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Original Article

Diagnostic value of PCT, SAA and presepsin in acute sepsis patients

Cheng Liu, Qiuju Qiu

Department of Emergency, Affiliated Nanhua Hospital, University of South China, Hengyang 421002, Hunan Province, China

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Abstract: Objective: This study aimed to analyze the levels of procalcitonin (PCT), amyloid A (SAA) and soluble cluster-of-differentiation 14 subtype (presepsin) in sepsis. Methods: Forty five patients with acute sepsis caused by burns and traffic accidents admitted in our hospital from January 2014 to January 2017 were selected as the research group (RG), and 49 patients with non-sepsis burns and traffic accidents in the same period were regarded as the control group (CG), for prospective analysis. The concentrations of PCT, SAA and presepsin in serum were detected. The diagnostic value of the three in sepsis and their correlation with APACHE II and SOFA scores were analyzed. To analyze the influence of PCT, SAA and presepsin on the prognosis of septic patients, they were followed up for 3 years. Results: The concentrations of PCT, SAA and presepsin in serum of the RG were higher than those of the CG ($P < 0.05$). ROC analysis identified that the sensitivity and specificity of the combined detection for sepsis in patients were 84.44% and 93.88% ($P < 0.001$). Pearson correlation coefficient analysis identified that PCT, SAA, presepsin were positively correlated with APACHEII scores ($P < 0.001$), and were also positively correlated with SOFA scores ($P < 0.001$). The three were positively correlated with APACHE II scores ($P < 0.001$) and were also positively correlated with SOFA scores ($P < 0.001$). Conclusion: PCT, SAA, presepsin are elevated in sepsis, which has high evaluation value for occurrence and prognosis and the combination has the potential to become good blood markers.

Keywords: Sepsis, PCT, SAA, presepsin, prognosis

Introduction

Sepsis is a systemic inflammatory response syndrome caused by infection, and it has a very high morbidity in the world [1]. Recently, the morbidity is showing a rising trend, and the affected population is also getting younger [2]. According to statistical investigation, the current global morbidity of sepsis is about 22/100,000 [3]. Sepsis can cause severe organ damage, diffuse intravascular coagulation, microcirculation disturbance, septic shock, etc., which is a great threat to the life and health of patients [4]. Some data show that it causes about 1 million deaths every year [5]. It is precisely because of the high morbidity and mortality of sepsis that it has been clinically classified as a key research disease. Researchers at home and abroad are constantly exploring new diagnosis and treatment methods for sepsis [6].

The occurrence of sepsis is relevant to the degree of immune ability and inflammatory reaction, so the studies of procalcitonin (PCT) in sepsis have been common in clinical study [7, 8]. A recent study has suggested that PCT can be used as a clinical indicator for early diagnosis of sepsis, but the specificity of PCT alone for diagnosing sepsis is not high, so it is necessary to combine other markers for joint screening [9]. With the deepening of research, clinical findings show that amyloid A (SAA) is also closely related to acute inflammatory reaction [10]. SAA is an acute phase protein that combines with plasma high density lipoprotein (HDL) and has a relatively similar effect with hypersensitive-C reactive protein (CRP), but currently has a higher specificity [11]. However, we found that soluble cluster-of-differentiation 14 subtype (presepsin) is a glycoprotein existing in monocytes/macrophages. It has been confirmed that the presepsin level in sep-

tic patients is dramatically higher than that in healthy people, and it is tied to disease severity [12]. Therefore, we speculate that if PCT and SAA are combined with presepsin, the diagnostic value for sepsis may be better than that in current clinical practice. In order to verify our conjecture, we will analyze the levels of PCT, SAA and presepsin in sepsis through experiments to provide a reliable theoretical basis for future clinical practice.

Materials and methods

General data

Forty-five patients with acute sepsis caused by burns and car accidents who were admitted to our hospital from January 2014 to January 2017 were selected as the research subjects, and 49 patients with non-septic burns and car accidents at the same time were selected, all for a prospective analysis. The subjects were all screened based on the inclusion criteria (those in line with sepsis diagnostic criteria [15]; those who had complete case data; those who agreed to cooperate with our hospital medical staff and arrangements; ICU severe patients) and exclusion criteria (pregnant women; patients with drug allergy; heart failure (≥ grade III); renal failure (Rifle grade ≥ F); liver failure (total plasma protein < 30 g/L, bilirubin > 85 mol/L); brain death; those transferred from one hospital to another; prolonged bed rest; mental illness; physical disability). Sepsis patients were included in the research group (RG) and non-sepsis patients were included in the control group (CG). All the subjects signed an informed consent form and all the investigations were carried out with the approval of the ethics committee of our hospital.

