Predictive Value of The Combined Detection of Platelets, D-Dimer, and Procalcitonin On Severe Heat Stroke

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Research

Keywords: TNI, PCT, MYO, heatstroke, ROC

Posted Date: June 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-618567/v1

Abstract

Background

To explore the clinical characteristics of patients with severe heat stroke, we explored the early sensitive indicators of heat stroke (HS) patients, with a view to early intervention for HS patients.

Methods

From July 30, 2015 to October 5, 2020, 70 inpatients with severe heat stroke admitted to the Second Affiliated Hospital of Nantong University, Jiangsu Province were selected as the research objects. The general information and clinical test indicators of the patients were recorded, and all patients were assessed for acute physiology (APACH) upon admission. According to the severity of heatstroke, they were divided into three groups: control group (heat cramps and heat exhaustion), EHS, and CHS to compare the differences in indicators of each group. Further draw the receiver operating characteristic curve (ROC).

Results

1. According to the severity of heat stroke, 28 cases were divided into the control group, 24 cases in the EHS group, and 18 cases in the CHS group. The body temperature of the EHS group and the CHS group was significantly higher than that of the control group (both P<0.05), but there was no statistical difference in the body temperature of the EHS group and the CHS group; the DD, PCT, and APACH of the EHS group were significantly higher than those of the control group and the CHS group (both P 0.05); PLT, CRP, Na, GLU of EHS group were lower than those of control group and CHS group (all P 0.05), and the decrease of PLT was more significant; CHS group HbA1C was significantly higher than that of control group and EHS group (all P <0.05).

2. ROC curve analysis the areas under the curves of DD, PCT, and PLT are 0.670, 0.705, 0.791, respectively, the sensitivity is 40.48%, 100%, 73.81%, and the specificity is 96.43%, 32.14%, 78.57%, respectively. Using the combined analysis of the three series tests, the area under the curve was 0.838, the sensitivity was 71.43%, and the specificity was 85.71%.

Conclusions

EHS patients have higher DD, PCT, APACH, but PLT, CRP, Na, and blood sugar are lower. At the same time, the significant decrease of PLT and the increase of PCT and DD may be early sensitive indicators of HS. The combined detection of the three can be used as a reference basis for early diagnosis of HS and critical illness.

Background

Heatstroke(HS) is a clinical syndrome in which the body is exposed to the thermal environment and/or strenuous exercise, which leads to the dysfunction of thermoregulation, which leads to the increase of core temperature and the potentially fatal disorder of the body. HS is a severe heat stroke, the core temperature of the body can rapidly rise to more than 40 ℃, accompanied by convulsions, delirium and coma and other central nervous system dysfunction [1–2]. According to the cause of the disease and the susceptible population, it can be divided into exertional heat radiation disease and classical heat radiation disease. There is no unified standard for the diagnosis of HS in the world [3], and there may be great individual differences in clinical manifestations. It is

often mixed with the manifestations of underlying diseases, which can easily lead to misdiagnosis. In addition, disturbance of consciousness in patients with HS is often complicated by craniocerebral trauma or aspiration, which makes the clinical manifestation and diagnosis more complicated. At present, with the normalization of the prevention and control of COVID-19 's epidemic situation, the General Office of the State Health Commission issued a notice on preventing and cooling Heat in 2020, requiring all localities to pay full attention to the health hazards of high temperature heatstroke and effectively avoid the occurrence of heatstroke. Therefore, the biomarkers that predict the occurrence and development of HS will help to quickly identify HS, and is of great significance to find effective brain protection therapy.

Methods

General information

A retrospective study was conducted to collect the clinical data of 70 adult inpatients diagnosed as severe heatstroke from July 30, 2015 to October 5, 2020 in the second affiliated Hospital of Nantong University in Jiangsu Province. This study has been reviewed by the Ethics Committee of the Second Affiliated Hospital of Nantong University (2015KT007).

All the patients met the "Diagnostic criteria of Occupational heatstroke" issued by the former Ministry of Health of the people's Republic of China [4]. The diagnosis of EHS and CHS refers to the "consensus of experts in the diagnosis and treatment of heat radiation disease in China" issued by the military critical Medicine Committee [5]. Informed consent forms were signed for all the tests and treatments in this study.

