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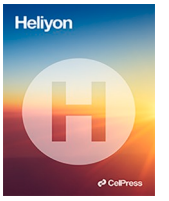

Clinical relevance of neutrophil/lymphocyte ratio combined with APACHEII for prognosis of severe heatstroke

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ABSTRACT

We evaluated clinical implication of neutrophil-lymphocyte ratio (NLR) for severe heatstroke and predictive value of combined acute physiology and chronic health evaluation (APACHEII) score for prognosis of severe heatstroke. Retrospectively, we studied 185 individuals that have been admitted at emergency department for severe heatstroke. On the basis of their prognosis, we sorted the patients into two categories, namely non-survival (n = 43) and survival groups (n = 142). The primary outcome was 30-day mortality. A considerably higher NLR was observed among the non-survivors compared to survivors ($P < 0.05$). After correction for confounders, statistical analysis using multi-variable Cox regression indicated NLR as an independent risk factor for patient death (HR = 1.167, 95%CI = 1.110–1.226, P < 0.001). Through receiver-operating characteristics (ROC) curve, we estimated area-under the curve (AUC) of NLR to be 0.7720 (95% CI [0.6953, 0.8488]). Also, transformation of NLR into a profile type analysis showed that the marker remained a risk factor for death, which showed trend variation (P for trend <0.001). Subgroup forest plot analysis showed robustness in the predictive ability of NLR after exclusion of confounders. Besides, we demonstrated through Kaplan-Meier (KM) survival analysis curve that high risk NLR mortality substantially exceeded low risk NLR. The combined prediction of NLR and APACHEII achieved higher efficacy than NLR and APACHEII alone (AUC = 0.880, 95% CI [0.8280, 0.9290]). Additionally, Delong test indicated that the combined prediction demonstrated a significantly greater ROC than NLR and APACHEII alone, while DCA showed a considerably higher clinical net benefit rate. Increased NLR is a high risk factor and has predictive value for death in individuals with severe heatstroke. Suggestively, combination of NLR and APACHEII have greater predictive value.

1. Introduction

A condition wherein the core temperature of human body exceeds 40° Celsius in a hot environment is severe heatstroke, which induces abnormalities in the central nervous system and consequently result in systemic multiple organ dysfunction (MODS) and mortality [1]. Heatstroke incidence is increasing as average global temperature rises [2] and despite aggressive treatment, the mortality rate remains very unacceptably high [3]. Due to this, early prognosis of severe heatstroke is therefore particularly important.

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Currently, there are no validated scoring tools for predicting severe heatstroke. In spite of this, the acute physiology and chronic health evaluation (APACHEII) score is being used to predict severe heatstroke [4]. However, prediction of severe heatstroke with APACHEII is controversial, amid the scoring being cumbersome and requiring multiple blood parameters which are not readily available at emergency department [5]. Therefore, a fast, easy and emergency room index that can appropriately predict mortality risk among severe heatstroke patients is needed.

Existing literature has revealed that severe heatstroke usually progresses to MODS through dysfunction of immune system and systemic-inflammatory response syndrome (SIRS) [6]. A recent study suggests an intricate interplay between SIRS and immune system culminates in MODS [7]. Close correlation of neutrophil-lymphocyte ratio (NLR) with SIRS and autoimmunity has been reported elsewhere [8]. Of note, when NLR is elevated it implies a state of severe SIRS, which can be used to efficiently assess sepsis [9], tumor [10], and severe pneumonia [11]. However, prognosis of severe heatstroke using the aforementioned index has not been studied enough.

Most previous studies of heatstroke have focused on young people, but many older farmers and outdoor workers in underdeveloped countries still suffer from this disease. The aforesaid individuals may have a more severe inflammatory response to heatstroke due to their older age and weakened immune function. Therefore, we aimed to investigate significance of NLR in these patients, as well as predict severe heatstroke prognosis by combining NLR and APACHEII.

