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Target temperature management versus normothermia without temperature feedback systems for out-of-hospital cardiac arrest survivors

Hui Jai Lee[1,2], Jonghwan Shin[1,2], Kyoung Min You[1,2], Woon Yong Kwon[2,3], Kyung Su Kim[2,3], You Hwan Jo[2,4] and Seung Min Park[2,4]

Abstract

Objective: The clinical benefit of automatic temperature control devices remains unclear. We investigated the outcomes of out-of-hospital cardiac arrest (OHCA) survivors who had undergone either target temperature management (TTM) with a temperature feedback system (TFS) or maintenance of normothermia without a TFS during post-resuscitation care.

Methods: This study was a retrospective analysis of a multicenter prospective cohort of OHCA survivors who had received postcardiac arrest care from August 2014 to December 2018. The overlap propensity score weighting method was applied for adjustment between groups.

Results: A total of 405 OHCA survivors were included. TTM with a TFS and normothermia without a TFS were applied to 318 and 87 patients, respectively. Fever events were more common in patients with normothermia without a TFS. After propensity score matching, no statistically significant differences were observed in the 1-month good neurologic outcome

[1]Department of Emergency Medicine, Seoul Metropolitan Government – Seoul National University Boramae Medical Center, 20, Boramae-ro 5-gil, Dongjak-gu, Seoul, Republic of Korea
[2]Department of Emergency Medicine, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul, Republic of Korea
[3]Department of Emergency Medicine, Seoul National University Hospital, 101, Daehak-ro Jongno-gu, Seoul, Republic of Korea
[4]Department of Emergency Medicine, Seoul National University Bundang Hospital 82, Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, Republic of Korea

Corresponding author:
Jonghwan Shin, Seoul Metropolitan Government – Seoul National University Boramae Medical Center, 20, Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Republic of Korea.
Email: skyshiner@naver.com

(odds ratio 0.99, 95% confidence interval [CI] 0.56–1.25) or survival rate (odds ratio 1.25, 95% CI 0.88–1.78).

Conclusion: No significant differences in the 1-month neurologic outcome were observed between patients receiving TTM with a TFS and those undergoing normothermia without a TFS.

Keywords

Out-of-hospital heart arrest, hypothermia, induced, treatment outcome, critical care, target temperature management, temperature feedback system

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Introduction

Target temperature management (TTM) is the key component of modern postcardiac arrest care for comatose patients after successful resuscitation from cardiac arrest. After two large randomized controlled trials showed the benefits of hypothermia for out-of-hospital cardiac arrest (OHCA) survivors with a shockable rhythm, the Millennium guidelines suggested that temperature regulation or therapeutic hypothermia could improve neurological outcomes in patients with ischemic brain injury after cardiac arrest.[1–3] During the nearly 20 intervening years, several preclinical and clinical studies have established the beneficial effects of therapeutic hypothermia. Accordingly, TTM has been recommended for most comatose patients after cardiac arrest.[4–7] However, after a multicenter prospective trial using temperature-feedback devices showed no difference in neurologic outcome in patients randomized to target temperatures of 33°C versus 36°C, TTM procedures were changed and overall adherence to TTM wavered.[5,8–10] Moreover, a recent TTM-2 trial comparing the use of TTM (33°C) with the maintenance of normothermia showed no difference in clinical outcomes.[11]

Automated temperature control devices with a temperature feedback system (TFS) have several advantages including rapid induction of hypothermia, maintenance of a consistent temperature, and avoidance of fever or hypothermia overshooting. Thus, these devices are regarded as an important component of TTM.[5,7,8] However, the clinical benefit of TFSs has not yet been fully evaluated and the evidence for their use is insufficient.[12]

This study was conducted to assess whether TFSs provide any beneficial effect on neurological outcomes in OHCA patients.

