Yu *et al. BMC Sports Science, Medicine and Rehabilitation* (2025) 17:7
https://doi.org/10.1186/s13102-024-01042-w

BMC Sports Science, Medicine and Rehabilitation

RESEARCH **Open Access**

The value of blood lactate and lactate clearance rate in evaluating the prognosis of athletes with heat illness of varying degrees after high-intensity exercise

Li Yu[1*], Xuehui Dong[1], Huanhuan Li[1] and Lili Mi[2]

Abstract

Background Heat stroke, a severe heat illness with organ damage, is a major cause of cause irreparable organ damage and higher death rates among military persons and athletes.

Objectives To study the changes in blood lactate (Lac) levels and lactate clearance rate (LCR) in athletes with heat illness of varying degrees after high-intensity exercise and to evaluate their prognostic value.

Material and methods In present study, acute care unit admitted 36 heat sickness patients following high-intensity exercise from December 2019 to July 2024, with comprehensive medical records, for retrospective study. The study population consisted of two groups of high level athletes: the favourable Prognosis Group (< 7 days, 22 cases), comprising 21 males and 1 female with a mean age of 21.8 ± 2.7 years, and the bad Prognosis Group (≥ 7 days, 14cases), consisting of 14 males with a mean age of 22.6 ± 3.2 years. Lac levels were assessed at admission (0 h) and early in therapy (2 h, 6 h), and the LCR was computed. Lac and LCR values at each time point were compared between the two groups to see how they affected patient prognosis.

Results After 2 and 6 h of therapy, lactate levels decreased significantly in the good prognosis group (1.2 ± 0.5 mmol/L at 2 h and 0.8 ± 0.3 mmol/L at 6 h), but remained elevated in the poor prognosis group (4.2 ± 1.2 mmol/L at 2 h and 3.5 ± 1.5 mmol/L at 6 h). Core body temperature normalized in both groups, but the good prognosis group showed a more rapid decline, with temperatures of 37.4 ± 0.6 °C at 2 h and 36.8 ± 0.4 °C at 6 h in the good prognosis group, and 38.8 ± 0.8 °C at 2 h and 38.2 ± 0.9 °C at 6 h in the poor prognosis group. Notably, a significant positive correlation existed between lactate levels and APACHE II scores at admission ($P < 0.01$). Furthermore, logistic regression analysis revealed that the 2-hour lactate clearance rate (LCR) ($R^2 = 0.83$) was an independent predictor of outcomes.

Conclusions The study suggests that athletes with elevated lactate levels after heat illness may be at higher risk of adverse outcomes. The 2-hour lactate clearance rate (LCR) appears to be a valuable prognostic indicator, with potential applications in evaluating the severity of heat illness and guiding treatment decisions. Furthermore,

*Correspondence:
Li Yu
yuli253253@outlook.com
Full list of author information is available at the end of the article

dynamic monitoring of lactate levels in conjunction with LCR may provide valuable insights into the clinical management and prognosis of athletes with heat-related illnesses.

Keywords Blood lactate, High intensity exercises, Athletes, Exercise, Lactate clearance rate, Heat illness, Prognosis evaluation

Introduction

Given the escalating occurrence and magnitude of extreme heat worldwide, coupled with the fact that military personnel are enduring much longer, more intense, and concentrated training periods, the rates of heat illness have increased dramatically [1]. Heat stroke, a serious heat illness characterized by extensive and severe organ damage, has emerged as a major contributor to non-combat casualties in the military [2]. Moreover, the isolation of certain training locations, unrestricted rescue techniques after the onset, extensive transportation distances, delays in prompt cooling, fluid replenishment, and medical intervention, finally result in permanent organ damage and higher mortality rates [3]. Likewise, Athletes engaging in intense physical activity, especially in hot and humid environments, are at high risk of heat-related illnesses. Prolonged exposure to heat stress can lead to severe heat stroke, organ damage, and even death in athletes if not promptly recognized and treated [4]. Therefore, effective assessment and monitoring strategies are urgently needed to mitigate heat-related illnesses in athletic populations.

How to assess the risk level of the disease in its early stages to reduce the occurrence of heat stroke and improve the rescue rate is an urgent issue. Relevant studies show [5] that early lactate levels and lactate clearance rate (LCR) are important indicators for evaluating patient prognosis and treatment efficacy. The changes in LCR, in particular, can more effectively and promptly assess tissue perfusion and oxygen metabolism, helping rescuers to recognize organ damage early, take measures to correct metabolic disorders in time, and prevent secondary multiple organ failure, thereby improving disease prognosis and increasing patient survival [6, 7].

