THE PROGNOSTIC VALUE OF SERUM STREM-1 AND PCT COMBINED WITH PRO-ADM IN PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA

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ABSTRACT

Objective: To analyse the prognostic value of serum soluble myeloid cell trigger receptor-1 (sTREM-1), procalcitonin (PCT) and adrenal myelinogen (pro-ADM) in patients with ventilator-associated pneumonia.

Methods: From May 2017 to May 2019 96 patients undergoing mechanical ventilation in our intensive care unit (ICU) were selected to be the observation group This group was further divided into the group of patients who died within 28 days (45 cases) and those who survived beyond that time (51 cases). In addition, 40 patients without VAP who underwent mechanical ventilation in our hospital during the same period were selected as the control group. Data collected for all patients included age, gender, the APACHE II score, the pulmonary infection score, and the duration of mechanical ventilation. The changes of sTREM-1, PCT and pro-ADM levels in each group on day 1, day 3 and day 5 were compared. ROC curve analysis examined the prognostic value of sTREM-1, PCT and pro-ADM in VAP patients, and logistic regression analysis was used to analyse the risk factors for death within 28 days.

Results: In the group that died, the APACHE II score and CPIS score were significantly higher than in the survival group, and the difference was statistically significant (p<.01). For the patients who died, the levels of sTREM-1, PCT and pro-ADM after VAP diagnosis were significantly higher on day 1, day 3 and day 5 than the levels in the survival group, and the difference was statistically significant (p<.05). Over time, the levels of sTREM-1, PCT and pro-ADM in the survival group were significantly lower (p<.05), while the levels of sTREM-1, PCT and pro-ADM in the group that died were significantly higher (p<.05). ROC curve analysis showed that the area under the curve (AUC) of sTREM-1, PCT and pro-ADM was 0.845, 0.702, 0.756 and 0.915, respectively, for predicting the prognosis of VAP patients independently and in combination. The value of the three indicators combined in predicting the prognosis of VAP patients was significantly higher than that of the separate tests. Logistic regression analysis showed that the APACHE II rating, sTREM-1, PCT, pro-ADM are independent risk factors for the development of patients who die within 28 days (p<.05).

Conclusion: Serum sTREM-1 and PCT combined with pro-ADM have clinical value in predicting the condition of patients with ventilator-associated pneumonia, and all three indicators are independent risk factors for death within 28 days.

Keywords: Serum sTREM-1, PCT, pro-ADM, ventilator-associated pneumonia, prognosis.

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Introduction

Ventilator-associated pneumonia (VAP) is a common and serious complication of mechanical ventilation. It refers to pulmonary parenchymal infection after 48 h of mechanical ventilation by tracheotomy or endotracheal intubation, and it is an important type of hospital-acquired pneumonia[1]. VAP can be divided into an early type (mechanical ventilation time between 48 h and 5 days) and a late type (mechanical ventilation time ≥5 days). Once VAP occurs in patients, it can be difficult to wean, significantly increases hospitalization time and mortality of patients, and creates serious economic burdens to patients' families. Therefore, it is of great significance to find sensitive laboratory indicators to accurately evaluate the condition of VAP patients and to identify different measures for intervention to reduce the morbidity and mortality of VAP patients. Studies have found that soluble triggering receptor 1

expressed on myeloid cell1 (sTREM-1) belonging to the immunoglobulin superfamily member can help the diagnosis and prognosis of infectious diseases such as lung infection assessment[2, 3]. Procalcitonin (PCT) is often used to evaluate the severity of the disease and diagnose the body's inflammatory response in clinics, and its effect is better than other laboratory indicators[4]. Proadrenaline (pro-ADM), an inflammatory indicator commonly used in clinics to predict pulmonary infection, has been found in recent years to have anti-infection and inflammatory regulation effects[5]. The purpose of this study is to analyse the value of serum sTREM-1 and PCT combined with pro-ADM in predicting the condition of patients with ventilator-associated pneumonia.