2. Methods

2.1. Patient selection

In this retrospective study, we included a total of 185 severe heatstroke patients, including 120 patients hospitalized in Changzhou City ICU of Second People's Hospital and 65 patients admitted to Changzhou Jintan First People's Hospital from June 2013 to September 2022. On the basis of their prognosis, we sorted the patients into two categories, namely non-survival (n = 43) and survival groups (n = 142). The diagnostic criteria for severe heatstroke are as follows [12,13]: Having a history of heat exposure (solar radiation) with physical labor, and having one of the following symptoms; a. Central nervous system damage, including coma, convulsions, delirium, behavioral abnormalities, and Glasgow coma scale (GCS) score $\leq$14); b. core temperature $\geq$40° Celsius; c. multiple organ dysfunction ($\geq$2) (liver, kidney, rhabdomyolysis, gastrointestinal, circulatory, and respiratory dysfunction); d. disseminated intravascular coagulation. The following were the exclusion criteria: 1) severe cardiopulmonary, hepatic, or renal dysfunction with life-threatening conditions before the onset of the disease. 2) missing blood routine parameters in the emergency room. 3) age<18 years old. The study did not involve human intervention hence it was qualified for exemption from informed consent. Importantly, approval for this study was given by Changzhou City's Ethics Committee of Second Human Hospital of (approval number: [2022] YLJSC014).

2.2. Data collection

General demographics, underlying morbidities, viz., diabetes mellitus (DM), coronary atherosclerotic heart disease (CHD), chronic obstructive pulmonary disease (COPD), history of neoplasia and high blood pressure (HBP), hospital complications (pneumonia and atrial fibrillation), usage of vasoactive drugs and invasive mechanical ventilation (IMV), as well as duration of stay in ICU were collected for both groups. Patients' blood parameters were obtained in the emergency room, while the APACHEII was obtained after hospitalization of the patients.

2.3. Statistical methods

Mean and standard deviation ($\overline{x} \pm s$) were used to express normal continuous data, while we performed independent two sample *t*-test to determine significant differences within the groups. Non-normal continuous data were presented as median (quartiles) [M (Q25, Q75)], while intergroup comparison was accomplished with nonparametric Mann Whitney *U* test. Percentages (%) were used to express categorical data after analysis with Chi square and Fisher's exact tests. We evaluated mortality risk factors analyses with univariate and multivariate Cox regression. Plotting of time variables was carried out via receiver-operating characteristic (ROC) curves to assess predictive value of NLR, while cutoff values were calculated. The patients were grouped according to cutoff values. The grouped patients were subjected to survival curve analysis with the help of the Kaplan-Meier (KM) method, while evaluation of the difference in survival rate within groups was accomplished with log rank test. Furthermore, multiple sensitivity analysis was performed to assess the predictive robustness of NLR, involving conversion of continuous numerical variables into rank and categorical variables to analyze risk factors. The NLR risk ratio was also fitted using modified Poisson regression, while the E-value was reported. In addition, regression analysis was performed for subgroup forest plots after excluding confounding factors. Consideration was given to $P < 0.05$ to be an accepted significant level, while data analysis was accomplished with R (version 4.1) and SPSS (26.0) softwares.

3. Results

3.1. Admitted severe heatstroke patients' characteristics

The general characteristics and clinical blood parameters of patients in both groups are depicted in Table 1. It was discovered that

the medians of gender, age, HBP, DM, COPD, CHD, tumor, pneumonia, and atrial fibrillation were not significantly different ($P > 0.05$) among the two groups. Patients in the non-survival group had a higher proportion of mechanical ventilation and used vasopressors than those in the survival group. In terms of vital signs, the respiratory rate, heart rate and body temperature of the non-survival group were higher compared to the survival group, but the peripheral systolic blood pressure of the survival group was lower than that of the survival cohort. Regarding blood routine parameters, the white blood count (WBC), neutrophil count (NEU), and NLR of the non-survival group were higher compared to survival group, but the lymphocyte (LYM) of the non-survival group was lower than that of the survival group. The APACHEII score of patients in the non-survival group was significantly higher than those in the survival group. These results suggest that all the patients had the same general condition, while the non-survival patients exhibited more severe organ dysfunction.

3.2. Mortality risk analysis of hematological parameters of inflammatory response in severe heatstroke

Our purpose was to study the inflammatory response of severe heatstroke, so we analyzed the parameters reflecting inflammatory response in blood routine. Table 2 displays the Cox regression analysis of prognostic mortality risk factors with severe heatstroke. Multivariate Cox regression analysis was corrected for confounders such as various comorbidities and organ dysfunction variables with clinically essential and statistical discrepancies. The results showed that after correction for confounders, the NEU, NLR and APACHEII were identified as risk factors for death from severe heatstroke, while LYM was a protective factor against death from this disease.

3.3. ROC curves analysis

The ROC curves analysis for the NLR's predictive value for death from severe heatstroke is indicated in Table 3. We discovered that

Table 1
Admitted severe heatstroke patients' characteristics.

