Journal of Biosciences and Medicines, 2026, 14(8), 55-61
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Advances in the Pathogenic Mechanisms and Treatment Strategies of Heat Stroke

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How to cite this paper: He, H. (2026) Advances in the Pathogenic Mechanisms and Treatment Strategies of Heat Stroke. *Journal of Biosciences and Medicines*, **14**, 55-61.
https://doi.org/10.4236/jbm.2026.148006

Received: May 16, 2026
Accepted: August 8, 2026
Published: August 11, 2026

Abstract

Heat stroke is medically defined as severe heat illness and represents a critical emergency with extremely rapid onset and swift progression. It is associated with high rates of disability and mortality and is regarded as a highly dangerous and potentially fatal condition. In recent years, the increasing frequency of extreme heat events and the ongoing intensification of climate warming have led to a significant rise in heat stroke incidence, showing a clear year-on-year upward trend. This public health concern has drawn widespread attention from all sectors of society. The pathogenesis of heat stroke is associated with systemic inflammatory responses, oxidative stress, and coagulation dysfunction. The interaction of these factors can lead to multiple organ dysfunction syndrome, resulting in high mortality if treatment is delayed. The key to effective management lies in early and rapid cooling together with multi-organ support. Close monitoring of organ function status and vital signs, along with timely symptomatic treatment, is essential to minimize systemic damage and improve patient survival. This article reviews recent progress in understanding the pathogenic mechanisms of heat stroke and focuses on analyzing current treatment strategies centered on cooling, combined with organ function support, pharmacological interventions, and comprehensive care, with the aim of providing a reference for future clinical management of the disease.

Keywords

Heat Stroke, Pathogenic Mechanisms, Cooling Strategies, Organ Function Support, Comprehensive Treatment

1. Introduction

Heat stroke is a fatal emergency caused by a rapid rise in the body's core temperature. The condition progresses rapidly, often leading to multiple organ dysfunction and carrying a high mortality rate [1]. According to differences in affected populations and predisposing factors, heat stroke is classified into classic heat stroke (CHS) and exertional heat stroke (EHS). CHS results from an imbalance between heat production and heat dissipation caused by passive exposure to a hot environment. It is commonly seen in elderly people, young children, frail individuals, and patients with chronic diseases. EHS is more common in healthy young adults, such as military personnel, athletes, firefighters, and construction workers, who develop symptoms after intense training or heavy physical labor in hot and humid environments. However, both types involve a series of abnormalities in the body caused by heat stress. Currently, with advances in understanding its pathogenesis, treatment strategies have evolved from simple cooling to a comprehensive rescue system based on life support. This article reviews the latest developments in heat stroke treatment.

2. Pathogenic Mechanisms of Heat Stroke

2.1. Inflammatory Response Mechanism

Heat stroke is a systemic inflammatory response syndrome induced by elevated body temperature. The core pathogenesis involves heat stress activating the innate immune system. Heat stress triggers the activation of the NOD-like receptor protein 3 (NLRP3) inflammasome, promoting the release of inflammatory cytokines and thereby exacerbating the systemic inflammatory response.

2.2. Oxidative Stress Mechanism

Under high-temperature conditions, the body generates large amounts of reactive oxygen species, leading to an oxidative stress state. This activates inflammatory pathways, further amplifying the inflammatory response in an exponential manner.

2.3. Cell Death Mechanisms

Patients with heat stroke may exhibit multiple forms of cell death, including ferroptosis associated with rhabdomyolysis, NLRP3 inflammasome-mediated apoptosis, and P53 protein-mediated mitochondrial apoptosis pathways. These diverse mechanisms of cell death collectively exacerbate tissue and organ damage.

2.4. Coagulation Dysfunction Mechanism

If not treated promptly, patients with heat stroke may progress to coagulation disorders, manifesting as heat stroke-induced coagulopathy or disseminated intravascular coagulation. High temperatures also damage vascular endothelial cells, leading to the exposure of tissue factor and activation of the coagulation cascade. Studies have further shown that neutrophil extracellular traps (NETs) released by neutrophils strongly promote thrombus formation.

