Journal of Hainan Medical University

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Clinical significance of NT−proBNP, myocardial enzymes, and inflammatory cytokines in diagnosis of acute coronary syndrome

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ARTICLE INFO

Article history:
Received 6 Jun 2017
Received in revised form 10 Jun 2017
Accepted 16 Jun 2017
Available online 28 Jun 2017

Keywords:
NT-proBNP
Myocardial enzyme
Serum inflammatory cytokines
ACS

ABSTRACT

Objective: To explore the clinical significance of NT-proBNP, myocardial enzymes, and inflammatory cytokines in diagnosis of acute coronary syndrome (ACS). **Methods:** A total of 120 patients with ACS confirmed by CAG who were admitted in our hospital from December, 2014 to December, 2016 were included in the study and divided into UAP group (n=28), NSTEMI group (n=41), and STEMI group (n=51) according to different lesion degrees. Moreover, 40 cases with negative CAG results were served as the control group. The standard Judkins method was used for CAG examination. Multi-position projection was performed to confirm the coronary lesion degrees. The peripheral venous blood was collected on admission, and the serum was separated. The fluorescence immunoassay was used to detect NT-proBNP and CK-MB levels. The chemiluminiscence was used to detect cTnI level. The immunoturbidimetry was used to detect hs-CRP level. ELISA was used to detect IL-18, TNF-α, and MMP-9 levels. **Results:** The serum NT-proBNP, CK-MB, cTnI, hs-CRP, IL-18, TNF-α, and MMP-9 levels were graudally increased in the control group, UAP group, NSTEMI group, and STEMI group, and the comparison among each group was statistically significant. **Conclusions:** The combined detection of serum NT-proBNP, CK-MB, cTnI, hs-CRP, IL-18, TNF-α, and MMP-9 is of great significance in diagnosis of ACS, evaluation of severity degree, risk stratification, and formulation of therapeutic schemes.

1. Introduction

Acute coronary syndrome (ACS) is a clinical syndrome with the main pathological basis of complete or incomplete occlusive thrombus due to atherosclerosis (AS) plaque rupture and erosion[1]. ACS can be divided into UAP, STEMI, NSTEMI, and meanwhile can reflect the continuous pathophysiological process of acute myocardial ischemia[2]. Some researches demonstrate that[3,4] NT-proBNP has a preferable application value in the diagnosis, screening, treatment monitoring, risk classification, and prognosis evaluation of cardiovascular disease[4]. cTnI and CK-MB has a higher specificity in diagnosis of myocardial necrosis[5]. It is proved by epidemiology that hs-CRP, TNF-α, MMP-9, and M-CSF are the indicators to predict the occurrence of cardiovascular events in the future[6]. The study is aimed to explore the clinical significance of NT-proBNP, myocardial enzymes, and inflammatory cytokines in diagnosis of ACS.

2. Materials and methods

2.1. General materials

A total of 120 patients with ACS confirmed by CAG who were admitted in our hospital from December, 2014 to December, 2016 were included in the study, among which 75 were male, and 45 were female; aged from 40 to 73 years old, with an average age of (57.5±9.3) years old. The patients were divided into UAP group (n=28), NSTEMI group (n=41), and STEMI group (n=51) according to different lesion degrees. Moreover, 40 patients with negative ACS

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Fund Project: The study was supported by the Scientific and Technological Progress Project of Hebei Province with the number of 20152297.

were served as the control group, among which 24 were male, and 16 were female; aged from 41 to 74 years old, with an average age of (57±9) years old. The comparison of age and gender between the two groups was not statistically significant (P>0.05).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) those who were in accordance with related diagnostic criteria of ISFC/WHO[7]; (2) those who had signed the informed consents. Those who had valvular heart disease, congenital heart disease, chronic heart failure, severe myocardiopathy, old myocardial infarction, liver and renal insufficiency, pulmonary heart disease, autoimmune disease, inflammatory reactive disease, metabolic disease, and malignant tumors were excluded from the study.

2.3. CAG and lesion estimation

The standard Judkins method was adopted for CAG. Multi-position projection was used to confirm the coronary lesion degree. The international common diameter method was used to estimate the coronary artery stenosis degree: (1) abnormal: at least 1 coronary artery lumen stenosis degree >50%; (2) normal: coronary artery lumen stenosis degree <50%.

2.4. Observation indicators

A volume of 5 mL peripheral venous blood was collected after admission, and centrifuged at 4 000 r/min for 10 min for the serum. The detection items were performed immediately. The fluorescence immunoassay was used to detect NT-proBNP and CK-MB levels, and the fluorescence immunoassay analyzer (Triage MeterPor) was adopted. The chemiluminiscence was used to detect cTnI and Naon checker 710 chemiluminescence apparatus (Nano-Ditech) was used. The immunoturbidimetry was used to detect hs-CRP level, and Hitachi 7600 biochemical analyzer (provided by Shanghai Shensuo Youfu Medical Diagnosis Appliance Co. Ltd). ELISA was used to detect IL-18, TNF-α, and MMP-9 levels, and Bio-Plex cytokine detector (provided by BIO-RAD biotechnology Co. Ltd) was applied.

