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Original article

Impact of heart rate on the outcome of hypothermic patients

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Abstract

Objective: This study aimed to identify prognostic factors for hypothermia, including hormone levels.

Materials and Methods: This retrospective analysis used data from our department's database from November 2018 to December 2023. Inclusion criteria comprised cases with a prehospital diagnosis of hypothermia (body temperature <35°C) established by emergency medical technicians. Patients in cardiac arrest upon arrival were excluded from the study. This study investigated various parameters, including age, sex, body temperature, systolic blood pressure, heart rate, Glasgow Coma Scale (GCS) score, and adrenocorticotropic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), C-reactive protein, total protein, albumin levels, and outcomes. Patients were categorized into two groups based on the discharge outcome: fatal and survival groups. This study compared the variables between the two groups.

Results: There were 28 and 53 patients in the fatal and survival groups, respectively. The average heart rate and FT3 levels in the fatal group were significantly lower than those in the survival group. The average cortisol and CRP levels in the fatal group were significantly higher than those in the survival group.

Conclusion: This is the first report to demonstrate that hypothermic patients with a fatal outcome tend to have low heart rate, low FT3 levels, high cortisol levels, and inflammation upon arrival at the hospital. Further studies with larger sample sizes are needed to confirm the clinical significance of our findings.

Key words: hypothermia, low T3 syndrome, heart rate

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Introduction

Hypothermia is an involuntary drop in the body temperature to below 35°C. Accidental hypothermia is not confined to regions or times of severe cold and can occur even in milder climates. Hypothermia occurs when the body loses more heat than it absorbs or generates, making it unable to produce sufficient heat to maintain homeostasis and proper bodily functions. The underlying cause of accidental hypothermia is excessive cold stress and inadequate heat generation from the body (thermogenesis); other factors also contribute to the risk of developing hypothermia. Functional central and peripheral nervous systems, along with proper behavioral adaptation, are crucial components[1–4]. Extremes of age, hypoglycemia, malnutrition, and endocrine disorders are examples of inadequate heat production. Skin disorders and improper peripheral vasodilation due to peripheral dysfunction exacerbate heat loss. Conditions such as cerebrovascular accidents, neurodegenerative disorders, and drug abuse may disrupt the hypothalamic thermoregulatory function. In addition to organic causes, impaired behavioral responses to cold stress may result in hypothermia in individuals with dementia, drug abuse disorders, or psychiatric conditions. Situational circumstances such as lack of shelter or clothing may occur among the homeless.

Data on the epidemiology of hypothermia are limited, and there are no reports on the analysis of hormonal data on hypothermia. At our facility, we measured thyroid function in patients with shock or abnormal body temperature. This study aimed to gather data on the epidemiology of hypothermia.

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Materials and Methods

The protocol for this retrospective study was approved by our institutional review board (approval number: 298), and the study was conducted in accordance with the standards of good clinical practice and the Declaration of Helsinki.

This study was a retrospective analysis of the database of the Department of Acute Critical Care Medicine at Shizuoka Hospital, Juntendo University, a tertiary care center located in the eastern region of Shizuoka Prefecture, approximately 130 km southwest of Tokyo, Japan. The eastern region of Shizuoka Prefecture is approximately 4,090 km^2 and has a population of approximately 2 million. Due to a shortage of medical resources in this area, the most severely ill or traumatized patients are transported to our hospital by ground ambulances or doctor helicopters. This study was conducted between November 2018 and December 2023. The inclusion criteria were a prehospital diagnosis of accidental hypothermia established by emergency medical technicians and subsequently registered in the medical database in our department, with a temperature <35°C measured by rectal or bladder temperature. The exclusion criteria were cases with cardiac arrest on arrival, temperature over 35°C on arrival, and unknown final outcomes. Patients' age, sex, body temperature, systolic blood pressure, heart rate, respiratory rate, Glasgow Coma Scale (GCS) score, and adrenocorticotropic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), FT3/TSH, C-reactive protein, total protein, and albumin levels, and outcomes were investigated, with all parameters measured at the time of arrival. Patients were divided into two groups: the fatal group, which included patients with a fatal outcome, and the survival group, which included patients with a survival outcome on discharge. The variables were compared between the two groups.

