International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 15, No. 3, 2026

Pre-culture Hypothermia and Short-term Mortality Among ICU Patients with Positive Blood Cultures: A Retrospective Cohort Study Using MIMIC-IV

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Abstract: Temperature is often treated as a simple trigger for infection work-up in the intensive care unit (ICU), yet the absence of fever can be clinically deceptive. We conducted a retrospective cohort study using MIMIC-IV v3.1 to examine whether temperature patterns before the first qualifying positive blood culture were associated with short-term mortality in adults with operationally defined ICU-acquired bloodstream infection (BSI). The index event was the first positive blood culture collected at least 48 hours after ICU admission; patients with an earlier positive blood culture in the same hospitalization before ICU hour 48 were excluded. Temperature patterns during the 24 hours before culture were classified as normothermic, febrile, hypothermic, or mixed dysregulated. Among 525 patients, pre-culture temperature data were available for 511. Hypothermia occurred in 51 patients and was associated with higher in-hospital mortality than normothermia after adjustment for age, sex, time from ICU admission to culture, vasoactive infusion, and invasive ventilation (odds ratio [OR] 2.20, 95% confidence interval [CI] 1.13-4.28). The association was similar for ICU mortality and observed 28-day mortality within available hospital/ICU follow-up. A complete-case laboratory-adjusted model showed a similar direction but wider uncertainty. These findings support pre-culture hypothermia as a nurse-sensitive surveillance signal rather than a causal claim or a stand-alone prediction rule.

Keywords: Bloodstream Infection; Hypothermia; Intensive Care Unit; MIMIC-IV; Nursing Surveillance; Temperature.

1. Introduction

Bloodstream infection acquired during critical illness rarely presents as a clean diagnostic event. [1,2] A positive blood culture after several ICU days may reflect a new infection, progression of an infection that was already incubating, device-related infection, or contamination. This uncertainty is not just a methodological inconvenience. It is the same uncertainty nurses and physicians face during handoff, when a patient is deteriorating but the microbiology result has not yet clarified the source or the organism.

Fever tends to dominate infection recognition. In practice, a febrile spike often prompts cultures, antimicrobial review, and renewed attention to lines, wounds, drains, and respiratory secretions. Low temperature receives less intuitive urgency, although hypothermia in severe infection may signal shock, impaired host response, active temperature intervention, sedation, or advanced physiologic exhaustion. Prior ICU and sepsis studies have reported nonlinear relationships between body temperature and mortality.[3,4] What remains less well characterized is the short interval before the first ICU blood culture becomes positive.

The nursing relevance is straightforward but easily underestimated. Temperature is measured repeatedly, passed through shift reports, and interpreted alongside perfusion, urine output, vasopressor changes, mental status, device status, and laboratory trends. A common ICU management scenario illustrates the problem: a ventilated patient with suspected infection may have no fever, but the handoff shows a new temperature of 35.7 C, increasing norepinephrine requirement, and delayed lactate recheck. In such a situation, the absence of fever should not soften the infection reassessment. It should sharpen it. This study was designed around that operational question rather than around an abstract prediction exercise.

We used MIMIC-IV to examine whether simple temperature-response patterns during the 24 hours before a qualifying positive blood culture were associated with short-term mortality. The exposure window was deliberately placed before microbiological recognition, because post-culture temperature can be shaped by treatment, survival time, and documentation intensity. We hypothesized that pre-culture hypothermia would identify a higher-risk bedside phenotype.[5] Mixed temperature dysregulation was treated as exploratory from the outset because it was expected to be uncommon.

2. Methods

2.1. Data Source and Study Design

This retrospective cohort study used a local PostgreSQL installation of MIMIC-IV v3.1, a de-identified critical-care database distributed through PhysioNet.[6,7] The study followed STROBE principles for observational research.[8] All analyses were conducted locally, and no patient-level analytic file is included in the manuscript package.

2.2. Cohort Definition

Adults aged 18 years or older were eligible during their first ICU stay. The index event was the first qualifying positive blood culture collected at least 48 hours after ICU admission and before ICU discharge. To reduce inclusion of infections already present at ICU entry, patients with any positive blood culture earlier in the same hospitalization before ICU hour 48 were excluded. This rule improves temporal clarity but does not transform the cohort into an adjudicated clinical hospital-acquired BSI cohort.

Blood-culture records required a blood specimen

description and a non-missing organism name. Cancelled records, screening or surveillance entries, and administrative non-organism labels were excluded. Common skin organisms were excluded unless the same organism appeared in at least two positive blood-culture records within 48 hours. Because structured microbiology records did not reliably distinguish peripheral from catheter-drawn samples, the analysis could not classify central line-associated bloodstream infection (CLABSI).

2.3. Temperature Exposure

Temperature was extracted from ICU charted events. Celsius values were used directly, and Fahrenheit values were converted to Celsius. Implausible values were removed. The primary exposure used all valid temperatures documented during the 24 hours before the index culture. Fever was defined as >=38.3 C, and hypothermia was defined as <=36.0 C, thresholds commonly used in critical-care and sepsis work.

