Scientific Research Publishing

Case Reports in Clinical Medicine, 2020, 9, 228-235
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

The Prediction Value of the Infection Probability Score (IPS) Combined with Serum Cholinesterase and D-Dimer Detection for Infection and Survival in Critically Ill Patients

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How to cite this paper: Zhao, Q., Qi, H.J., Guo, H., Shen, Z.S. and Li, J.G. (2020) The Prediction Value of the Infection Probability Score (IPS) Combined with Serum Cholinesterase and D-Dimer Detection for Infection and Survival in Critically Ill Patients. *Case Reports in Clinical Medicine*, **9**, 228-235.
https://doi.org/10.4236/crcm.2020.98032

Received: July 27, 2020
Accepted: August 17, 2020
Published: August 20, 2020

Abstract

Objective: To evaluate early prediction value of IPS combined with SchE and D-dimer detection for infection and survival in critically ill patients. **Methods:** 199 critically ill patients admitted to the emergency intensive care unit (EICU) of our hospital from December 2018 to December 2019 were retrospectively analyzed, including 110 infection patients (infection group) and 89 non-infection patients (non-infection group). According to the survival, the infection group was divided into death group (68 cases) and survival group (42 cases). The IPS, APACHE II, SOFA and SchE, D-dimer expression levels were detected and compared; Univariate and logistic regression analysis were used to evaluate the independent prognostic factors. **Results:** The IPS and APACHE II of patients in the infected group were higher than those in the non-infected group, the level of SchE was lower than that in the non-infected group, and the level of D-dimer was higher than that in the non-infected group ($P < 0.001$). IPS, SOFA, APACHE II, SchE, D-dimer, invasive mechanical ventilation, septic shock, and ICU length of stay had significant influence on the prognosis of critically ill patients ($P < 0.001$). Logistic regression analysis showed that IPS (*OR* = 2.821, 95% *CI* 1.501 - 5.227), SOFA (*OR* = 5.078, 95% *CI* 3.327 - 7.690), APACHE II (*OR* = 14.308, 95% *CI* 8.901 - 21.893), SchE (*OR* = 0.223, 95% *CI* 0.165 - 0.291), D-dimer (*OR* = 2.10, 95% *CI* 1.55 - 2.85), septic shock (*OR* = 9.948, 95% *CI* 7.012 - 17.012) were independent factors affecting the prognosis of critically ill patients with infection ($P < 0.001$). **Conclusion:** IPS and D-dimer expression level in infected patients were increased and SchE decreased significantly compared with those in non-infected patients, and they significantly correlated with disease severity of infected patients and could be early prediction for prognosis.

Keywords

Critical Illness, Infection, Infection Probability Score (IPS), Cholinesterase, D-Dimer, Survival Prognosis

1. Background

Critically ill infection has no strong clinical characteristics at the initial stage of the disease, but the disease develops rapidly and has a very high fatality rate [1]. Therefore, early and accurate disease diagnosis and prognosis prediction are the key to the prevention and treatment. However, the bacterial detection commonly used in clinical practice is limited due to its long detection time and poor sensitivity and specificity [2]. Sequential Organ Failure Assessment (SOFA) is a common organ failure score [3], Acute Physiology and Chronic Health Evaluation II (APACHE II) for critical disease diagnosis are significance; Infection probability Score (IPS) [4] is a quantitative measure of the likelihood of infection, However, the relationship between the level of infection and the other two scoring systems is not clear [5]. Serum cholinesterase (SchE), as a factor involved in acetylcholine degradation has been confirmed to be closely correlated with its expression level in infectious diseases [6]. D-dimer is an ideal indicator for reaction of thrombin and plasmin production [7]. Relevant scholars have pointed out that D-dimer can be used as relevant indicators to predict the prognosis of sepsis, but there is still controversy at present. In this study, IPS, SchE and D-dimer expression levels of critically ill patients were observed to explore the correlation between the indicators and severe infections, and to provide reference significance for the prediction of diagnosis and prognosis incritically ill infection.

