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Original Article

Serum C reactive protein and procalcitonin are valuable predictors of coronary heart disease and poor prognosis in the elderly

Lei Yu[1], Jianbin Sun[1], Xinguang Liu[2]

[1]*Department of Clinical Laboratory, Wuhan City No. 3 Hospital, Wuhan 430060, Hubei, China;* [2]*Guangdong Medical University, Dongguan 523000, Guangdong, China*

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Abstract: Objectives: To investigate the potential of serum C-reactive protein (CRP) and procalcitonin (PCT) for predicting coronary heart disease (CHD) in elderly patients, as well as their impact on prognosis. Methods: This retrospective analysis included 120 elderly patients with CHD (CHD group) and 100 patients without cardiovascular disease (control group). CHD patients were followed up for 12 months after discharge. Patients with readmission due to adverse cardiovascular events were incorporated into a poor prognosis group, and the rest were considered a good prognosis group. Serum CRP and PCT were measured by Latex immunoturbidimetric assay and enzyme-linked fluorescent assay. Results: Serum CRP and PCT levels in the CHD group were considerably higher than those in the control group. Serum CRP and PCT were found to be predictive factors for CHD by logistic regression study, and the area under the curve (AUC) of the combination examination of CRP and PCT was greater than that of CRP or PCT alone, suggesting that the combination was most valuable for the prediction of CHD in the elderly. Furthermore, the levels of CRP and PCT in the poor prognosis group were substantially higher than those in the good prognosis group. Logistic regression found that serum CRP and PCT were independent factors affecting the prognosis of CHD. The AUR of the combined examination of CRP and PCT was greater than that of the CRP or PCT alone, suggesting that the combination had a better prognostic value. Conclusions: Serum PCT and CRP levels are abnormally elevated in elderly patients with CHD, and higher levels of PCT and CRP are associated with higher risk of CHD and poor prognosis. The determination of PCT and CRP is of great significance in guiding clinical treatment.

Keywords: Coronary heart disease, procalcitonin, C-reactive protein, diagnosis, prognosis

Introduction

Coronary heart disease (CHD) exhibits high incidence in the elderly [1]. According to statistics, the prevalence of CHD in people over 60 years old is 27.8% in China [2]. Due to the aging of the population and the changes in living habits and environment, the incidence and mortality of CHD are still on the rise [3, 4]. The majority of patients with CHD seek medical treatment after physical discomfort or onset, and are diagnosed by cardiac ultrasound and transcoronary angiography [5, 6]. If the risk of CHD can be detected early, the occurrence of critical conditions and mortality can be reduced. However, there is currently a lack of hematologic indicators for early diagnosis of CHD. C-reactive protein (CRP), a sensitive marker for the chronic inflammation, is significantly increased in tissue damage and acute inflammation [7, 8]. In addition, CRP is also an independent risk factor for atherosclerotic thrombosis, including future cardiovascular events [9, 10]. Procalcitonin (PCT) is a biomarker that has long been used in the diagnosis of sepsis since it indicates the severity of bacterial infection, especially for monitoring the progression of sepsis, pneumonia, or septic shock [11-13]. In patients with sepsis, PCT levels rise more rapidly than CRP or erythrocyte sedimentation rate, suggesting that PCT may be of more importance in early diagnosis of conditions typically associated with elevated PCT, CRP, and erythrocyte sedimentation rate [14]. Recent research has shown that the levels of PCT in patients with CHD are associated with the severity and

Table 1. Basic information of the two groups of patients

Group	Sex		Age		
	Male	Female		Max	Min
CHD	67	53	73.18±8.34	93	60
Control	59	41	74.56±7.69	95	61
X^2/t	0.113		1.266		
p	0.737		0.27		

CHD: Coronary heart disease.

adverse outcomes of atherosclerosis [15]. In recent years, there have been various reports on the effects of serum PCT and CRP levels on predictionf the prognosis of liver, lung and kidney diseases, but few reported their effects on the prognosis of CHD [16-18]. The aim of this research was to investigate the predictive value of serum CRP and PCT levels for CHD in elderly patients, as well as their impact on prognosis.

