RESEARCH ARTICLE

Changes and significance of serum monocyte chemoattractant protein-1 and Lp-PLA2 in patients with hypertension and coronary heart disease

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Abstract

Objective: To explore the combined application value of serum monocyte chemoattractant protein-1 and lipoprotein-associated phospholipase A2 in the diagnosis of hypertension and coronary heart disease.

Methods: The cross-sectional case-control study was conducted at Baoji Hospital of Traditional Chinese medicine, Shaanxi, China, from April 2018 to May 2020, and comprised patients with suspected hypertension and coronary heart disease. Patients with both hypertension and coronary heart disease formed Group A, and those with simple hypertension formed Group B. Healthy individuals formed the control Group C. Receiver operating characteristic curve was used to evaluate the value of serum monocyte chemoattractant protein-1 combined with lipoprotein-associated phospholipase A2 in the diagnosis of hypertension complicated with coronary heart disease. Data was analysed using SPSS 25.

Result: Of the 306 subjects, there were 122(40%) in Group A; 68(55.7%) males and 54(44.3%) females with mean age 68.77±5.76 years. There were 92(30%) cases in Group B; 51(55.4%) males and 41(44.6%) females with mean age 68.80±5.28 years. Group C had 92(30%) cases; 50(54.3%) males and 42(45.7%) females with mean age 67.85±5.29 years. Serum monocyte chemoattractant protein-1 and lipoprotein-associated phospholipase A2 levels were higher in Group A than the other two groups ($p<0.001$), and the levels in patients with carotid plaque total score <2 were lower than those with carotid plaque total score ≥2 ($p<0.001$). Area under receiver operating characteristic curve of the combination of the serum markers was 0.883 (95% confidence interval: 0.837-0.929, $p<0.001$), which was greater than that of two serum markers alone ($p<0.05$).

Conclusion: Monocyte chemoattractant protein-1 and lipoprotein-associated phospholipase A2 may be involved in pathogenesis of elevated blood pressure and coronary artery disease. Combined detection of the two serum markers can provide a certain basis for the diagnosis and treatment of hypertension and coronary heart disease.

Keywords: Hypertension, Coronary heart disease, Serum, Monocyte chemoattractant protein-1, Lp-PLA2.

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Introduction

Hypertension (HTN) has become a disease seriously threatening human health, and is one of the main causes of death from cardiovascular diseases. Coronary heart disease (CHD), a disease caused by coronary atherosclerosis, is currently the most common cardiovascular disease with high mortality. HTN is closely related to CHD.[1] It has been shown that HTN is an independent risk factor affecting the occurrence and prognosis of CHD events.[2] CHD is a common complication of HTN.[3] If blood pressure (BP) is not controlled well, inflammatory response continues to exist in the body. The abnormal expression of various inflammatory factors leads to cardiovascular functional and structural abnormalities, causes damage to target organs, such as heart, kidneys and brain, and prematurely induces cardiovascular events and death. Early diagnosis and treatment of CHD can reduce the incidence of cardio-cerebrovascular events, such as myocardial infarction (MI) and heart failure (HF).[4]

Monocyte chemoattractant protein-1 (MCP-1), a class of inflammatory cytokines with chemotactic function, may be related to the infiltration of monocytes during inflammation.[5] MCP-1 can be secreted by fibroblasts, vascular endothelial cells, and monocytes/macrophages that infiltrate the injury site.[6] Studies have confirmed that serum MCP-1 has certain clinical significance in judging the vulnerability of coronary atherosclerotic plaques. It may be an independent risk factor for CHD and can be used as an ideal indicator for the diagnosis of acute coronary syndrome (ACS).[7] It has also been shown that MCP-1 is related to the onset of essential HTN.[8] MCP-1, able to chemoattract monocytes, plays a key role in the formation of atherosclerosis in essential HTN and the remodelling of hypertensive heart.[9]

Lipoprotein-associated phospholipase A2 (Lp-PLA2), a member of the phospholipase A superfamily, is secreted