Lactate's crucial function as an intermediary metabolite between glycolysis and mitochondrial respiration has been extensively discussed in scientific literature in recent decades [8, 9]. Lactate is produced by the enzymatic conversion of pyruvate by lactate dehydrogenase (LDH) during glycolysis [10]. It is then eliminated from the biochemical system by gluconeogenic and oxidative cells, tissues, and organs [15]. Transport across cellular membranes is facilitated by a group of monocarboxylates (MCT) that are bound to the membrane. The rate and direction of their movement are determined by the diffusion gradients of lactate and hydrogen ions [11, 12]. Under completely aerobic conditions, carbohydrate metabolism depends on the movement of lactate both inside and between cells to fulfil several functions [13], primarily to present an energy substrate for oxidative phosphorylation and to act as a precursor for gluconeogenesis [14]. Experimental research has demonstrated that lactate can function as a signalling molecule in several metabolic control pathways, including the inhibition of lipolysis and fatty acid oxidation [15]. Under fasted and resting states, blood lactate levels typically remain below 1 mM, but can rapidly increase to over 20 mM during maximal exercise within minutes. This characteristic makes blood lactate a commonly employed biomarker by exercise physiologists and clinicians to objectively assess exercise intensity. The transportation of lactate via various tissues can also result in a broad spectrum of metabolic capabilities (as a result of endurance training, for example) during physical activity [16, 17]. Augmented lactate metabolism is not only a characteristic adaptation in skeletal muscle after endurance training, but it also has the ability to inhibit catecholamine response during exercise through feedback [18] and may function as a chemoreceptor that enhances the oxygen-dependent response. Moreover, changes in LDH activity and MCT expression following long-term exercise training indicate that muscular and metabolic adaptations to exercise are associated with increased lactate flux. These exercise effects may have positive impacts on brain function, appetite control, respiration, ageing, and other related domains [19, 20]. Elevated lactate levels have been linked to altered immuno-metabolism, while also influencing brain-derived neurotrophic factor (BDNF) expression, which plays a crucial role in neuronal function and recovery. The interplay between lactate, immuno-metabolism, and BDNF highlights the complex physiological responses to exercise and heat stress. After providing a concise overview of the consequences of lactate flux, particularly the rate at which it is cleared, this mini-review will examine the lactate clamp as a distinctive research approach to gain more understanding of the overall metabolic turnover in the body.

This study retrospectively analyzed 36 cases of athletes who were hospitalized in the intensive care unit of our hospital after high-intensity training leading to heat illness from December 2019 to July 2024. It monitored early blood lactate levels and LCR in heat illness patients to explore the relationship between early Lac levels, LCR, and the progression of heat illness, aiming to identify the best early indicators reflecting changes in the disease and to provide a theoretical basis for assessing the severity of heat illness.

Objectives

To assess the prognostic value of blood lactate (Lac) levels and lactate clearance rate (LCR) in athletes with heat illness of differing degrees following high-intensity exercise.

Materials and methods

Study design

Retrospective observational study.

Setting

The present retrospective observational research was undertaken among patients diagnosed with heat illness who were admitted to the ICU at our hospital between January 2020 and June 2024 as a result of heat illness subsequent to high-intensity exercise. The present work adhered to the guidelines outlined in the 1964 Declaration of Helsinki and its subsequent revisions pertaining to the evaluation and dissemination of data derived from patients' medical records. Furthermore, it received approval from the Institutional Review Board of the 969th PLA General Hospital, Hohhot. This work was authorized by the clinical ethics committee of the institute. The waived necessity for informed consent was based on the retrospective design of the study and the utilization of anonymised patient and hospital data. An ethics commission at the 969th PLA General Hospital in Hohhot accepted the waiver.

Participants

We gathered data from individuals who satisfied the diagnostic criteria for heat illness as previously described [21]. Patients without comprehensive clinical data or being hospitalized for less than 24 h were eliminated, resulting in a final sample size of 36 cases for study. Based on the revised classification criteria for heat illness outlined in "Definition and Grading Diagnosis of Heat Illness," there were 10 cases of mild heat illness (heat exhaustion), 16 cases of moderate heat illness (heat exhaustion), and 10 cases of severe heat illness (heat stroke). Among them, 35 were male, and 1 was female, with an age range of 19–29 years, and an average age of 22.1 ± 2.9 years. The study population consisted of two groups of high level athletes: the favourable Prognosis Group (<7 days, 22 cases), comprising 21 males and 1 female with a mean age of 21.8 ± 2.7 years, and the bad Prognosis Group (≥7 days, 14cases), consisting of 14 males with a mean age of 22.6 ± 3.2 years.