Data collection and grouping

Record the time of onset and hospitalization of patients. Maximum body temperature (T max), leukocyte (WBC), neutrophil (N), hemoglobin (HB), platelet (PLT), procalcitonin (PCT), erythrocyte sedimentation rate (ESR), blood lactate (LAC), hypersensitive C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea nitrogen (BUN), creatinine (SCR), venous blood glucose (GLU), glycosylated hemoglobin (HbA1C), Arterial blood gas analysis PH, actual bicarbonate (AB), serum potassium (K), serum sodium (Na), serum chloride (Cl), troponin (TNI), myoglobin (MYO), creatine kinase isoenzyme (CKMB), B-type brain natriuretic peptide (BNP), D-dimer (DD). Among them, PCT, TNI, MYO, CKMB, BNP and DD were tested by rapid bedside (POCT) [Shanghai Redumite Medical equipment Co., Ltd., time-resolved fluorescence immunoassay, reference range: PCT (0.072-0.94ng/L, TNI (0.010-0.023ng/L), MYO (23-112ng/L), CKMB (2.0-7.2ng/ml), BNP (300-450ng/L), DD (260ng/ml)]. All patients were assessed with acute physiology score (APACH) on admission.

According to the severity of heatstroke, the patients were divided into three groups: control group (heat spasm and heat exhaustion), EHS and CHS.

Statistical analysis

SPSS 21.0 software was used for data processing and analysis. The measurement data were expressed by mean ± standard deviation(± S) in accordance with normal distribution such as age, body temperature, WBC, N and Hb, and by median and quartile interval (median [IQR]) in accordance with skewness distribution such as onset time, DD and hospitalization days, and the counting data were compared by χ 2 test. Draw the working characteristic

curve of the subjects and analyze the significance of PLT, PCT and DD in the early diagnosis of HS by (ROC). The difference was statistically significant ($P < 0.05$).

Results

General result

Among the 70 patients with severe heatstroke, there were 46 males (65.7%) and 24 females (34.3%), aged from 22 to 96 years old, with an average age of (65.72 ± 16.64) years. The length of hospital stay was 15.58 ± 14.49 days, the highest body temperature was 39.66 ± 1.08 ℃, 9 cases died and 61 cases improved. Among them, 13 cases were admitted to ICU, 22 cases were treated by mechanical ventilation, 1 case was treated with blood purification, 20 cases were treated with vasoactive drugs, and 35 cases were complicated with more than one basic disease (20 cases of hypertension, 12 cases of diabetes, 3 cases of coronary heart disease, atrial fibrillation, 3 cases of uremia and 1 case of chronic obstructive pulmonary disease).

Comparison of clinical data of patients with heat stroke

70 patients were divided into three groups: 28 cases of heat cramps and heat exhaustion (control group), 24 cases of EHS group, and 18 cases of CHS group. The body temperature of the EHS group and the CHS group was significantly higher than that of the control group (both $P < 0.05$), but the body temperature of the EHS group and the CHS group were not statistically different; the DD, PCT, and APACH of the EHS group were significantly higher than those of the control group and the CHS group (both $P<0.05$); PLT, CRP, Na, GLU of EHS group were lower than those of control group and CHS group (all $P<0.05$), and the decrease of PLT was more significant; CHS group HbA1C was significantly higher than that of control group and EHS group (all $P < 0.05$).

None in each group in terms of age, gender, publication time, days of hospitalization, and PH, AB, BNP, ALT, AST, WBC, N, HB, ESR, LAC, SPO2, K, Cl, TNI, MYO, CKMB, BNP, BUN Statistical significance (all $P > 0.05$). Table 1

