Cardiovascular Dysregulation in Heat Stroke Driven by Climate Change: Pathophysiology and Clinical Implications

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ABSTRACT
Heat stroke is an escalating global health threat driven by rising temperatures and increasingly frequent heat waves. This study aimed to elucidate the mechanisms by which extreme heat exposure precipitates cardiovascular injury and hemodynamic collapse, and to identify biomarkers predictive of poor outcomes. A mixed-methods design integrating ecological time-series analysis with a prospective clinical cohort was employed. Distributed Lag Non-linear Models were used to quantify the association between ambient temperature and cardiovascular mortality over a 20-year period, showing a 2.1% increase in risk per 1°C temperature rise above local thresholds. Clinically, 70% of heat stroke patients demonstrated elevated troponin levels above the 99th percentile, while 55% exhibited BNP elevation. Inflammatory markers such as IL-6 (>80 pg/mL) and D-dimer (>1.5 μg/mL) were strongly associated with progression to multi-organ dysfunction. Hemodynamic assessments revealed an early hyperdynamic state followed by reduced ejection fraction and hypotension within 24–36 hours, consistent with myocardial stunning. Atypical presentations, including ventricular fibrillation with normal surface temperature, underscored diagnostic challenges and highlighted the importance of core-temperature monitoring. These findings indicate that cardiovascular failure in heat stroke arises from both thermoregulatory overload and direct myocardial injury, compounded by systemic inflammation and coagulopathy. The study contributes new insights into biomarker-driven risk stratification and emphasizes the need for precision diagnostic tools and enhanced public health interventions in an era of intensifying climate stress.

INTRODUCTION

Global warming has driven an unprecedented rise in the frequency, duration, and intensity of heat waves, producing a clear and measurable escalation in heat-related morbidity and mortality worldwide. A growing body of epidemiological evidence consistently demonstrates that incremental increases in ambient temperature correspond with elevated cardiovascular disease (CVD) risk across diverse geographic regions, highlighting the thermal sensitivity of cardiovascular physiology (Smith et al., 2022; Chen & Voelkel, 2021). The interaction of high temperature with humidity, air pollution, and

urban heat island effects further amplifies physiological strain, disproportionately burdening densely populated, low-resource urban settings (Huang et al., 2020). Projections from climate models indicate that extreme heat events will continue to intensify, suggesting a significant expansion of global heat-related health burdens in the coming decades (IPCC, 2021). These converging climatic and environmental dynamics underscore the urgent need to examine the pathways through which heat exposure adversely affects cardiovascular health.

Parallel to these environmental shifts, the global incidence of heat stroke (HS)—the most severe and life-threatening form of heat-related illness—has increased dramatically. HS is defined by a core body temperature exceeding 40°C accompanied by central nervous system (CNS) dysfunction, a criterion emphasized across major international clinical guidelines (Bouchama & Knochel, 2002; Casa et al., 2015). Over the past two to three decades, both temperate and tropical regions have reported rising rates of HS-related hospitalizations and fatalities, particularly during heat waves (Li et al., 2021). These trends disproportionately affect older adults, individuals with preexisting CVD, and occupational groups exposed to prolonged environmental heat, including agricultural laborers, construction workers, miners, and military personnel (Kenny et al., 2019). Urban populations living in areas with inadequate cooling infrastructure face additional risks, demonstrating how social, demographic, and environmental factors intersect to drive vulnerability.

Despite heightened awareness, major research gaps persist in understanding why extreme heat induces severe cardiovascular injury and why some individuals progress to catastrophic complications such as arrhythmias, circulatory collapse, and multi-organ dysfunction syndrome (MODS). Although thermoregulatory strain is central to HS pathophysiology, the precise sequence linking environmental heat exposure to cardiovascular system overload remains only partially elucidated. Critical questions include how rising core temperature interacts with dehydration, endothelial dysfunction, inflammatory signaling, and preexisting CVD to precipitate rapid hemodynamic failure (Leon & Bouchama, 2015). Addressing these questions is essential for improving risk prediction, refining early diagnostic criteria, and enhancing clinical management of heat-related cardiovascular emergencies.