Material and methods

Subjects

In this retrospective analysis, 120 elderly patients with CHD who attended Wuhan City No. 3 Hospital between October 2020 and November 2022 were included in a CHD group. In addition, 100 patients without cardiovascular disease admitted to Wuhan City No. 3 Hospital during the same time period were included in a control group. Inclusion criteria for the CHD group: 1) patients were diagnosed with CHD by coronary angiography due to chest pain, chest tightness, and other symptoms; 2) patients received medical treatment; 3) patients were followed up for 12 months; 4) patients with complete clinical data. Exclusion criteria for both groups: 1) patients with congenital heart disease, coronary artery bypass grafting, myocardial disease, or rheumatic heart disease; 2) patients with chronic infectious diseases or autoimmune diseases. This study was approved by the Ethics Committee of Wuhan City No. 3 Hospital.

Evaluation of blood test

Fasting elbow venous blood 2 mL were collected in all subjects. Following manufacturer's instructions, PCTs were determined by enzyme-linked fluorescent assay using an enzyme-linked fluorescent assay kit (vidas, BioMérieux, France), and CRPs were determined by Latex immunoturbidimetric assay using a Latex immunoturbidimetric assay kit (BC5390CRP, Mindray, China). The MultiskanFC microplate reader was purchased from Thermo Fisher Technology (China) Co., LTD.

Follow-up visit

All patients in the CHD group received conventional treatment and were followed up for 12 months after discharge to record the occurrence of cardiovascular adverse events. Patients readmitted to the hospital due to adverse cardiovascular events were incorporated into a poor prognosis group, and the others were grouped into a good prognosis group.

Statistical analysis

SPSS26.0 was utilized for statistical analysis, and graphs were plotted using GraphPad Prism 9. The counted data were represented by the number of cases and percentage [N (%)], and Chi-square test was used to compare the incidence between the two groups. The t test was used to assess the measured data. The prognostic factors of CHD patients were analyzed by multivariate Logistic regression, and receiver operating characteristic (ROC) curve was used to evaluate the predictive value. Statistical significance was considered when $P<0.05$.

Results

Comparison of general data between the CHD group and the control group

In the CHD group, there were 67 males and 53 females, with an age range of 60 to 93, and a median age of 73.17±8.34 years old. In the control group, there were 59 males and 41 females, aged 61-95 years old, with a median age of 75.56±7.69 years old. There was no significant difference in the general data between the two groups ($P>0.05$), as shown in **Table 1**.

Comparison of serum CRP and PCT between the CHD group and the control group

The levels of CRP and PCT in the CHD group were 8.40±1.98 mg/L and 1.85±0.77 ng/mL, respectively, which were significantly higher than 6.61±1.34 mg/L and 1.08±0.29 ng/mL in the control group ($P<0.05$), as shown in **Table 2**.

Table 2. Comparison of serum CRP and PCT in the CHD group and the control group ($\bar{X}$ ± SD)

Group	n	CRP (mg/L)	PCT (ng/mL)
CHD	120	8.40±1.98	1.85±0.77
Control	100	6.61±1.34	1.08±0.29
t		7.690	9.475
P		0.009	<0.001

CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin.

Correlation for serum CRP and PCT with CHD

CHD was the dependent variable and serum CRP and PCT were covariables.

Serum CRP (P<0.001) and PCT (P<0.001) were identified as independent risk variables for CHD by logistic regression analysis, as shown in **Table 3**.

Predictive value of serum CRP and PCT for CHD

The ROC curves of serum CRP and PCT for the diagnosis of CHD in elderly patients were plotted. The area under the curve (AUC), critical value, sensitivity, and specificity of CRP were 0.869, 5.935 mg/L, 93.3% and 62%, respectively, and those of PCT were 0.785, 1.527 ng/mL, 59.2%, and 89%, respectively. The AUC, sensitivity, and specificity of CRP with PCT were 0.926, 70.8%, and 98%, respectively. See **Figure 1** and **Table 4**.