Methods

Study design and setting

We conducted a retrospective analysis of prospectively registered data on OHCA patients who had undergone post-resuscitation care after the sustained return of spontaneous circulation (ROSC) in three hospitals between July 2014 and December 2018. All hospitals were tertiary university hospitals with an emergency department volume of approximately 60,000 (site A, south of Seoul), 90,000 (site B, Gyeonggi Province), and 70,000 (site C, north of Seoul) patients per year. All participating hospitals were equipped with facilities, equipment, and trained medical personnel to provide advanced cardiovascular life

support and post-resuscitation care to OHCA patients. Prospective data on prehospital management, advanced cardiovascular life support, and postcardiac arrest care were previously collected in accordance with the standardized Utstein-style guidelines[13,14] (ClinicalTrials.gov number, NCT03695718). All patient details were de-identified.

Participants

Comatose (Glasgow Coma Scale less than 8) OHCA survivors over the age of 18 years were included in the study. The exclusion criteria were as follows: 1) terminal illness or withdrawal of additive treatment after ROSC, 2) awake after ROSC, 3) active internal or external bleeding, 4) pregnancy, 5) hemodynamic instability (i.e., persistent shock despite adequate fluid resuscitation and vasopressor support), and 6) poor baseline functional status or cerebral performance category (CPC) 3 or less before cardiac arrest.

Treatment of postcardiac arrest patients was performed in accordance with each hospital's treatment protocol and was based on international guidelines.[15] Core temperature, mainly of the esophagus or bladder, was monitored for all patients. TTM was defined as the application of an automatic TFS for the control of temperature during post-resuscitation care. A surface cooling device—the Artic Sun® Temperature Management System (Bard, Murray Hill, NJ, USA) or Blanketrol® (Cincinnati Sub Zero Products, LLC, Cincinnati, OH, USA)—was used for TTM with a TFS. The target temperature was maintained for 24 hours. Rewarming was actively performed at a rate of approximately 0.25°C to 0.5°C per hour. After rewarming, normothermia was maintained with surface cooling devices during the initial 72 hours. Occurrences of core temperatures over 38°C were regarded as fever events.

A strategy of normothermia maintenance with fever control was used if the patient's caregivers did not consent—for cost or other reasons—to TTM with an automatic TFS. Acetaminophen or a cooling bag was applied at the treating clinician's discretion.

The Institutional Review Board of Seoul Metropolitan Government - Seoul National University Boramae Medical Center, Seoul, Korea approved the study and all hospitals waived informed consent because only de-identified registry data were analyzed (24 September 2021, IRB No. 10-2021-106). This study was performed in accordance with the principles of the Declaration of Helsinki, and reporting conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement guidelines.[16]

Statistical analysis

The primary outcome of a good CPC (i.e., CPC 1 or 2) at 1 month was compared between the groups. Subgroups were further identified based on initial rhythm, cause of arrest, or the presence of a witness during the arrest.

The Shapiro–Wilk test was used to evaluate the normality of the continuous variables. The continuous variables were expressed as the mean ± standard deviation or median and interquartile ranges, as appropriate. The Student's t-test or Mann–Whitney U test was used, as appropriate. Categorical variables were presented as a frequency with the corresponding percentage and were compared using the chi-square test or Fisher's exact test, as appropriate.

Because the application of TTM can be affected by the patient's clinical condition and because the clinical parameters of the two groups were expected to be considerably different, the overlap propensity score weighting method was applied.[17,18]

A propensity score for receiving TTM was calculated from a multivariable logistic regression analysis incorporating the following variables: age, sex, baseline CPC, diabetes, hypertension, witnessed arrest, bystander cardiopulmonary resuscitation, initial shockable rhythm, prehospital ROSC, no flow time, low flow time, presence of ST-elevation myocardial infarction, emergency percutaneous coronary intervention, Sequential Organ Failure Assessment score, Acute Physiology And Chronic Health Evaluation II score, and the cause of cardiac arrest. Multiple imputations by chained equations were applied for missing values. Ten copies of the dataset were created and pooled results were calculated using Rubin's rule. The results of the logistic regression analysis were presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Modified Poisson regression was used to estimate adjusted relative risks (with 95% CIs) of fever events for a good outcome. The following variables were used for covariate adjustment: age, sex, baseline CPC, diabetes, hypertension, witnessed arrest, bystander cardiopulmonary resuscitation, initial shockable rhythm, prehospital ROSC, no flow time, low flow time, presence of ST-elevation myocardial infarction, emergency percutaneous coronary intervention, Sequential Organ Failure Assessment score, Acute Physiology And Chronic Health Evaluation II score, and the causes of cardiac arrest.