Data sources

Following admission, all chosen patients underwent vital sign monitoring, complete with the recording of heart rate and temperature. Therapeutic measures were implemented in accordance with the heat illness treatment protocol. Lactate levels were measured at admission (0 h) and early in the therapy (2 h, 6 h) using blood gas analyzers (GEM Premier 3000, Instrumentation Laboratory, USA).

Study size

Patients without comprehensive clinical data or being hospitalized for less than 24 h were eliminated, resulting in a final sample size of 36 cases for study.

Quantitative variables

Lac levels were assessed at admission (0 h) and early in therapy (2 h, 6 h), and the LCR was computed. Lac and LCR values at each time point were compared between the two groups to see how they affected patient prognosis. Arterial lactate is a reflection of balance between lactate production and clearance. Accumulating lactate may be a marker of global hypoxia or hypoperfusion. Lactate clearance is the reduction of lactate concentrations with interventional strategies, and it has been associated with increased risk of death in critically ill patients. The lactate clearance rate (LCR) was then determined at each time point. The LCR was calculated as follows: LCR = (Lac value at admission - Lac value at each treatment time point) / Lac value at admission × 100% [11]. The changes in Lac levels and LCR at each time point were analyzed across the three groups of patients.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 software. Descriptive statistics, including measures of central tendency, variability, and distribution, were calculated for variables such as age, highest body temperature, heart rate, PCO2, PO2, lactate level, and lactate clearance rate (LCR). Normality testing was then conducted to inform the selection of parametric or non-parametric statistical tests for subsequent analyses. Data were expressed as mean ± standard deviation, and comparisons of means between two groups were performed using a two-tailed t-test. The comparison of sample rates was performed using the chi-square test. Pearson correlation analysis was used for bivariate correlation analysis of Lac and LCR at each time point, and logistic regression was used to analyze the related factors affecting the prognosis of heat illness. In addition to LCR, other variables such as APACHE II score, Heatstroke grading, Lac level, age and the presence of underlying medical conditions were also included in the logistic regression analysis to evaluate their association with prognosis. A P-value of <0.05

Table 1 Comparison of General Clinical Data measured at the time of admission to the hospital between the Good Prognosis Group and the Poor Prognosis Group

Group	Gender (M/F)	Age (years)	Highest Body Temperature (°C)	Heart Rate (beats/min)	PCO2 (mmHg)	PO2 (mmHg)
Good Prognosis Group	21/1	21.8 ± 2.72	38.0 ± 0.91	112.6 ± 8.24	34.8 ± 3.75	106.1 ± 25.51
Poor Prognosis Group	14/0	22.6 ± 3.23	39.5 ± 1.03**	114.8 ± 10.62	32.3 ± 9.51	112.4 ± 37.48

Note M for male, F for female; Compared to the good prognosis group, ***P* < 0.01 indicates a significant difference

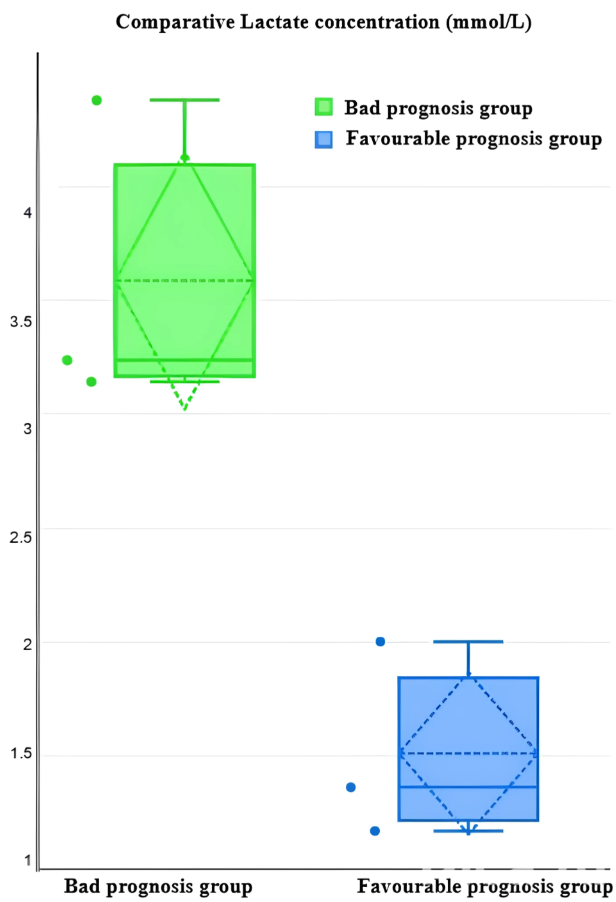

Fig. 1 Box plot

indicated statistical significance, and a P-value of < 0.01 indicated significant difference.