	Survivor (N = 142)	Non-survivor (N = 43)	$Z/t/\chi^2$	*P*
Male (n, %)	106 (74.6)	30 (69.8)	0.404	0.525
Age (years)	59 (49–73)	65 (50–74)	0.937	0.349
Highest temperature (°C)	40.8 (40.0–41.5)	41.0 (40.1–42.0)	1.456	0.145
R	23.3 ± 8.5	26.8 ± 7.0	−2.460	0.015
HR	116.0 ± 20.4	129.4 ± 10.4	−4.144	<0.001
SBP(mmHg)	106.4 ± 13.9	95.8 ± 16.0	4.228	<0.001
Mechanical Ventilation (n,%)	38 (26.8)	31 (72.1)	29.003	<0.001
Vasopressor (n,%)	42 (29.6)	34 (79.1)	33.401	<0.001
Concomitant disease (n,%)				
HBP	23 (16.2)	8 (18.6)	0.137	0.711
DM	17 (12.0)	6 (14.0)	0.119	0.730
COPD	13 (9.2)	6 (14.0)		0.393△
CHD	12 (8.5)	4 (9.3)		1.000△
Tumor	6 (4.2)	3 (7.0)		0.436△
Complication (n, %)				
pneumonia	70 (49.3)	22 (51.2)	0.046	0.830
Atrial fibrillation	20 (14.1)	8 (18.6)	0.525	0.469
cramp	48 (33.8)	17 (39.5)	0.476	0.490
coma	125 (88.0)	36 (83.77)	0.542	0.461
Hematological parameters				
WBC($\times 10^9$/L)	9.94 (6.71–12.95)	12.38 (8.02–17.23)	2.142	0.032
NEU($\times 10^9$/L)	7.98 (4.83–11.20)	10.14 (7.06–15.63)	2.602	0.009
LYM($\times 10^9$/L)	1.41 (0.86–2.16)	0.99 (0.43–1.76)	−3.327	0.001
NLR	5.59 (3.34–9.48)	10.86 (7.71–18.40)	5.549	<0.001
BUN (mmol/L)	6.8 (5.2–9.0)	8.0 (5.9–10.0)	1.780	0.075
CR (μmol/L)	122.4 (91.2–167.1)	136.7 (122.8–183.8)	2.560	0.010
AST (U/L)	74.2 (41.0–142.0)	146.5 (76.0–239.0)	4.000	<0.001
ALT (U/L)	68.7 (35.8–168.1)	100.1 (68.1–392.5)	3.101	0.002
ALB (g/L)	37.41 ± 5.37	32.23 ± 6.90	−4.200	<0.001
TNI (ng/ml)	0.087 (0.030–0.268)	0.267 (0.123–1.100)	4.809	<0.001
BNP (pg/mL)	376.5 (166.5–1285.8)	712.6 (178.0–3470.0)	2.113	0.035
LDH (U/L)	303.5 (254.2–407.7)	391.9 (320.5–765.5)	4.322	<0.001
CK (mmol/L)	354.5 (181.9–1083.8)	503.0 (327.7–1069.0)	2.045	0.041
CKMB (mmol/L)	19.8 (10.5–35.2)	51.0 (28.8–105.0)	5.454	<0.001
ICU days	9 (6–14)	7 (5–9)	−2.586	0.010
APACHE-II	16 (13,21)	26 (19,31)	5.244	<0.001

Abbreviation: ALB: human serum albumin; ALT: Alanine transaminase; APACHE: Acute Physiology and Chronic Health Evaluation score; AST: Aspartate transaminase; BNP: Brain natriuretic peptide; BUN: Blood urea nitrogen; CHD: Coronary atherosclerotic heart disease; CKMB: Creatine kinase myocardial band; CK: Creatine phosphate kinase; COPD: Chronic obstructive pulmonary disease; Cr: Blood creatinine; DM: Diabetes mellitus, R: breaths per minute; HBP: High blood pressure; HR: Heart beats per minute; LDH, Lactate dehydrogenase; LYM: Lymphocyte count; NEU: Neutrophil count; SBP: Peripheral systolic blood pressure; TNI, troponin I; WBC: White blood cell count. △It Means Fisher's exact test.