Comparison of serum CRP and PCT between poor and good prognosis groups

Follow-up data demonstrated that there were 52 patients in the poor prognosis group and 68 patients in the good prognosis group. The CRP and PCT levels in the poor prognosis group were 9.17±2.26 mg/L and 1.53±0.60 ng/mL, respectively, considerably greater than those in the good prognosis group (9.17±2.26 mg/L and 2.26±0.77 ng/mL, respectively), with a statistically significant differences (P<0.05). See **Table 5**.

Correlation analysis of serum CRP and PCT with prognosis of CHD

With good prognosis as the dependent variable and serum CRP and PCT as covariables, serum CRP (P<0.001) and PCT (P<0.001) were identified as independent influencing variables for CHD prognosis by logistic regression analysis, as shown in **Table 6**.

Prognostic value of serum CRP and PCT in elderly patients with CHD

The ROC curve of serum CRP and PCT levels for the prognosis CHD was plotted. The AUC, critical value, sensitivity, and specificity of CRP were 0.789, 7.295 mg/L, 42.6% and 84.6%, respectively, and those of PCT were 0.661, 1.774 ng/mL, 79.4%, and 73.1%, respectively. The AUC, sensitivity, and specificity of CRP combined with PCT were 0.828, 83.8%, and 76.9%, respectively. See **Table 7** and **Figure 2**.

Discussion

CHD is a worldwide major cause of death [19]. It is characterized by high incidence and poor prognosis in the elderly population, seriously threatening their life [20, 21]. With the acceleration of the aging process, the incidence and mortality of CHD are also increasing in China [22]. It is also a common chronic disease among the elderly worldwide [23]. Early diagnosis and intervention can effectively reduce the occurrence of serious adverse outcomes, as well as reduce the risk of disability and death. In addition, early detection of the risk of poor prognosis can also help reduce the recurrence of cardiovascular disease events and improve quality of life.

CRP is a common biomarker. It is associated with endothelial dysfunction, prethrombotic state, remodeling of atherosclerotic plaques, and instability [24]. In patients with coronary artery disease, major adverse cardiovascular events are often associated with elevated CRP levels, so CRP level is associated with an increased atherosclerotic burden [25]. In recent years, CRP has been identified as an important predictor of the onset of cardiovascular disease [26].

PCT, a non-hormonally active propeptide, is typically secreted by thyroid C cells during normal metabolism and is rarely detected in the sera of healthy people [27]. This makes PCT a preferable marker with greater sensitivity towards bacterial infections, also for distinguishing between bacterial infections, viral infections, and other non-communicable dis-

Table 3. Logistic regression analysis of CPR and PCT levels as risk factors for CHD

Variable	B	SE	Wald	P	OR	95% CI
CRP (mg/L)	-0.868	0.138	39.750	<0.001	0.420	0.321-0.550
PCT (ng/mL)	-2.857	0.601	22.609	<0.001	0.057	0.018-0.187

CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin.