Our standard methods for the treatment of hypothermia include the infusion of warm lactated Ringer's solution and warming with a forced-air warming body blanket. Percutaneous cardiopulmonary support is not routinely employed for rewarming, except in patients experiencing cardiac arrest.

All statistical analyses were performed using JMP software (version 13.0; SAS Japan Incorporation, Tokyo, Japan). Data were analyzed using a non-paired Student's t-test or χ^2 test for comparisons between the two groups. Statistical significance was set at $P<0.05$. difference. All data are presented as mean ± standard deviation.

Results

During the study period, 353,582 patients were registered in the database. Of these patients, there were 105 patients who were diagnosed with accidental hypothermia. After excluding 12 patients with cardiac arrest on arrival, 7 with temperatures over 35°C on arrival, and 5 with unknown final outcomes, 81 patients were included in this study. There were 28 patients in the fatal group and 53 in the survival group.

The results of the analyses of the two groups are pre-

Table 1 Analysis results

	Fatal	Survival	*P*-value
	n=28	n=53	
Sex (male/female)	13/15	30/23	0.38
Age (years)	78.0 ± 19.0	78.8 ± 11.1	0.48
Glasgow Coma Scale	6 (8, 11)	10 (7, 13)	0.27
Systolic blood pressure (mmHg)	97.1 ± 34.4	104.0 ± 34.4	0.41
Heart rate (beats per minute)	52.7 ± 20.5	74.8 ± 29.6	0.0007
Respiratory rate	16.3 ± 5.8	18.2 ± 4.7	0.11
Body temperature	29.0 ± 2.5	29.8 ± 2.5	0.22
ACTH (pg/mL)	98.1 ± 143.3 (n=8)	50.5 ± 53.1 (n=23)	0.54
Cortisol (μg/dL)	49.7 ± 24.0 (n=8)	29.7 ± 14.8 (n=23)	0.01
FT3 (pg/mL)	1.38 ± 0.63 (n=24)	1.90 ± 0.71 (n=42)	0.001
FT4 (ng/dL)	1.20 ± 0.55 (n=24)	1.30 ± 0.31 (n=42)	0.25
TSH (μIU/mL)	40.9 ± 131.2 (n=25)	4.73 ± 9.1 (n=41)	0.25
FT3/TSH	0.78 ± 0.92	1.40 ± 1.73	0.08
C reactive protein (mg/dL)	7.64 ± 7.26	3.75 ± 5.35	0.005
Total protein (g/dL)	6.30 ± 1.04	6.51 ± 0.78	0.35
Albumin (g/dL)	3.10 ± 0.70	3.26 ± 0.69	0.69

ACTH: adrenocorticotropic hormone; TSH: thyroid-stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine.

sented in Table 1. There were no statistically significant differences in sex, age, GCS score, systolic blood pressure, respiratory rate, body temperature, and ACTH, FT4, TSH, FT3/TSH, total protein, and albumin levels between the two groups. However, the average heart rate and FT3 levels were significantly lower in the fatal group than in the survival group. The average cortisol and CRP levels in the fatal group were significantly lower than those in the survival group.

There were 3 cases in the fatal group and 1 case in the survival group that had over 10 μIU/mL of TSH and under 1.0 ng/dL of FT4, which was compatible with hypothyroidism (no significant difference, P=0.10). Additionally, 14 cases of low T3 syndrome (under 2.4 pg/mL of FT3 but levels of TSH and FT4 were within the normal limit) in the fatal group were significantly greater than the 19 cases of low T3 syndrome in the survival group (P=0.04).

Discussion

This study demonstrated that hypothermic patients with fatal outcomes tend to have low heart rates, low FT3 levels, high cortisol levels, and inflammation upon arrival at the hospital.