Table 2
Analysis using univariate and multi-variate Cox regression.

variables	Univariable analysis			Multivariable analysis		
	HR	95%CI	P	HR	95%	P
WBC	1.074	1.016–1.136	0.012	1.076	0.998–1.160	0.055
NEU	1.099	1.044–1.158	<0.001	1.125	1.043–1.214	0.002
LYM	0.517	0.335–0.800	0.003	0.456	0.236–0.879	0.019
NLR	1.104	1.067–1.143	<0.001	1.202	1.117–1.292	<0.001
APACHE	1.098	1.060–1.137	<0.001	1.086	1.037–1.137	<0.001

Multivariate analysis adjusted for gender, age, mechanical ventilation, Vasopressor, HBP, DM, COPD, CHD, tumor, TNI, BNP, Cr, BUN, CPK, CKMB, AST, ALT, LDH, ALB, APACHE.

AUC of NLR was 0.7720 (95% CI [0.6953, 0.8488]). Compared with WBC, the NEU, LYM and NLR demonstrated better predictive value for severe heatstroke.

3.4. KM survival analysis curves

We calculated the ROC curves' cutoff values to be 7.27. Grouping of the patients was carried out in accordance with ROC curve cutoff values, viz., the low risk cohort (below the cutoff) and high risk batch (above the cutoff). Determination of patients' survival rates in both groups was accomplished with the KM survival analysis curves (Fig. 1). The outcomes showed that the 30-day patients' survival rate in low risk cohort obviously exceeded ($P < 0.001$) that of patients in high risk batch, wherein the difference within the groups was statistically significant. We further evaluated organ dysfunction in both groups (Table 4), wherein it was found that high risk patients showed poorer liver and kidney functions, coupled with myocardial damage. Moreover, breathing and heart rates of the aforementioned patients were significantly faster, thus suggesting a more severe SIRS.

3.5. Multiple sensitivity analysis

We screened out the high risk patients and calculated the cutoff value again utilizing ROC and obtained a second cutoff value of 15.57. The patients were grouped according to cutoff values, with NLR $\leq$7.27, 7.27 < NLR $\leq$15.77 and NLR >15.77 respectively defined as low risk, medium risk and high risk groups (Table 5). Following this strategy, we performed regression analysis after converting NLR into rank and categorical information. The results showed that the risk value of NLR was enhanced after correction for confounders, wherein a trend change was observed (P for trend <0.001). Both unadjusted and multivariable adjusted models demonstrated that NLR is an increased risk of death among individuals with heatstroke, amid the E-value being 1.346. We used modified Poisson regression to refit the risk ratio of NLR, which remained a mortality risk factor (RR = 1.087, 95%CI = 1.062–1.111, p < 0.001). As a result of concomitant chronic diseases in some of our patients, the Cox regression analysis was repeated after exclusion of the aforesaid diseases because they affected the risk values of NLR. The subgroup forest plot results (Fig. 2) showed that the predictive power of NLR was not diminished by these chronic diseases, thus revealing the robust predictive ability of NLR.

3.6. Combined predictive value of NLR and APACHEII

Although NLR and APACHEII have good predictive values for severe heatstroke, it is essential to note that none of these factors strongly predict prognosis. Therefore, we examined the combined predictive value of these factors. Consequently, we performed ROC curves (Fig. 3) to assess the combined prediction. Combined NLR and APACHEII yielded larger AUC, which was 0.880 (95% CI [0.8280, 0.9290]). Delong test showed that the combined ROC was significantly higher than NLR (z = 2.8874, P = 0.0038) and APACHEII (z = 3.0543, P = 0.0023) alone. These results indicate a better predictive value of combined NLR and APACHEII. Considerably, net clinical gains of the combined model were shown via DCA to be relatively higher compared to that of NLR and APACHEII. In addition, further assessment of deviation within actual conditions and combined model's prediction was carried out with a calibration curve according to bootstrap sampling (repeated 1000 times). This combined model's results were coherent with actual clinical situations. Therefore, we drew a nomogram (Fig. 4) to facilitate clinical practice.

Table 3
ROC curves of white blood cells (WBC), neutrophil count (NEU), lymphocytes (LYM), neutrophil-lymphocyte ratio (NLR), and acute physiology and chronic health evaluation (APACHEII) for predicting death in severe heatstroke.