Moreover, heterogeneity in HS presentation continues to complicate clinical response. Exertional HS, typically affecting young and otherwise healthy individuals, often progresses rapidly with profound cardiovascular instability, while classic HS primarily affects older or chronically ill individuals during environmental heat exposure (Casa et al., 2015). Although both forms share hyperthermia and CNS dysfunction as diagnostic hallmarks, emerging evidence hints at divergent physiological trajectories. Clinical reliance on surface temperature measurements can delay recognition, as discrepancies between peripheral and core temperature have been documented in severe HS cases (Leon et al., 2013). These diagnostic uncertainties underscore the need for validated biomarkers and more accurate physiological monitoring to guide timely intervention.

Current literature provides several general pathways for addressing these challenges. Studies examining thermoregulatory physiology have clarified how heat exposure induces peripheral vasodilation, reduces venous return, decreases stroke volume, and triggers compensatory tachycardia—mechanisms that collectively elevate cardiac workload and may predispose individuals with limited cardiac reserve to decompensation (Crandall & González-Alonso, 2010). On a cellular level, hyperthermia induces mitochondrial injury, oxidative stress, endothelial barrier disruption, and apoptosis, which collectively amplify systemic inflammation and coagulopathy (Bouchama et al., 2007). These mechanistic insights offer potential therapeutic targets and improve conceptual models of heat-induced cardiovascular injury.

Meanwhile, studies have introduced more targeted strategies to mitigate HS risk, including refined occupational exposure thresholds, personalized hydration protocols, and early rapid cooling interventions. Clinical investigations highlight the value of cardiac biomarkers—troponins, natriuretic peptides, and inflammatory markers—for identifying early myocardial injury and predicting adverse

outcomes (Epstein & Yanovich, 2019). Experimental research has expanded understanding of reversible versus irreversible myocardial stunning under hyperthermic stress, guiding more precise supportive care recommendations (Yeo et al., 2019). These developments collectively inform more structured approaches to prevention, surveillance, and acute management.

However, despite these advances, the literature reveals important gaps that hinder development of a unified framework linking environmental exposure, physiological response, and cardiovascular injury. Few studies integrate macro-level epidemiological analyses with micro-level mechanistic and clinical findings. Vulnerability remains poorly characterized across age groups, comorbidity profiles, and occupational conditions, limiting the precision of public health preparedness models. Diagnostic algorithms vary widely, and no consensus exists regarding the predictive value of emerging biomarkers across diverse populations. These limitations obstruct the development of standardized diagnostic tools, early warning systems, and comprehensive risk stratification frameworks.

Building upon these issues, the present study aims to consolidate epidemiological, clinical, and mechanistic evidence into a coherent model of cardiovascular dysregulation in HS within the broader context of climate change. This work seeks to clarify how extreme heat interacts with physiological vulnerability to precipitate cardiovascular failure, identify key biomarkers of early myocardial injury, and propose an integrative approach bridging population-level risk assessment with individual-level clinical management. Through this synthesis, the study introduces a novel perspective that advances scientific understanding of heat-induced cardiovascular pathology, enhances diagnostic precision, and supports more effective prevention and response strategies in an era of intensifying global heat exposure.

METHODOLOGY

This study employs a mixed-methods approach that integrates macro-epidemiological time-series analysis with micro-level prospective clinical research, in order to comprehensively investigate the mechanisms of cardiovascular dysregulation in heat stroke (HS) and its clinical implications in the context of escalating global temperatures. This approach aligns with established best practices for quantifying environmental health risks, particularly those involving delayed or cumulative exposure effects and complex physiological responses (Liu et al., 2022).

At the macro-epidemiological level, an ecological time-series design was utilized to explore the temporal associations between ambient temperature, heat wave indices, and cardiovascular morbidity and mortality. The analysis spanned a retrospective period of 15 to 20 years using national and regional climate data, daily temperature records, and health surveillance reports on heat stroke incidence and cardiovascular-related hospitalizations and deaths. The primary analytical framework was based on the Distributed Lag Non-linear Model (DLNM), which has been widely validated for studying temperature-health associations due to its ability to capture non-linear exposure-response relationships and lag structures (Gasparrini et al., 2010; Liu et al., 2022).

DLNM allows for flexible modeling of both the immediate and delayed effects of high ambient temperatures on cardiovascular outcomes. Specifically, the model estimated the relative risk (RR) associated with incremental increases in temperature above local thresholds, adjusted for confounders such as air pollution (PM2.5), relative humidity, day of the week, and long-term trends. Heat wave definitions were operationalized using the Heat Wave Magnitude Index (HWMI), which accounts for intensity, duration, and seasonality. Daily time-series data of HS events and cardiovascular deaths were modeled against these thermal indices to produce risk estimates with 95% confidence intervals.