R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for the statistical analysis. A P-value less than 0.05 was considered statistically significant.

Results

Enrolled patients

During the study period, 1045 patients received postcardiac arrest care and 405 were enrolled in the study (Figure 1). Among enrolled patients, 318 and 87 patients received TTM and underwent maintenance of normothermia strategy without a TFS, respectively. Several characteristics—such as no flow time and Sequential Organ Failure Assessment score—and some laboratory results differed. However, differences in functional outcomes were not observed between the groups (Table 1).

Temperature changes

Core temperatures were higher in the normothermia without TFS group (Figure 2), and fever (i.e., body temperature $\geq$38°C) events were more frequent than in the TTM group during the initial 24 hours (18, 20.7% vs. 15, 4.7%, $P < 0.001$; Table 1, Supplemental Table).

The number of patients experiencing a fever event within 72 hours did not differ statistically between the groups (24, 27.6% vs. 58, 18.2%). In the TTM group, 8 patients (15.4%) with a target temperature of 36°C and 50 patients (18.8%) with a target temperature less than 36°C experienced fever events (Table 1). Fever events during the initial 24 hours were not related to the outcome in either group. Fever events within 72 hours were more frequent in the good-outcome patients of the TTM group (Tables 2 and 3); however, this difference disappeared after adjustment (Table 3).

Propensity score matching

After propensity score weighting, a good CPC outcome at 1 month was not different between the groups (OR 0.99, 95% CI 0.56–1.25). Furthermore, no difference in survival was observed at 1 month (OR 1.25, 95% CI 0.88–1.78; Supplemental Figure).

Propensity-score-adjusted logistic regression analyses were conducted for several

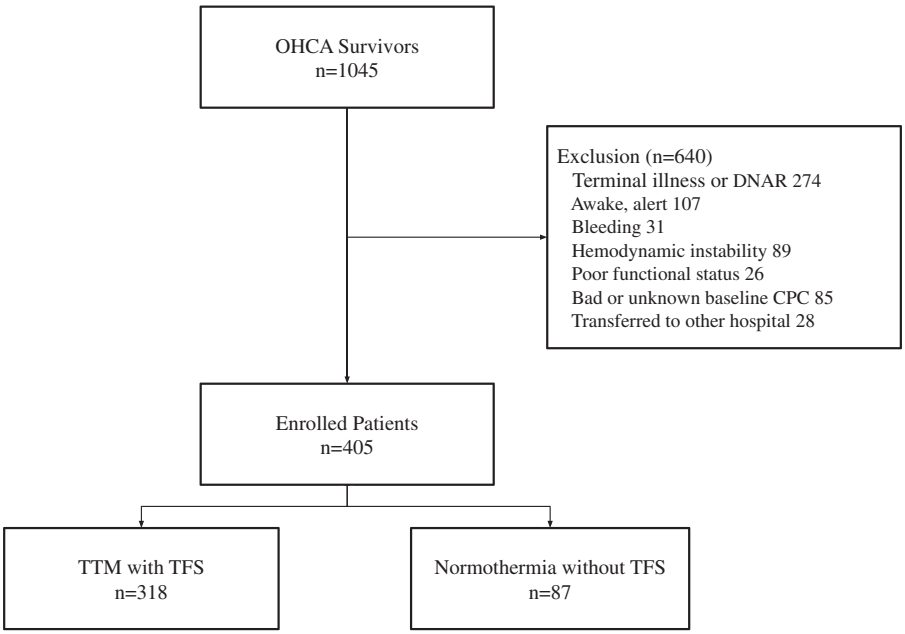

Figure 1. Enrollment of study patients.
OHCA: out-of-hospital cardiac arrest, DNAR: do not attempt resuscitation, CPC: cerebral performance category, ICU: intensive care unit, TTM: target temperature management, TFS: temperature feedback system.

subgroups. No differences in outcome were observed between TTM and normothermia without a TFS for the various subgroups (Figure 3).