	AUC	95%CI	sensitivity	specificity	NPV	PPV	cutoff
WBC	0.5936	0.4906,0.6965	0.6047	0.5915	0.8317	0.3095	11.30
NEU	0.6141	0.5163,0.7119	0.7674	0.4366	0.8611	0.2920	7.00
LYM	0.3370	0.2367,0.4374	0.6744	0.6408	0.8667	0.3625	0.60
NLR	0.7720	0.6953,0.8488	0.8372	0.6338	0.9278	0.4091	7.27
APACHE	0.7594	0.6762,0.8426	0.8139	0.6479	0.9200	0.4118	18.00

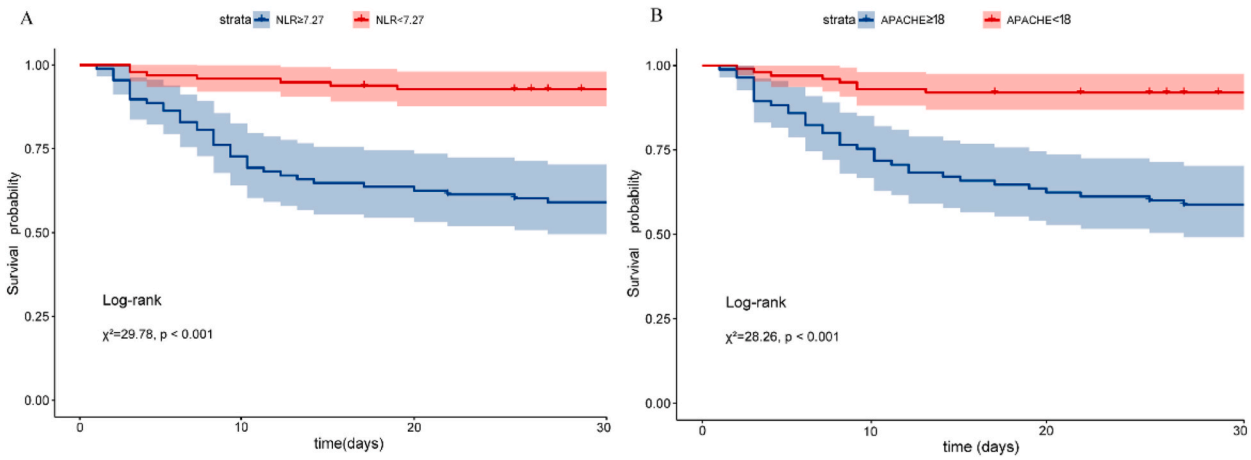

Fig. 1. Kaplan-Meier (KM) survival curve analysis based on different cutoff values. (A) The low risk cohort (below the cutoff); (B) High risk batch (above the cutoff).

Table 4
Clinical characteristics of patients at high and low risk for neutrophil-lymphocyte ratio (NLR).

	NLR<7.27 (n = 97)	NLR≥7.27 (n = 88)	Z/t/χ^2	P
R	19.1 ± 6.4	29.7 ± 6.3	−11.328	<0.001
HR	106.7 ± 17.2	132.7 ± 10.4	−12.611	<0.001
SBP (mmHg)	113.2 ± 10.1	93.7 ± 12.8	11.552	<0.001
TNI (ng/mL)	0.081 (0.018–0.331)	0.150 (0.748–0.561)	3.181	0.001
BNP (pg/mL)	364.5 (181.5–852.2)	671.1 (153.7–2135.0)	1.673	0.094
CR (μmol/L)	111.9 (85.4, 148.0)	151.8 (116.9, 190.0)	1.464	0.143
BUN (mmol/L)	6.6 (5.4–8.7)	7.6 (5.3–10.0)	4.484	<0.001
CK (mmol/L)	305.0 (165.9, 677.9)	518.4 (285.6, 1530.1)	3.358	<0.001
CKMB (mmol/L)	17.5 (10.4, 30.9)	33.9 (18.5, 59.2)	3.821	<0.001
AST (U/L)	49.3 (37.1, 93.4)	88.8 (55.8, 196.1)	3.035	0.002
ALT (U/L)	70.2 (39.8–134.8)	116.9 (60.7–186.7)	4.080	<0.001
LDH (U/L)	295.9 (253.5, 417.1)	355.6 (288.1, 518.6)	−3.607	<0.001
ALB (g/L)	37.7 ± 6.0	34.6 ± 5.9	3.519	0.001

Table 5
Hierarchical regression analysis of neutrophil-lymphocyte ratio (NLR) stratified by cutoff value.

	Model1	Model2	Model3
NLR	HR (95%CI)	HR (95%CI)	HR (95%CI)
≦7.27	1	1	1
7.27–15.57	4.91 (2.05,11.77)	7.33 (2.82,19.08)	7.70 (2.95,20.12)
≧15.57	11.69 (4.87,28.08)	15.72 (6.21,39.81)	17.80 (6.85,46.27)
P for trend	<0.001	<0.001	<0.001

Model 1: Unadjusted.
Model 2: Adjusted for age, sex.
Model 3: Adjusted for variables in Model 1, plus HBP，DM、COPD、CHD、tumor.