2.5. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. The measurement data were expressed as mean ± SD, and the enumeration data were expressed as percentage. The independent-sample t test was used for the comparison between the two groups. ANOVA and SNK-q was used for the comparison among groups. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of NT-proBNP, CK-MB, and cTnI levels among groups

The serum NT-proBNP, CK-MB, and cTnI levels were graudally increased in the control group, UAP group, NSTEMI group, and STEMI group, and the comparison among each group was statistically significant (P<0.01) (Table 1).

3.2. Comparison of hs-CRP, IL-18, TNF-α, and MMP-9 levels among groups

The serum hs-CRP, IL-18, TNF-α, and MMP-9 levels were graudally increased in the control group, UAP group, NSTEMI group, and STEMI group, and the comparison among each group was statistically significant (P<0.01) (Table 2).

Table 1.
Comparison of NT-proBNP, CK-MB, and cTnI levels among groups.

Groups	n	NT-proBNP (pg/mL)	CK-MB (μg/L)	cTnI (μg/L)
Control group	40	54.46±10.79	3.12±0.24	0.53±0.17
UAP group	28	539.64±84.45*	42.71±1.73*	4.87±0.31*
NSTEMI group	51	1 146.38±274.73*#	54.26±2.44*#	5.32±0.55*#
STEMI group	41	1 529.67±239.61*#△	69.84±3.57*#△	8.26±0.73*#△
F		426.4093	5 815.2193	1 733.8886
P		0.0000	0.0000	0.0000

*P<0.01, when compared with the control group, #P<0.01, when compared with UAP group, △P<0.01, when compared with NSTEMI group.

Table 2.
Comparison of hs-CRP, IL-18, TNF-α, and MMP-9 levels among groups.

Groups	n	hs-CRP (mg/L)	IL-18 (pg/mL)	TNF-α (pg/mL)	MMP-9 (ng/L)
Control group	40	3.76±1.38	117.64±13.76	0.51±0.13	114.71±24.61
UAP group	28	9.58±2.21*	238.75±26.24*	1.28±0.24*	252.36±35.28*
NSTEMI group	51	13.76±2.36*#	321.17±39.57*#	1.72±0.38*#	379.68±21.57*#
STEMI group	41	16.55±3.23*#△	371.54±58.35*#△	2.12±0.29*#△	554.68±38.84*#△
F		218.8001	326.9630	236.7458	1 555.4429
P		0.0000	0.0000	0.0000	0.0000

*P<0.01, when compared with the control group, #P<0.01, when compared with UAP group, △P<0.01, when compared with NSTEMI group.

4. Discussion

ACS is a series of clinical syndrome caused by acute myocardial ischemia, is an emergency of coronary heart disease, with clinical manifestations of chest distress, chest pain, short of breath, sweat, dizzy, and nausea, and is a high-risk disease with complications of ischemia and cardiac death[8]. It is argued by the modern study that[9] the repeated ischemia attack after ACS event is associated with coronary lesions and inflammatory reaction, and the corresponding inflammatory markers are involved in the vascular inflammation, myocardial ischemia, necrocytosis, AS plaque rupture, and function insufficiency; therefore, according to ACS pathophysiolcal mechanism, the combined detect of biomarkers at different stages can provide a forceful evidene the early diagnosis, risk stratification, and treatment strategy.

Various enzymes are involved in the physiological activity of human myocardial cells. When ACS patients have chest pain and chest distress, the myocardial enzymes are elevated and released into the blood, among which CK-MB is the most sensitive, and its activity begins to elevate 5 h after the symptoms occur, and reaches peak within 24 h; therefore, detection of the changes of serum myocardial enzymes can estimate the myocardial damage. It should pay attention to that when there are skeletal muscle and renal diseases, CK-MB will be elevated, which will affect the diagnosis; therefore, detection of other specific indicators is required[10]. In recent years, due to the unique biological characteristics, cTnI has been the highly specific and sensitive indicator of myocardial cell damage, and has a higher clinical value in the diagnosis, condition monitoring, therapeutic effect, and prognosis evaluation of perioperative myocardial damage and AMI[11]. cTnI can regulate the mutual action of myosin and actin through adjusting ATP activity of calcium ion striated muscle actin, and is a more sensitive and specific marker to reflect the myocardial damage[12,13]. It is indicated that[12] cTnI elevation is associated with the death rate in ACS patients, and the more level ACS is, the more death risk will increase; therefore, cTnI can be served as an important marker in the diagnosis and prognosis estimation of ACS. BNP is mainly secreted and stored in the ventricle. When there is a cardiac volume load or excessive pressure, the ventricular wall pressure is increased and the myocardium is pulled, resulting in the elevation of BNP concentration[15]. NT-proBNP and BNP are originated from the same precursor, but NT-proBNP has a long half-life period than BNP, with stable concentration in the blood, whose level will not only be elevated when there is a heart failure, but also in a condition when there is no cardiac insufficiency. Currently, NT-proBNP is served as a marker to reflect the cardiac function, and is of great significance in the diagnosis, treatment, and prognosis estimation of ACS[16]. NT-proBNP level is elevated in ACS patients, and is closely associated with the prognosis. In multi-factor logistic analysis, NT-proBNP predictive ability is independent of prognosis variables including LVEF[17]. The higher concentrations of BNP and NT-proBNP are in AMT patients, the greater probability of fatality rate or heart failure. BNP and NT-proBNP are independent of other prognosis variables, and have higher value in evaluating the prognosis of ACS patients[18]. The results in the study showed that the serum NT-proBNP, CK-MB, and cTnI levels in UAP group, NSTEMI group, and STEMI group were significantly higher than those in the control group; the serum NT-proBNP, CK-MB, and cTnI levels were graudally increased in the control group, UAP group, NSTEMI group, and STEMI group, the levels of biological markers are closely associated with the development of myocardial damage in ACS patients, but the comparison of CK-MB and cTnI between UAP group and NSTEMI group was not statistically significant, suggesting that myocardial enzymology reflecting that cardiac damage has a certain boundedness, which is consistent with related reports.