3. Timing of Cooling in Heat Stroke

Timely and effective cooling is critical to successful treatment. According to the

2025 Chinese Expert Consensus and Treatment Guidelines for Heat Stroke, the key to management lies in the "golden half hour" and achieving an adequate cooling rate. If the core body temperature (rectal temperature) can be lowered to below 40.0˚C within 30 minutes of onset, treatment is usually successful, with mortality approaching zero. In contrast, if the core temperature is ≥41.0˚C upon arrival and remains elevated for a prolonged period, mortality rises sharply and can reach up to 80%. Both domestic and international guidelines strongly recommend "rapid cooling immediately after removal from the heat source" as the highest-priority intervention.

Beyond timing, the cooling rate also significantly affects prognosis. A rate below 0.15˚C/min is considered insufficient and is associated with a higher risk of multi-organ damage. An ideal rate of approximately 0.19˚C/min has been shown to improve outcomes. There is currently no complete consensus on the target temperature. Most experts agree that hypothermia should be avoided, and the majority of guidelines recommend stopping active cooling when the temperature reaches 37.5˚C - 38.5˚C, although some studies support 39.0˚C as the endpoint. Recent evidence suggests that the cooling endpoint should not be based solely on a fixed temperature threshold but should also consider clinical improvement, such as restored consciousness and behavioral changes. In summary, early, rapid, and moderate cooling remains the core principle in the treatment of heat stroke.

4. Treatment Strategies for Heat Stroke

4.1. Cooling Therapy

Rapid and effective cooling immediately after patient arrival is critical for determining treatment outcomes [2]. The core principle of management is "cooling first, transport second", with the goal of minimizing heat-induced damage to the body. For patients with exertional heat stroke, cold water immersion is the most appropriate on-site cooling method. This approach provides rapid cooling, effectively lowering the core temperature to a safe range within a short time and thereby creating a window for subsequent treatment. Physical cooling plays an irreplaceable role in halting heat-induced injury and can also be extended to patients with classic heat stroke or those in special circumstances. For example, evaporative cooling—combining cold water sprays with fan-assisted airflow—may be employed. In advanced medical centers, intravascular cooling techniques and extracorporeal blood purification therapy may also be used. The latter not only allows precise control of the patient's core temperature, but can also remove excessive inflammatory mediators from the body within a short period of time. Intravascular cooling technology was previously used mainly for temperature management after neurosurgery, cardiac surgery, stroke, and treatment of patients with cardiac arrest, and it enables precise control of core body temperature. The system typically consists of a temperature control unit and a heat exchange catheter. The catheter contains multiple lumens with a heat exchange balloon at its tip. Through connection with the body's circulatory system, it enables rapid blood cooling via extracorporeal heat exchange, thereby regulating core temperature. According to available data [3], intravascular cooling can achieve precise temperature control, with cooling rates of 3.0˚C/h - 6.0˚C/h and temperature accuracy within 0.1˚C. It avoids skin vasoconstriction commonly seen with rapid surface cooling and has not been associated with increased complications. However, its widespread use is limited by the high technical skill required and the need for specialized equipment, making it unsuitable for prehospital or transport settings. It is primarily applied in hospital environments. In the future, the emphasis should be placed on promoting early and effective cooling. After patient arrival, the optimal cooling strategy should be selected based on the patient's condition and disease severity.

The *Chinese Guidelines for the Diagnosis and Treatment of Heat Stroke* (2025 Edition) [4] divides the rescue process into five key stages: rapid identification, on-site first aid, evacuation and transport, hospital treatment with rehabilitation, and return to duty. In-hospital management of heat stroke should follow the principle of "ten early interventions and one contraindication": early cooling, early fluid resuscitation, early sedation, early intubation (early airway management), early anticoagulation, early anti-infection treatment, early anti-inflammatory treatment, early blood purification, and early gastrointestinal management; when coagulopathy is present, surgical procedures are contraindicated. It emphasizes that cooling measures must be maintained continuously throughout the entire rescue chain to ensure seamless and effective intervention. This structured approach highlights the need to strengthen training for emergency responders to improve their ability to quickly recognize heat stroke and initiate the rescue process in a timely manner. Future efforts should include regular professional training for emergency personnel, focusing on rapid identification and initial management of heat stroke. Training content should cover the latest guidelines, practical skills, and scenario-based simulations to ensure responders can promptly identify patients and activate emergency protocols.