Patients were classified as normothermic, febrile, hypothermic, or mixed dysregulated. Normothermia meant no recorded fever and no recorded hypothermia. The febrile group had at least one temperature >=38.3 C without hypothermia; the hypothermic group had at least one temperature <=36.0 C without fever. The mixed dysregulated group had both fever and hypothermia in the same pre-culture window. Because charted temperature density varied, sustained hypothermia for 6 consecutive hours could not be reliably defined across the cohort.

2.4. Outcomes and Covariates

The primary outcome was in-hospital mortality. Secondary outcomes were ICU mortality after the index culture and observed 28-day mortality within available hospital/ICU follow-up. The observed 28-day endpoint should not be read as complete post-discharge 28-day all-cause mortality.

Primary adjustment variables were age, sex, log-transformed time from ICU admission to culture, vasoactive infusion during the 24 hours before culture, and invasive ventilation during the same window. Vasoactive infusion and invasive ventilation were coded as binary variables. Dose, duration, ventilator mode, and intensity of support were not modeled. Important confounders such as chronic kidney disease, diabetes, malignancy, immunosuppression, infection source, antimicrobial timing, source control, antipyretics, and warming or cooling interventions were not reliably available in the structured analysis dataset.

2.5. Statistical Analysis

Continuous variables were summarized as medians and interquartile ranges; categorical variables were summarized as counts and percentages. Logistic regression estimated ORs and 95% CIs, using normothermia as the reference group. Sensitivity analyses excluded fungal BSI and retained common-commensal organisms. Laboratory-adjusted models added pre-culture lactate, creatinine, white blood cell count, and platelet count. Because lactate was missing in nearly half of the cohort, the laboratory-adjusted analyses were interpreted as exploratory.

To address concern that the 24-hour temperature pattern might reflect measurement fluctuation, we also examined temperature nadir and temperature standard deviation. A post-culture landmark analysis was restricted to patients who remained in ICU for at least two days after the index culture and had post-culture temperature data. Cox or competing-risk models were not fitted because reliable post-discharge survival time was not available for this analysis.

3. Results

The stricter operational definition yielded 525 patients. In-hospital mortality was 194 of 525 (36.9%), ICU mortality was 167 (31.8%), and observed 28-day mortality within available hospital/ICU follow-up was 185 (35.2%). Pre-culture temperature was available in 511 patients. Lactate was missing in 252 patients (48.0%), which is clinically important because lactate is often ordered selectively rather than randomly.

The most common organisms were Staphylococcus aureus, Enterococcus faecium, retained coagulase-negative staphylococci, Staphylococcus epidermidis, Candida albicans, and Candida glabrata. Candida bloodstream infection accounted for 93 patients (17.7%). This mixture is typical of a broad ICU blood-culture cohort[9], but it also means that the results should not be interpreted as CLABSI-specific.

Table 1. Temperature patterns and mortality.

Pre-culture temperature pattern	N	In-hospital mortality	ICU mortality
Normothermic	219	84 (38.4%)	70 (32.0%)
Febrile	225	61 (27.1%)	53 (23.6%)
Hypothermic	51	31 (60.8%)	30 (58.8%)
Mixed dysregulated	16	10 (62.5%)	7 (43.8%)
Missing pre-culture temperature	14	8 (57.1%)	7 (50.0%)

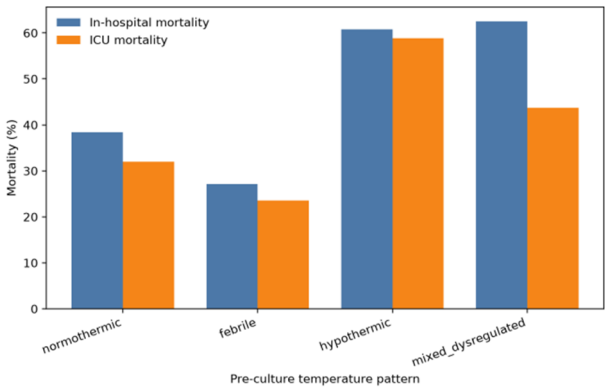

Fig 1. In-hospital and ICU mortality by pre-culture temperature pattern

Compared with normothermia, pre-culture hypothermia was associated with in-hospital mortality (OR 2.20, 95% CI 1.13-4.28), ICU mortality (OR 2.69, 95% CI 1.38-5.24), and observed 28-day mortality (OR 2.30, 95% CI 1.19-4.45). The febrile pattern was not associated with higher mortality. Its apparent lower risk in the primary model weakened after laboratory adjustment, which argues against interpreting fever as protective.

The mixed dysregulated group had high crude mortality, but only 16 patients fell into this category. The estimate is therefore unstable and should not be used as an independent clinical phenotype. After excluding retained common-contaminant organisms, the hypothermia estimate remained elevated (OR 2.42, 95% CI 1.15-5.09). In non-fungal BSI, the direction was similar but less precise (OR 2.01, 95% CI 0.89-4.52).

Table 2. Selected regression estimates for in-hospital mortality.