Methods

Sepsis patients underwent routine treatment, including bed rest, strengthening nutrition and supplementing appropriate amount of vitamins, maintaining water, electrolyte and acid-base balance. Blood transfusion, plasma, albumin and gamma globulin were given when necessary. According to etiological examination, appropriate antibacterial drugs were selected for treatment. A total of 3 mL fasting venous blood was extracted from patients in the RG and CG. Next, it was placed into a coagulation accelerator, left for 30 min at room temperature and then centrifuged 20 min in a centrifuge (1505 × g, 4°C), and the upper serum was obtained and then placed in a freezer at -80°C for testing. PCT in serum was detected by immunoluminescence method, and the kit was purchased from Shanghai Caiyou Industry Co., Ltd. SAA concentration and presepsin were detected through enzyme linked immunosorbent assay (ELISA). The kits were purchased from Shanghai Jingkang Bioengineering Co., Ltd. and Wuhan Feien Biotechnology Co., Ltd. Within 24 h after sepsis patients entered the Emergency Department, APACHEII score and sequential organ failure assessment (SOFA) score were calculated based on the worst clinical indicators. The patients were followed up for 3 years in the form of hospital reexamination, and the prognosis in the RG was recorded.

Outcome measures

Main outcome measures: The serum concentrations of PCT, SAA and presepsin in sepsis patients, and the diagnostic value of PCT, SAA and presepsin in sepsis were taken into account (The ROC curve analysis was performed using PCT, SAA and presepsin concentrations of the RG and the CG).

Secondary outcome measures: The correlation between PCT, SAA and presepsin concentrations and APACHEII and SOFA scores in serum of septic patients, and effect of PCT, SAA and presepsin on prognosis of patients were included (according to the median results of PCT, SAA and presepsin, the patients were divided into low PCT group and high PCT group; low SAA group and high SAA group; low presepsin group and high presepsin group. The prognosis and survival of the two groups were compared).

Statistical methods: The data results were analyzed and processed by SPSS 22.0. The counting data were recorded in the form of (rate) and the comparison was assessed via chi-square test. The measurement data were recorded in the form of (mean ± standard deviation), and the inter-group comparison was assessed by independent-samples T test. The comparison before and after treatment was analyzed through paired T test, and that among groups was analyzed with one-way analysis of variance

Table 1. Comparison of general data between the two groups [n (%)]

	Research group (n=45)	Control group (n=49)	t or X^2	P
Age (year)	48.3±14.8	46.7±15.2	0.516	0.6069
BMI (kg/cm^2)	20.54±4.26	20.84±5.02	0.311	0.757
Gender			0.010	0.921
Male	28 (62.22)	30 (61.22)		
Female	17 (37.78)	19 (38.78)		
Nationality			0.876	0.349
Han	44 (97.78)	46 (93.88)		
Minority nationality	1 (2.22)	3 (6.12)		
Marital status			0.251	0.616
Married	28 (62.22)	28 (57.14)		
Unmarried	17 (37.78)	21 (42.86)		
Place of residence			0.517	0.472
Cities and towns	34 (75.56)	40 (81.63)		
Countryside	11 (24.44)	9 (18.37)		
Cause of injuries			0.104	0.747
Traffic accidents	29 (64.44)	30 (61.22)		
Burns	16 (35.56)	19 (38.78)		
Smoking			0.563	0.453
Yes	26 (57.78)	32 (65.31)		
No	19 (42.22)	17 (34.69)		

and LSD back testing. Pearson correlation coefficient was used for correlation analysis, and the diagnostic value was analyzed by ROC curve. The joint formula was calculated through SPSS binary regression analysis in joint diagnosis, and then assessed by ROC curve analysis. The survival rate was calculated by Kaplan-Meier method and compared by Log-rank test. The difference was considered statistically significant when $P < 0.05$.

Results

Comparison of general data in both groups

There was no marked difference in general data such as age and gender between the two groups ($P > 0.05$) (**Table 1**).

Comparison of PCT, SAA and presepsin concentrations in serum of both groups

Through detection, we found that the concentrations of PCT, SAA and presepsin in the serum of the RG were higher than those of the CG ($P < 0.05$) (**Figure 1**).

Diagnostic value of PCT, SAA and presepsin in sepsis

ROC curve analysis identified that the predictive sensitivity and specificity of PCT detection for sepsis were 62.22% and 85.71%, respectively ($P < 0.001$); the sensitivity and specificity of SAA detection were 53.33% and 85.71%, respectively ($P < 0.001$); the sensitivity and specificity of presepsin detection were 77.78% and 73.47%, respectively ($P < 0.001$). However, through SPSS regression analysis, the combined formula log (P) =-30.444+0.765 × PCT+0.034 × SAA+0.147 × presepsin was obtained first. Then, ROC analysis showed that the sensitivity and specificity of the combined detection for sepsis in patients were 84.44% and 93.88% ($P < 0.001$) (**Figure 2**; **Table 2**).