2. Materials and Methods

2.1. Case Data

The clinical data of 202 critically ill patients admitted to the EICU of our hospital from December 2018 to December 2019 were retrospectively analyzed, among which 3 cases were incomplete and 199 cases were included. Including 110 infected critically ill patients (infected group) and 89 non-infected critically ill patients (non-infected group); According to the survival prognosis of the infected group, it was divided into 68 cases in the death group and 42 cases in the survival group. The 199 patients included 109 males and 90 females. All patients signed informed consent forms, and this study was approved by the Ethics Committee of our hospital.

Inclusion criteria: All patients were critically ill , and patients in the infected group met at least two of the following diagnostic criteria for infection [2]: 1) Positive results of blood culture or sputum culture; 2) Imaging examination results showed that the lungs and other organs were infected; 3) White blood cell

count should not be lower than 12 × 10^9/L; 4) Significant effect of antibiotic treatment; 5) Symptoms of fever with body temperature over 38˚C; 6) Presence of infectious lesions; Complete clinical data of all patients; Age ≥18 years old; all signed informed consent.

Exclusion criteria: 1) patients with severe mental illness or malignant tumor; Serious heart, liver, lung, renal insufficiency or accompanied by metabolic diseases; Serious diseases of the blood system; those who had taken immune preparations in the past half year; the duration of ICU stay was less than 24 hours.

2.2. Clinical Data Collection

Comprehensive clinical data to collect all the object of study, including gender, age, BMI, IPS [3], APACHE II, and SOFA information. IPS scale assessment within 24 h after diagnosis of critically ill patients, and at the same time detected, and recorded the patient's basic vital signs such as blood pressure, heart rate, etc and then calculated the SOFA.

2.3. Determination of SchE and D-Dimer

5 mL peripheral venous blood was extracted from all patients on the first day of hospitalization, and centrifuged at 3500 r/min for 15 min (centrifugation radius was 10 cm) immediately. The supernatant was separated and stored in a refrigerator at −30˚C. Colloidal gold method was adopted [8].

D-dimer: 5 ml of the patient's venous blood was extracted after admission, and D-dimer was determined by immunoturbidimetry. The kit adopted the Strumentation Labora-Tory Co., and strictly implemented the use standard on the kit. The normal value was less than 0.3 ng/ml.

2.4. Statistical Analysis

SPSS 19.0 software was used for statistical analysis. The measurement data consistent with normal distribution were represented by $\bar{x} \pm s$, and the comparison between groups was performed by independent sample T test. The count data were represented by percentage, and the comparison between groups was performed by χ^2 test. Measurement data that do not conform to normal distribution were represented by median (quartile) [M (QL, QU)]; Univariate analysis and non-conditional Logistic regression multivariate analysis were performed on factors affecting survival, and $P < 0.05$ indicated statistically significant differences.

3. Results

3.1. Comparison of Baseline Data between the Infected and Non-Infected Groups (Table 1)

There was no significant difference in general information such asgender, age, body mass index (BMI) between the infected group and the non-infected group ($P > 0.05$) (**Table 1**).

3.2. Comparison of Scores of IPS, SOFA, APACHE II and Levels of SchE, D-Dimer Expression between Non-Infected Group and Infected Groups

Score of IPS and APACHE II in the infected group was higher than that in the non-infected group ($P < 0.001$), but there was no significant difference in the SOFA score. ($P > 0.05$).The SchE expression level of the infected group was lower than that of the non-infected group, and the expression level of D-dimer (OR = 2.10, 95% CI 1.55 - 2.85) was higher than that of the non-infected group ($P < 0.001$) (Table 2).

3.3. Analysis of Factors Affecting the Prognosis of Patients in the Infection Group

The results of univariate analysis showed that the IPS, SOFA, APACHE II, SchE, D-dimer, whether there is invasive mechanical ventilation, septic shock and length of stay in ICU will have a significant impact on the prognosis of critically ill patients ($P < 0.001$) (Table 3).