Model	Predictor	OR	95% CI	p value
Primary model	Febrile pattern	0.67	0.43-1.04	0.074
Primary model	Hypothermic pattern	2.20	1.13-4.28	0.020
Primary model	Mixed dysregulated pattern	2.96	1.00-8.77	0.050
Laboratory model, complete case	Hypothermic pattern	1.98	0.73-5.34	0.180
No retained commensals	Hypothermic pattern	2.42	1.15-5.09	0.020

Temperature nadir analysis supported the same clinical signal. Crude in-hospital mortality was 61.2% when the lowest pre-culture temperature was <=36.0 C, 42.3% at 36.1-36.5 C, 33.1% at 36.6-37.0 C, and 23.8% at 37.1-37.5 C. Temperature standard deviation was not independently associated with mortality after adjustment.

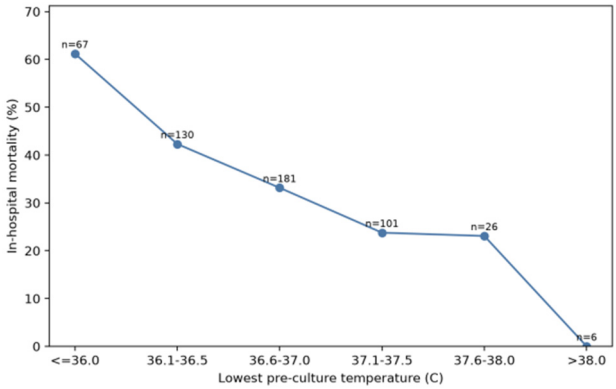

Fig 2. In-hospital mortality by lowest pre-culture temperature.

4. Discussion

This study points to a clinically familiar but underemphasized problem: some high-risk ICU patients with bloodstream infection do not announce themselves with fever. Hypothermia before positive blood-culture collection was associated with higher short-term mortality across several outcomes. The association persisted in direction when the analysis was restricted, but the laboratory-adjusted complete-case model became imprecise. That pattern is believable. It suggests a bedside signal worth acting on, not a clean causal mechanism.

The finding should be read against the realities of ICU infection management. A nurse receiving handoff on a patient with a new positive culture risk does not see a regression coefficient. The nurse sees a trajectory: a cooler patient, changing vasopressor needs, delayed labs, a central line that may or may not be implicated, and a team deciding whether the current antimicrobial plan is enough. The practical value of this work is to make hypothermia harder to dismiss in that moment. A temperature of 35.8 C during suspected infection deserves the same disciplined reassessment that a fever spike often receives.

A reasonable surveillance response is not complicated. When pre-culture or suspected-infection hypothermia appears, bedside staff should review perfusion, mental status, urine output, vasopressor trajectory, lactate when available, and recent antimicrobial decisions.[10,11] Lines, drains, wounds, respiratory secretions, and urinary devices should be reconsidered as possible sources. If these concerns cluster, the issue should be escalated during multidisciplinary rounds or directly to the responsible clinician. This is not a treatment protocol. It is a structured way to prevent a low-temperature signal from being lost because the patient is not febrile.

Several implementation problems deserve attention. Temperature documentation is uneven; some patients are measured continuously, others intermittently. Active warming, cooling blankets, antipyretics, sedation, and procedures can all distort the apparent host response. During a real ICU quality-improvement effort, these issues would need to be handled through documentation standards, handoff prompts, and periodic audit. A simple improvement would be to add a line to infection reassessment templates: 'hypothermia or falling temperature present?' That line would not decide care, but it would force a pause at the right point in the workflow.

The study also cautions against an easy story about fever. Fever was not a mortality-risk signal in this cohort, and its apparent lower risk attenuated after laboratory adjustment. One possible explanation is that fever sometimes reflects a more preserved inflammatory response, whereas hypothermia can reflect shock or impaired reserve. That remains a hypothesis. The present analysis does not include immune status, antipyretic exposure, active warming/cooling, or granular antimicrobial timing, so biological interpretation must remain modest.

5. Limitations

The limitations are not minor. The BSI definition was operational, not adjudicated. Excluding earlier positive cultures before ICU hour 48 reduced misclassification but could not eliminate infection already incubating at ICU entry. Sampling site information was incomplete, preventing reliable separation of peripheral and catheter-drawn cultures and preventing CLABSI classification.

The mixed dysregulated group was too small for independent inference. Post-culture temperature analyses are vulnerable to survival and observation bias. The study is also based on a single-center public database, so external validation is needed before embedding the signal into formal risk tools.

6. Conclusion

In operationally defined ICU-acquired BSI, hypothermia during the 24 hours before positive blood-culture collection was associated with higher in-hospital, ICU, and observed 28-day mortality. The association should be used cautiously: it is a bedside surveillance signal, not proof of causation. For ICU nursing practice, the actionable message is narrow and important. A patient with suspected infection who is hypothermic should not be considered reassuring simply because fever is absent.

Data Availability and Ethics

MIMIC-IV v3.1 is distributed by PhysioNet under credentialed-access terms. This study used de-identified data and did not attempt patient re-identification. Reproduction requires authorized MIMIC-IV access and local execution of the SQL and analysis scripts.

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