Materials and methods

Research objects

A total of 96 patients admitted to the intensive care unit (ICU) of our hospital from May 2017 to May 2019 for mechanical ventilation treatment were selected as the observation group. This study was approved by the hospital ethics committee.

Inclusion criteria were:
• Patients met the diagnostic criteria of VAP formulated by the Chinese society of critical care medicine;
• Age >18 years;
• Mechanical ventilation treatment time ≥48 h;
• No clinical symptoms or signs such as pulmonary infection occurred during the treatment;
• Complete clinical data;
• The patients and their families were informed and signed the consent form.

Exclusion criteria were:
• Pulmonary infection and VAP before ICU admission;
• Complicated with other organ or tissue infection responders;
• Infection with other pathogens;
• Lung cancer or other malignant tumour diseases;
• Pregnant and nursing women;
• Admitted in very serious condition (the patient died within 3 days).

The patients were divided into two groups, those who died within 28 days (45 cases) and those who survived beyond that time (51 cases). In addition, 40 patients without VAP who underwent mechanical ventilation in our hospital during the same period were selected as the control group.

VAP diagnostic criteria

The following diagnostic criteria were formulated by the Chinese society of critical care medicine[6]: pneumonia occurred after 48 h of mechanical ventilation after tracheotomy or endotracheal intubation, including 48 h after removal of the tube, and at least two of the following conditions were met simultaneously: body temperature was below 36ºC or above 38oC; white blood cell count in peripheral blood was <4 × 109/L or >10 × 109/L[3] purulent secretion appeared in the bronchus of the patient's organs.

Observation indicators

For patients who met the diagnostic and treatment guidelines for the treatment of VAP, the following data were collected: age, gender, the Acute Physiology and Chronic Health Evaluation II (APACHE II) grade, Clinical pulmonary infection score (CPIS), and length of mechanical ventilation.

For each patient, 5 ml of fasting venous blood was collected on the morning of day 1, day 3 and day 5 and held at room temperature for 30 min. After centrifugation at 3000 r/min for 10 min, the changes in sTREM-1 and PCT levels in the supernatant were detected by Enzyme-linked immunosorbent assay (ELISA), and the changes in pro-ADM levels were detected by a double-antibody sandwich assay. The sTREM-1 and PCT kits were purchased from Rapid-bio, and pro-ADM kits were purchased from Huamei Biological Engineering Co., LTD.

Statistical methods

This study measured data in the following ways ($\bar{x} \pm s$): t-test to compare groups of data; all counts used [n] and (%); χ^2 test to compare groups; ROC curve analysis of the value of sTREM-1, PCT, and pro-ADM in patients with VAP to predict the condition of patients with VAP; and logistic regression analysis of factors influencing the patients at risk of death within 28 d, p<.05 as statistically significant. This research used SPSS 21.0 software for analysis.

Results

Comparison of general data of patients in each group

There were no statistically significant differences in the general data of age, gender, mechanical ventilation duration, etc. (p>.05). The APACHE II scores and CPIS scores were significantly higher in

the patients who died than in the survival group, and the difference was statistically significant (p < .01). See Table 1

	Observation group (n = 96)		Control (n = 40)	χ²/F	p
	Survived (n = 51)	Died (n = 45)			
M/F	29/22	25/20	22/18	0.035	.982
Age	51.12±8.06	50.68±7.13	51.23±8.75	0.06	.943
APACHE II score	18.33±5.14	24.55±5.42	18.11±5.46	21.18	< .001
CPIS score	3.79±1.16	6.85±1.26	3.78±1.33	91.22	< .001
Mechanical ventilation time	13.22±3.75	12.63±3.41	13.26±4.02	0.46	.635

Table 1: Comparison of general data of patients in each group.

Comparison of sTREM-1, PCT and pro-ADM levels between the survival group and the group that died

For patients who died, the levels of sTREM-1, PCT and pro-ADM on day 1, day 3 and day 5 after VAP diagnosis were significantly higher than those in the survival group, and the difference was statistically significant (p<.05).