4. Discussion

In this study, NLR was observed to be considerably higher in individuals who died from severe heatstroke than in those who survived. The NLR as an independent risk factor for patients' death was disclosed by Multi-variable Cox regression analysis after correction for confounders, wherein ROC curve evidenced a good predictive value of NLR for death. KM survival analysis after correction for confounders showed significantly lower mortality in patients with high risk NLR, while multiple sensitivity analysis showed that the predictive model of NLR was robust.

Severe heatstroke is often accompanied by MODS, wherein previous epidemiologic studies have shown that once it is combined with organ dysfunction, the mortality rate increased significantly [14,15]. The specific mechanisms underlying the high mortality rate of severe heatstroke are unknown and may be due to multiple factors, which make it impossible to accurately determine its prognosis at an early stage. Current research suggests that severe SIRS is vital for severe heatstroke progression to MODS, which is secondary to

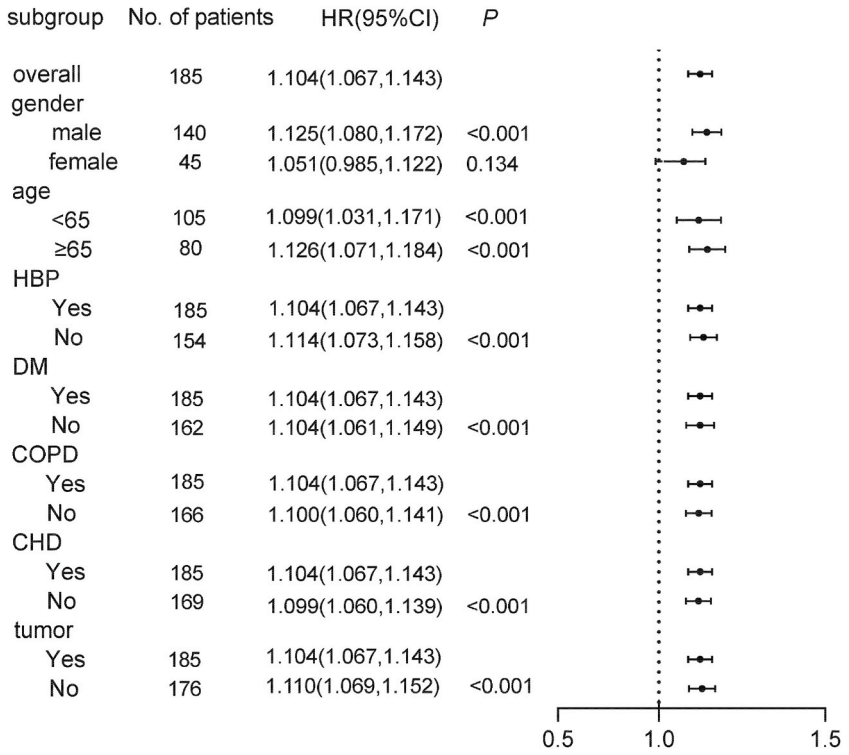

Fig. 2. The forest plot shows subgroup analysis in different populations. We reintroduced the neutrophil-lymphocyte ratio (NLR) into the regression analysis after excluding the patient's comorbidities.