Furthermore, intergroup differences in 1-month functional outcomes were not observed in a sensitivity analysis after propensity weighting and removal of missing cases (OR 0.94, 95% CI 0.83–1.02).

Discussion

In our study, the neurological outcome of normothermia with a TFS did not differ from that of conventional TTM. Hyperthermia during postcardiac arrest care, especially within the first 72 hours, is believed to worsen brain injury. The use of temperature-management devices with a TFS has been encouraged for rapid induction, minimization of overcooling risk, and consistent temperature control.[5,15] However, the beneficial effects of positive-feedback devices were never fully evaluated. A meta-analysis of randomized and non-randomized clinical trials showed a lower probability of unfavorable neurological outcomes when using a TFS. A difference in outcomes between with-TFS and without-TFS cohorts was observed in only one large-scale observational study and not in an analysis of exclusively randomized clinical trials.[12] Multivariable analyses revealed that only the use of invasive cooling methods—not external cooling devices—is related to good outcomes when compared with conventional cooling methods without a TFS.[12,19] Given many clinical studies have not proved that invasive cooling devices are more effective than external cooling devices in improving functional outcomes or survival, the benefits of

Table 1. Base characteristics of enrolled patients.

	Normothermia (N = 87)	TTM (N = 318)	P-value
Age, years	59.0 [49.5; 72.0]	58.5 [47.0; 74.0]	0.755
Male	57 (65.5%)	224 (70.4%)	
Baseline CPC			>0.999
1	67 (77.0%)	245 (77.0%)	
2	20 (23.0%)	73 (23.0%)	
Initial body temperature, °C	35.8 [35.0; 36.0]	35.5 [34.9; 36.2]	0.400
Diabetes mellitus	21 (24.1%)	87 (27.6%)	0.609
Hypertension	27 (31.0%)	137 (43.5%)	0.049
Dyslipidemia	7 (8.0%)	23 (7.3%)	0.997
Witness arrest	68 (78.2%)	214 (67.3%)	0.069
Bystander CPR	46 (53.5%)	154 (48.6%)	0.493
Shockable rhythm	30 (34.5%)	96 (30.2%)	0.525
Prehospital defibrillation	32 (37.2%)	109 (35.0%)	0.808
Prehospital ROSC	27 (31.0%)	83 (26.3%)	0.454
No flow time	0.0 [0.0; 5.0]	3.0 [0.0; 8.0]	0.001
Low flow time	23.0 [12.0; 31.0]	24.0 [14.0; 32.0]	0.722
Emergency CAG	37 (42.5%)	113 (35.5%)	0.284
Emergency PCI	19 (21.8%)	50 (15.7%)	0.237
SOFA score	11.0 [8.0; 13.0]	9.0 [7.0; 12.0]	0.038
APACH II score	27.0 [20.0; 34.5]	28.0 [23.0; 32.0]	0.649
GCS	3.0 [3.0; 6.0]	3.0 [3.0; 4.0]	0.051
Laboratory results			
WBC	11.6 [8.4; 15.5]	13.7 [10.2; 18.9]	0.006
Hemoglobin	12.3 [10.3; 14.3]	13.2 [11.1; 14.9]	0.045
Platelet	175.0 [124.0; 237.0]	199.0 [152.0; 249.0]	0.067
Na^+	139.0 [136.2; 142.4]	139.4 [136.0; 143.0]	0.862
K^+	4.5 [3.7; 5.4]	4.2 [3.6; 5.2]	0.235
Cl^-	104.0 [100.0; 109.0]	104.0 [100.3;108.0]	0.757
TCO_2	15.0 [12.0; 18.0]	15.6 [12.0; 19.0]	0.266
Blood urea nitrogen	19.0 [14.0; 27.0]	19.0 [14.5; 27.5]	0.653
Creatinine	1.4 [1.1; 2.1]	1.3 [1.0; 1.7]	0.323
Total bilirubin	0.7 [0.5; 1.0]	0.7 [0.4; 0.9]	0.166
Glucose	228.0 [163.0; 313.0]	251.0 [187.5; 329.5]	0.162
AST	146.0 [69.0; 424.5]	167.5 [78.5; 411.0]	0.725
ALT	84.0 [40.0;184.5]	106.0 [49.0; 256.5]	0.136
PT/INR	1.3 [1.2; 2.0]	1.2 [1.1; 1.5]	0.002
aPTT	47.3 [35.1;75.8]	38.0 [29.8; 54.8]	0.001
C-reactive protein	0.3 [0.3; 5.2]	0.3 [0.1; 1.6]	0.004
Troponin I	0.2 [0.0; 0.6]	0.1 [0.0; 1.2]	0.826
NSE	37.6 [29.2; 57.1]	42.4 [31.0; 63.0]	0.445
Lactate	11.9 [8.7; 15.8]	12.4 [9.5; 15.0]	0.936
Cardiac cause	44 (50.6%)	148 (46.5%)	0.071
Discharge CPC	4.0 [2.0; 5.0]	4.0 [3.0; 5.0]	0.549
1-month survival	39 (44.8%)	164 (51.6%)	0.320