Over time, the levels of sTREM-1, PCT and pro-ADM in the survival group were significantly lower (p<.05), while the levels of sTREM-1, PCT and pro-ADM in the group that died were significantly higher (p<.05). See Table 2.

Group	Index	1d	3d	5 days
Survival	sTREM-1 (pg/mL)	54.10±11.68	50.36±10.45	43.26±10.75
	PCT (ng/mL)	3.16±0.42	2.88±0.35	2.16±0.28
	pro-ADM (nmol/L)	3.20±1.12	2.99±1.24	1.64±0.77
Death	sTREM-1 (pg/mL)	89.49±17.34*	95.26±16.32*	99.36±16.32*
	PCT (ng/mL)	4.80±0.56*	5.43±0.63*	6.40±0.73*
	pro-ADM (nmol/L)	4.18±1.67*	4.55±1.62*	5.14±1.79*

Table 2: Comparison of sTREM-1, PCT and pro-ADM levels between the survival group and the group that died. *Note. Comparison with the survival group at each time point p<.05.*
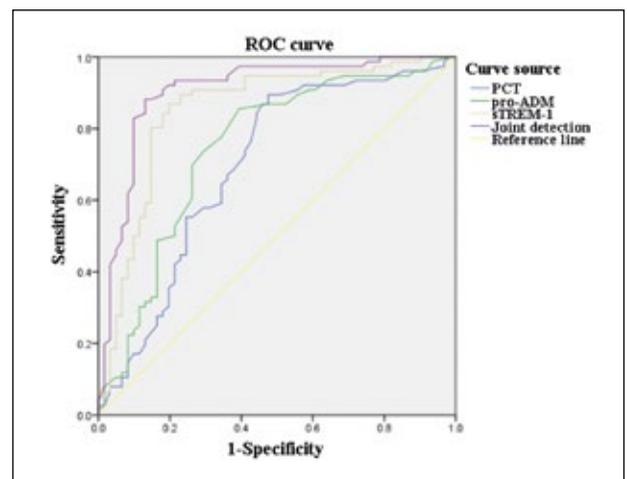
ROC curve analysis of the prognostic value of sTREM-1, PCT and pro-ADM in patients with VAP

ROC curve analysis showed that the AUC of sTREM-1, PCT, and pro-ADM were 0.845, 0.702, 0.756, and 0.915, respectively; sensitivity was 82.38%, 88.24%, 82.02%, 89.49%, respectively

and specificity was 79.30%, 47.69%, 60.75%, and 82.88%, respectively. The value of three indicators combined to predict the condition of VAP patients was significantly better than that of each test separately. See Table 3.

Index	AUC	95% CI	p	Cut-off point	Sensitivity	specificity
sTREM-1	0.845	0.751~0.958	.039	75.00 pg/mL	82.38%	79.30%
PCT	0.702	0.626~0.798	.014	4.82 ng/mL	88.24%	47.69%
pro-ADM	0.756	0.701~0.862	.003	4.23 nmol/L	82.02%	60.75%
Joint detection	0.915	0.851~0.960	.003	-	89.49%	82.88%

Table 3: ROC Curve analysis of the prognostic value of sTREM-1, PCT and pro-ADM in patients with VAP.

Figure 1: ROC curve analysis of the prognostic value of sTREM-1, PCT and pro-ADM in patients with VAP.

Logistic regression analysis of risk factors influencing death within 28 days

Logistic regression analysis showed that the APACHE II rating, sTREM-1, PCT, and pro-ADM are independent risk factors for the development of patients die within 28 d (p<.05). Shown in table 4.

Index	B value	Wald value	OR value	95% CI	p
APACHE II score	0.332	11.656	1.403	1.152~1.678	<.001
CPIS score	1.465	1.302	0.867	0.672~1.113	.265
Mechanical ventilation time	1.203	1.245	3.337	0.402~27.852	.282
sTREM-1	0.085	12.903	1.074	1.033~1.126	<.001
PCT	0.004	0.049	1.003	0.978~1.065	.002
pro-ADM	0.752	1.364	1.342	0.856~1.563	.005

Table 4: Logistic regression analysis of risk factors influencing mortality within 28 days.