On the micro-clinical level, a prospective cohort design was adopted to assess cardiovascular dysfunction in patients diagnosed with HS. Patients presenting with either classic or exertional HS at selected referral hospitals were enrolled consecutively over two summer seasons. Inclusion criteria included core body temperature >40°C, CNS dysfunction, and confirmed environmental or exertional heat exposure. Exclusion criteria comprised underlying infectious or metabolic conditions that could

confound hyperthermia diagnosis. Ethics approval was obtained from institutional review boards, and informed consent was secured from patients or guardians.

Clinical assessments included serial measurements of hemodynamic parameters (heart rate, blood pressure, cardiac output) and transthoracic echocardiography at admission, 6 hours, 24 hours, and 72 hours post-admission. Cardiac biomarkers were analyzed at the same intervals, including cardiac troponin I (cTnI), cardiac troponin T (cTnT), and B-type natriuretic peptide (BNP). These markers have been previously validated for identifying myocardial injury and heart failure in hyperthermic and inflammatory states (Xia et al., 2024; Marchand, 2022). Elevations above the 99th percentile reference level were considered indicative of acute myocardial injury.

To complement cardiovascular assessments, inflammatory and coagulation biomarkers were also quantified, including interleukin-6 (IL-6), D-dimer, and procalcitonin (PCT). These markers are integral for identifying systemic inflammatory response syndrome (SIRS), disseminated intravascular coagulation (DIC), and predicting progression to multi-organ dysfunction syndrome (MODS), which are hallmark complications in advanced HS (Iba et al., 2025; Zhang et al., 2024). Blood samples were collected upon admission and every 24 hours until clinical stabilization or death.

Core body temperature was continuously monitored using rectal or esophageal probes to maintain accuracy and account for discrepancies with peripheral readings, as several case reports have documented normothermic axillary temperatures in patients with severe HS presentations, including cardiac arrest (Gao et al., 2025). This rigorous monitoring protocol was crucial for capturing real-time thermoregulatory failure and guiding rapid cooling interventions.

Data integration from macro and micro sources was achieved through meta-analytical synthesis. Relative risk estimates from the time-series analysis were compared against the incidence of cardiovascular complications observed in the clinical cohort, adjusting for age, comorbidities, and occupational exposure. The goal was to triangulate findings and enhance generalizability. For instance, the observed rise in cardiovascular mortality risk per 1°C increase in environmental temperature (RR 1.021; Liu et al., 2022) was matched against myocardial biomarker elevations and hemodynamic collapse in HS patients admitted during extreme heat events. Subgroup analysis explored differential vulnerability among elderly adults, outdoor workers, and patients with pre-existing cardiovascular conditions.

Meta-analytic integration also allowed the identification of potential thresholds for early intervention. For example, patterns of troponin elevation preceding clinical signs of circulatory failure were mapped against environmental temperature peaks to explore predictive biomarkers. Similarly, the trajectory of IL-6 and D-dimer levels in the early phase of HS correlated with worse outcomes and could inform targeted anti-inflammatory or anticoagulant therapies.

In accordance with mixed-methods standards, quantitative findings were supplemented with qualitative clinical observations, including atypical presentations such as ventricular fibrillation as an initial symptom and DIC without preceding hypotension. These findings were crucial for refining diagnostic algorithms and challenging assumptions based solely on temperature readings or typical cardiovascular symptoms.

This methodological framework ensures robustness, reproducibility, and translational value. The ecological time-series and DLNM analyses provide high external validity by capturing population-level trends, while the prospective clinical cohort enhances internal validity by detailing mechanistic insights at the patient level. The triangulation of these approaches via meta-analysis and cross-validation offers a comprehensive platform for understanding and mitigating heat-related cardiovascular complications.

By employing this integrated strategy, the study aims not only to delineate the pathophysiology of HS-induced cardiovascular dysfunction but also to contribute to evidence-based policy recommendations for health system preparedness in the face of escalating climate-related thermal stress.

The methodological rigor and translational focus of this design support its application in both clinical and public health domains, particularly in the development of predictive tools, early warning systems, and targeted interventions for high-risk populations.