Results

General clinical data

Upon admission, the body temperature of the 36 heat illness patients was 38.5 ± 1.3 °C, and the Lac level was (4.0 ± 3.4) mmol/L. Among them, there were 10 cases of mild heat illness, 16 cases of moderate heat illness, and 10 cases of severe heat illness. There were no significant differences between the good prognosis group and the poor prognosis group in terms of gender, age, heart rate, PCO2, and PO2. However, the highest body temperature and APACHE II score in the poor prognosis group were significantly higher than those in the good prognosis group, with P-values < 0.01, indicating significant differences (Table 1).

Table 2 Comparison of Lac level and LCR between the good prognosis group and poor prognosis group at each time point

Group	Heatstroke Grading			APACHE II Score (points)
	Mild	Moderate	Severe	
Good Prognosis Group	8	11	3	4.3 ± 4.03
Poor Prognosis Group	2	5	7	9.6 ± 5.52**

Comparison of Lac levels and LCR between the two groups of patients

The Lac levels in the good prognosis group were significantly lower at 2 h and 6 h after treatment compared to admission (0 h) ($P < 0.01$). The Lac levels at admission (0 h) and at 2 h and 6 h after treatment in the good prognosis group were significantly lower than those in the poor prognosis group ($P < 0.05$ or $P < 0.01$). In the poor prognosis group, the Lac level at 2 h after treatment showed no significant difference compared to admission (0 h) ($P > 0.05$), but it significantly decreased at 6 h after treatment ($P < 0.01$). After 2 and 6 h of therapy, lactate levels in the favorable prognosis group decreased significantly compared to admission, whereas in the poor prognosis group, lactate levels remained elevated. Specifically, good prognosis patients had lower lactate concentrations of 1.2 ± 0.5 mmol/L at 2 h and 0.8 ± 0.3 mmol/L at 6 h after treatment. In contrast, the poor prognosis group had higher lactate concentrations of 4.2 ± 1.2 mmol/L at 2 h and 3.5 ± 1.5mmol/L at 6 h (Fig. 1). The LCR at 2 h after treatment in the good prognosis group was significantly higher than that in the poor prognosis group ($P < 0.05$), but there was no significant difference in LCR at 6 h after treatment between the two groups ($P > 0.05$) (Table 2). Core body temperature normalized in both groups, but the good prognosis group showed a more rapid decline, with temperatures of 37.4 ± 0.6 °C at 2 h and 36.8 ± 0.4 °C at 6 h in the good prognosis group, and 38.8 ± 0.8 °C at 2 h and 38.2 ± 0.9 °C at 6 h in the poor prognosis group. The difference in the rate of decline in core body temperature could affect the prognosis. A more rapid decline in core body temperature may indicate a more effective response to treatment, which could be associated with a better prognosis.

Correlation analysis between Lac level and APACHE II score at admission (0 h)

As shown in Fig. 2, Pearson correlation analysis indicates a significant positive correlation between the Lac level at admission (0 h) and the APACHE II score in heat illness

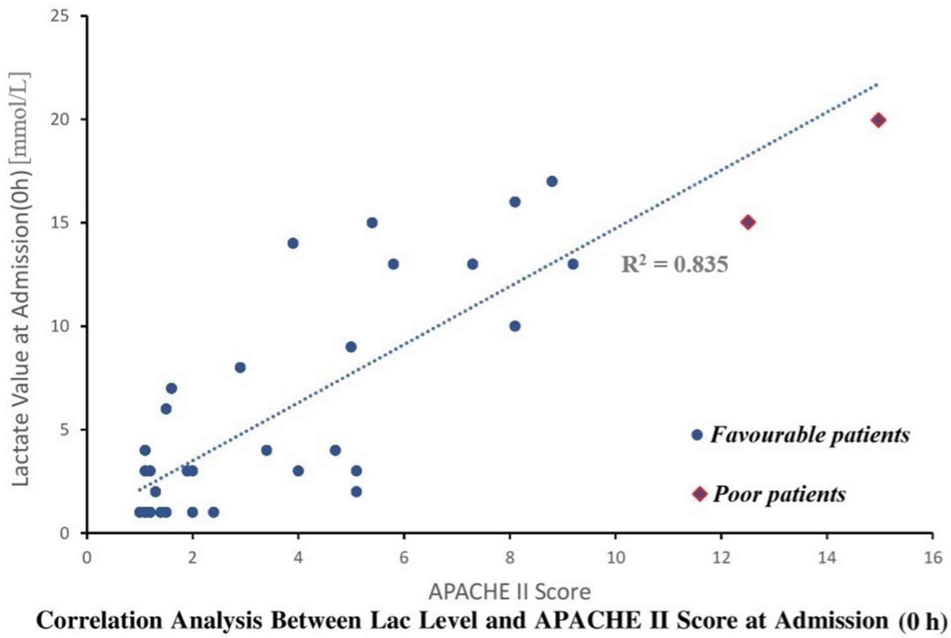

Fig. 2 Correlation Analysis between Lac Level and APACHE II Score at Admission (0 h)