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by mature lymphocytes and macrophages. It is a newly-discovered inflammatory factor.[10] Lp-PLA2 can degrade the oxidised phospholipids in low-density lipoprotein cholesterol (LDL-C), leading to enhanced inflammatory response mediated by monocytes and macrophages, causing oxidative stress (OS) and endothelial damage.[11] It has been confirmed that Lp-PLA2 is closely related to CHD.[12]

The current study was planned to analyse the changes of serum MCP-1 and Lp-PLA2 in patients with HTN and CHD, and to explore the combined application value of serum MCP-1 and Lp-PLA2 in the diagnosis of HTN and CHD.

Patients and Methods

The cross-sectional case-control study was conducted at Baoji Hospital of Traditional Chinese medicine, China, from April 2018 to May 2020. After approval from the institutional ethics review committee, the sample size was calculated using G-Power software at significance level 0.05 and power 90% suing two-tailed test for difference between two independent means.[13] The sample was raised from among those who met the HTN diagnostic criteria for hypertension entailing systolic blood pressure (SBP) ≥140mmHg or/and diastolic blood pressure (DBP) ≥90 mmHg (1mmHg=0.133kpa),[14] and who met the World Health Organisation (WHO) diagnostic criteria for CHD which comprised coronary angiography showing the degree of stenosis to be 50-100% in at least 1 of the 4 vessels, which are the left main (LM) stem, left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA).[15] Those excluded were patients with diabetes, rheumatism, thyroid diseases, infectious diseases, tumours, congenital heart disease, and secondary HTN. Also excluded were patients receiving regular antihypertensive treatment or having taken statins and aspirin in the preceding 2 weeks, those who were mentally abnormal, and women during pregnancy or lactation.

Patients with both HTN and CHD formed Group A, and those with simple HTN formed Group B. Healthy people who had physical examination in the hospital to rule out the presence of HTN, heart, brain, lung and kidney disease were selected to form control Group C. Written informed consent was taken from all the participants.

All subjects were kept on an overnight fast for 12 hours, and 5mL fasting peripheral venous blood was drawn, and centrifuged before the upper serum was extracted. Serum MCP-1 and Lp-PLA2 levels of the subjects were determined by enzyme-linked immunosorbent assay (ELISA).

Doppler ultrasound was used to examine the degree of the patients' carotid artery atherosclerosis and to determine the intima-media thickness (IMT) value. Carotid plaque total score, called the Crouse score, was used to determine the degree of carotid atherosclerosis. IMT <1mm without thickening intima is scored as 0; IMT 1-1.1mm with partially thickened intima is scored as 1; IMT 1.2-1.4mm with plaque formation is scored as 2; IMT 1.5-1.9mm with mild stenosis is scored as 3; and IMT 2mm or greater with arterial stenosis is scored as 4.[16]

Data was analysed using SPSS 25. Kolmogorov-Smirnov test was used to check data normality. Measurement data was expressed as median with interquartile range (IQR) and mean ± standard deviation (S), and count data was expressed as frequencies and percentages. Measurement data were compared among the groups using one-way analysis of variance (ANOVA). Pairwise comparison among the groups was tested by least significant difference (LSD) test. Measurement data was compared using independent sample t test between two groups. The receiver operating characteristic (ROC) curve was used to evaluate the value of serum MCP-1 combined with Lp-PLA2 in the diagnosis of HTD complicated with CHD. P<0.05 was considered statistically significant.

Results

Of the 306 subjects, there were 122(40%) in Group A; 68(55.7%) males and 54(44.3%) females with mean age 68.77±5.76 years, mean SBP 153.68±13.19mmHg, mean DBP 95.64±8.22mmHg, and mean HTN duration 6.32±0.55 years.

There were 92(30%) cases in Group B; 51(55.4%) males and 41(44.6%) females with mean age 68.80±5.28 years, mean SBP 152.25±11.87mmHg, mean DBP 94.54±7.37mmHg and mean HTN duration 3.57±0.28 years.