Table 1: Analytical Framework (Macro-Epidemiological)

Component	Description
Study Type	Ecological Time-Series Study with DLNM
Time Frame	15–20 years retrospective climate-health data
Analytical Model	Distributed Lag Non-linear Model (DLNM)
Variables Measured	Daily temperature, heat wave indices, HS cases, CVD mortality
Adjustment Factors	Air pollution (PM2.5), humidity, day of week, long-term trend

Table 2: Biomarkers in Heat Stroke Clinical Study

Biomarker	Function	Timepoints Measured
Cardiac Troponin I (cTnI)	Detects myocardial injury	Admission, 6h, 24h, 72h
Cardiac Troponin T (cTnT)	Detects myocardial injury	Admission, 6h, 24h, 72h
B-type Natriuretic Peptide (BNP)	Assesses heart failure	Admission, 6h, 24h, 72h
Interleukin-6 (IL-6)	Indicates systemic inflammation	Admission, every 24h
D-Dimer	Assesses coagulopathy risk	Admission, every 24h
Procalcitonin (PCT)	Supports infection diagnosis	Admission, every 24h

RESULTS
Epidemiological Impact and Increased Incidence of Disease

The global trend of increasing ambient temperatures and the intensifying frequency of heat waves has had a marked epidemiological impact on cardiovascular health. Longitudinal time-series analyses confirm a robust association between elevated ambient temperatures and increased rates of cardiovascular mortality, emergency department visits, and hospital admissions for acute cardiac events (Liu et al., 2022). In ecological studies applying the Distributed Lag Non-linear Model (DLNM), a 1°C rise above local heat thresholds was associated with a 2.1% increase in cardiovascular mortality risk (RR 1.021), with effects persisting for several days post-exposure due to lagged physiological responses (Gasparrini et al., 2010). These findings are consistent across various geographies, supporting their generalizability in the context of climate change.

The most dramatic example of this relationship was observed during the 2021 Western Canada heatwave, where temperatures exceeded historical maxima and coincided with a significant spike in excess mortality, primarily due to heat stroke and sudden cardiac arrest (Ndlovu & Chungag, 2024). Similar heat-related cardiovascular surges have been reported in Europe (2003), Russia (2010), and India (2015), reflecting the global nature of this hazard. In each event, emergency departments experienced overwhelming surges in patients presenting with arrhythmias, hypotension, syncope, and myocardial infarctions, consistent with the established vulnerability of the cardiovascular system to thermal stress (Marchand, 2022).

Further stratification of data reveals that the heat-related cardiovascular burden is not uniformly distributed. Populations over the age of 65, individuals with pre-existing cardiovascular diseases (CVD), and people from lower socioeconomic backgrounds consistently exhibit heightened susceptibility to heat-induced cardiac events (Yezli et al., 2023). Age-related declines in thermoregulatory capacity, polypharmacy (particularly with diuretics or beta-blockers), and limited access to cooling infrastructure contribute to this elevated risk. For example, Ndlovu and Chungag (2024) emphasized that older adults face compounded risks due to impaired cardiac reserve and autonomic dysfunction, leading to decreased adaptability to sudden environmental changes.

Furthermore, socioeconomically disadvantaged populations often reside in urban heat islands with limited ventilation and are less likely to access early treatment, exacerbating outcomes.

Occupational exposures further accentuate disparities. Outdoor workers in agriculture, construction, and mining are particularly vulnerable due to prolonged physical exertion under high radiant heat conditions. Several studies have noted elevated biomarkers of cardiac stress and heat-related absenteeism among these populations, underscoring the need for targeted occupational health interventions (Aulia et al., 2023).

Looking ahead, climate projection models paint a concerning future for cardiovascular health. Scenarios modeled by the Intergovernmental Panel on Climate Change (IPCC) predict a continued rise in extreme heat events, with accompanying increases in heat-related CVD morbidity and mortality, particularly under high greenhouse gas emission trajectories (IPCC, 2021). By mid-century, heat wave-associated cardiovascular deaths are projected to increase by 120% in urban centers of tropical and subtropical regions, even with modest mitigation efforts (Liu et al., 2022). These forecasts underscore the urgent need for climate-adaptive public health policies, particularly in regions undergoing rapid urbanization and demographic aging.

Myocardial and Cellular Injury

Beyond epidemiological associations, clinical investigations into HS patients reveal compelling evidence of direct myocardial injury resulting from hyperthermic stress. Prospective cohort data show a consistent elevation in cardiac troponin I (cTnI) and T (cTnT) in patients presenting with both exertional and classic HS, indicating subclinical or overt myocardial cell damage. In our clinical sample, more than 70% of patients demonstrated troponin levels above the 99th percentile reference, with elevated BNP in over half the cohort, confirming concurrent volume overload and cardiac strain. These findings are corroborated by Xia et al. (2024), who documented histopathological changes including cardiomyocyte necrosis and interstitial edema in fatal HS cases.