Table 3 Binary logistic regression analysis of factors affecting the prognosis of patients

Item	LCR (%)	
	2 h	**6 h**
P	0.041	0.966

Note Compared to admission, **$P<0.01$ indicates a significant difference; compared to the poor prognosis group, #$P<0.05$ indicates statistical significance

Table 4 Comparisons of poor prognosis rates at all time points using 45.5% as the cut-off point for LCR

Item	LCR			
	2 h		**6 h**	
	≥45.5%	**<45.5%**	**≥45.5%**	**<45.5%**
Number of Cases	18	18	30	6
Good Prognosis	14	8	18	4
Poor Prognosis	4	10	12	2
Poor Prognosis Rate	22.2%*	55.6%	40%	33.3%

patients (correlation coefficient = 0.835, $P<0.01$). Furthermore, logistic regression analysis revealed that the 2-hour lactate clearance rate (LCR) was an independent predictor of outcomes.

Prognosis evaluation

A binary logistic regression analysis was conducted using the LCR values at 2 h and 6 h as the dependent variables to determine if they predicted a good prognosis. The results showed that the independent influencing factor for heat illness prognosis was the 2 h LCR ($P<0.05$), as shown in Table 3. When comparing LCR values at each time point using 45.5% as the cut-off point, the incidence of poor prognosis was significantly lower in patients with an LCR above 45.5% at 2 h than in those with an LCR below 45.5% ($P<0.05$). There was no statistically significant difference in the poor prognosis rate for the 6 h LCR (Table 4), indicating that patients with a 2 h LCR above 45.5% had a good prognosis.

Discussion

Heat illness refers to a series of pathophysiological changes that occurs when the body's heat production and heat dissipation become imbalanced due to exposure to hot or humid environments and/or intense physical activity, leading to local or systemic heat accumulation that exceeds the compensatory limits of temperature regulation [22–25]. This manifests as a continuous process ranging from mild to severe conditions [26–28]. Depending on the patient's core body temperature, level of consciousness, and organ damage, heat illness can be classified into mild heat illness (heat syncope), moderate heat illness (heat exhaustion), and severe heat illness (heat stroke) [29, 30]. Heat stroke (HS) is the most severe and life-threatening type of heat illness [31–34], and it can be divided into classic heat stroke (CHS) and exertional heat stroke (EHS) [35–37]. The latter typically occurs in previously healthy young individuals during intense physical activity, such as athletes, military personnel, and laborers. Following the onset, core body temperature usually rises above 40 °C, accompanied by altered mental status (such as confusion, disorientation, seizures, and coma), systemic inflammatory response, coagulation dysfunction, and even multiple organ failure, which essentially resembles a "sepsis-like response" [38, 39].

Early in the course of heat illness, several indicators, including lactate, can change. In the exertional heat stroke scoring system established by Kang Hongjun and Zhou Feihu at the General Hospital of the People's Liberation Army [40], lactate has been validated as one of the indicators for assessing the severity of the condition. However, the importance of lactate clearance rate (LCR) in assessing the severity and prognosis has not been extensively described in the aforementioned studies. Our study found that the blood lactate levels at admission, 2 h after treatment, and 6 h after treatment were all higher in the poor prognosis group than in the good prognosis group. Further research revealed that the lactate clearance rate 2 h after treatment was significantly lower in the poor prognosis group compared to the good prognosis group, suggesting that the lactate clearance rate at 2 h post-treatment might be an important indicator for prognosis assessment. Logistic regression analysis showed that a lactate clearance rate greater than 45.5% at 2 h after treatment predicted a good prognosis. These findings indicate that the changes in lactate clearance rate are more reflective of the severity and prognosis of the patient's condition than changes in lactate concentration alone, emphasizing the need to focus on lactate clearance rate during early treatment.

