Early risk stratification and workflow acceleration in the emergency department: from thermal emergencies to triage-driven decision support

PhD Thesis

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1. INTRODUCTION

Extreme temperatures are an increasingly important indicator of the link between climate change and severe health consequences, including death. In Europe, it is estimated that approximately 47,690 people died from heat-related causes in 2023, rising to 62,775 in 2024. These numbers are expected to rise further due to ongoing climate change and an ageing population. In temperate climates, thermal exposure occurs not only outdoors, but also indoors and within institutions. This increases the need for a structured approach to assessing vulnerability to thermal loads in emergency departments (ED).

Both heatstroke and severe accidental hypothermia are potentially fatal conditions. In cases of heatstroke, there is a sudden rise in core body temperature, which can lead to neurological symptoms, organ failure and coagulation disorders. Hypothermia is defined as a condition in which core body temperature drops below 35 °C. In such cases, metabolism is disrupted, breathing and circulation become irregular, blood clotting deteriorates, and the risk of arrhythmia—or even cardiac arrest—increases. In both cases, time is of the essence: the sooner the condition is recognised and treatment begins, the greater the chance of survival.

When EDs become overwhelmed, patients have to wait longer for assessment and diagnostic workup, during which conditions can deteriorate. Digital questionnaires are a valuable tool for collecting patient data immediately after triage. This can shorten the interval from triage to clinician laboratory ordering, enabling earlier risk stratification and escalation decisions. However, such tools require rigorous oversight and continuous performance monitoring.

Vulnerability to temperature-related emergencies in the ED is influenced by personal factors such as comorbidities, medication use and housing instability. This transforms the problem from a predictable outdoor phenomenon into a more challenging and less visible issue. Current hypothermia staging systems, which primarily rely on level of consciousness, are not very accurate in heterogeneous urban populations where intoxication, neurological disease and polypharmacy can complicate clinical assessment.

This dissertation examines a front-end strategy in which objective signals identified at the triage level indicate risk. A limited early laboratory panel then refines this risk in selected patients, while dynamic monitoring supports escalation without replacing clinical judgement. Six original studies, conducted at a single academic emergency department (ED), progress from identifying prognostic signals (Pillar 1) and investigating their mechanisms (Pillar 2), to developing decision support concepts for practical implementation (Pillar 3).

2. OBJECTIVES

This dissertation aims to develop and evaluate pragmatic risk-stratification concepts for ED patients exposed to thermal stress, and to explore how these concepts can be translated into protocols to accelerate and, where appropriate, escalate workflows.

Objective 1 – Early risk stratification in thermal emergencies (Papers I–III): To characterise early clinical and laboratory risk signals in heat stroke (Paper I) and accidental hypothermia (Papers II–III), and to evaluate whether triage-level variables—triage category and admission temperature—can predict early critical outcomes in a temperate-climate ED.

Objective 2 – Biomarker dynamics and coagulopathy during hypothermic rewarming (Papers IV–V): To assess the dynamics of biomarkers and coagulopathy during rewarming in the early phase of ED care in accidental hypothermia, and whether these trajectories differ between critical and non-critical outcomes.

Objective 3 – Machine-learning-based workflow acceleration (Paper VI): To develop and internally validate a machine-learning-based model that predicts clinician laboratory orders from patient-reported symptoms collected at triage, and to estimate the potential time savings of an anticipatory workflow before clinician laboratory ordering.

3. METHODS

This dissertation comprises six original publications from the Department of Emergency Medicine at Semmelweis University in Budapest. The studies

combine retrospective analysis of ED data, prospective pilot sampling, and development of machine-learning-based models within a unified framework.

Heat stroke study (Paper I)

A retrospective cohort study (n = 8) of patients with body temperature ≥40 °C between June and July 2024, identified through ICD-10 hyperthermia codes with manual chart review confirmation. Heat stroke was defined as documented temperature ≥40 °C with central nervous system dysfunction. Survivors and non-survivors were compared using Mann–Whitney U tests with Cliff's delta effect sizes. Ethics: SE RKEB 198/2021.