Table-1: Comparison of serum MCP-1 and Lp-PLA2 levels between the three groups.

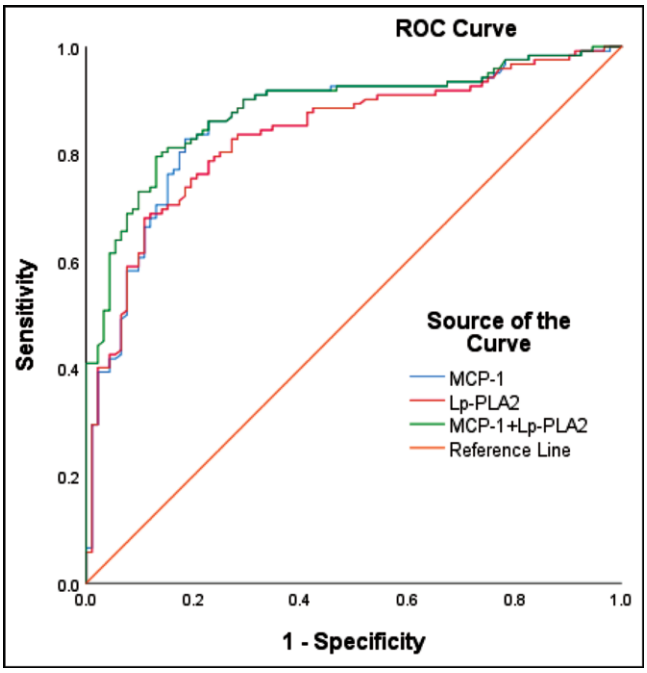
Parameter	Group A (n=122)	Group B (n=92)	Normal control group (n=92)	P value
Serum MCP-1(pg/mL)	150.63±12.17	109.10±8.69	77.52±6.18	<0.001
Serum Lp-PLA2(μg/mL)	451.87±36.46	384.98±30.52	245.66±19.54	<0.001

MCP-1: Monocyte chemoattractant protein-1, Lp-PLA2: Lipoprotein-associated phospholipase A2.

Table-2: Comparison of serum MCP-1 and Lp-PLA2 levels in patients with different Crouse points.

Parameter	Crouse score < 2 (n=57)	Crouse score ≥ 2 (n=65)	P value
Serum MCP-1(pg/mL)	141.82±10.37	158.37±7.48	<0.001
Serum Lp-PLA2(μg/mL)	427.09±30.48	477.15±24.03	<0.001

MCP-1: Monocyte chemoattractant protein-1, Lp-PLA2: Lipoprotein-associated phospholipase A2.



MCP-1: Monocyte chemoattractant protein-1, Lp-PLA2: Lipoprotein-associated phospholipase A2.

Figure-1: Receiver operating characteristic (ROC) curve evaluation of the value of serum MCP-1 combined with Lp-PLA2 in the diagnosis of hypertension complicated with coronary heart disease.

Group C had 92(30%) cases; 50(54.3%) males and 42(45.7%) females with mean age 67.85±5.29 years, mean SBP 125.63±9.79mmHg, and mean DBP 79.11±6.16mmHg. Serum MCP-1 and Lp-PLA2 levels were higher in Group A than the other two groups ($p<0.001$), and the levels were higher in Group B than those in Group C ($p<0.001$) (Table-1).

In Group A, 57(46.7%) patients had Crouse score <2, and 65(53.3%) had ≥2. Serum MCP-1 and Lp-PLA2 levels of patients with Crouse score <2 were lower than those with score ≥2 ($p<0.001$) (Table-2).