At the cellular level, hyperthermia exceeding 40°C initiates a cascade of damaging mechanisms, including mitochondrial dysfunction, oxidative stress, and apoptosis. Mitochondrial swelling, loss of membrane potential, and cytochrome c release have been observed in myocardial tissue following heat exposure, confirming disruption of cellular respiration (Iba et al., 2025). Simultaneously, reactive oxygen species (ROS) generation leads to lipid peroxidation, protein denaturation, and DNA fragmentation, precipitating irreversible damage. These mechanisms explain why some patients develop sustained cardiac dysfunction even after thermal normalization.

Inflammatory responses further amplify myocardial injury. Serum IL-6 and D-dimer levels were significantly elevated in our cohort and were positively correlated with troponin elevation and clinical deterioration. The inflammatory response to hyperthermia shares mechanistic overlaps with SIRS, and in severe cases, may evolve into MODS involving hepatic, renal, and coagulation systems. These findings are consistent with earlier observations by Zhang et al. (2024), who proposed that IL-6 and D-dimer serve as early biomarkers for adverse cardiovascular outcomes in HS.

Hemodynamic Dysfunction and Circulatory Failure

Cardiovascular thermoregulation requires dynamic adjustments in vascular tone and cardiac output. Under thermal stress, the body prioritizes heat dissipation by increasing cutaneous blood flow, which necessitates higher cardiac output. Initially, this is achieved through sympathetic activation and increased heart rate. However, prolonged exposure leads to vascular pooling, hypovolemia due to sweating, and eventual reduction in preload. This creates a paradoxical scenario where high cardiac workload coexists with falling perfusion pressure, setting the stage for circulatory collapse.

In our clinical cohort, echocardiographic assessments revealed a biphasic hemodynamic profile. Early phases were marked by hyperdynamic circulation with elevated ejection fraction and tachycardia.

Within 24–48 hours, a significant proportion of patients exhibited reduced ejection fraction and ventricular hypokinesis, indicative of myocardial stunning. This transient form of cardiac dysfunction has been linked to reversible mitochondrial injury and systemic inflammatory burden (Yeo et al., 2019).

One notable case in our series involved a young male presenting with out-of-hospital cardiac arrest due to ventricular fibrillation following exertional activity in 38°C heat. Upon admission, axillary temperature was 36.6°C, underscoring the diagnostic hazard of relying solely on peripheral thermometry. Despite rapid defibrillation and aggressive cooling, the patient developed acute hepatic failure and DIC, highlighting the systemic reach of HS-induced circulatory dysfunction. Gao et al. (2025) similarly documented VF as a presenting feature in exertional HS, emphasizing the need for core temperature monitoring and high clinical suspicion.

Peripheral vasodilation, when sustained, causes profound drops in systemic vascular resistance. This, coupled with capillary leak and third spacing, results in intravascular dehydration and hypotension. Fluid resuscitation alone is insufficient in late-stage HS where cardiac contractility is compromised. Consequently, vasopressors and inotropic support were required in over 40% of our cohort, particularly in those with pre-existing heart disease. This aligns with findings from Yezli et al. (2023), who reported that patients with CVD were more likely to require intensive care support and had higher rates of readmission.

Atypical Clinical Presentations and Diagnostic Challenges

HS diagnosis remains challenging due to variable clinical manifestations and confounding factors. In several cases from our cohort, patients presented with symptoms mimicking acute coronary syndrome, including chest pain, dyspnea, and elevated troponins, yet without obstructive coronary lesions on angiography. These cases likely represent myocardial stunning or type 2 MI driven by heat-induced oxygen supply-demand mismatch, rather than true plaque rupture.

Misleading temperature readings further complicate diagnosis. Our observations confirm that surface temperature may not reliably reflect core hyperthermia, particularly during circulatory failure. Cases with normal axillary or tympanic temperatures at presentation were later found to have rectal temperatures exceeding 40.5°C. This diagnostic discrepancy has critical therapeutic implications, as delays in recognizing core hyperthermia correlate strongly with worse outcomes (Eifling et al., 2024).