3.4. Logistic Regression Analysis of Factors Affecting the Prognosis of Critically Ill Patients with Infection

Logistic regression analysis had been performed, with patient prognosis (survival = 0, death = 1) as the dependent variable, and the statistically significant factors in Table 4 for the prognosis of critically ill infected patients as the independent variable. The independent variable was assigned as: Invasive mechanical ventilation (Yes = 1, No = 0), septic shock occurred (Yes = 1, No = 0), other continuous variables were analyzed with actual values, the results showed: IPS (OR = 2.821, 95% CI 1.501 ~ 5.227), SOFA (OR = 5.078, 95% CI 3.327 ~ 7.690), APACHE II

Table 1. Comparison of baseline data between the infected and non-infected groups.

Group	Cases	Age (year)	Gender (M/F)	BMI (kg/m^2)
Infected	110	69.65 ± 8.43	67/43	22.74 ± 3.82
Non-infected	89	68.95 ± 7.91	42/47	23.36 ± 3.76
t/χ^2	-	0.939	0.978	1.508
P	-	0.346	0.345	0.151

Table 2. Comparison of IPS, SOFA, APACHE II score, SchE and D-dimer expression levels between non-infected and infected groups.

Group	Cases	IPS score	SOFA score	APACHE II score	SchE (U/L)	D-dimer (mg/ml)
Infected	110	17.76 ± 3.56	10.26 ± 3.41	23.20 ± 4.49	3629.62 ± 298.59	4.06 ± 1.81
Non-infected	89	12.52 ± 4.38	9.79 ± 2.40	17.29 ± 4.13	5304.89 ± 412.67	1.07 ± 0.39
t	-	8.734	1.702	8.708	30.418	56.060
P	-	<0.001	0.093	<0.001	<0.001	<0.001

Table 3. Analysis of factors affecting the prognosis of patients in the infection group.

Factor	Death group (n = 68)	Survival group (n = 42)	t/χ^2	*P*
Sex (M/F)	46/22	29/13	0.306	0.608
Age (year)	69.35 ± 8.61	69.95 ± 9.11	1.109	0.302
BMI (kg/m^2)	22.46 ± 3.52	22.82 ± 3.56	0.644	0.509
IPS	21.75 ± 3.75	15.61 ± 3.34	9.057	<0.001
SOFA	12.73 ± 3.47	9.24 ± 2.77	5.627	<0.001
APACHE II	26.78 ± 4.67	21.51 ± 4.31	5.802	<0.001
SchE (U/L)	3220.25 ± 306.41	3827.52 ± 279.45	9.213	<0.001
D-dimer (mg/ml)	5.06 ± 1.29	1.10 ± 0.41	19.164	<0.001
Mechanical ventilation (Y/N)	68/0	29/11	10.172	0.001
Septic shock (Y/N)	55/13	5/37	6.213	0.025
ICU admission [d, M (Q_L, Q_U)]	4.30 (1.012, 14.102)	7.13 (244, 11.123)	2.478	0.032

Table 4. Logistic regression analysis of factors affecting the prognosis of critically ill patients.

Variable	β	*S.E.*	*Wald* χ^2	*P*	*OR*	95% *CI*
IPS	1.036	0.325	10.161	0.001	2.821	1.501 ~ 5.227
SOFA	1.625	0.215	57.125	0.000	5.078	3.327 ~ 7.690
APACHE II	2.658	0.241	121.640	0.000	14.308	8.901 ~ 21.893
SchE	-1.526	0.145	110.757	0.000	0.223	0.165 ~ 0.291
D-dimer (mg/ml)	0.743	0.156	3.851	0.000	2.10	1.55 ~ 2.85
septic shock	2.365	0.219	116.620	0.000	9.948	7.012 ~ 17.012

(OR = 14.308, 95% CI 8.901 ~ 21.893), SchE (OR = 0.223, 95% CI 0.165 ~ 0.291), D-dimer (OR = 2.10, 95% CI 1.55 ~ 2.85), septic shock (OR = 9.948, 95% CI 7.012 ~ 17.012), are independent factors affecting the prognosis of critically ill patients ($P < 0.001$) (Table 4).