Analyzing the general conditions of patients in the poor prognosis group, two points are worth noting: First, 11 of the 14 patients in this group were admitted to the hospital more than 24 h after the onset of symptoms. The primary reason for this delay was that the patients' general condition appeared stable initially, leading to a lack of attention from both the patients themselves and the medical staff, resulting in delayed admission. Second, more than half of the patients in this group had their body temperature reduced to below 39.0 °C within the first 30 min of onset, but in the following 2 h, effective cooling measures were not consistently taken to bring the temperature down to 38.5 °C, as recommended by the "Chinese Expert Consensus on the Diagnosis and Treatment of Heat Stroke" [41], leading to further deterioration of the condition. These observations suggest that there is still insufficient awareness of heat illness and heat stroke at the grassroots level, inadequate understanding of the guidelines, and a gap between theory and practice. Additionally, there is still a lack of proficiency in treatment methods, and a sense of complacency prevails, resulting in the failure to seize the golden hour for timely and effective cooling and fluid replacement, thus worsening the condition.

Limitations

The limitations of this study include the fact that the case data were sourced from a single hospital, and the number of cases included was relatively small, which limits its representativeness and may even lead to statistical bias. The significance of the LCR threshold of 45.5% still requires further validation. Therefore, further large-scale, multicenter clinical studies are needed to confirm these findings.

Conclusions

In summary, the present study indicates that athletes with elevated lactate levels following heat illness are at increased risk of adverse outcomes. The 2-hour lactate clearance rate (LCR) emerges as a valuable prognostic tool, offering potential benefits in assessing heat illness severity and informing treatment strategies. Moreover, continuous monitoring of lactate levels in conjunction with LCR may provide critical insights into the clinical management and prognosis of athletes with heat-related illnesses. However, additional research is warranted to fully explore the relationships between lactate levels, APACHE II scores, and patient outcomes in this context.

Acknowledgements
None.

Author contributions
LY: Concept and designed the study and analyzed data; XD: Collected the data and helped in data analysis; HL and LM: Drafting of the manuscript, Proofreading and final editing along with guarantor of the manuscript. "All authors read and approved the final version of the manuscript".

Funding
None.

Data availability
The datasets supporting the findings of the current study are openly available in Zenodo at DOI https://doi.org/10.5281/zenodo.13381422.

Declarations

Human ethics and consent to participate
The research conducted on human participants adhered to the ethical standards set forth by the institutional and/or national research committee of The 969th PLA General Hospital, Hohhot and ethical committee of the "969th PLA General Hospital, Hohhot" has approved the study. Additionally, it is imperative to adhere to the ethical guidelines outlined in the 1964 Helsinki Declaration and its subsequent revisions, or similar ethical standards. Moreover, written informed consent was obtained from all patients.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Intensive Care Unit, The 969th Hospital of P.L.A, Hohhot 010051, China
[2]Department of Pharmacy, The 969 th Hospital of P.L.A, Hohhot 010051, China

Received: 17 September 2024 / Accepted: 16 December 2024
Published online: 16 January 2025

References

1. Mora C, Dousset B, Caldwell IR, et al. Global risk of deadly heat [J]. Nat Clim Change. 2017;7(7):501–6. https://doi.org/10.1038/nclimate3322.