Correlation between PCT, SAA, presepsin and APACHE II, SOFA scores

The APACHE II score was (18.62±4.26) and the SOFA score was (8.42±1.41) before treatment in the RG. Pearson correlation coefficient analysis identified that PCT, SAA, presepsin were positively associated with APACHE II scores ($P < 0.001$), and were also positively associated with SOFA scores ($P < 0.001$) (**Figure 3**).

Relationship between PCT, SAA, presepsin and prognosis of septic patients

According to the median detection results of PCT, SAA and presepsin, patients in the RG were divided into low PCT group (≤ 10.57, n= 19) and high PCT group (> 10.57, n=26), low SAA group (≤ 310.70, n=23) and high SAA group (> 310.70, n=22), low presepsin group (≤ 97.35, n=22) and high presepsin group (> 97.35, n=23). Prognostic follow-up results manifested that the survival rate of low PCT group, low SAA group and low presepsin group was better than that of high PCT group, high SAA group and high presepsin group ($P < 0.05$) (**Figure 4**).

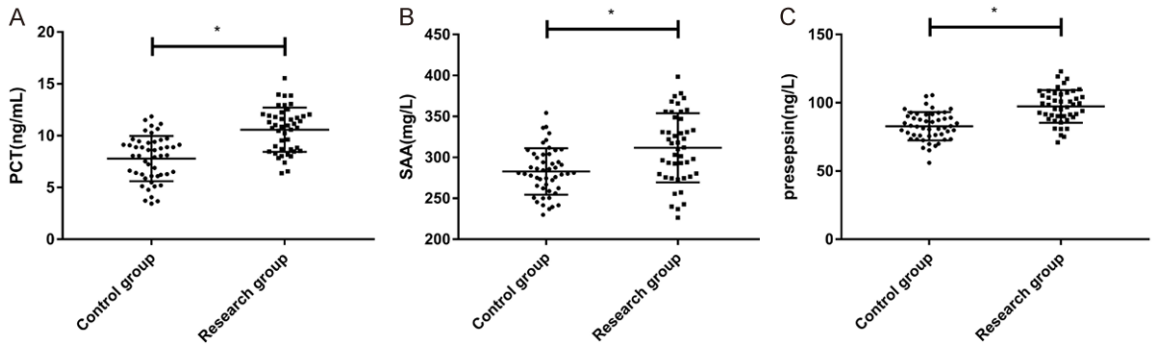

Figure 1. Comparison of PCT, SAA and presepsin concentrations in serum of both groups. A. Comparison of PCT concentration in serum between research group and control group; B. Comparison of SAA concentration in serum between research group and control group; C. Comparison of presepsin concentration in serum between research group and control group (*P < 0.05).

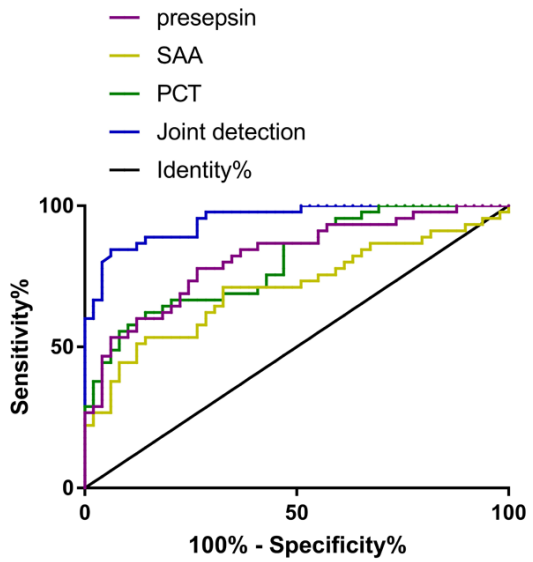

Figure 2. ROC curves of PCT, SAA and presepsin predicting sepsis.