Table 1
Comparison of clinical data of three groups of patients

Factors	Control group	EHS	CHS	F/Z	P
N	28	24	18	-	-
Age (years)	66.89 ± 14.83	64.08 ± 21.46	66.11 ± 12.68	0.183	0.833
Gender(male/female)	20/8	16/8	10/8	1.240	0.538
Time of onset(h)	22(40)	24(36)	23(42)	0.796	0.672
Hospitalization days(d)	13.57 ± 9.41	15.46 ± 17.82	18.83 ± 16.62	0.707	0.497
T max(℃)	38.73 ± 0.49	40.71 ± 0.58 [a]	40.64 ± 0.69 [a]	97.020	0.00
DD(ug/mL)	1880.00(3365.25)	10946.00(11265.00)[a]	2110.00(3497.50)[b]	10.160	0.006
WBC(*109/L)	11.66 ± 5.38	9.16 ± 3.46	10.80 ± 4.12	2.026	0.14
N(*109/L)	8.94 ± 3.23	7.34 ± 2.33	9.53 ± 3.81b	2.897	0.62
HB (g/L)	127.21 ± 24.77	123.83 ± 18.20	122.94 ± 14.16	0.299	0.743
PCT(ng/L)	1.79(9.81)	21.98(57.97)[a]	2.88(8.28)[b]	15.204	0.000
PLT(*109/L)	113(74.75)	40(16)[a]	100.5(91.5)[b]	35.515	0.000
ESR(mm)	13(24.75)	23(20)	18(22.75)	2.834	0.242
CRP(mg/L)	39.98(130.6)	13(13.56)[a]	38.84(78.96)[b]	7.927	0.019
PH	7.41 ± 0.06	7.39 ± 0.09	7.40 ± 0.86	0.190	0.827
LAC(mmol/L)	3.41 ± 1.45	2.88 ± 1.45	2.88 ± 0.99	1.319	0.274
SPO2(%)	93.74 ± 4.36	95.57 ± 3.98	93.78 ± 5.81	0.946	0.393
K (mmol/L)	4.1(0.93)	3.56(1.4)	3.7(0.74)	1.685	0.431
Na(mmol/L)	139.31 ± 8.13	128.77 ± 28.33[a]	140.97 ± 5.86 [b]	3.227	0.046
Cl (mmol/L)	104.99 ± 8.52	97.86 ± 22.35	103.78 ± 6.65	1.674	0.195
AB(mmol/L)	20.31 ± 4.08	22.78 ± 4.50	22.02 ± 3.91	2.376	0.101
GLU(mmol/L)	7.166(3.82)	5.95(1.95)[a]	7.45(5.68)[b]	6.3	0.043
HbA1C(%)	5.85 ± 0.74	5.62 ± 0.67	7.09 ± 2.04 [ab]	8.701	0.000
TNI(ng/ml)	0.120(0.9)	0.145(1.3)	0.125(0.6)	2.015	0.365
Myo(ng/ml)	341(653.75)	677(860.88)	469(715.93)	1.897	0.387
CKMB(ng/ml)	25.5(38.25)	48(40)	29.5(38.65)	2.435	0.296
BNP(ng/L)	1055.2(1252.55)	975.1(3187)	453.5(1275.58)	1.192	0.551

Factors	Control group	EHS	CHS	F/Z	P
ALT(U/L)	41.5(41)	34(49)	52.5(94.25)	4.159	0.125
AST(U/L)	50.5(52)	69(101)	76(63.5)	2.449	0.294
SCR(mmol/L)	86(73.25)	81(93)	80.5(51.75)	0.783	0.676
BUN(mmol/L)	8.11(5.22)	6.53(4.73)	7.85(8.73)	0.512	0.774
APACH	16.25 ± 6.94	14.13 ± 5.55	21.83 ± 9.54 [ab]	5.973	0.004

Compared with the control group, a $P<0.05$; compared with the EHS group, b $P<0.05$.

The predictive value of clinical related indicators for the early diagnosis and treatment of severe heat stroke

Comparing the above three groups of patients with statistically different factors, the ROC curve was performed. Comparing the clinical related indicators of patients with different degrees of heatstroke, CRP and APACH have higher sensitivity, 95.24% and 85.71%, respectively, but the specificity is low; Na, GLU, HbA1C% have high specificity, respectively 89.29%, 85.71%, 82.14%, but the sensitivity is low. ROC curve analysis DD, PCT, PLT area under the curve (AUC) were 0.670, 0.705, 0.791, respectively, the sensitivity was 40.48%, 100%, 73.81%, and the specificity was 96.43%, 32.14%, 78.57%, respectively. Using the combined analysis of the three series tests, the AUC was 0.838, the sensitivity was 71.43%, and the specificity was 85.71%. The three tests further increase the Youden index. (Table 2, Fig. 1).