The 2023 Expert Consensus on Cooling Methods for Heat Stroke Prevention and Treatment in Military Training [5] recommends prioritizing immersion in ice water (2˚C - 8˚C) or cold water (8˚C - 14˚C). This method can achieve a cooling rate of 0.16˚C/min - 0.26˚C/min, effectively halting heat-induced damage as quickly as possible. When cold water is unavailable, immersion in room-temperature water (around 26˚C) can serve as an effective alternative. During immersion, continuous agitation of the water is advised to enhance convection and improve cooling efficiency.

4.2. Organ Function Support

This treatment approach requires advanced medical equipment and is therefore widely applied in large hospitals. The key to its implementation lies in early intervention and continuous dynamic monitoring to maintain internal homeostasis and prevent secondary injury. Studies [6] have shown that early application of continuous renal replacement therapy (CRRT) in heat stroke patients with acute kidney injury can temporarily substitute for renal function while effectively removing inflammatory cytokines and myoglobin, thereby improving prognosis [7]. For patients with coagulation disorders, treatment strategies should be dynamically adjusted according to coagulation parameters. Anticoagulation may be appropriately administered in the absence of active bleeding, while replacement therapy should be initiated when bleeding occurs, aiming for precise and individualized management. Subsequent interventions should emphasize continuous dynamic assessment of organ function to facilitate the transition from supportive care to functional recovery.

4.3. Pharmacological and Supportive Therapy

Pharmacological therapy plays an important adjunctive role in alleviating excessive inflammatory responses, providing symptomatic care, and protecting organ function. For example, in patients with heat stroke, the use of benzodiazepines for sedation and analgesia can facilitate subsequent treatment, reduce oxygen consumption, and help control symptoms such as convulsions and agitation. Similarly, drugs such as chlorpromazine can effectively terminate skeletal muscle spasms associated with heat stroke. However, the majority of Chinese experts currently hold a negative view toward pharmacological cooling in heat stroke and do not recommend the use of medications for this purpose [8]. Agents such as Xuebijing and ulinastatin can inhibit excessive systemic inflammatory responses and provide protective effects on organs in heat stroke patients. When administering pharmacological therapy, emphasis should be placed on targeted mechanisms and optimal timing to ensure maximum therapeutic efficacy. Ulinastatin, a protease inhibitor, can suppress excessive inflammatory responses, reduce leukocyte activation, and improve endothelial function, thereby alleviating organ damage caused by heat stroke. Xuebijing injection works by inhibiting the release of inflammatory mediators and modulating immune function, offering protective effects against organ injury in heat stroke patients.

For coagulation abnormalities, targeted therapy should be guided by coagulation monitoring. In cases of active bleeding or consumptive coagulopathy due to significant clotting factor deficiency, replacement therapy with platelets, prothrombin complex concentrate, or fresh frozen plasma may be administered. For hypercoagulable states without active bleeding, anticoagulation therapy—such as heparin, thrombomodulin, or antithrombin—should be initiated promptly. Although glucocorticoids have anti-inflammatory effects in certain inflammatory conditions, their use in heat stroke remains controversial. Some experts [9] argue that glucocorticoids may mask clinical symptoms and potentially delay diagnosis and treatment; therefore, routine use is not recommended. However, in selected cases with severe sepsis or systemic inflammatory response syndrome, cautious use may be considered after careful risk-benefit evaluation.

Heat stroke patients often present with hypovolemia and electrolyte disturbances in the early stage, so timely fluid resuscitation is essential to maintain fluid and electrolyte balance. For patients with impaired intestinal mucosal barrier function, early administration of gut microbiota regulators can help preserve intestinal immunity and reduce the risk of bacterial translocation. Overall, pharmacological management of heat stroke should follow the principle of "rapid cooling-dynamic monitoring-targeted intervention". Treatment should be individualized based on the patient's evolving condition to maximize therapeutic efficacy and reduce mortality.