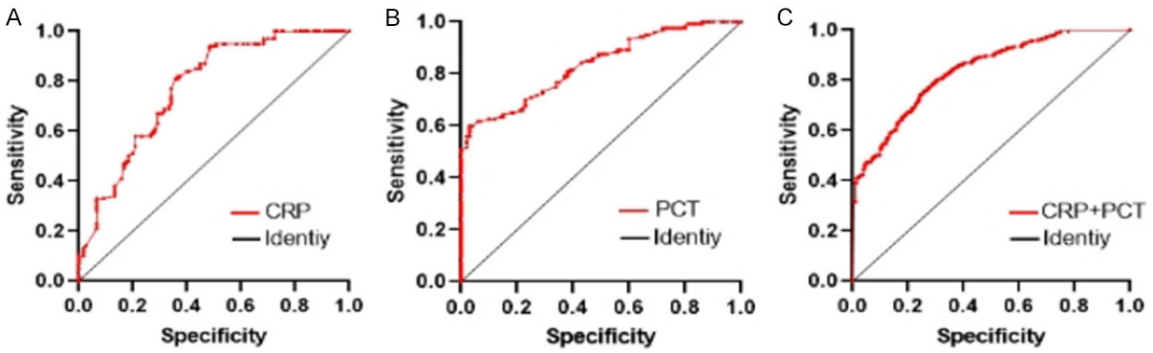

Figure 1. ROC curves of serum CRP (A), PCT (B) and their combined values (C) for the diagnosis of CHD. CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin.

Table 4. Predictive value of serum CRP and PCT levels for CHD

Variable	AUC	Cut-off	Sensitivity (%)	Specificity (%)	P
CRP (mg/L)	0.869	5.935	93.3	62	0.003
PCT (ng/mL)	0.785	1.527	59.2	89	<0.001
CRP+PCT	0.926	0.234	70.8	98	<0.001

CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin. AUC: area under the curve.

Table 5. Comparison of serum CRP and PCT between good and poor prognosis groups ($\bar{X}$ ± SD)

Group	n	CRP (mg/L)	PCT (ng/mL)
Good prognosis	68	7.81±1.54	1.53±0.60
Poor prognosis	52	9.17±2.26	2.26±0.77
t		3.943	0.028
P		5.832	0.007

CRP: C-reactive protein. PCT: procalcitonin.

eases [28]. In recent years, there is recognition of the value of PCT in patients with cardiovascular diseases [29].

Previous studies have shown that the inflammatory response contributes to the development of coronary atherosclerosis, exhibiting a direct correlation [30]. As shown by Medina-Leyte et al., coronary atherosclerosis could cause inflammation and elevated CRP levels, which is a factor for inducing CHD [31]. The findings of this research demonstrated that serum CRP in the CHD group was significantly higher than that in the control group. Serum CRP (P<0.001) was identified as an independent risk variable for CHD by logistic regression analysis. Cheng et al. [32] reported that CRP plays a dual role in promoting atherosclerosis by facilitating leukocyte adhesion to the vascular wall and promoting the transformation of monocytes into foam cells through the oxidation of LDL cholesterol. This may be the mechanism underlying the significantly higher serum CRP levels in CAD patients.

PCT acts as a chemoattractant, initially produced in adherent monocytes, which then recruit parenchymal cells in inflamed tissues to further produce PCT [33]. The findings of this research demonstrated that serum PCT level in the CHD group was higher than that of the control group by a significant amount. Serum PCT (P<0.001) was identified as an independent risk factor for CHD by logistic regression analysis. Previous studies have found that the expression of PCT mRNA in peripheral blood monocytes is directly stimulated by lipopolysaccharide in vitro, and indirectly by the pro-inflammatory cytokine interleukin-1β, Interleukin-2,

Table 6. Logistic regression analysis of CPR and PCT levels as risk factors for CHD prognosis

Variable	B	SE	Wald	P	OR	95% CI
CRP (mg/L)	-0.390	0.125	9.709	0.002	0.677	0.865-0.865
PCT (ng/mL)	-1.536	0.349	19.379	<0.001	0.215	0.427-0.427

CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin.

Table 7. Prognostic value of serum CRP and PCT for the prognosis of CHD

Variable	AUC	Cut-off	Sensitivity (%)	Specificity (%)	P
CRP (mg/L)	0.789	7.295	42.6	84.6	0.003
PCT (ng/mL)	0.661	1.774	79.4	73.1	<0.001
CRP+PCT	0.828	0.610	83.8	76.9	<0.001

CRP: C-reactive protein. PCT: procalcitonin.