Discussion

Sepsis, as a very serious malignant disease, and it poses a great threat to the life and health of patients [13]. Therefore, it is extremely important to adopt effective monitoring methods for the occurrence of sepsis. At present, the clinical monitoring of sepsis is extremely complicated, which requires multiple examinations such as vital signs, hemodynamics, organ function and pathogenic bacteria [14]. Seeking effective blood markers is quite significant for sepsis, one of which is to assist the clinical diagnosis of sepsis in the early stage and to carry out timely and effective interventions for patients. Besides, it can be used as a guide to judge the disease process of patients and to understand the disease development more intuitively. What's more, we know the prognosis and rehabilitation of patients through the detection of markers, which is of great significance to their prognosis. In this study, we can effectively preliminarily reveal the potential significance of PCT, SAA and presepsin in sepsis by analyzing the situation of the three in sepsis and provide a basis for future further clinical research.

This experiment showed that PCT, SAA and presepsin were all higher in sepsis than those in healthy subjects, suggesting that the three might be involved in disease development and progression. This is also similar to the results in previous studies, which can support the results of this experiment [15-17]. Through reviewing previous studies, we found that presepsin consists of 64 amino acid residues, which may directly act on T cells and B cells to regulate cellular immunity and humoral immunity [18]. Mathias et al. [19] pointed out that the occurrence of sepsis was closely related to the abnormal reduction of immune ability. Therefore, we speculate that the increase of presepsin in sepsis may be due to the increase of inflammatory factors and the decrease of immune function caused by the infection of pathogenic bacteria. At this time, presepsin is activated and released in a large amount, and tissues and organs suffer from obvious pathological changes and necrosis, which eventually leads to sepsis. However, previous studies have suggested that the occurrence of sepsis is strongly linked to the release of inflammatory factors. For example, IL-6, a common inflam-

Table 2. Diagnostic value of PCT, SAA and presepsin for sepsis

	PCT	SAA	Presepsin	Joint detection
Cut-off	> 9.980	> 309.900	> 89.260	> 0.628
AUC	0.803	0.708	0.817	0.949
95% CI	0.716-0.889	0.600-0.816	0.732-0.902	0.910-0.989
Sensitivity (%)	62.22	53.33	77.78	84.44
Specificity (%)	85.71	85.71	73.47	93.88
P	< 0.001	< 0.001	< 0.001	< 0.001

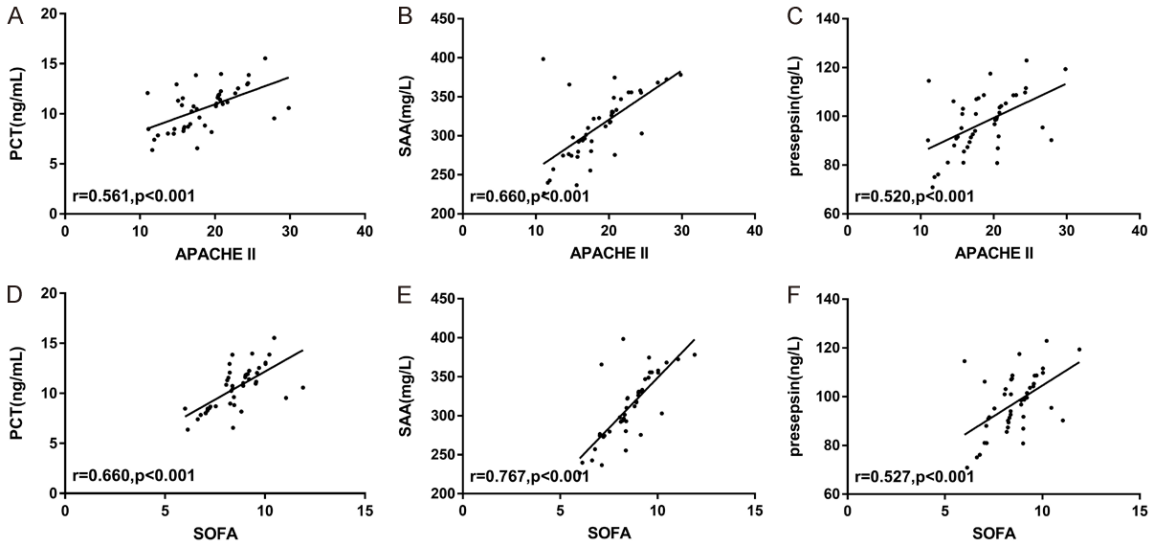

Figure 3. Correlation between PCT, SAA, presepsin and APACHE II, SOFA scores. A. Correlation analysis between PCT and APACHE II score (r=0.561, P < 0.001); B. Correlation analysis between SAA and APACHE II score (r=0.660, P < 0.001); C. Correlation analysis between presepsin and APACHE II score (r=0.520, P < 0.001); D. Correlation analysis between PCT and SOFA score (r=0.660, P < 0.001); E. Correlation analysis between SAA and SOFA score (r=0.767, P < 0.001); F. Correlation analysis between presepsin and SOFA score (r=0.527, P < 0.001).