Concerning the low level of FT3, hypothyroidism should be evaluated. Some patients in the present study may have had decompensated hypothyroidism (myxedema coma), which is associated with significant morbidity and mortality[5]. However, most patients did not meet the definition of hypothyroidism. During illness, deiodination of thyroxine (T4) to triiodothyronine (T3) is downregulated, a condition known as "low T3 syndrome", representing an adaptive metabolic mechanism that reduces energy expenditure and prevents catabolism[6]. In the present study, low T3 syndrome was predominant in the fatal group. Recently, low T3 syndrome has been reported as a poor prognostic marker for multiple conditions or diseases[7–11]. However, there have been no reports indicating that low T3 syndrome is associated with a poor prognosis in hypothermic patients, making this the first study to demonstrate such an association. The use of hormone replacement therapy in the treatment of patients with low T3 syndrome remains controversial. Nevertheless, hormone replacement therapy has been shown to significantly improve the survival rates of neurocritical patients. However, hormone replacement therapy in hypothermic patients has not been studied; therefore, this is another issue that needs to be investigated in the future.

The present study demonstrated that hypothermic patients with fatal outcomes tend to exhibit inflammation. Infections are common causes of inflammation. Infected patients who develop hypothermia experience significantly worse outcomes than those who develop fever or maintain normal body temperature[12–14]. Therefore, infected patients may have been included in the fatal group. The pathophysiology of hypothermia in Systemic Inflammatory Response Syndrome and sepsis remains unclear, despite various theories proposed to explain it. Hypothermia in sepsis was previously attributed to a lack of pro-inflammatory cytokines, such as IL-6 and TNF-α. However, studies have failed to demonstrate a decrease in the inflammatory response during hypothermic sepsis[12]. Conversely, another proposed mechanism for the onset of hypothermia is an increased anti-inflammatory response, either through elevated anti-inflammatory cytokines such as IL-10 or reduced responsiveness of white blood cells to inflammatory signals[12]. While this study remains purely descriptive, the results suggest a causal relationship between elevated CRP levels and poor prognosis in hypothermic patients. Further research is required to explore this potential relationship and provide deeper insights into the roles of inflammation and infection in these conditions.

This study showed that hypothermic patients with fatal outcomes tend to have high cortisol levels. Cortisol concentrations increase during stress[15]. Generally, in response to cold stress, the hypothalamus attempts to stimulate heat production through shivering and increases thyroid, catecholamine, and adrenal activities[15]. However, the present study found no significant difference in body temperature upon arrival between the two groups. In contrast, the inflammatory response was greater in the fatal group than in the survival group. Inflammatory stress can lead to the release of cortisol from the adrenal glands[16]. Further studies are required to investigate the relationship and mechanisms of cortisol levels in patients with accidental hypothermia.

This study demonstrated that hypothermic patients with fatal outcomes tend to have a low heart rate upon arrival at a hospital. However, no previous studies have described this tendency. Because compensatory mechanisms to prevent hypothermia are overwhelming, patients with mild hypothermia initially demonstrate tachypnea, tachycardia, and hyperventilation[15]. However, moderate hypothermia is characterized by proportionate reductions in pulse rate and cardiac output, hypoventilation, central nervous system depression, and hyporeflexia. Severe hypothermia can lead to pulmonary edema, oliguria, areflexia, coma, hypotension, bradycardia, and ventricular arrhythmia[15, 17]. Bradycardia may be physiological in severe hypothermia; however, a low heart rate was a risk factor for fatal outcomes in the present study.

This study had some limitations. First, it had a small sample size, retrospective nature, and restricted selection criteria, limiting the generalizability of the results across different settings and environments. Moreover, establishing a clear mechanistic relationship between the poor outcomes of hypothermia and low heart rate, low FT3 levels, high cortisol levels, and inflammation requires further investigation

using a larger cohort to enhance the study's statistical power and confidence in the findings.

Conclusion

This study demonstrated that hypothermic patients with fatal outcomes tend to have low heart rates, low FT3 levels, high cortisol levels, and inflammation upon arrival at the hospital. Further studies with larger sample sizes are needed to confirm the clinical significance of our findings.

Conflicts of interest: The authors declare no conflicts of interest in association with this study.

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Consent for publication: All authors endorse the data and conclusions.

Data availability statement: We do not have data for availability.

Author contributions: All the authors made substantive contributions to this study. Soichiro Ota wrote the manuscript. Hiroki Nagasawa, Hiroaki Taniguchi, Tatsuro Sakai, Hiromichi Ohsaka, Kazuhiko Omori, and Youichi Yanagawa edited the manuscript.

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