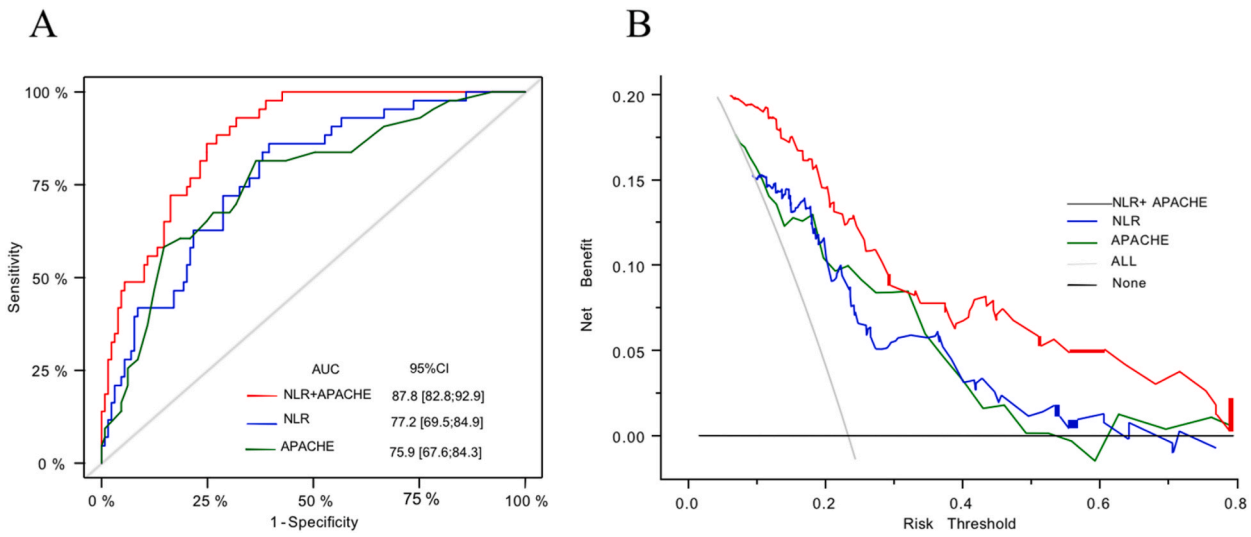

Fig. 3. Neutrophil-lymphocyte ratio (NLR), acute physiology and chronic health evaluation (APACHEII), and (A) NLR combined receiver-operating characteristics (ROC) and (B) DCA curves of APACHEII.

heat stress injury [16]. Our study revealed obvious faster breathing and heart rate in these patients who died of severe heatstroke, which suggests more life-threatening SIRS. Besides, Bouchama et al. [17] found a significant increase in peripheral blood neutrophils in individuals with severe heatstroke. When the body is under stress due to infection or non-inflammatory injury, the level of neutrophil surface marker CD11b is upregulated, thereby leading to neutrophil proliferation and migration [18], which may be one of the mechanisms of enhanced neutrophil function under hyperthermia. These innately immune neutrophils are integral to recognition and clearance of pathogens. However, the mechanism underlying lymphocyte reduction in hyperthermia is not clear and may be related to increased apoptosis. The body secretes large amounts of inflammatory factors during hyperthermia which induce

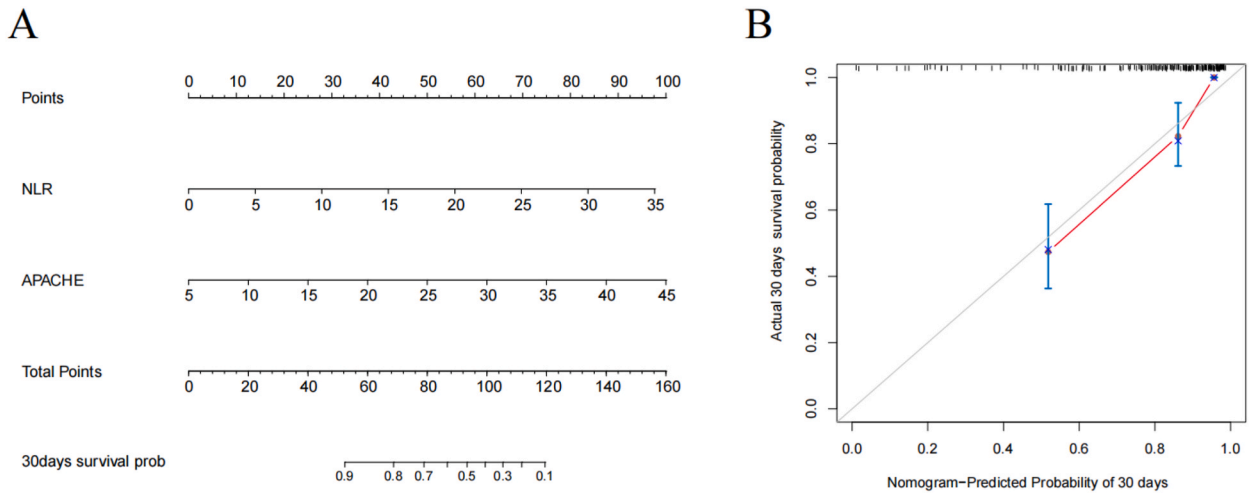

Fig. 4. (A) Nomogram and calibration curve of neutrophil-lymphocyte ratio (NLR); (B) Acute physiology and chronic health evaluation (APACHEII).

lymphocyte apoptosis. In a mouse heatstroke model, it was shown that lymphocytopenia leads to an increase in inflammatory factors, which further promotes lymphocyte apoptosis and thus enters a vicious cycle [19]. Additionally, in humans, a significantly lower number of lymphocytes was observed in patients who died due to heatstroke when compared with surviving patients [20]. This evidence suggests that lymphocyte changes are strongly associated with severe heatstroke. Herein, the absolute values of neutrophils were observed to be higher in deceased individuals with severe heatstroke than in surviving patients, while those of lymphocytes were lower in comparison with survival cohort, thus suggesting a close relation of neutrophil and lymphocyte changes with severe heatstroke's prognosis.