Discussion

VAP is a complication of mechanical ventilation infection with a high incidence in ICUs. The artificial airway can destroy normal respiratory defence mechanisms. Protease released by white blood cells destroys the protective fibronectin layer of the airways, exposing receptors on the surface of epithelial cells, and bacteria are easily adsorbed by epithelial cells[7]. During mechanical ventilation, endotracheal intubation can directly injure the pharynx and larynx, destroy the natural defence function of the airway, and inhibit the cough mechanism, causing lower respiratory tract infection.

In addition, the reflux of oropharyngeal colonizing bacteria mistakenly inhaled in the lung, stomach- and duodenum-colonizing bacteria, pulmonary inhalation, and exogenous bacterial infection are all important factors for the occurrence of VAP[8].

Epidemiological investigations showed that the incidence of VAP was 4.7% ~ 55.8% and the mortality rate was 19.4% ~ 51.6%[9]. In recent years, with the promotion of preventive measures in the VAP population, the incidence of VAP has been controlled to a certain extent. However, the mortality of patients is still high, which significantly prolongs the mechanical ventilation of patients and their treatment time in the ICU, increasing the family and social and economic burden. At present, the clinical diagnosis of VAP patients mainly relies on clinical symptoms, signs and pulmonary imaging examination. Although these methods have high sensitivity, they have low specificity. Therefore, it is of great significance for clinical treatment of VAP to find early indicators to evaluate the prognosis of patients.

TREM-1, a member of the immunoglobulin superfamily, is selectively expressed on the surface of neutrophils and mononuclear macrophages in the form of transmembrane glycoproteins. sTREM-1 is a secreted subtype of TREM-1, which can largely synthesize inflammatory factors in the early stage of infection and release them into the blood. The role of airway expansion in the inflammatory response is often used as a reliable indicator for early diagnosis and evaluation of infectious diseases[10]. Some scholars have found that the sensitivity and specificity of serum sTREM-1 in patients with VAP on the 3rd day of mechanical ventilation were 95.68% and 92.33%, respectively, but its value in determining the prognosis of patients still needs further discussion[11]. PCT is a glycoprotein molecule which the body produces in response to serious infection and systemic inflammation or when the immune system functions poorly or patients are in a state of immunosuppression. The synthesis of bacterial endotoxin can stimulate and release a large number of liver cells, so the expression level of serum PCT will rise rapidly. This is positively correlated with the severity of the inflammation, so it is the indicator commonly used to monitor the body's inflammatory response sensitivity index[12, 13]. ADM is a vasoactive peptide with a wide range of biological functions, including vasodilating, lowering blood pressure and inhibiting the production of vascular smooth muscle endothelin. As a precursor of ADM, pro-ADM has been proven to be more stable than ADM, and it has a long half-life. It can directly reflect the rapidly degraded ADM level in vivo[14]. Relevant data show that pro-ADM has certain clinical value in the prognosis of pulmonary infection, sepsis and other diseases, and it can also be used as a biomarker for the severity of bacterial infectious diseases[15].

By observing the dynamic change rules of the survival group and the group that died, this study found that the sTREM-1, PCT, and pro-ADM levels were significantly higher on day 1, day 3, and day 5 in the group that died than in the survival group (p<.05). In addition, the levels of sTREM-1, PCT and pro-ADM in the survival group decreased with time (p < .05), but for the group that died all three indexes trended significantly higher (p<.05). This suggests that dynamic monitoring of three indicator levels can be helpful in evaluating the efficacy of VAP treatment. Moreover, ROC curve analysis showed that sTREM-1, PCT and pro-ADM combined could be used as specific indicators to predict the condition of VAP patients.

In conclusion, serum sTREM-1 and PCT combined with pro-ADM have certain clinical value in predicting the condition of patients with ventilator-related pneumonia, and all three indicators are independent risk factors for death within 28 days.

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