Hypothermia triage and temperature model (Paper II)

A retrospective single-centre study (2020–2024) of 131 patients with accidental hypothermia (ICD-10 T68, tympanic temperature <35 °C). Triage category, assigned according to the Hungarian Emergency Triage System (MSTR), and admission temperature were evaluated as predictors of early critical outcome (ED death or intensive care unit [ICU] admission). Discrimination was assessed by the area under the receiver operating characteristic curve (ROC-AUC); calibration was reported graphically with Brier score, calibration intercept, and calibration slope. Ethics: SE RKEB 274/2024.

Hypothermia comorbidity and staging study (Paper III)

A retrospective cohort study of 125 patients (March 2021–March 2025) examining comorbidities, chronic medications, homelessness, and consciousness–temperature discordance across temperature-defined severity categories. Exploratory Firth penalised logistic regression was performed. Ethics: SE RKEB 274/2024.

Biomarker dynamics during rewarming (Paper IV)

A prospective pilot study (December 2024–October 2025) of 18 patients with paired biomarker measurements during ED rewarming. Hypothermic-state and rewarmed-state (≥35 °C) draws were compared. Parameters included blood glucose, haematocrit, complete blood count, high-sensitivity troponin

T (hs-TnT), C-reactive protein (CRP), and lactate. Ethics: SE RKEB 274/2024.

Coagulation pilot with viscoelastic testing (Paper V)

A prospective pilot study (December 2024–March 2025) of 16 patients assessing routine coagulation tests and viscoelastic testing (ClotPro®, measured at 37 °C) during hypothermia and after rewarming. Extrinsic pathway and ecarin-based assay clotting time, clot formation time, and clot firmness were recorded. Patients on anticoagulants were excluded. Ethics: SE RKEB 274/2024.

Machine-learning laboratory order prediction (Paper VI)

A non-interventional observational study (October 2023–February 2025; n = 3,925) using prospectively collected digital symptom questionnaire data linked to retrospective electronic health record (EHR) laboratory orders. Separate random forest models were trained for six laboratory tests using 10-fold nested cross-validation. The interval between questionnaire completion and physician ordering was used to simulate potential time savings. Ethics: BM/18039-3/2023.

4. RESULTS

Heat stroke (Paper I)

Among eight patients meeting the case definition, three (37.5%) died in the ED. Non-survivors had significantly lower pH (7.07 vs. 7.40), higher potassium (7.3 vs. 3.2 mmol/L), higher lactate (10.9 vs. 3.5 mmol/L), higher $PaCO_2$ (57.2 vs. 28 mmHg), and higher ionised calcium (1.19 vs. 0.97 mmol/L; all $p = 0.036$). Core temperature was paradoxically lower in non-survivors (40.6 vs. 42.2 °C; $p = 0.294$), possibly reflecting heterogeneity in measurement timing relative to cooling initiation.

Hypothermia triage model (Paper II)

In 131 patients (median age 67 years; 67.2% male; median tympanic temperature 29.3 °C), early critical outcome occurred in 33.6% of cases (28

ED deaths, 16 ICU admissions). Triage category alone achieved an ROC-AUC of 0.683 (95% confidence interval [CI] 0.598–0.767), improving to 0.740 (95% CI 0.644–0.829) when combined with admission temperature. This combined model yielded a higher point-estimate discrimination than Swiss staging (0.644) or Wilderness Medical Society (WMS) staging (0.637) applied to this cohort.

Comorbidity and staging patterns (Paper III)

Among 125 patients, ED mortality was 18.4%. Nearly half (44.0%) had no registered residence. Consciousness level frequently diverged from temperature-defined severity: 30.0% of Stage III and 18.2% of Stage IV patients were alert, while 34.6% of Stage I patients responded only to pain or were unresponsive. Alcoholism and cardiovascular diseases were the most common comorbidities across all stages. Each 1 °C increase in tympanic temperature was associated with lower odds of ED mortality (odds ratio [OR] 0.83; 95% CI 0.72–0.95; $p = 0.005$).

Biomarker dynamics (Paper IV)

Among 18 patients with paired sampling, 8 had early critical outcomes. During rewarming to ≥35 °C, significant within-patient changes included decreases in blood glucose, haematocrit, red blood cell count, lymphocyte count, and lymphocyte percentage, alongside increases in hs-TnT and CRP. These biomarker changes are exploratory, and the troponin T signal in particular cannot be separated from resuscitation intensity and illness severity. At the first normothermic assessment, the neutrophil-to-lymphocyte ratio was significantly higher in the critical group (median 18.52 vs. 2.22; Cliff's $\delta = 0.92$; $p = 0.016$). Five of eight critical patients failed to achieve normothermia within the observation window, compared with one of ten non-critical patients.