(continued)

Table 1. Continued.

	Normothermia (N = 87)	TTM (N = 318)	P-value
1-month CPC			0.082
1	20 (23.0%)	49 (15.4%)	
2	7 (8.0%)	27 (8.5%)	
3	3 (3.4%)	24 (7.5%)	
4	9 (10.3%)	64 (20.1%)	
5	48 (55.2%)	154 (48.4%)	
Fever event			
Within 24 hours	18 (20.7%)	15 (4.7%)	<0.001
Within 72 hours	24 (27.6%)	58 (18.2%)	0.076

Data are n (%) or median [interquartile range].
TTM: target temperature management, CPC: cerebral performance category, CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation, CAG: coronary angiography, PCI: percutaneous coronary intervention, SOFA: Sequential Organ Failure Assessment Score, GCS: Glasgow Coma Scale, WBC: white blood cell count, AST: aspartate transaminase, ALT: alanine transaminase, PT/INR: prothrombin time/international normalized ratio, aPTT: activated partial thromboplastin time, NSE: neuron-specific enolase, APACHE: Acute Physiology And Chronic Health Evaluation.

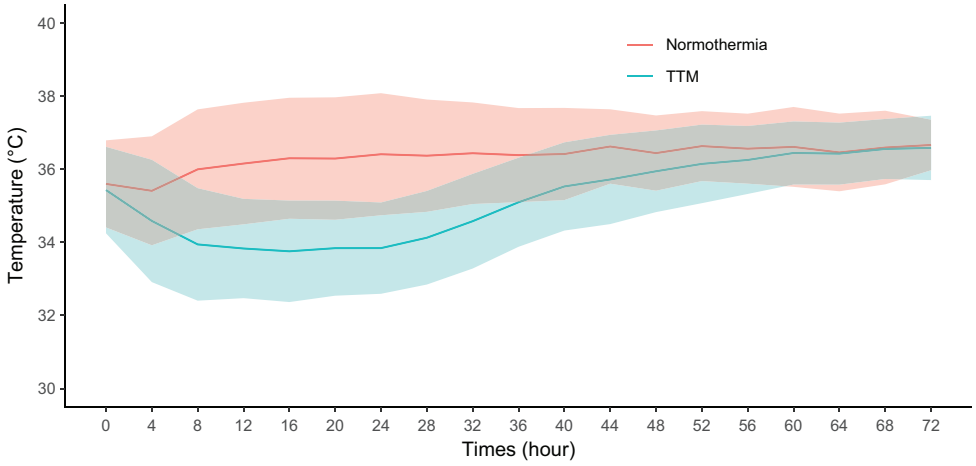

Figure 2. Temperature of enrolled patients during initial 72 hours. Lines indicate the mean temperature of each group and shaded areas indicate the 2 SDs.
TTM: target temperature management, SD: standard deviation.

