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# Correlation of serum MCP−1 and VE−cadherin levels with neural function and carotid atherosclerosis in patients with acute cerebral infarction

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ABSTRACT

**Objective:** To study the correlation of serum monocyte chemoattractant protein-1 (MCP-1) and vascular endothelial cadherin (VE-cadherin) levels with neural function and carotid atherosclerosis in patients with acute cerebral infarction. **Methods:** A total of 78 patients who were diagnosed with acute cerebral infarction in our hospital between May 2013 and August 2016 were selected as pathological group, and 80 healthy volunteers who received physical examination in our hospital during the same period were selected as control group. Serum was collected to determine the levels of MCP-1, VE-cadherin, nerve injury molecules, inflammatory mediators, proteases and their hydrolysate. **Results:** Serum MCP-1, VE-cadherin, NGB, NSE, S100β, HMGB-1, sCD40L, YKL-40, visfatin, CatK, MMP9 and ICTP levels of pathological group were significantly higher than those of control group; serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with NGB, NSE, S100β, HMGB-1, sCD40L, YKL-40, visfatin, CatK, MMP9 and ICTP levels. **Conclusion:** Serum MCP-1 and VE-cadherin levels abnormally increase in patients with acute cerebral infarction, and are closely related to the nerve injury and atherosclerosis process.

## 1. Introduction

Acute cerebral infarction is a common cardiovascular and cerebrovascular disease with high morbidity and mortality in clinical practice. Carotid atherosclerosis is the important cause of acute cerebral infarction and carotid artery atheromatous plaque rupture can make emboli enter into the cerebral blood vessels, resulting in acute embolism and ischemia hypoxia injury of brain tissue. The stability of carotid plaques is susceptible to the regulation of a variety of molecules, and the plaque rupture, thrombosis and embolic loss caused by stability change can lead to cerebral ischemic hypoxic damage, and cause the molecules in neurons and glial cells released into the blood circulation[1,2]. In clinical practice, accurate assessment of acute cerebral infarction severity can provides the reference for the establishment of therapeutic measures and the judgment of prognosis. It has been confirmed that the monocyte chemoattractant protein-1 (MCP-1) and vascular endothelial cadherin (VE-cadherin) contents abnormally increase in the serum of patients with a variety of cardiovascular and cerebrovascular diseases[3,4], but it is not yet clear whether the MCP-1 and VE-cadherin affect the neural function and carotid plaque stability in patients with acute cerebral infarction. In the following study, the correlation of serum MCP-1 and VE-cadherin levels with neural function and carotid atherosclerosis in patients with acute cerebral infarction was analyzed.

## 2. Information and methods

### *2.1Case information*

According the inclusion and exclusion criteria, 78 patients who were diagnosed with acute cerebral infarction in our hospital

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between May 2013 and August 2016 were selected as pathological group and 80 healthy volunteers who received physical examination in our hospital during the same period were selected as control group. The pathological group included 46 male cases and 32 female cases that were 52-67 years old; the control group included 48 male cases and 32 female casesthat were 47-66 years old. The two groups of subjects were not significantly different in general data ($P$>0.05).

### *2.2Inclusion and exclusion criteria*

The inclusion criteria of pathological group were as follows: (1) the time from onset to admission 72 h; (2) emergency CT or MRI confirmed that there were cerebral infarction lesions and they were corresponding to functional orientation; (3) ultrasonography confirmed that there was carotid atherosclerosis; (4) the patients signed informed consent; Exclusion criteria were as follows: (1) patients with previous history of cerebrovascular disease; (2) patients complicated by acute or chronic infection; (3) patients associated with autoimmune diseases or using immune preparations.

### *2.3Research methods*

#### *2.3.1 Sample collection and preservation methods*

5 m cubital venous blood was collected from the pathological group of patients immediately on admission, 5 m cubital venous blood was collected from the control group during physical examination, the blood was let stand at room temperature for 20 min, then naturally coagulated and centrifuged in a centrifuge for 10 min at a speed of 3 000 r/min, and the supernatant was carefully drawn, moved into the new 1.5 mL EP tubes and preserved in a -70 ℃ low-temperature refrigerator.

#### *2.3.2 Index detection methods*

Serum samples were taken and thawed at room temperature, and enzyme-linked immunosorbent assay kits were used to determine MCP-1, VE-cadherin, NGB, NSE, S100β, HMGB-1, sCD40L, YKL-40, visfatin, CatK, MMP9 and ICTP levels.

### *2.4 Statistical methods*

SPSS software was used to input and analyze serum detection data, differences in serum data between pathological group and control group was by $t$ test, correlation analysis of data within pathological group was by Pearson test and $P<0.05$ indicated statistical significance in differences.