4.4. Integrated Treatment Approach

Current clinical management of heat stroke emphasizes a systematic and integrative strategy, in which various effective interventions are applied in combination or sequentially to form a timely and comprehensive treatment protocol. The guiding principle of "ten early interventions and one prohibition" represents the core of this integrated approach. Through multi-target and multi-stage interventions, disease progression can be maximally interrupted. Previous clinical practice has demonstrated that combining rapid on-site cooling, efficient in-hospital life support, continuous organ function monitoring, and targeted pharmacological therapy can act through different pathways and significantly improve treatment success rates [10]. The integrated model leverages the strengths and complementary effects of each measure—for instance, pharmacological interventions target specific pathological processes, organ support lays the foundation for functional recovery, and cooling creates a therapeutic window for organ function restoration.

5. Conclusion

The management of heat stroke is a multidisciplinary, multi-step systematic endeavor. Early cooling of patients is essential for interrupting disease progression within a short time, while subsequent targeted pharmacological therapy plays a critical role in reducing mortality. Implementing the principle of "ten early interventions and one prohibition" throughout the entire treatment process, along with bundled and individualized comprehensive strategies, contributes to improved patient outcomes. Future research should focus on establishing and promoting multidisciplinary collaboration and standardized treatment protocols for heat stroke, while emphasizing long-term prognosis improvement and restoration of heat tolerance, ultimately providing patients with a full-cycle management pathway.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Li, Z.Z. and Luo, X. (2023) Manifestations and Prevention of Multi-Organ Damage in Heatstroke. *Chinese Journal of Geriatric Multi-Organ Diseases*, **22**, 624-628. (In Chinese)

[2] Bouchama, A., Abuyassin, B., Lehe, C., Laitano, O., Jay, O., O'Connor, F.G., *et al.* (2022) Classic and Exertional Heatstroke. *Nature Reviews Disease Primers*, **8**, Article No. 8. https://doi.org/10.1038/s41572-021-00334-6

[3] Filep, E.M., Murata, Y., Endres, B.D., Kim, G., Stearns, R.L. and Casa, D.J. (2020) Exertional Heat Stroke, Modality Cooling Rate, and Survival Outcomes: A Systematic Review. *Medicina*, **56**, Article 589. https://doi.org/10.3390/medicina56110589

[4] Song, J.C., Song, Q., Zhang, W., *et al.* (2025) Guidelines for the Diagnosis and Treatment of Heatstroke in China (2025 Edition). *PLA Medical Journal*, **50**, 367-386. (In Chinese)

[5] Song, Q., Ning, B., *et al.* (2023) Military-Wide Expert Group for the Prevention and Treatment of Heatstroke. Expert Consensus on Cooling Methods for Preventing Heatstroke/Heat Exhaustion during Military Training. *PLA Medical Journal*, **48**, 871-878. (In Chinese)

[6] Hu, X.Y., Liu, L.X., Yang, L.Y., *et al.* (2023) Clinical Characteristics and Efficacy Analysis of Central Nervous System Damage in Heatstroke. *Beijing Medical Journal*, **45**, 807-810. (In Chinese)

[7] Wang, X.S., Chen, H.O., Li, W.C., *et al.* (2021) Nursing Care of Patients with Heatstroke during Emergency Treatment Using Continuous Blood Purification Combined with Hypothermia Therapy. *Modern Practical Medicine*, **33**, 227-229. (In Chinese)

[8] Monseau, A.J., Hurlburt, G.A., Balcik, B.J., Oppenlander, K.E., Chill, N.M. and Martin, P.S. (2021) Status of US Emergency Medical Service Protocols Regarding Pre-Transfer Cooling for Exertional Heat Stroke. *Cureus*, **13**, e19505. https://doi.org/10.7759/cureus.19505

[9] Roberts, W.O., Armstrong, L.E., Sawka, M.N., Yeargin, S.W., Heled, Y. and O'Connor, F.G. (2021) ACSM Expert Consensus Statement on Exertional Heat Illness: Recognition, Management, and Return to Activity. *Current Sports Medicine Reports*, **20**, 470-484. https://doi.org/10.1249/jsr.0000000000000878

[10] Glahn, K.P.E., Bendixen, D., Girard, T., Hopkins, P.M., Johannsen, S., Rüffert, H., *et al.* (2020) Availability of Dantrolene for the Management of Malignant Hyperthermia Crises: European Malignant Hyperthermia Group Guidelines. *British Journal of Anaesthesia*, **125**, 133-140. https://doi.org/10.1016/j.bja.2020.04.089