invasive cooling with a TFS versus conventional cooling without a TFS remain unclear.[20–22]

Moreover, a recently published TTM-2 trial showed no differences in outcome between normothermia and hypothermia groups—a finding consistent with our results. However, whereas all patients in the normothermia group were treated with a cooling device in our study, only 46% of patients were treated with surface and intravascular cooling devices in the TTM-2 trial, which did not evaluate the TFS itself.

The results of a recent comprehensive meta-analysis further indicated no

Table 2. One-month neurological outcomes and fever events per group.

	Normothermia without TFS			TTM with TFS		
	Good	Bad	P-value	Good	Bad	P-value
Fever within 24 hours	6 (22.2%)	12 (20.0%)	>0.999	5 (6.6%)	10 (4.1%)	0.570
Fever within 72 hours	9 (33.3%)	15 (25.0%)	0.586	28 (36.8%)	30 (12.4%)	<0.001

Data are n (%).
TFS: temperature feedback system, TTM: target temperature management.

Table 3. Relative risks of fever events for good outcome.

	Fever within 24 hours		Fever within 72 hours	
	Unadjusted RR (95% CI)	Adjusted RR (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Normothermia without TFS	1.10 (0.40–2.55)	1.81 (0.58–5.36)	1.31 (0.56–2.85)	1.89 (0.69 –5.30)
TTM with TFS	1.42 (0.50– 3.18)	0.89 (0.26–2.35)	2.61 (1.62–4.14)	1.43 (0.84–2.40)
Overall	1.35 (0.68– 2.41)	1.16 (0.55–2.18)	2.21 (1.46–3.28)	1.42 (0.91–2.18)

RR: relative risk, TFS: temperature feedback system, TTM: target temperature management, CI: confidence interval.

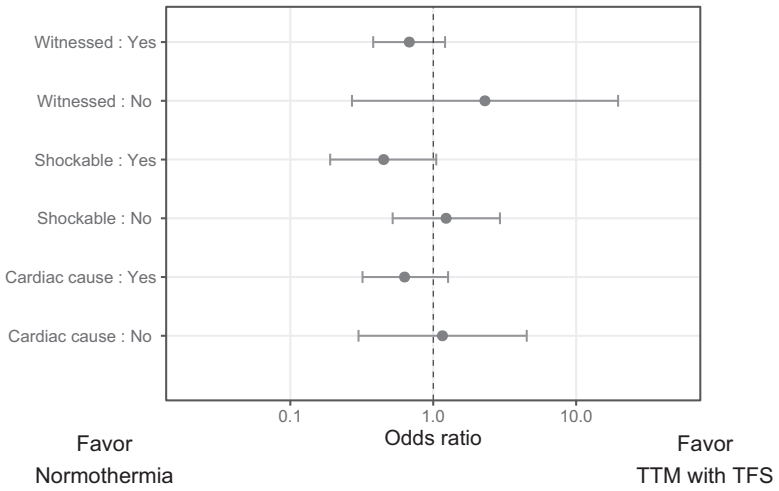

Figure 3. Subgroup analysis for 1-month good neurologic outcomes (odds ratios and 95% confidence intervals). The x-axis represents the log (10) scale of the odds ratio of good neurologic outcomes between the groups.

differences in neurological or survival outcomes between targeted hypothermia (32–34°C) and normothermia (≥36°C with fever control) for comatose OHCA patients.[23]

The European Resuscitation Council–European Society of Intensive Care Medicine (ERC-ESCIM) guidelines still recommend TTM with a TFS. Active fever control with simple surface cooling using wet towels and ice can be considered in low-resource settings.[24] However, the evidence for active fever control without

Table 4. Differences in characteristics between patients with good and bad outcomes.