Table 2
Predictive value of clinical related indicators for early diagnosis and treatment of severe heat stroke

Factors	Sensitivity	Specificity	Youden Index	AUC	95%CI
T max(℃)	100	100	1	1	0.949-1.000
CRP(mg/L)	95.24	32.14	0.2738	0.588	0.464–0.704
Na(mmol/L)	26.19	89.29	0.1548	0.578	0.454–0.695
GLU(mmol/L)	40.48	85.71	0.2619	0.597	0.472–0.712
HbA1C(%)	35.71	82.14	0.1786	0.541	0.418–0.661
APACH	85.71	0	0.1429	0.512	0.390–0.634
DD(ug/mL)	40.48	96.43	0.3690	0.670	0.547–0.777
PCT(ng/L)	100	32.14	0.3214	0.705	0.584–0.808
PLT(*109/L)	73.81	78.57	0.5238	0.791	0.677–0.879
DD%PCT&PLT	71.43	85.71	0.5714	0.838	0.731–0.916

Discussion

An incomplete epidemiological survey showed that during the summer heat wave abroad, the incidence of HS was 17.6–26.5 per 100,000 people, the hospital mortality rate was 14%-65%, and the ICU patient mortality rate was > 60% [5]. At present, the exact pathogenesis of severe heat stroke-related multiple organ dysfunction is not fully understood [8, 9], including the direct cytotoxic effects of high temperature and activation of sepsis-like inflammation cascades. Severe heat stroke damages the function of multiple organs throughout the body. The clinical manifestations mainly include: central nervous system damage (consciousness, mental disorders, cerebral edema, seizures, etc.), coagulation disorders (diffuse intravascular coagulation, prolonged coagulation time), liver and kidney Dysfunction, rhabdomyolysis, respiratory failure and cardiovascular complications (arrhythmia, hypovolemic shock) cause changes in the corresponding system detection indicators [10]. The severity of organ tissue damage is directly proportional to the prognosis [11]. At present, there is no unified standard for the diagnostic indicators of HS, and there is no specific method for evaluating the prognosis of HS. Leon LR [12] and others believe that a single systematic research indicator or score does not fully evaluate the interaction between multiple factors, and the prognosis of heat stroke is not Completely reliable. We analyzed more than two thousand data collected from 70 critically ill hospitalized patients. According to the severity of heatstroke, the patients were divided into three groups: control group (heat cramps and heat exhaustion), EHS, and CHS to compare the differences of indicators in each group. Try to find the test indicators that can judge the prognosis of severe heatstroke, and it can be carried out in clinic effectively, simply and quickly.

Among the 70 patients with severe heatstroke, 46 were males (65.7%) and 24 were females (34.3%); they were 22–96 years old, with an average age of (65.72 ± 16.64) years old. Considering that there are more men than women doing outdoor work in summer, the time and labor intensity of high temperature exposure are higher than women, but there is no statistical difference between men and women in each group ($P > 0.05$). we found that there were differences in body temperature in the mechanical ventilation group, combined with higher body temperature. High fever can cause hyperventilation and rapid respiratory rate. In foreign animal experiments, it has been found that the respiratory rate of pigs in severe heat stroke models is significantly faster than normal, suggesting that respiratory frequency may be an influencing factor for the prognosis of severe heat stroke [13].

We found that most of the patients with severe heat stroke in the above group have differences in liver function. Due to hypoxia and direct heat damage, the liver is found to be the most vulnerable organ. Liver transaminase is a very sensitive indicator of organ damage. Serum creatinine and blood urea nitrogen did not increase with the degree of damage. Previous data believe that the liver is the main site of heat damage, and most patients with heat stroke have liver tissue damage [14, 15]. Wagner M et al. [16] believed that the prognosis of patients with abnormal liver function due to heat stroke is extremely poor. A1zeer AH [17] found that serum ALT and AST increased during heat stroke, which can be used as an important reference index for the judgment and prognosis of heat stroke. We further analyzed that there was no statistical difference in liver function damage among severe heatstroke patients, suggesting that liver function may be an influencing factor for the onset of heatstroke, not a risk factor for prognostic assessment.