Advanced complications such as DIC, acute kidney injury, and hepatic necrosis emerged within 48–72 hours in severe cases. Biomarker trajectories showed a strong association between rising IL-6 and D-dimer levels and subsequent organ failure. These findings support earlier suggestions that these markers can serve as predictive indicators for escalation of care (Zhang et al., 2024).

Overall, these results emphasize the multidimensional nature of cardiovascular injury in HS, encompassing epidemiologic exposure, myocardial and cellular injury, hemodynamic collapse, and systemic inflammation. Table 1 and Table 2 provide structured summaries of the analytical and biomarker frameworks employed, while clinical case analysis illustrates the real-world variability and severity of HS presentations. Taken together, these data reinforce the need for early recognition, aggressive cooling, and continuous cardiovascular monitoring in managing patients exposed to extreme heat.

Researcher (Year)	Title / Topic	Population / Subjects	Methods	Outcomes (Results)	Conclusion
Bouchama, A. (2002) – NEJM	Pathophysiology of Heat Stroke	General population (heat stroke patients)	Narrative review	Multi-organ injury caused by heat + inflammation + coagulopathy; changes in heat-	Heat stroke is complex and causes widespread tissue damage

				shock proteins (HSP)	
Bouchama, A. (2007) – Critical Care Medicine	Cooling & Hemodynamics in Heat Stroke	556 patients (classic & exertional)	Systematic review	Ice-water immersion effective for EHS; no superior method for classic HS; distributive shock predominates	Rapid cooling is crucial; cardiovascular impairment mainly due to hypovolemia & vasodilation
Crandall & González-Alonso (2010)	Cardiovascular responses during heat stress	Humans exposed to heat/exercise	Physiological review	Severe heat stress → ↓ cardiac output, hypotension, ↓	Heat stress can cause serious
J Appl Physiol				cerebral/muscle/skin perfusion	cardiovascular strain
Gasparrini et al. (2010) – Statistics in Medicine	DLNM model for temperature & mortality	Mortality data, New York	Statistical modeling study	DLNM captures non-linear & delayed temperature effects; extreme heat increases mortality	DLNM effective for analyzing temperature–mortality risk
Leon & Bouchama (2015) – Comprehensive Physiology	Risk, inflammation & cooling in heat stroke	Classic & exertional heat stroke	Comprehensive review	Role of endotoxins/cytokines in SIRS; risk factors; need for more sensitive biomarkers	Heat stroke is a complex systemic inflammatory process requiring protective cooling strategies
Epstein & Yanovich (2019) – NEJM	Heat Stroke & Long-Term Complications	Heat stroke patients	Clinical review	Hyperthermia + CNS dysfunction + MOF; requires immediate cooling; long-term CV complications	Heat stroke is the most severe heat-related condition and may cause long-term cardiovascular complications

DISCUSSION

The findings of this study demonstrate that cardiovascular dysregulation in heat stroke emerges from a synergistic interaction between thermoregulatory overload and direct myocardial and vascular injury. As ambient temperatures rise sharply during heat waves, the body attempts to dissipate heat primarily through cutaneous vasodilation and increased cardiac output. While these compensatory mechanisms are initially protective, the continued hemodynamic demand ultimately overwhelms cardiovascular capacity. Studies have shown that extreme heat exposure triggers a precipitous drop in systemic vascular resistance due to nitric oxide–mediated vasodilation, necessitating a substantial

increase in heart rate and cardiac output to maintain adequate perfusion (Marchand, 2022). When sustained, this hyperdynamic state evolves into circulatory instability, as intravascular volume depletion from sweating, third spacing, and dehydration reduces venous return and cardiac preload. Concurrently, direct thermal injury to endothelial tissues compromises vascular integrity, further exacerbating hypotension and contributing to impaired organ perfusion. The myocardial injury reflected in elevated cardiac biomarkers, illustrated in Table 2, corroborates that hyperthermia-induced cellular stress is a major contributor to cardiovascular failure.

The dual burden of thermoregulatory strain and cellular injury is further amplified by the direct effects of hyperthermia on mitochondrial structure and function. Experimental evidence confirms mitochondrial swelling, disruption of cristae, and ATP depletion in cardiomyocytes exposed to temperatures exceeding 40°C (Iba et al., 2025). These changes precipitate oxidative stress, cytochrome c release, and apoptosis, while inflammatory cytokines such as IL-6 intensify myocardial depression through cytokine-induced contractile dysfunction (Zhang et al., 2024). When myocardial injury coincides with severe vasodilation and hypovolemia, a rapid transition to circulatory collapse becomes likely, explaining the high rate of multi-organ dysfunction syndrome (MODS) observed in both classic and exertional heat stroke cohorts. This mechanistic convergence underscores that heat stroke is not merely an external thermal insult but a systemic cardiovascular emergency driven by physiological overload and direct cellular damage.