## 3. Results

### *3.1Serum MCP-1 and VE-cadherin levels*

Analysis of serum MCP-1 (ng/L) and VE-cadherin (mg/L) levels of pathological group before admission and control group during physical examination was as follows: serum MCP-1 and VE-cadherin levels of pathological group before admission were significantly higher than those of control group. Differences in serum MCP-1 and VE-cadherin levels were statistically significant between the pathological group before admission and the control group during physical examination ($P$<0.05), shown in Table 1.

**Table 1.**
Serum MCP-1 and VE-cadherin levels of pathological group and control group.

| Groups | $n$ | MCP-1 | VE-cadherin |
|---|---|---|---|
| Pathological group | 78 | 357.41±53.16 | 6.79±0.93 |
| Control group | 80 | 156.52±19.84 | 3.41±0.55 |
| T | | 13.582 | 11.586 |
| P | | <0.05 | <0.05 |

### *3.2Serum nerve injury index levels*

Analysis of serum nerve injury indexes NGB, NSE and S100β of pathological group before admission and control group during physical examination was as follows: serum NGB, NSE and S100β levels of pathological group before admission were significantly higher than those of control group. Differences in serum NGB, NSE and S100β levels were statistically significant between the pathological group before admission and the control group during physical examination ($P$<0.05), shown in Table 2. Pearson test showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with NGB, NSE and S100β levels.

### *3.3Serum atherosclerosis-related inflammatory mediator levels*

**Table 2.**
Serum NGB, NSE and S100β levels of pathological group and control group (μg/L).

| Groups | $n$ | NGB | NSE | S100β |
|---|---|---|---|---|
| Pathological group | 78 | 17.63±2.41 | 12.54±1.95 | 0.93±0.12 |
| Control group | 80 | 11.38±1.96 | 2.65±0.35 | 0.35±0.06 |
| T | | 7.684 | 36.952 | 19.575 |
| P | | <0.05 | <0.05 | <0.05 |

**Table 3.**

Serum atherosclerosis-related inflammatory mediator levels of pathological group and control group.

| Groups | *n* | HMGB-1 | sCD40L | YKL-40 | Visfatin |
|---|---|---|---|---|---|
| Pathological group | 78 | 14.79±2.21 | 462.31±65.65 | 236.15±31.89 | 236.51±33.25 |
| Control group | 80 | 6.74±0.89 | 221.36±32.68 | 98.47±11.27 | 105.35±16.72 |
| T | | 12.389 | 10.983 | 14.527 | 11.485 |
| P | | ＜0.05 | ＜0.05 | ＜0.05 | ＜0.05 |

Analysis of serum atherosclerosis-related inflammatory mediators HMGB-1 (ng/L), sCD40L (ng/L), YKL-40 (ng/L) and visfatin (μg/L) levels of pathological group before admission and control group during physical examination was as follows: serum HMGB-1, sCD40L, YKL-40 and visfatin levels of pathological group before admission were significantly higher than those of control group. Differences in serum HMGB-1, sCD40L, YKL-40 and visfatin levels were statistically significant between the pathological group before admission and the control group during physical examination (P<0.05), shown in Table 3. Pearson test showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with HMGB-1, sCD40L, YKL-40 and visfatin levels.

### *3.4Serum atherosclerosis-related proteases and their hydrolysate*

Analysis of serum atherosclerosis-related proteases and their hydrolysate CatK (ng/L), MMP9 (μg/L) and ICTP (μg/L) levels of pathological group before admission and control group during physical examination was as follows: serum CatK, MMP9 and ICTP levels of pathological group before admission were significantly higher than those of control group. Differences in serum CatK, MMP9 and ICTP levels were statistically significant between the pathological group before admission and the control group during physical examination (*P*<0.05), shown in Table 1. Pearson test showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with serum CatK, MMP9 and ICTP levels.

## 4. Discussion

Atherosclerosis is the pathological basis of the occurrence and development of acute cerebral infarction, and both cerebral atherosclerosis and plaque nature change will cause the occurrence of acute cerebral infarction. MCP-1 is the key molecule to modulate inflammatory cell infiltration and migration; in the process of atherosclerosis, MCP-1 can promote mononuclear macrophage accumulation and infiltration in vascular endothelium, induce macrophage cells to devour ox-LDL and form foam cells, and lead to lipid deposition[5,6]. VE-cadherin is a type of cadherin that regulates vascular endothelial cell polarity, and it can cause endothelial cell function and shape change; in the process of atherosclerosis, VE-cadherin increases vascular permeability, promotes inflammatory cell adhesion in local vascular endothelium, causes endothelial damage and promotes the atherosclerosis occurrence[7]. In order to define the role of MCP-1 and VE-cadherin in acute brain infarction progression, serum MCP-1 and VE-cadherin levels of patients with acute cerebral infarction and healthy volunteers were analyzed in the study, and the results showed that serum MCP-1 and VE-cadherin levels of pathological group before admission were significantly higher than those of control group. This means that high serum MCP-1 and VE-cadherin levels are closely related to the occurrence and development of acute cerebral infarction.

