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A comparison of intravascular and surface cooling devices for targeted temperature management after out-of-hospital cardiac arrest

A nationwide observational study

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Abstract

This study aimed to compare prognostic difference between intravascular cooling devices (ICDs) and surface cooling devices (SCDs) in targeted temperature management (TTM) recipients.

Adult TTM recipients using ICD or SCD during 2012 to 2016 were included in this nationwide observational study. The outcome was survival to hospital discharge and good neurological outcome at hospital discharge.

Among 142,905 out-of-hospital cardiac arrest patients, 1159 patients (SCD, n=998; ICD, n=161) were investigated. After propensity score matching for all patients, 161 matched pairs of patients were available for analysis (SCD, n=161; ICD, n=161). We observed no significant differences in the survival to hospital discharge (SCD, n=144 [89.4%] vs ICD, n=150 [93.2%], $P=.32$) and the good neurological outcomes (SCD, n=86 [53.4%] vs ICD, n=91 [56.5%], $P=.65$). TTM recipients were categorized by age groups (elderly [age >65 years] vs nonelderly [age $\leq$65 years]) to compare prognostic difference between ICD and SCD according to the age groups. In the nonelderly group, the use of ICD or SCD was not a significant factor for survival to hospital discharge or good neurologic outcome. Whereas, the use of ICD was significantly associated with good neurological outcome (odds ratio, 3.97; 95% confidence interval, 1.19 – 13.23, $P=.02$) compared with SCD in the elderly group.

There were no significant differences in the survival to hospital discharge and the good neurological outcomes between SCD and ICD recipients. However, the use of ICD might be more beneficial than SCD in elderly patients.

Abbreviations: CI = confidence interval, CPC = cerebral performance category, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, EMS = emergency medical service, ICD = intravascular cooling device, KCDC = Korean Centres for Disease Control and Prevention, OHCA = out-of-hospital cardiac arrest, OHCAS = Out-of-Hospital Cardiac Arrest Surveillance, OR = odds ratio, PCI = percutaneous coronary intervention, ROSC = return of spontaneous circulation, SCD = surface cooling device, TTM = targeted temperature management.

Keywords: observational study, out-of-hospital cardiac arrest, prognosis, survival, targeted temperature management

1. Introduction

Severe brain injury after cardiopulmonary resuscitation (CPR) has been known to be the most common cause of death in out-of-hospital cardiac arrest (OHCA) patients.[1] The American Heart Association recommends targeted temperature management (TTM) as part of critical care for a comatose patient receiving post-cardiac arrest management.[2]

TTM can be induced by conventional or active methods. Conventional cooling methods include exposure to air, cold intravenous fluids, ice slurry, or cooling pads.[3–5] Active devices include intravascular cooling devices (ICD) or surface cooling devices (SCD) that have automated temperature feedback control.[6–8] The American Heart Association and European Resuscitation Council recommend targeting a core temperature between 32°C and 36°C for 24 hours, followed by strict fever management. Therefore, there is a need for accurate core temperature control during TTM.[4,9] Because conventional methods are associated with overcooling and rebound hyperthermia,[10–12] SCD and ICDs are more acceptable with respect to strict temperature control.

Active devices have more rapid induction with less temperature variation compared to conventional cooling methods.[13–16] However, there may be significant mechanical differences in cooling performance between ICD and SCD.[17–22] ICD cooling of circulating blood could be likened to convective cooling. In contrast, SCD relies on perfusion to transfer coldness from the surface to the core of the body.[23]

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We hypothesized that the mechanical difference in cooling between ICD and SCD could affect the outcome of TTM recipients. Thus, the aim of this study was to compare survival to hospital discharge and neurological outcome of TTM in OHCA patients according to ICD or SCD through analyzing nationwide OHCA data.

2. Methods

2.1. Study design and settings

This was a retrospective observational study using nationwide data from the Out-of-Hospital Cardiac Arrest Surveillance (OHCAS) of the Korean Centres for Disease Control and Prevention (KCDC) from January 2012 to December 2016.

OHCAS was conducted in 17 provinces of South Korea (about 50 million people) and contained patient information from the moment of cardiac arrest to outcomes at hospital discharge. The local ethics committee approved this study in 2018 (Kangnam Sacred Heart Hospital Institutional Review Board; IRB No. 2019-01-018) and informed consent was waived because of the retrospective nature of the study and the use of anonymous clinical data for the analysis. The KCDC approved the use of the data for this study. The methodology of this study was consistent with the Strengthening the Reporting of Observational Studies in Epidemiology checklist for observational studies.

2.2. Data source

The OHCAS is a population-based, emergency medical service (EMS)-assessed OHCA registry and retrospective patient cohort. The information on OHCA patients was obtained from the EMS records entered by EMS providers immediately after the transport of OHCA patients, and the data of OHCA patients for hospital care and outcomes at hospital discharge were provided by the KCDC. Medical record reviewers of KCDC visited all emergency departments and hospitals to where the OHCA patients were transported and reviewed the medical records.