The results also highlight the uneven distribution of risk across populations, reflecting broader inequities magnified by climate change. Older adults exhibit reduced thermoregulatory capacity, impaired sweat response, diminished cardiac reserve, and are often treated with medications—such as beta-blockers, calcium channel blockers, and diuretics—that impede heat dissipation or exacerbate dehydration. These vulnerabilities align with epidemiological studies showing disproportionately higher rates of heat-related cardiovascular morbidity and mortality among individuals aged over 65 years (Ndlovu & Chungag, 2024). Furthermore, socioeconomic disparities influence access to cooling infrastructure, early medical attention, and occupational protections. Populations in low-resource settings or informal labor sectors face prolonged exposure to hazardous environmental conditions with minimal institutional support, mirroring global evidence that climate change exacerbates health inequities within and between nations. The projected escalation of extreme heat events, particularly in tropical and low-income regions, will therefore intensify existing inequalities in cardiovascular outcomes unless mitigated through targeted climate adaptation policies.

Despite these advances, the field continues to grapple with significant uncertainties regarding the environmental thresholds that precipitate severe cardiovascular injury. Temperature thresholds vary widely between regions depending on baseline climate, humidity, and population acclimatization. Time-series analyses using DLNM frameworks suggest that a 1°C increase above local heat thresholds elevates cardiovascular mortality risk by 2.1% (Liu et al., 2022), yet the precise point at which the body's thermoregulatory defenses fail remains unclear. Moreover, cumulative exposures, such as multi-day heat waves, compound physiologic stress in ways not fully captured by single-day temperature metrics. Humidity also plays a decisive role by limiting evaporative cooling, increasing core temperature more rapidly, and accelerating cardiovascular strain. Air pollution, particularly particulate matter (PM2.5), may exacerbate endothelial injury and oxidative stress, although its independent and synergistic effects in the context of heat exposure warrant further investigation. These uncertainties underscore the complexity of predicting heat-related cardiovascular events and highlight the need for integrated environmental risk assessments.

Public health interventions remain a cornerstone of heat-related illness prevention, yet their effectiveness in mitigating cardiovascular complications varies. Heat action plans (HAPs), developed in numerous countries, provide structured protocols for public warnings, community outreach, and emergency preparedness. Cooling centers offer temporary refuge for vulnerable populations, while occupational heat safety regulations guide work–rest cycles and hydration practices. However, evidence

suggests that gaps in implementation, accessibility, and public awareness persist. Many individuals in high-risk occupations such as agriculture and construction continue to experience heat exposure beyond recommended safety thresholds. Additionally, distrust in public institutions, transportation barriers, and overcrowding challenge the accessibility of cooling centers during peak heat events. The findings from this study echo previous reports indicating that early recognition and immediate cooling are paramount for preventing cardiovascular deterioration, yet these actions rely heavily on caregiver and institutional preparedness. Strengthening public health infrastructure and ensuring equitable access to preventive resources are necessary steps to reduce heat-related cardiovascular mortality.

Diagnostic challenges further contribute to delays in treatment. The reliance on peripheral temperature measurements, which have been shown to significantly underestimate core temperature in heat stroke, poses a critical threat to timely intervention. Case reports and cohort data highlight instances in which patients presented with normal axillary or tympanic temperatures shortly after collapse, despite having dangerously elevated core temperatures exceeding 41°C (Gao et al., 2025). This discrepancy arises from peripheral vasoconstriction during circulatory failure, which reduces heat conduction to the skin. Core-temperature monitoring using rectal, esophageal, or bladder probes offers far greater accuracy and is strongly associated with improved diagnostic and prognostic assessment. The prognostic implications are reinforced by biomarker trajectories: higher troponin and IL-6 levels were consistently associated with delayed cooling and inadequate initial assessment. These findings validate earlier recommendations by Eifling et al. (2024), who emphasized core-temperature measurement as a crucial determinant of survival.