The APACHE Ⅱ score is currently a commonly used clinical evaluation system for critical illness. It consists of the sum of acute physiology, age, and chronic health conditions [18]. The highest theoretical score is 71 points, the higher the score, the more severe the condition. Studies have found that the APACHE II score is closely related to the severity of heatstroke, the higher the score, the more severe the disease [19, 20]. This study found that the APACHE Ⅱ score of the CHS group was higher than that of the control group, suggesting that the APACHE Ⅱ score has a certain significance for the prognosis of CHS, while the EHS score is lower than that of the control group.

Considering that CHS patients are mostly elderly with underlying diseases, the general condition at the time of admission Poor, higher score. It was further found that the specificity and sensitivity of APACHE Ⅱ score were 0 and 85.71%, respectively, and the specificity was low. The AUC was 0.512, and the 95% confidence interval was 0.390–0.634. It suggests that APACHE Ⅱ is not of high predictive value in evaluating the prognosis of severe heat stroke.

In previous studies, serum PCT is a relatively specific marker of severe bacterial infection and sepsis [21]. Tong Hua sheng [22] compared the positive rate of serum PCT and blood culture in EHS and sepsis patients, and found that the PCT level and positive rate of blood culture in the EHS group were higher than those in the sepsis group. They believed that for EHS patients with elevated PCT, combined with blood culture and clinical analysis, in patients with significantly elevated serum PCT levels or patients with positive blood cultures, even if no direct focus of bacterial infection is found, active anti-infective treatment should be adopted. In our study, we collected the PCT of severe heatstroke patients. The PCT of the EHS group and the CHS group were higher than those of the control group, especially in the EHS group. In the middle and late stages of the disease, 25 patients developed systemic infections, mainly the following respiratory tract infections (EHS :12 vs CHS:9). PCT reflects the active degree of systemic inflammation, and its production is affected by many factors. Even if there is no bacterial infection or bacterial lesions, there will be obvious abnormalities. Therefore, we believe that a significant increase in PCT can greatly reflect the severity and prognosis of HS.

In the study, the DD of the EHS group was significantly higher than that of the control group and the CHS group (all $P < 0.05$); the PLT of the EHS group was significantly lower than the control group and the CHS group (all $P < 0.05$). Coagulation dysfunction is also involved in the important pathological process of severe heat stroke [23, 24]. Studies have shown that abnormalities in platelet and coagulation function can reflect the severity of severe heat stroke. The application of anticoagulant therapy may help improve the survival rate of patients [25]. The current abnormalities in the blood coagulation mechanism caused by heat stroke may be related to the direct cytotoxic effect of thermal stimulation and the cellular inflammatory response induced by thermal stimulation, which leads to vascular endothelial damage and micro thrombosis [26–27]. In addition, thermal stimulation can cause platelet aggregation, decrease in number, and consumption of coagulation factors, thereby inhibiting bone marrow production and releasing platelets [28–30].

Conclusion

In this study, a single-center retrospective study was used to collect early case data of 70 patients to explore the early sensitive indicators of HS. The included cases were all heatstroke patients admitted to the Second Affiliated Hospital of Nantong University, and there may be selective bias. In the future, we will continue to combine multi-center, large-scale randomized controlled studies, and at the same time, we can add multiple time nodes to comprehensively observe the changing trends of PLT, PCT and DD in patients with severe heatstroke to further verify the significance of the three-joint testing.

Declarations

Ethical Approval and Consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, this study has been reviewed by the Ethics Committee of the Second Affiliated Hospital of Nantong University (2015KT007).

Consent for publication

The authors affirm that human research participants provided informed consent for publication of their data.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there are no competing interests.

Funding

This research was supported by the Top Six Types of Talents 'Financial Assistance of Jiangsu Province Grant (2019-WSW-199).