	Good outcome (N = 103)	Bad outcome (N = 302)	P-value
Age, years	53.0 [44.5; 60.0]	64.0 [50.0; 75.0]	<0.001
Male	81 (78.6%)	200 (66.2%)	0.025
Baseline CPC			<0.001
1	93 (90.3%)	219 (72.5%)	
2	10 (9.7%)	83 (27.5%)	
Initial body temperature, °C	36.0 [35.1; 36.6]	35.3 [34.7; 36.0]	<0.001
Diabetes mellitus	14 (13.7%)	94 (31.3%)	0.001
Hypertension	39 (38.2%)	125 (41.7%)	0.622
Dyslipidemia	10 (9.8%)	20 (6.7%)	0.41
Witness arrest	89 (86.4%)	193 (63.9%)	<0.001
Bystander CPR	67 (65.0%)	133 (44.3%)	<0.001
Shockable rhythm	61 (59.2%)	65 (21.5%)	<0.001
Prehospital defibrillation	71 (68.9%)	70 (23.8%)	<0.001
Prehospital ROSC	68 (66.7%)	42 (14.0%)	<0.001
No flow time	1.0 [0.0; 4.0]	3.0 [0.0; 8.0]	<0.001
Low flow time	12.5 [9.0; 22.5]	26.0 [18.0; 35.0]	<0.001
Emergency CAG	77 (74.8%)	73 (24.2%)	<0.001
Emergency PCI	37 (35.9%)	32 (10.6%)	<0.001
SOFA score	21.0 [16.0; 27.0]	29.0 [24.0; 34.0]	<0.001
APACH II score	7.0 [5.0; 9.0]	10.0 [8.0; 13.0]	<0.001
GCS	4.0 [3.0; 7.0]	3.0 [3.0; 3.0]	<0.001
Laboratory results			
WBC	14.0 [10.2; 19.0]	13.2 [9.5; 18.4]	0.286
Hemoglobin	14.4 [12.7; 15.4]	12.5 [10.4; 14.0]	<0.001
Platelet	227.0 [184.5; 271.0]	184.5 [138.0; 238.0]	<0.001
Na^+	139.0 [136.2; 141.3]	139.5 [136.0; 143.0]	0.097
K^+	3.7 [3.3; 4.3]	4.5 [3.7; 5.4]	<0.001
Cl^-	104.0 [102.0; 107.6]	104.0 [100.0; 108.2]	0.738
TCO_2	16.0 [14.0; 19.0]	15.0 [11.9; 18.0]	0.001
Blood urea nitrogen	17.0 [14.0; 21.0]	20.0 [15.0; 31.0]	0.002
Creatinine	1.1 [0.9; 1.4]	1.4 [1.1; 1.9]	<0.001
Total bilirubin	0.6 [0.5; 0.9]	0.7 [0.4; 1.0]	0.904
Glucose	228.0 [166.0; 276.0]	267.0 [187.5; 342.5]	0.003
AST	133.0 [85.0; 248.0]	184.0 [72.0; 499.0]	0.03
ALT	105.0 [54.0;192.0]	103.0 [46.0; 265.0]	0.687
PT/INR	1.1 [1.0; 1.2]	1.3 [1.1; 1.7]	<0.001
aPTT	31.7 [27.4; 38.5]	44.5 [32.5; 66.8]	<0.001
C-reactive protein	0.3 [0.1; 0.3]	0.3 [0.2; 3.7]	<0.001
Troponin I	0.1 [0.0; 0.9]	0.2 [0.0; 1.1]	0.196
NSE	38.2 [29.9; 50.9]	44.8 [30.4; 70.5]	0.024
Lactate	9.3 [6.9; 14.6]	12.6 [9.7; 15.0]	0.01
Cardiac cause	88 (85.4%)	104 (34.4%)	<0.001
Discharge CPC	2.0 [1.0; 2.0]	5.0 [4.0; 5.0]	<0.001
Survival (28D)	103 (100.0%)	100 (33.1%)	<0.001

(continued)

Table 4. Continued.