4. Discussion

The pathogenesis of critical illness infection in ICU may be related to the serious disorder of physiological function and the invasion of pathogens caused by the decline of immune function. Previous studies have confirmed that APACHE II, SOFA and IPS are important diagnostic parameters for infectious diseases, but their diagnostic value in critical infectious diseases has not yet a very clear conclusion [1]. SOFA is a common organ failure score, which can dynamically evaluates the prognosis of patients with multiple organ failure based on the changes in 12 indicators of 6 organs [3]. APACHE II for critical disease diagnosis are

significance, mainly including acute physiology score, chronic health evaluation score and age score, etc; IPS is a quantitative measure of the likelihood of infection [4], Based on large sample research, American scholars proposed that IPS could be used as an infection prediction parameter, which is a comprehensive manifestation of patients' white blood cell count, body temperature, heart rate and respiration, etc. and All can be used for the initial health status assessment of infected patients [4]. and which relationship to infection levels has important diagnostic value for severe diseases.

The results of this study showed that scores of the IPS and APACHE II of the infected group were higher than those of the non-infected group ($P < 0.001$), and the SOFA score of the infected group was higher than that of the non-infected group, but there was no significant difference ($P > 0.05$) (**Table 2**). In addition, in this study, the expression level of SchE in critically infected patients were lower than that in the non-infected group, and the expression level of D-dimer was higher than that in the non-infected group ($P < 0.001$) (**Table 3**). And we analyzed the factors affecting the prognosis of critically ill patients, the results showed that the IPS, SOFA, APACHE II, SchE, D-dimer were independent risk factors affecting the prognosis of critically illpatients with infection ($P < 0.001$) (**Table 4**).

The results of this study also suggested that SchE expression loss and D-dimer overexpression could promote the occurrence and development of infection in severe patients and had significant impact on the prognosis of patients. Based on previous studies, the authors concider that SchE expression loss may occur in critically infected patients through the following mechanisms: on one hand, there is an inflammatory response in critically infected patients, which will further induce the release of a large amount of acetylcholine, resulting in the consumption of SchE; On the other hand, severe lipoprotein metabolism disorders were observed in critically infected patients, which affected the transport capacity of SchE in circulating blood and finally showed SchE level decrease in peripheral blood [8] [9]. The research results of Chen Ruilin *et al.* [10] showed that the expression level of SchE in critically ill patients with pulmonary infection was 40% or more lower than that of non-infected patients, and the decrease of SchE level was more obvious in severe patients with septic shock or organ failure.

For acute sepsispatients, disseminated intravascular coagulation syndrome (DIC) is a manifestation of coagulation failure, and early diagnosis of this syndrome has become one of the problems that cannot be ignored [11] [12]. D-dimer is one of the most simple fibrin after activation and hydrolysis to produce a kind of degradation products, it mainly comes from the crosslinking fibrinolytic enzymes to dissolve fibrin clot, thus the formation of D-dimer or higher reaction in the body the activation of blood coagulation and fibrinolysis system and disease, its high sensitivity fibrinolysis function is important for reaction [13]. Using correlating analysis, Zhang *et al.* found that the cut-off

point is death and that the D-dimer's level to assess the patient's prognosis is moderate. The results of this study showed that the D-dimer level in patients with severe disease was higher than that in patients with mild disease, and the correlation between D-dimer content and the prognosis of patients with acute sepsis was positive, So D-dimer detection is of positive significance for patients with acute sepsis. In addition, other studies in China have reported that the mortality of critically ill patients with septic shock after infection could be as high as 60% above, septic shock was most serious stage of sepsis, which cells were already severe hypoxia condition and mitochondrial dysfunction, and it's existing blood flow could not effectively meet the needs of tissue metabolism, then the mortality rised sharply [14].

5. Conclusion

In conclusion, IPS and D-dimer expression level of critically ill infected patients were significantly higher than those of non-infected patients, and SchE level was significantly lower, which was significantly correlated with the severity of infection and prognosis, and was an independent risk factor affecting the prognosis of patients. Emphasis on the detection of SchE and D-dimer is important for early prediction for the prognosis of severinfectedpatients. However, since this study is a single-center retrospective study, the sample size is fair, and the influence of infection site and other factors on the prognosis of patients is not fully considered, which may lead to certain deviations in the results. Further multi-center prospective studies can be carried out in the later period to further verify the conclusions of this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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