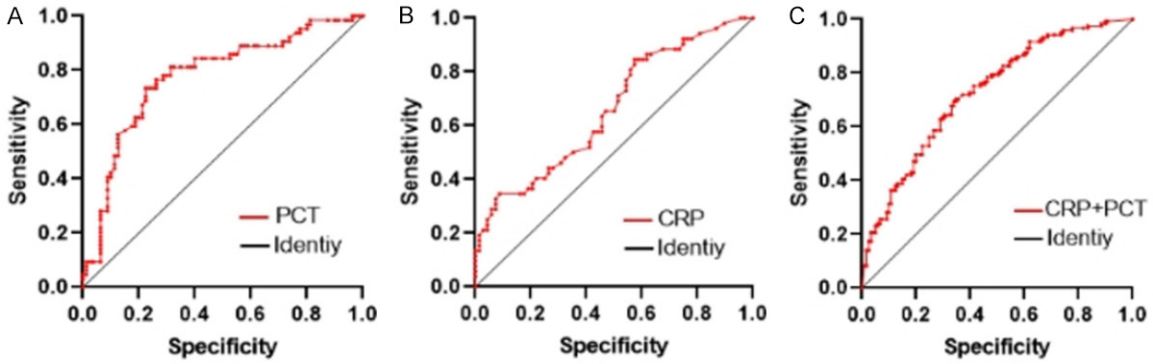

Figure 2. ROC curves of serum CRP (A), PCT (B) and their combined value (C) for thr prognosis of CHD. CHD: Coronary heart disease. CRP: C-reactive protein. PCT: procalcitonin.

Interleukin-6, and tumor necrosis factor-α. These cytokines also play a key role in the procession of atherosclerosis [34, 35]. This may be the mechanism underlying the significantly higher serum PCT levels in CAD patients.

The predictive value of serum CRP and PCT for cardiovascular diseases has been shown by prior research [26, 29], and this study further confirmed their ability to predict CHD. ROC curve showed that the AUCs of CRP and PCT were 0.869 and 0.785, respectively, indicating that they had good diagnostic value for CHD. The AUC of the combination examination of CRP and PCT was 0.926, indicating that the combination of these two indicators has a higher diagnostic efficiency.

Previous studies have found that CRP is not only an independent risk predictor of cardiovascular diseases but also associated with poor prognosis [36, 37]. Similarly, elevated levels of PCT are also associated with the degree of atherosclerosis and adverse outcomes in patients with CHD [38, 39]. Therefore, the value of serum CRP and PCT levels in predicting the prognosis of elderly patients with CHD was further analyzed in this study. Our findings revealed that serum CRP and PCT levels in the poor prognosis group were significantly higher than those in the good prognosis group. According to the results of logistic regression, serum CRP (P< 0.001) and PCT (P<0.001) were both independent risk factors for poor prognosis of CHD. Therefore, increased serum CRP and PCT levels were associated with high risk of poor prognosis of CHD, confirming their predictive value. Previous studies also reported the predictive value of CRP and PCT for the prognosis of diseases such as sepsis and pneumonia [40, 41]. In this study, ROC curve showed that the AUCs of CRP and PCT for the prognosis CHD were 0.789 and 0.661, respectively, indicating their good predictive value for the prognosis of CHD. The AUC of the combined examination of CRP and PCT was 0.828, indicating that the combi-

nation demonstrated a higher prognostic value for CHD.

However, this study has some limitations, because the included patients with CHD were all elderly, who have other basic diseases, which may cause some interference to the two main detection indicators. However, it is difficult to collect data of healthy elderly patients in China. In future research we hope to collect more data of healthy volunteers and conduct a more comprehensive analysis.

In summary, serum PCT and CRP levels are both abnormally elevated in elderly patients with CHD, and higher levels are associated with higher risk of CHD and adverse prognosis. The determination of PCT and CRP is of great significance in guiding clinical treatment.

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Disclosure of conflict of interest

None.

Address correspondence to: Lei Yu, Department of Clinical Laboratory, Wuhan City No. 3 Hospital, No. 241, Pengliuyang Road, Wuchang District, Wuhan 430060, Hubei, China. Tel: +86-027-65399897; E-mail: yl20230129zza@163.com

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