	Good outcome (N = 103)	Bad outcome (N = 302)	P-value
CPC (28D)			<0.001
1	69 (67.0%)	0 (0.0%)	
2	34 (33.0%)	0 (0.0%)	
3	0 (0.0%)	27 (8.9%)	
4	0 (0.0%)	73 (24.2%)	
5	0 (0.0%)	202 (66.9%)	
Fever event			
Within 24 hours	11 (10.7%)	22 (7.3%)	0.379
Within 72 hours	37 (35.9%)	45 (14.9%)	<0.001

Data are n (%) or median [interquartile range].
CPC: cerebral performance category, CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation, CAG: coronary angiography, PCI: percutaneous coronary intervention, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow Coma Scale, WBC: white blood cell count, AST: aspartate transaminase, ALT: alanine transaminase, PT: prothrombin time, aPTT: activated partial thromboplastin time, NSE: neuron-specific enolase, APACHE: Acute Physiology And Chronic Health Evaluation.

a TFS remains insufficient. Moreover, the results of the present study support the ERC-ESICM guidelines.

Consistent with the TTM-2 trial results, 20.7% of patients with normothermia without a TFS developed fever events during the initial 24 hours of our study. Fever is believed to worsen brain damage in various types of brain injury. Fever during post-resuscitation care is related to poor prognosis.[25,26] Clinical practice has changed following the TTM trial; patients' target and lowest temperatures have risen and fever events have increased. Nonetheless, changes in outcome have not been evident.[5,9,27–30] Similarly, in our study, although fever events during the initial 24 hours were more frequent in the normothermia without TFS group, no differences in outcomes were observed (Table 4).

Because of enhanced knowledge of post-cardiac arrest pathophysiology, physicians' responses have improved versus historical hypothermia practices. If adequate efforts toward achieving temperature control follow, the harmful effects of hyperthermia can be further minimized.[11] However, although a TFS can provide constant and convenient temperature control, it can cause complications necessitating expensive devices that incur additional costs. The average cost of TTM with a TFS was approximately USD 3,000 per patient in our centers during the study period. We believe that maintenance of normothermia without a TFS may be regarded as a temperature management option for post-resuscitation patients.

In our study, fever events were more common in good-outcome patients who underwent TTM with a TFS (Table 2). Thermal activity can be a sign of brain metabolic activity and preserved brain function. Preserving heat production ability during TTM is further related to good clinical outcomes.[31,32] These phenomena may have affected our study results by masking the harmful effects of fever. However, heat production during the rewarming period was not related to clinical outcomes in a recent clinical study and most fever events developed after 24 hours in our study.[33]

This study has several limitations. First, this was a retrospective analysis and

treatment groups were not randomly selected or blinded. We attempted to overcome this limitation by using propensity score weighting; however, uncontrolled bias remains a possibility. Second, a small number of patients received TTM with a target temperature of 36°C because the clinical significance of the fever event was not fully evaluated given the limited number of patients. Third, long-term neurological outcomes were not evaluated in our study. Finally, the reasons for non-consent to TTM with a TFS were not recorded and matched for propensity analysis. This may have caused unadjusted differences in socioeconomic status between the groups.

Conclusion

No significant differences in the 1-month neurologic outcome were observed between patients receiving TTM with a TFS and those undergoing maintenance of normothermia without a TFS during post-resuscitation care.

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Author contributions

HJL: formal analysis, data curation, writing – original draft, and visualization; **JS**: conceptualization methodology, writing – original draft, review and editing, and supervision; **KMY**: resources, writing – review and editing; **WYK**: methodology and writing – review and editing; **KSK**: resources and writing – review and editing; **YHJ**: methodology and writing – review and editing; **SMP**: data curation and writing – review and editing.

Declaration of conflicting interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The data that support the findings of this study are available on request from the corresponding author, JS, after IRB approval. The data are not publicly available given they contain information that could compromise the privacy of research participants.

ORCID iDs

Hui Jai Lee https://orcid.org/0000-0002-9064-4680
Seung Min Park https://orcid.org/0000-0002-3594-8403

Supplemental material

Supplemental material for this article is available online.

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