
LVIDd (cm)	5.60 ± 0.64	4.97 ± 0.45	4.82 ± 0.37*
MCP-1 (pg/ml)	194.91 ± 54.4	166.57 ± 23.6*	160.95 ± 47.4*#
WBC (x109/L)	7.03 ± 2.06	7.41 ± 1.84	6.86 ± 1.45

Table 2: Comparison of the general data and laboratory test results of patients with different LVEF levels [M ± DS，M (min～max)].

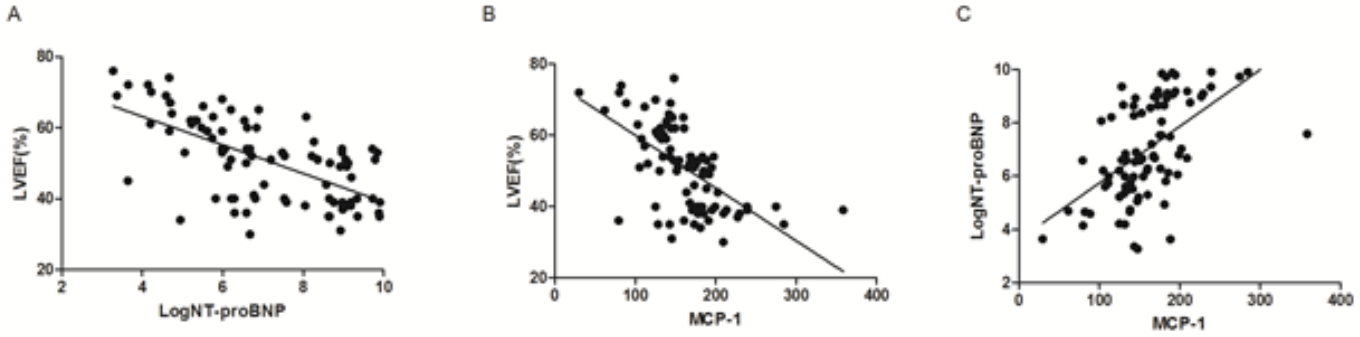

Figure 1: Correlation scatter LVEF with LogNT-pro BNP（A. r=-0.636，p<0.01）, LVEF with MCP-1（B. r=-0.609，p<0.01）and LogNT-pro BNP with MCP-1（C. r=0.551，p<0.01).

Group	n	MCP-1(pg/ml)	LogNT-proBNP	LVEF (%)
Group AMI	62	164.52 ± 47.04	7.07 ± 1.80	49 ± 11
Group UA	27	152.77 ± 48.06	6.96 ± 1.93	54 ± 11
t		1.076	0.260	-1.997
P		0.285	0.795	0.049

Table 3: The Comparison of MCP-1, LogNT-proBNP, LVEF in Different types of ACS patients' (M ± DS).

when LVEF below 40% indicates a poor prognosis [11,12]. Therefore, from the point of view of research data in this group, serum MCP-1 levels increased have important value for assessment of prognosis in patients with ACS.

BNP is quantitative marker for the severity of heart failure, which is a peptide hormone. Its synthesis and secretion by ventricular myocytes when they subjected to stretch stimulation or ischemia, is generated by the brain natriuretic peptide (pro-BNP) degradation. NT-pro BNP is generated simultaneously along with degradation, and the release were equimolar with BNP, but the NT-pro BNP concentration in plasma is more stable, Longer half-life same as BNP. It can be indicators for cardiovascular disease diagnosis, treatment monitoring and prognosis, it is widely used in clinical [13]. This study shows negative correlation between NT-pro BNP and LVEF (r=-0.609, p<0.01, it indicated that NT-pro BNP was important guiding significance for risk stratification in patients with ACS, and is the same result reported in the literature domestic and foreign [14,15]. Meanwhile, the study also the first time do correlation analysis between the MCP-1 and NT-pro BNP, the results is a positive correlation (r = 0.551, p <0.01), but what is cause and effect as well as its exact mechanism remains to be elucidated. The results of this study also showed no statistical significant difference about NT-proBNP between the A/B groups while there were significant differences about MCP-1 between the three groups which indicating that MCP-1 and LVEF have a good correlation in ACS patients. Of course, we could not exclude the sampling error due to the content of the less sample, so further large sample was needed to confirm our conclusion.

In addition, analysis of variance showed that there were differences between the three groups about LVIDd. But after further two-two comparing, it was found that there were statistically significant difference only between group C and group A. We could infer that left ventricular remodeling has big impact on LVEF in patients with ACS. Different from previous research, this study did not introduce the healthy controls, but divided patients according to the clinical types of ACS. Although MCP-1 in the UA group is lower than in the AMI group, but there were no statistically significant difference after statistics analysis (p>0.05) which showed that whether MCP-1 had the value for judging the types of ACS [16]. Unlike literatures reported before, it showed no statistically significant difference about NT-proBNP between the two groups which may be related to the less content of the sample.

In summary, this study proved both in the application value in patients with ACS by analyzing correlation between MCP-1, NT-pro BNP and LVEF .at the same time, This experiment further analyzed correlation between MCP-1 and NT-pro BNP, From another angle confirmed MCP-1 serum levels increased in ACS patients, can play important guiding significance for ACS risk stratification and prognosis.

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