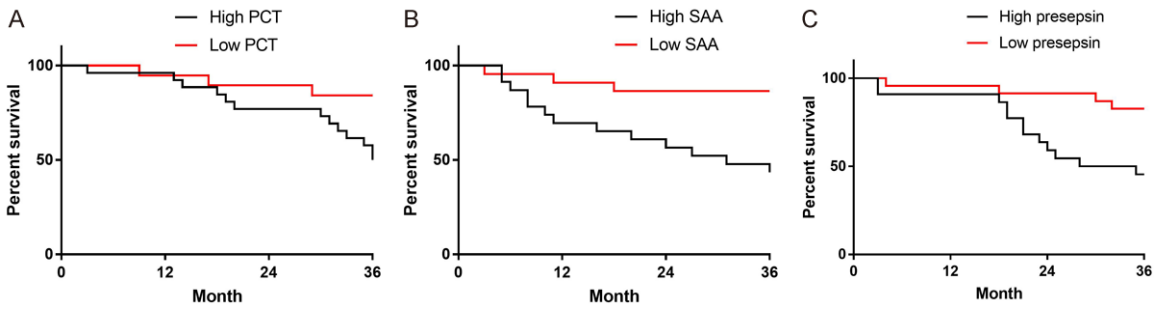

Figure 4. Relationship between PCT, SAA, presepsin and prognosis of septic patients. A. 3-year survival curve of prognosis in low PCT group and high PCT group (P=0.03); B. 3-year survival curve of low SAA group and high SAA group (P=0.004); C. 3-year survival curve of low presepsin group and high presepsin group (P=0.009).

matory factor, is also released in large quantities when septic bacterial infection occurs [20]. A recent study has found that the production of presepsin is greater than to IL-6 [21], so presepsin may play a more vital role in sepsis occurrence. However, the elevation of PCT and SAA is also consistent with the disease situation of sepsis. Previous studies have explained the relationship between PCT, SAA and sepsis, so this article will not go into details. PCT and

SAA are both closely related to the occurrence of inflammation, and both have been confirmed as one of the diagnostic indicators of many infectious diseases [22, 23]. However, in sepsis, although some studies have suggested that PCT and SAA have certain diagnostic significance, due to their obvious activation reactions, their ability to differentiate sepsis is not strong. In this study, we analyzed the diagnosis results of PCT and SAA for sepsis by ROC curve, which could confirm this point. Through the joint detection of PCT, SAA and presepsin, we found that the sensitivity to predict sepsis reached 84.44% and the specificity reached 93.88%. This shows that the combined detection of the three can effectively improve the differential and diagnosis rates of sepsis, and it has more reliable reference significance for preventing sepsis occurrence. Above, we have preliminarily confirmed the diagnostic value of PCT, SAA and presepsin for sepsis, but we believe that the three are strongly linked to sepsis occurrence and should have wider application. Thus, we analyzed the relationship between PCT, SAA, presepsin and APACHE II and SOFA scores, and found that the three were also relevant to the changes of APACHE II and SOFA scores. APACHE II and SOFA scores, as objective guidelines for clinical evaluation of sepsis, are self-evident in relation to sepsis [24, 25]. The results also confirmed the important role of PCT, SAA and presepsin in sepsis development. Not only that, we also found that patients' PCT, SAA and presepsin decreased after treatment, but through prognosis follow-up, we found that the higher PCT, SAA and presepsin were, the greater the probability of death of patients was. This suggested that we could evaluate the changes of PCT, SAA, presepsin in the prognosis examination of septic patients as early as possible for readmission treatment selection, and reduce the prognosis mortality of sepsis.

Of course, there are still many limitations in this experiment that need improvement. For example, the results of ROC curve analysis need to be more accurate with large-data experimental sample analysis, but the number of patients included is small and needs further expansion. Moreover, the mechanism of PCT, SAA, presepsin and sepsis is ambiguous, so we need to conduct more in-depth experiments. However, different detection methods or kits may cause errors in the detection results of PCT, SAA and presepsin. We need to conduct more experiments to verify PCT, SAA and presepsin expression in sepsis.

To sum up, PCT, SAA and presepsin are elevated in sepsis, which has high evaluation value for disease occurrence and prognosis and has the potential to become good blood markers.

Disclosure of conflict of interest

None.

Address correspondence to: Qiuju Qiu, Department of Emergency, Affiliated Nanhua Hospital, University of South China, No. 336 Dongfeng South Road, Zhuhui District, Hengyang 421002, Hunan Province, China. Tel: +86-0734-8303797; E-mail: qiuqiuju918@163.com

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