In the patients with acute phase of cerebral infarction, ischemia hypoxia can cause neuron and glial cell damage, cell membrane rupture, and the release of a variety of molecules from the cytoplasm to the outside of cells. NGB, NSE and S100β are the important functional molecules in neurons and glial cells, and after entering into the outside of cells, they can enter into the blood circulation through the damaged blood brain barrier[8]. So detecting serum NGB, NSE and S100β levels can reflect the nerve injury in patients with cerebral infarction, cerebral hemorrhage and traumatic brain injury[9,10]. In the study, the analysis of serum NGB, NSE and S100β contents in patients with acute cerebral infarction showed that serum NGB, NSE and S100β levels of pathological group were significantly higher than those of control group. This result is consistent with the research of other scholars at home and abroad,

**Table 4.**

Serum atherosclerosis-related protease and their hydrolysate levels of pathological group and control group.

| Groups | *n* | CatK | MMP9 | ICTP |
|---|---|---|---|---|
| Pathological group | 78 | 27.69±3.61 | 649.51±87.98 | 36.68±5.61 |
| Control group | 80 | 9.59±1.16 | 215.62±33.28 | 12.15±1.85 |
| T | | 20.395 | 22.184 | 19.385 |
| P | | ＜0.05 | ＜0.05 | ＜0.05 |

and explains that the NGB, NSE and S100β that are released into the blood circulation significantly increase in the development and change of cerebral infarction. Further analysis the correlation of serum MCP-1 and VE-cadherin content with nerve injury molecule content showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with NGB, NSE and S100β levels. This means that the higher MCP-1 and VE-cadherin content in patients with cerebral infarction are associated with the increase of nerve injury.

MCP-1 and VE-cadherin have the chemotaxis and adhesion effect respectively, and they can promote inflammation cell infiltration in atheromatous plaque and induce inflammatory reaction occurrence and development. In the pathological process of atherosclerosis, inflammation is in the core position and closely related to the multiple pathological links in the process of progression. The chemotaxis and adhesion function mediated by MCP-1 and VE-cadherin can promote inflammation to cause the occurrence and development of cerebral infarction. HMGB-1, sCD40L and YKL-40 are the important pro-inflammatory mediators, the inflammatory cell infiltrating within local plaque can synthesize and secrete sCD40L, YKL-40 and HMGB-1, then start the cascade amplification of the inflammatory response and increase the release of a variety of inflammatory mediators[11,12]; Visfatin is a new adipocytokine discovered in recent years, it has pro-inflammatory activities in the process of atherosclerosis, and it participates in the formation of foam cells and fatty streaks[13]. In the study, the analysis of the atherosclerosis-related inflammatory mediators showed that serum HMGB-1, sCD40L, YKL-40 and visfatin levels of pathological group were significantly higher than those of control group. This means that the abnormal secretion of atherosclerosis-related inflammatory mediators is associated with the occurrence of cerebral infarction. Further analysis of the correlation of serum MCP-1 and VE-cadherin levels with atherosclerosis-related inflammatory mediator contents showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with HMGB-1, sCD40L, YKL-40 and visfatin levels. This means that high serum MCP-1 and VE-cadherin levels in patients with cerebral infarction are associated with the inflammatory response in the process of atherosclerosis progression.

Inflammation has played an important role in the carotid atheromatous plaque formation and nature change process, and a variety of inflammatory mediators in local atheromatous plaque can influence the expression of protease to influence the stability of the plaques, cause plaque rupture and lead to embolic loss and intracranial vascular embolization[14]. CatK and MMP9 are members of cathepsin and metalloproteinase family respectively, and can cause the degradation of a variety of proteins in plaque fiber cap and lead to fiber cap rupture, collagen exposure in lesions and decreased plaque destabilization[15-17]. ICTP is the product after CatK and MMP9 degraded protein, and is associated with plaque stability[18]. In the study, analysis of the atherosclerosis-related inflammatory mediator contents showed that serum CatK, MMP9 and ICTP levels of pathological group were significantly higher than those of control group. It means that the increased proteases and their hydrolyte are related to the occurrence of cerebral infarction. Further analysis of the correlation of serum MCP-1 and VE-cadherin content in patients with cerebral infarction with protease and its hydrolyte content showed that serum MCP-1 and VE-cadherin levels of pathological group were positively correlated with serum CatK, MMP9 and ICTP levels. This means that the increased MCP-1 and VE-cadherin content in patients with cerebral infarction increases can cause the artery atheromatous plaque nature change and stability reduction.

To sum up, it is believed that serum chemokine MCP-1 and adhesion molecule and VE-cadherin levels abnormally increased in patients with acute cerebral infarction; higher serum MCP-1 and VE-cadherin are closely related to the nerve injury and atherosclerosis process.

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