The inflammatory reaction plays a vital role in the pathophysiology of ACS, is not only an internal factor to form the plaque, but also is an external factor to promote the plaque rupture; therefore, it is argued that the inflammatory factors can reflect the stability of plaques, and predict the occurrence of adverse reactions[19]. Some scholars argue that[20] the vascular endothelial cell damage, collagen exposure, platelet adhesion, plaque rupture are involved in ACS patients, which can produce the monocyte chemotactic factors and adhesion molecules, promote the infiltration of lymphocytes and monocyte-macrophages, synthetize various chemotactic factors and cytokines, elevate the expressions of inflammatory cytokines to induce an inflammatory reaction, and accelerate the progression of ACS. Some researches demonstrate that[21] the elevation of serum hs-CRP level is positively correlated with CAG lesion parameters in ACS patients and the severity degree, and is an independent factor to predict the occurrence of cardiovascular events. Hs-CRO an acute phase inflammatory reactive protein, is a specific marker of inflammatory reaction, deposits in the vascular endothelial lesions caused by inflammation, activate the inflammatory cells, excite the damaged vessels through the receptors, cause vasospasm and abnormal lipid metabolism, and promote the expression of MMP-9 by the macrophages[22]. The strengthened activity and expression of MMP-9 can degrade the unstable AS plaque fibrous cap should fiber tissues, and cause plaque rupture. After AMI, the inflammatory cells are invaded into the ischemic myocadium, which can aggravate the secondary myocardial damage and remodeling[23]. Some scholars argue that[24] MMP-9 is an independent factor to predict the progression of coronary artery lesions, and can be served as an active and specific marker of ACS. TNF-α is mainly synthetized by the activated mononuclear macrophages, can directly or indirectly damage the vascular endothelial cells, cause the inflammatory reaction, facilitate the synthesis of a large amount of chemotactic factors and growth factors, and promote the formation of AS and plaques. TNF-α can promote the expressions of interstitial collagenase and MMP, increase the degradation of extracellular matrix, degrade the synthesis of large molecule matrix interstitial collagen, be involved in the endothelial cell damage,

result in the instability of AS plaques, and promote the occurrence and development of ACS[25]. IL-18 is mainly synthetized by the mononuclear macrophages. IL-18 in a high level is one of the important factors for the occurrence of ACS, can accelerate the progression of AS, cause the instability of AS plaques, even plaque rupture[26]. It is reported by some scholars that by adoption of rosuvastatin in the treatment of ACS, CRP, TNF- α , and IL-18 levels before treatment are significantly higher than those in the healthy control group, those in STEMI group > NSTEMI group > UAP group, indicating that CRP, TNF- , and IL-18 are closely associated with the severity degree[27]. Study on the correlation of serum inflammatory cytokines with ACS shows that CRP, TNF- , and MMP-9 are involved in the formation and development of AS plaque, and are closely associated with the severity degree, whose elevation is an important marker for the instability of AS plaques[28]. The results in the study showed that the serum hs-CRP, IL-18, TNF- α , and MMP-9 levels in UAP group, NSTEMI group, and STEMI group were significantly higher than those in the control group (P<0.05); the serum hs-CRP, IL-18, TNF- α , and MMP-9 levels were gradually increased in the control group, UAP group, NSTEMI group, and STEMI group, and the comparison among each group was statistically significant (P<0.05), indicating that the mutual action of inflammatory cytokines can promote the occurrence and development of ACS.

In conclusion, the combined detection of serum NT-proBNP, CK-MB, cTnI, hs-CRP, IL-18, TNF- , and MMP-9 is of great significance in diagnosis of ACS, evaluation of severity degree, risk stratification, and formulation of therapeutic schemes.

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