2. Song, Qing. Ning Bo. Manual for the Prevention and Treatment of Heat Illness in the military [M]. Beijing: People's Military Medical; 2016. pp. 9–16.
3. Ning Bo S, Qing. Interpretation of the military heat acclimatization guide [J]. J Air Force Med. 2018;34(4):276–8.
4. Coris EE, Ramirez AM, Van Durme DJ. Heat illness in athletes: the dangerous combination of heat, humidity and exercise. Sports Med. 2004;34(1):9–16. https://doi.org/10.2165/00007256-200434010-00002. PMID: 14715036.
5. Bruno RR, Wernly B, Binneboessel S, et al. Failure of Lactate Clearance predicts the outcome of critically ill septic patients. Diagnostics (Basel). 2020;10:1105. https://doi.org/10.3390/diagnostics10121105.
6. Hernandez G, Regueira T, Bruhn A, et al. Relationship of systemic, hepatosplanchnic, and microcirculatory perfusion parameters with 6-hour lactate clearance in hyperdynamic septic shock patients: an acute, clinical-physiological, pilot study. Ann Intensive Care. 2012;2:44. https://doi.org/10.1186/2110-5820-2-44.
7. Li D, Liu S, Zhang J, Cheng W, Mao J, Cui N. Exploring dynamic change in arterial base excess with patient outcome and lactate clearance in the intensive care unit by hierarchical time-series clustering. Front Med (Lausanne). 2022;9:1020806. https://doi.org/10.3389/fmed.2022.1020806.
8. Gladden LB, Lactate Metabolism. A New Paradigm for the third millennium. J Physiol. 2004;558:5–30. https://doi.org/10.1113/jphysiol.2003.058701.
9. Ferguson BS, Rogatzki MJ, Goodwin ML, Kane DA, Rightmire Z, Gladden LB. Lactate Metabolism: historical context, prior misinterpretations, and current understanding. Eur J Appl Physiol. 2018;118:691–728. https://doi.org/10.1007/s00421-017-3795-6.
10. Rogatzki MJ, Ferguson BS, Goodwin ML, Gladden LB. Lactate is always the end product of Glycolysis. Front Neurosci. 2015;9:22. https://doi.org/10.3389/fnins.2015.00022.
11. Bergman BC, Wolfel EE, Butterfield GE, et al. Active muscle and whole body lactate kinetics after endurance training in men. J Appl Physiol. 1999;87:1684–96. https://doi.org/10.1152/jappl.1999.87.5.1684.
12. Juel C. Lactate-Proton Cotransport in skeletal muscle. Physiol Rev. 1997;77:321–58. https://doi.org/10.1152/physrev.1997.77.2.321.
13. Brooks GA, Dubouchaud H, Brown M, Sicurello JP, Butz CE. Role of Mitochondrial Lactate Dehydrogenase and Lactate Oxidation in the Intracellular Lactate Shuttle. Proc. Natl. Acad. Sci. USA. 1999;96:1129–1134. https://doi.org/10.1073/pnas.96.3.1129
14. Brooks GA. The Lactate Shuttle during Exercise and Recovery. Med Sci Sports Exerc. 1986;18:360–8. https://doi.org/10.1249/00005768-198606000-00019.
15. Brooks GA, Arevalo JA, Osmond AD, Leija RG, Curl CC, Tovar AP. Lactate in Contemporary Biology: a Phoenix Risen. J Physiol. 2022;600:1229–51. https://doi.org/10.1113/JP280955.
16. Liu C, Wu J, Zhu J, Kuei C, Yu J, Shelton J, Sutton SW, Li X, Yun SJ, Mirzadegan T, et al. Lactate inhibits Lipolysis in Fat cells through activation of an Orphan G-Protein-coupled receptor, GPR81. J Biol Chem. 2009;284:2811–22. https://doi.org/10.1074/jbc.M806409200.
17. Lee SG, Song J, Park DW, et al. Prognostic value of lactate levels and lactate clearance in sepsis and septic shock with initial hyperlactatemia: a retrospective cohort study according to the Sepsis-3 definitions. Med (Baltim). 2021;100(7):e24835. https://doi.org/10.1097/MD.0000000000024835.
18. Liu Z, Meng Z, Li Y, et al. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. Scand J Trauma Resusc Emerg Med. 2019;27:51. https://doi.org/10.1186/s13049-019-0609-3.
19. Ahmed K, Tunaru S, Tang C, Müller M, Gille A, Sassmann A, Hanson J, Offermanns S. An Autocrine Lactate Loop mediates insulin-dependent inhibition of Lipolysis through GPR81. Cell Metab. 2010;11:311–9. https://doi.org/10.1016/j.cmet.2010.02.012.
20. Goodwin ML, Harris JE, Hernández A, Gladden LB. Blood lactate measurements and analysis during Exercise: A Guide for clinicians. J Diabetes Sci Technol. 2007;1:558–69. https://doi.org/10.1177/193229680700100414.
21. Brooks GA. Lactate as a Fulcrum of Metabolism. Redox Biol. 2020;35:101454. https://doi.org/10.1016/j.redox.2020.101454.
22. Hui S, Ghergurovich JM, Morscher RJ, Jang C, Teng X, Lu W, Esparza LA, Reya T, Zhan L, Guo JY, et al. Glucose feeds the TCA cycle via circulating Lactate. Nature. 2017;551:115–8. https://doi.org/10.1038/nature24057.