The area under the ROC curve (AUC) for serum MCP-1 and Lp-PLA2 in the diagnosis of HTN with CHD was 0.861 (95% confidence interval [CI]: 0.810-0.913, $p<0.001$) and 0.836 (95% CI: 0.782-0.890, $p<0.001$), respectively. When the cut-off value of serum MCP-1 was 117.94pg/mL, the diagnostic sensitivity was 90.20% and specificity was 70.70%. When the cut-off value of serum Lp-PLA2 was 414.32μg/mL, the diagnostic sensitivity was 80.30% and specificity was 75.00%. The AUC of serum MCP-1 combined with Lp-PLA2 in the diagnosis of HTN with CHD was 0.883 (95% CI: 0.837-0.929, $p<0.001$), which was greater than that of serum MCP-1 or serum Lp-PLA2 alone ($p<0.05$). Its diagnostic sensitivity was 90.2% and specificity was 70.7% (Figure-1).

Discussions

HTN is a disease in which the systemic arterial pressure is higher than the normal BP range.[17] CHD is an organic myocardial disease or dysfunction caused by coronary artery stenosis and insufficient blood supply to the myocardium.[18] HTN and CHD are diseases with independent pathogenesis, but they can promote each other, aggravate the disease, and seriously threaten the life of patients.

As a main risk factor of CHD, essential HTN can play a pro-inflammatory effect by up-regulating the expression of some inflammatory mediators, such as MCP-1.[19] Serum MCP-1 level was significantly higher in Group A than in Group B and Group C, and the serum MCP-1 level was higher in Group B than that in Group C. It is speculated that elevated plasma MCP-1 levels can induce monocyte/macrophage infiltration and activation, phagocytose lipid to become foamy cells, aggravate instability and rupture of plaques, and ultimately lead to cardiovascular events in CHD patients.[20]

The carotid Crouse scores, with high reliability in the quantitative evaluation of carotid atherosclerosis, can reflect the severity of carotid atherosclerosis to a certain extent.[21] The higher the carotid Crouse score is, the more severe the degree of atherosclerosis will be.[22] The current study revealed that the serum MCP-1 level of patients with Crouse score <2 was lower than those with score ≥2. Serum MCP-1 was positively correlated with Crouse score in Group A. It is speculated that MCP-1 induces and accelerates the instability of coronary plaques, which is similar to earlier studies.[23] The reason may be that on the one hand, increased serum MCP-1 can directly induce damage to the blood vessel wall, while on the other hand, it induces the liver to produce C-reactive protein (CRP), promoting platelet aggregation and vascular smooth muscle cell proliferation to participate in the pathological development of atherosclerosis.[24,25]

The current study also revealed that serum Lp-PLA2 level was higher in Group A than in Group B and Group C. The serum Lp-PLA2 level of patients with Crouse score <2 was lower than those with score ≥2 points. The reason may be that the predominant role of serum Lp-PLA2 is to connect to LDL through apolipoprotein B, and convert LDL lecithin into oxidised lecithin. Then Lp-PLA2 has a hydrolysis effect on oxidised LDL and produces oxidised fatty acids and lysolecithin, both of which, as pro-inflammatory mediators, can stimulate the secretion of adhesion factors, thereby accelerating the accumulation of monocytes in the inner membrane.[26] Inflammatory mediators in the

arterial intima maintain a positive feedback relationship with Lp-PLA2, and ultimately promote plaque progression.

Studies have shown that MCP-1 can predict the occurrence of coronary artery disease (CAD).[27] The level of Lp-PLA2 also has a certain predictive value in the risk assessment of patients with ACS.[28] The current study showed that AUC of serum MCP-1 combined with Lp-PLA2 in the diagnosis of HTN with CHD was greater than that of serum MCP-1 and Lp-PLA2 alone. Therefore, the combined detection of serum MCP-1 and Lp-PLA2 levels can be used to determine CAD and prognosis in hypertensive patients.

Conclusion

MCP-1 and Lp-PLA2 may be involved in the pathogenesis of elevated BP and CAD. The combined detection of serum MCP-1 and Lp-PLA2 can provide a certain basis for the diagnosis and treatment of HTN and CHD.

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Conflict of Interest: None.

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