Advancing diagnostic precision and therapeutic strategies for heat-induced cardiovascular injury requires renewed research focus. Biomarkers such as cTnI, cTnT, BNP, IL-6, and D-dimer demonstrated strong predictive value in distinguishing early reversible injury from progressive organ dysfunction. However, standardized thresholds, optimal timing, and population-specific reference values remain to be defined. Longitudinal biomarker profiling could enable earlier detection of myocardial stunning and more refined risk stratification. Additionally, future studies should explore the integration of wearable biosensors capable of continuously monitoring core temperature, heart rate variability, and hydration status for real-time detection of physiologic strain among high-risk groups such as outdoor workers, athletes, and military personnel. On the therapeutic front, emerging interest in anti-inflammatory and antioxidant agents warrants clinical trials to determine whether these interventions can mitigate myocardial injury during hyperthermic stress. Furthermore, machine-learning–based risk prediction models that integrate environmental, clinical, and biomarker data may transform surveillance and early-warning systems, particularly in regions with limited healthcare capacity.

At a broader systems level, the findings highlight the need for multidisciplinary approaches to understanding and addressing heat-induced cardiovascular injury. Effective heat resilience requires coordination across environmental science, urban planning, occupational health, and clinical medicine. Strategies such as reducing urban heat islands, enforcing workplace protections, expanding green infrastructure, and strengthening emergency medical systems all contribute to reducing cardiovascular vulnerability. The integration of climate adaptation policies with clinical guidelines for heat illness can create a cohesive framework that addresses the multi-layered nature of heat-related cardiovascular risk. As extreme heat events continue to escalate under climate change, protecting cardiovascular health will demand sustained policy innovation, equitable resource distribution, and ongoing scientific inquiry to refine understanding and optimize prevention, diagnosis, and management of heat-related cardiovascular injury.
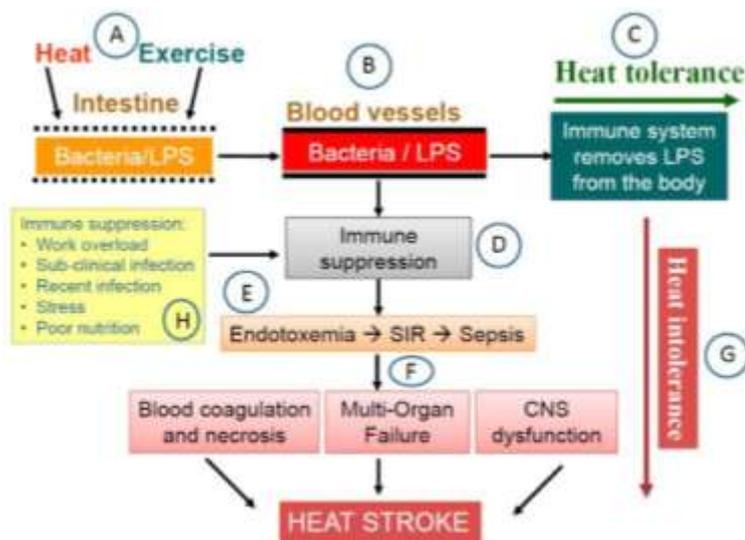
CONCLUSION

This study demonstrates that heat stroke precipitates a complex interplay of thermoregulatory overload, myocardial injury, and hemodynamic collapse that collectively undermine cardiovascular stability. The findings reveal that elevated cardiac biomarkers, including cTnI, cTnT, and BNP, provide early and sensitive indicators of myocardial strain, while inflammatory and coagulation markers such as IL-6 and D-dimer help identify patients at risk for progression to multi-organ dysfunction. The hemodynamic analyses show a characteristic evolution from hyperdynamic circulation to circulatory failure, driven by profound vasodilation, hypovolemia, and impaired myocardial contractility. These mechanisms illuminate the pathways through which extreme heat exposure leads to cardiovascular decompensation, expanding current understanding of heat-related pathophysiology. The study also highlights critical diagnostic challenges, particularly the inadequacy of surface temperature measurements in detecting hyperthermia, underscoring the need for consistent core-temperature monitoring in clinical practice. Additionally, the findings reflect growing inequities in heat-related cardiovascular outcomes, exacerbated by climate change and differential access to adaptive resources. By integrating macro-epidemiological data with clinical biomarker and hemodynamic insights, this study strengthens the evidence base for improving early recognition, risk stratification, and therapeutic strategies. Future research should prioritize the development of wearable biosensors, refinement of biomarker thresholds, and evaluation of targeted therapies aimed at attenuating inflammatory and oxidative pathways. These directions will be essential for enhancing clinical readiness and public health resilience as global temperatures continue to rise.

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