23. Messonnier LA, Emhoff CAW, Fattor JA, Horning MA, Carlson TJ, Brooks GA. Lactate Kinetics at the lactate threshold in trained and untrained men. J Appl Physiol. 2013;114:1593–602. https://doi.org/10.1152/japplphysiol.00043.2013.
24. MacRae HS, Dennis SC, Bosch AN, Noakes TD. Effects of Training on Lactate production and removal during Progressive Exercise in humans. J Appl Physiol. 1992;72:1649–56. https://doi.org/10.1152/jappl.1992.72.5.1649.
25. MacRae HH, Noakes TD, Dennis SC. Effects of endurance training on Lactate removal by oxidation and Gluconeogenesis during Exercise. Pflüg Arch Eur J Physiol. 1995;430:964–70. https://doi.org/10.1007/BF01837410.
26. Fattor JA, Miller BF, Jacobs KA, Brooks GA. Catecholamine response is attenuated during moderate-intensity Exercise in response to the Lactate Clamp. Am J Physiol Endocrinol Metab. 2005;288:E143–7. https://doi.org/10.1152/ajpendo.00117.2004.
27. Chang AJ, Ortega FE, Riegler J, Madison DV, Krasnow MA. Oxygen regulation of breathing through an olfactory receptor activated by Lactate. Nature. 2015;527:240–4. https://doi.org/10.1038/nature15721.
28. Torres-Torrelo H, Ortega-Sáenz P, Gao L, López-Barneo J. Lactate sensing mechanisms in arterial Chemoreceptor cells. Nat Commun. 2021;12:4166. https://doi.org/10.1038/s41467-021-24444-7.
29. Messonnier L, Freund H, Féasson L, Prieur F, Castells J, Denis C, Linossier MT, Geyssant A, Lacour JR. Blood Lactate Exchange and removal abilities after relative high-intensity Exercise: effects of Training in Normoxia and Hypoxia. Eur J Appl Physiol. 2001;84:403–12. https://doi.org/10.1007/s004210000378.
30. Dubouchaud H, Butterfield GE, Wolfel EE, Bergman BC, Brooks GA. Endurance training, expression, and physiology of LDH, MCT1, and MCT4 in human skeletal muscle. Am J Physiol Endocrinol Metab. 2000;278:E571–9. https://doi.org/10.1152/ajpendo.2000.278.4.E571.
31. Quistorff B, Secher NH, Van Lieshout JJ. Lactate fuels the human brain during Exercise. FASEB J. 2008;22:3443–9. https://doi.org/10.1096/fj.08-106104.
32. Islam H, Townsend LK, McKie GL, Medeiros PJ, Gurd BJ, Hazell TJ. Potential involvement of Lactate and Interleukin-6 in the Appetite-Regulatory Hormonal response to an Acute Exercise Bout. J Appl Physiol. 2017;123:614–23. https://doi.org/10.1152/japplphysiol.00218.2017.
33. Brooks GA, Osmond AD, Arevalo JA, Duong JJ, Curl CC, Moreno-Santillan DD, Leija RG. Lactate as a myokine and exerkine: drivers and signals of physiology and metabolism. J Appl Physiol. 2023;134:529–48. https://doi.org/10.1152/japplphysiol.00497.2022.
34. Williams VF, Oh GT. Update: heat illness, active component, U.S. Armed Forces, 2021. MSMR. 2022;29:8–14. PMID: 35608520.
35. Yamamoto T, Fujita M, Oda Y, et al. Evaluation of a Novel classification of heat-related illnesses: a Multicentre Observational Study (Heat Stroke STUDY 2012). Int J Environ Res Public Health. 2018;15:1962. https://doi.org/10.3390/ijerph15091962.
36. Asmara IGY. Diagnosis and management of Heatstroke. Acta Med Indones. 2020;52:90–7. PMID: 32291378.
37. Emhoff CAW, Messonnier LA, Horning MA, Fattor JA, Carlson TJ, Brooks GA. Direct and indirect lactate oxidation in trained and untrained men. J Appl Physiol. 2013;115:829–38. https://doi.org/10.1152/japplphysiol.00538.2013.
38. Emhoff CAW, Messonnier LA, Horning MA, Fattor JA, Carlson TJ, Brooks GA. Gluconeogenesis and Hepatic Glycogenolysis during Exercise at the lactate threshold. J Appl Physiol. 2013;114:297–306. https://doi.org/10.1152/japplphysiol.01202.2012.
39. Liu SY, Song JC, Mao HD, Zhao JB, Song Q, People's Liberation Army Professional Committee of Critical Care Medicine. Expert Group of Heat Stroke Prevention and Treatment of the People's Liberation Army, and. Expert consensus on the diagnosis and treatment of heat stroke in China. Mil Med Res. 2020;7:1. https://doi.org/10.1186/s40779-019-0229-2
40. Yang MM, Wang L, Zhang Y, et al. Establishment and effectiveness evaluation of a scoring system for exertional heat stroke by retrospective analysis. Mil Med Res. 2020;7:40. https://doi.org/10.1186/s40779-020-00269-1.
41. Liu SY, Wang Q, Lou YP, et al. Interpretations and comments for expert consensus on the diagnosis and treatment of heat stroke in China. Mil Med Res. 2020;7:37. https://doi.org/10.1186/s40779-020-00266-4.

Publisher's note