The NLR is closely related to immune function and SIRS, wherein it can rapidly reflect the degree of inflammation and immune status of patients and assess severity of the disease [8,21]. As the disease progresses and immunosuppression is accompanied by increased neutrophils and significant decreased lymphocytes, the NLR is considered as a better indicator of systemic inflammation and immune homeostasis than a single NEU or LYM [11]. In this work, it was discovered that the NLR predictive value was significantly greater than that of both NEU and LYM. We believe that high NLR during rapidly progressive deterioration of severe heatstroke represents a life-threatening disruption of SIRS and immune function, amid suggestion of a poor prognosis. Significantly faster breathing and heart rate in these high risk NLR patients indicate more severe SIRS. Elevated NLR was estimated to be an independent risk factor for patients' death from severe heatstroke (HR = 1.167) via Multi-variable Cox regression analysis, while KM survival analysis curves displayed considerably higher mortality in individuals with higher NLR. Also, the sensitivity analysis we performed showed that the predictive efficacy of NLR was not affected by confounding factors, thus indicating the robustness of NLR. Possibly, these chronic diseases may be mild for farmers and outdoor workers. This is because if these patients have serious chronic diseases, they may not be able to work outdoors during summer heat. Interestingly, we found a discrepancy in NLR between male and female patients. This is explained that male patients usually engage in higher-intensity labor, which is closely associated with heatstroke injuries.

A frequently used tool to predict severe heatstroke in clinical practice is APACHEII score. Several human studies have shown the effectiveness of APACHEII score to predict severe heatstroke prognosis [22,23], but some studies have also pointed out limitations associated with existing scores [22]. It is believed that most farmers and outdoor workers with severe heatstroke go into a coma, which is why they are sent to hospitals. In this case, the APACHEII score may reduce the role of GCS scores. Prognostic prediction of severe heatstroke using APACHEII score alone may be biased because this disease is often associated with severe coagulation abnormalities and rhabdomyolysis, which are not included in APACHEII score [24]. Also, it has been shown that there is no significant difference in blood creatinine and bilirubin between surviving and deceased individuals with severe heatstroke, amid these factors reducing the predictive efficacy [23,25]. Our ROC results showed that combination of NLR and APACHEII score was significantly better for predicting death of severe heatstroke patients than using the two individually. Table 4 showed that liver and kidney functions, rhabdomyolysis, and myocardial injury were more severe in high risk NLR patients, which indicates that high NLR reflected MODS. Therefore, the combined prediction of NLR and APACHEII can more comprehensively include clinical characteristics of patients with heatstroke, hence exhibiting more excellent prediction efficiency.

This paper is limited to some extent; that is we carried out a two centers retrospective analysis, with the population of heatstroke composing of farmers and outdoor workers. Therefore, its applicability to a younger population needs further validation. All patients were treated with active cooling after entering the emergency room. Still, the time of hyperthermia outside the hospital is unknown, while the time of exposure to a high-temperature environment may affect NLR. Moreover, all the patients we studied lived in a humid and hot environment, hence it is not clear whether our findings are applicable to a dry and hot environment.

5. Conclusions

NLR is a low-cost, rapid, and an easily accessible clinical indicator that is particularly suitable for use in the emergency room to help clinicians quickly determine prognosis of severe heatstroke patients. Combination of NLR with APACHEII is more effective in predicting severe heatstroke prognosis, amid further guiding individualized treatment.

Ethics declarations

This study was reviewed and approved by Changzhou City's Ethics Committee of Second Human Hospital, with the approval number: [2022] YLJSC014.

Informed consent was not required for this study because the study did not involve human intervention.

Author contribution statement

Yun Tang; Tijun Gu: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Dongyue Wei; Dong Yuan: Contributed reagents, materials, analysis tools or data.

Fujing Liu: Analyzed and interpreted the data.

Data availability statement

Data will be made available on request.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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