The OHCAS included information on patients and place of CPR, bystander CPR, procedures during transportation, survival to hospital discharge, and neurological outcome at hospital discharge using an appropriately devised survey form. The registry form was based on the Utstein style guideline and Resuscitation Outcome Consortium Project.

2.3. Study population

From January 2012 to December 2016, a total of 142,905 OHCA patients were registered in the OHCAS. Among them, adult OHCA patients (older than 18 years) who received TTM after return of spontaneous circulation (ROSC) as a result of CPR in EMS or hospital were included in the study. OHCA patients were excluded from the study on the basis of any traumatic cause, younger than 18 years of age, invalid data on neurological status or survival data, and missing information on TTM devices.

Patients who received TTM by any SCD were assigned to the SCD group, whereas those who received TTM via intravascular cooling catheter were assigned to the ICD group. Patients who received both types of cooling devices were excluded from this study.

2.4. Variables

Information on demographic factors (age, sex), geographical factors of the OHCA (metropolitan city versus nonmetropolitan city), etiological factors (cardiac origin versus non-cardiac origin), places of CPR (public places versus non-public places), initial monitored rhythm (shockable vs non-shockable), witnessed cardiac arrest, bystander CPR, cooling devices of TTM (ICD vs SCD), percutaneous coronary intervention (PCI), CPR methods (conventional CPR versus mechanical CPR), and extracorporeal membrane oxygenation (ECMO) were collected.

Public places were defined as the places generally open and near to people such as roads, public buildings, parks and beaches. Shockable rhythm was defined as ventricular fibrillation and pulseless ventricular tachycardia. ROSC was defined for all rhythms as conversion to spontaneous rhythm that was sustained for more than 20 minutes. Based on the description in the medical records, we classified the etiology of cardiac arrest as being of cardiac or non-cardiac origin. Conditions such as ischemic heart disease, arrhythmias and cardiac tamponade were classified as being of cardiac origin. In conditions such as trauma, drowning, poisoning, burn, asphyxia, or hanging, we assumed the cause of cardiac arrest as being of non-cardiac origin. PCI included balloon angioplasty and implantation of stents. Information on witnessed cardiac arrest, CPR methods and application of ECMO were also obtained from the medical records.

Cooling methods of TTM were categorized as surface or ICDs. SCDs utilize an external pad or blanket on the body surface to lower the body temperature, such as Arctic Sun (Medivance Corp, Louisville, KY), Gaymar (Gaymar Industries, Orchard Park, NY), Blanketrol III (Cincinnati Sub-Zero Products, Cincinnati, OH), or Emcools Flex. Pad (Emcools, Vienna, Austria). ICDs use an intravascular catheter in a large vessel to lower the body temperature, such as CoolGard 3000 Thermal Regulation System (Alsius Corporation, Irvine, CA). The application and type of TTM methods were determined by the physicians and hospital protocol.

2.5. Outcome measures

The primary outcome was survival to hospital discharge and good neurological outcome at hospital discharge, assessed using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC) scale. CPC 1 and 2 were classified as good neurological status. CPC 3, 4, and 5 were classified as poor neurological status. The status was based on the discharge summary in the medical records.

2.6. Statistical analysis

The data including demographic characteristics according to cooling devices are presented as the median and interquartile range for continuous data or as frequencies and percentages for categorical data. Normality of each continuous variable was assessed using the Kolmogorov–Smirnov test.

The independent sample *t* test for parametric data or Mann–Whitney *U* test for nonparametric data were used for continuous variables and Pearson χ^2 test or Fisher exact test was used for categorical variables.

To minimize the impact of potential confounders and selection bias, propensity score matching was used to compensate for the differences in baseline patient characteristics between the 2 groups of patients. We performed 1:1 propensity score matching (nearest neighbor) to select the participants in both the SCD and ICD groups. After estimating the propensity scores, we performed a multivariate logistic regression analysis to determine the prognostic factors influencing survival to hospital discharge and good neurological outcomes of TTM recipients.

The model of multivariate logistic regression was stepwise backward elimination. Any variables with $P<.2$ in univariate analyses were included in the multivariate regression analysis. All statistical analyses were conducted by SPSS version 20.0 software (IBM, Armonk, NY) and R package (R version 3.3.2) and $P<.05$ was considered statistically significant.

3. Results

3.1. Characteristics of study patients

Of 142,905 OHCA patients who were registered during the study period, 141,746 patients were excluded for the following reasons: did not receive TTM (n=140,301), younger than 18 years of age (n=402), traumatic OHCA (n=210), received conventional cooling (n=563), and invalid data for CPC score or survival (n=270). The remaining 1159 OHCA patients were finally enrolled in this study. Of these, 998 (86.1%) patients were included in the SCD group and 161 (13.8%) in the ICD group (Fig. 1).