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Authors' contributions

All authors conducted and contributed to the literature search. All authors contributed to the study design. JHY and SJH collected the data. JDS interpreted the data. WL and ZY wrote the article. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

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Figures

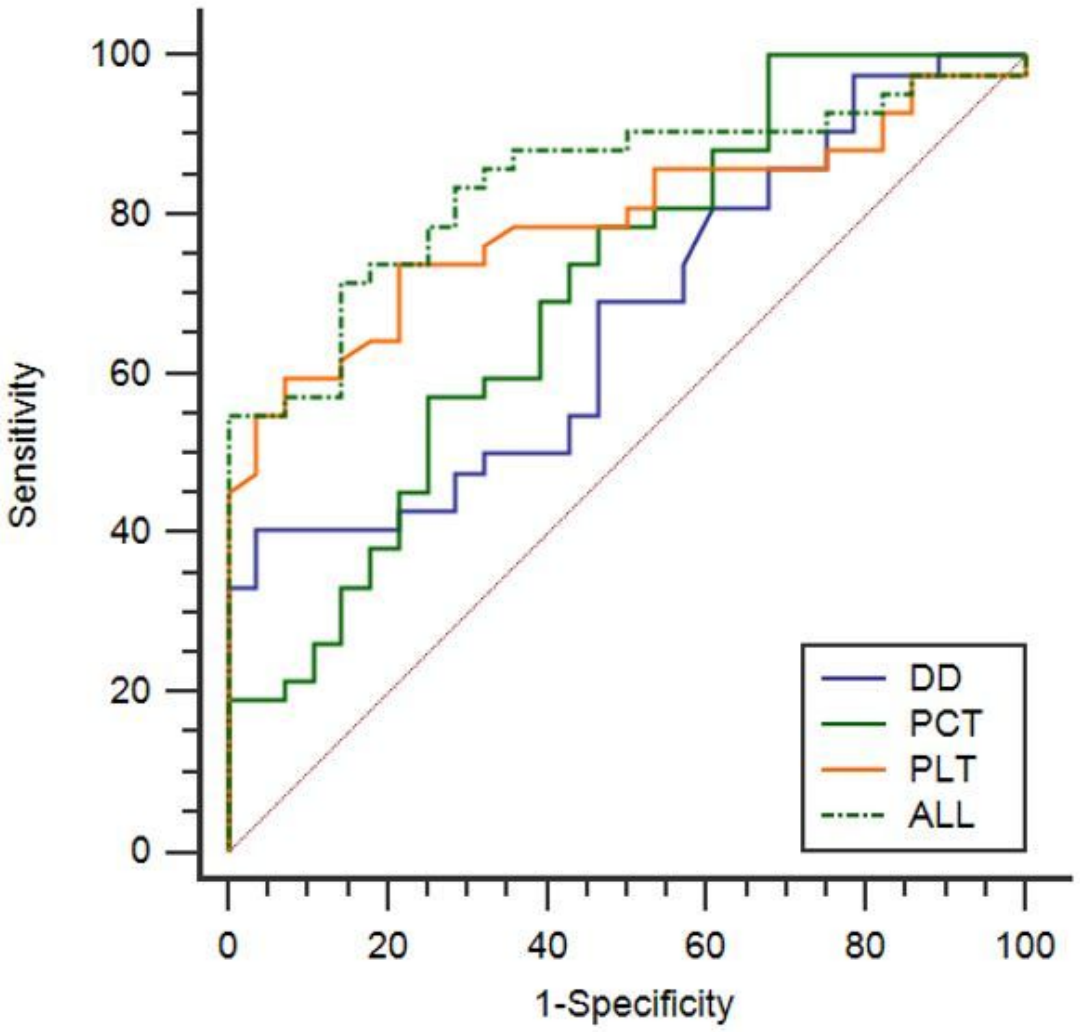

Figure 1

ROC curve analysis of D dimer, procalcitonin and platelet on the early severe heat stroke DD：D dimer；PCT：procalcitonin, PLT：platelets; ALL ：D dimer & procalcitonin & platelet combined detection.