Coagulation and viscoelastic testing (Paper V)

Among 16 patients (8 early critical outcomes), ecarin-based clotting time (ECA-CT) and clot formation time (ECA-CFT) were significantly prolonged in the critical group during hypothermia (ECA-CT: 112.0 vs. 65.0 s, $p = 0.025$; ECA-CFT: 100.0 vs. 70.0 s, $p = 0.003$). After rewarming, ecarin-

based times shortened, with greater magnitude of change in the critical group (Δ ECA-CT between groups: −39.5 s, p = 0.019). Only 3 of 8 critical patients reached normothermia, compared with all 8 non-critical patients (p = 0.026).

ML laboratory order prediction (Paper VI)

Random forest models achieved ROC-AUC values of 0.74–0.88 for predicting clinician laboratory orders from triage symptom data. The highest discrimination was observed for glutamic-oxaloacetic transaminase/aspartate aminotransferase (GOT/AST; ROC-AUC 0.88) and the highest precision–recall AUC (PR-AUC) for CRP (0.95, corresponding to 90% ordering prevalence). Median potential time savings ranged from 1 h 12 min (procalcitonin, PCT) to 1 h 53 min (D-dimer), with 95th-percentile values reaching 4 h 19 min to 6 h 28 min.

5. CONCLUSIONS

The dissertation, based on six original studies, shows that variables available in the early stages of emergency department care, such as triage category, measured temperature, mental status as a risk modifier and a narrow admission laboratory panel, can support the pragmatic risk stratification of thermal emergencies. The integrated conclusions are as follows:

In cases of heat stroke, early ED mortality was found to be associated with severe acid–base and electrolyte disturbances. This supports the use of low-threshold arterial blood gas and electrolyte testing in suspected cases. It should be noted that these findings remain hypothesis-generating in view of the small sample size.

In cases of accidental hypothermia, using a combination of the triage category and the admission tympanic temperature provided a more accurate prediction of early critical outcomes than the hypothermia-specific staging systems examined. However, confidence intervals overlapped across models. This could inform decisions regarding higher-level care, resource planning and intensive care consultations, particularly when accurate staging data are unavailable at admission. Conceptually, this triage-level model is a precursor to hospital-level prognostic tools, such as the Hypothermia Outcome

Prediction after Extracorporeal Life Support (HOPE) score, which is used at a later stage when more detailed physiological data are available.

In a diverse urban population, consciousness level often differed from temperature-defined severity, supporting the prioritisation of objective temperature measurement, ideally core temperature. If tympanic measurement is used, the measurement site should be documented. Altered mental status should be interpreted as an important risk modifier rather than a substitute for temperature.

Prospective pilot studies identified trajectories consistent with haemodilution, inflammation and hypothermia-associated coagulopathy during the ED rewarming phase. Elevated neutrophil-to-lymphocyte ratios and prolonged ecarin-based clotting times in critical cases suggest that dynamic monitoring during rewarming could help to identify deterioration. However, these observations require validation in larger cohorts.

Models based on patient-reported symptoms were able to predict certain laboratory orders with moderate to strong internal discrimination and projected time savings that were clinically meaningful. However, modelling clinical decisions does not equate to determining actual medical needs. Strict professional governance, continuous monitoring of model drift, and auditing of subgroup-level performance are essential prerequisites for the safe implementation of such models.

Several considerations can already be incorporated into practice during the emergency admission phase. It is important to take an early temperature reading and to record where the measurement was taken. Level of consciousness should not be treated as a substitute for severity determined by temperature. In cases of suspected accidental hypothermia, the triage classification and admission temperature together can serve as an early risk indicator. In cases of suspected heatstroke, it is advisable to order blood gas and electrolyte tests with a low threshold.

Routine monitoring of biomarker changes during the rewarming phase, the application of viscoelastic thresholds, and machine learning-based predictive lab ordering remains exploratory. Each of these requires prospective, multicentre studies before they can become part of routine patient care.

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