Baseline characteristics of the surface and intravascular cooling groups before propensity score matching are summarized in Table 1. There were significant differences between the 2 groups in terms of witnessed cardiac arrest (776 [77.8%] vs 112 [69.6%], $P=.02$) and PCI (170 [17.0%] vs 46 [28.6%], $P<.01$).

3.2. Characteristics of patients matched for propensity scores

After propensity score matching was performed for all patients, 161 matched pairs of patients were available for analysis (Table 2). There were no significant differences for all variables among the matched patients between the 2 groups.

3.3. Outcomes for propensity-matched patients

In the outcome analysis, we observed no significant difference in the survival to hospital discharge (144 [89.4%] vs 150 [93.2%], $P=.32$) and the good neurological outcomes (86 [53.4%] vs 91 [56.5%], $P=.65$) between the SCD and ICD groups.

3.4. Multivariate logistic analysis of survival to hospital discharge and good neurological outcomes

3.4.1. Prognostic factor for survival to hospital discharge in propensity-matched patients. After multivariate logistic regression analysis, 2 variables were significantly associated with hospital survival.

Prehospital ROSC (odds ratio [OR], 5.05; 95% confidence interval [CI], 1.06–24.14, $P=.04$) was associated with survival to hospital discharge. However, increase in age (OR, 0.96; 95% CI, 0.93–0.99, $P<.01$) was associated with hospital mortality (Fig. 2, Supplementary Table 1, http://links.lww.com/MD/D134).

3.4.2. Prognostic factors for good neurological outcome in propensity-matched patients. After multivariate logistic regression analysis, prehospital ROSC (OR, 5.57; 95% CI, 3.06–10.15, $P<.01$), witnessed cardiac arrest (OR, 2.55; 95% CI, 1.42–4.60, $P<.01$), public places (OR, 2.07; 95% CI 1.15–3.72, $P=.01$), and initial shockable rhythm (OR, 1.79; 95% CI, 1.01–3.19, $P=.04$) were associated with good neurological outcome. However, only 1 variable was associated with poor neurological outcome: increase in age (OR, 0.95; 95% CI, 0.93–0.97, $P<.01$) (Fig. 3, Supplementary Table 2, http://links.lww.com/MD/D134).

3.5. Subgroup analysis of elderly patients (age >65 years) and nonelderly patients (age ≤65 years) for survival to hospital discharge and good neurological outcomes

From the results of multivariate logistic analysis, the increase of age was significantly associated with in-hospital mortality. Thus, we performed additional subgroup analysis for different age groups (elderly [age >65 years] vs non-elderly [age ≤65 years]) to evaluate the efficacy of ICD and SCD for outcomes.[24,25]

3.5.1. Analysis of prognostic factors for survival to hospital discharge in the elderly and non-elderly groups. In multivariate logistic regression analysis, no variables were significantly associated with survival to hospital discharge in the nonelderly group. However, 2 variables were significantly associated with survival to hospital discharge in the elderly group. Witnessed CPR (OR, 7.54; 95% CI 1.80–31.51, $P<.01$), prehospital ROSC (OR, 14.55; 95% CI, 1.62–130.86, $P=.01$) were associated with survival to hospital discharge. The cooling devices did not influence the in-hospital survival in both subgroups (Table 3).

3.5.2. Analysis of prognostic factors for good neurological outcome in the elderly and nonelderly groups. After multivariate logistic regression analysis, public place (OR, 3.17; 95% CI 1.58–6.39, $P<.01$), witnessed cardiac arrest (OR, 3.14; 95% CI, 1.61–6.13, $P<.01$), prehospital ROSC (OR, 7.18; 95% CI, 3.51–14.67, $P<.01$), and initial shockable rhythm (OR, 2.17; 95% CI, 1.11–4.24, $P=.02$) were associated with good neurological outcome in the nonelderly group. The cooling devices did not influence the neurological outcome in the non-elderly group. In the elderly group, pre-hospital ROSC (OR, 9.41; 95% CI, 2.80–31.57, $P<0.01$), and the use of ICD compared with SCD (OR, 3.97; 95% CI, 1.19–13.23, $P=0.02$) was significantly associated with good neurological outcome (Table 3).

4. Discussion

We compared ICD with SCD in survival to hospital discharge and good neurological outcomes in recipients of TTM. Our nationwide, retrospective, observational, multicenter study indicated that the rates of good neurological outcome and in-hospital survival were similar in both cooling devices groups; however, in the subgroup analysis of the elderly group, the use of ICD exhibited an increase in good neurological outcome compared with SCD.

In their 2008 consensus statement, the Committee recommended the use of devices that incorporate continuous temperature feedback to achieve the temperature maintenance.[26] They emphasized the potential disadvantages of using simple surface cooling such as ice packs, namely, increased labor intensity, greater temperature fluctuations, and inability to control body temperature precisely during maintenance and reversal of hypothermia.[14,18]

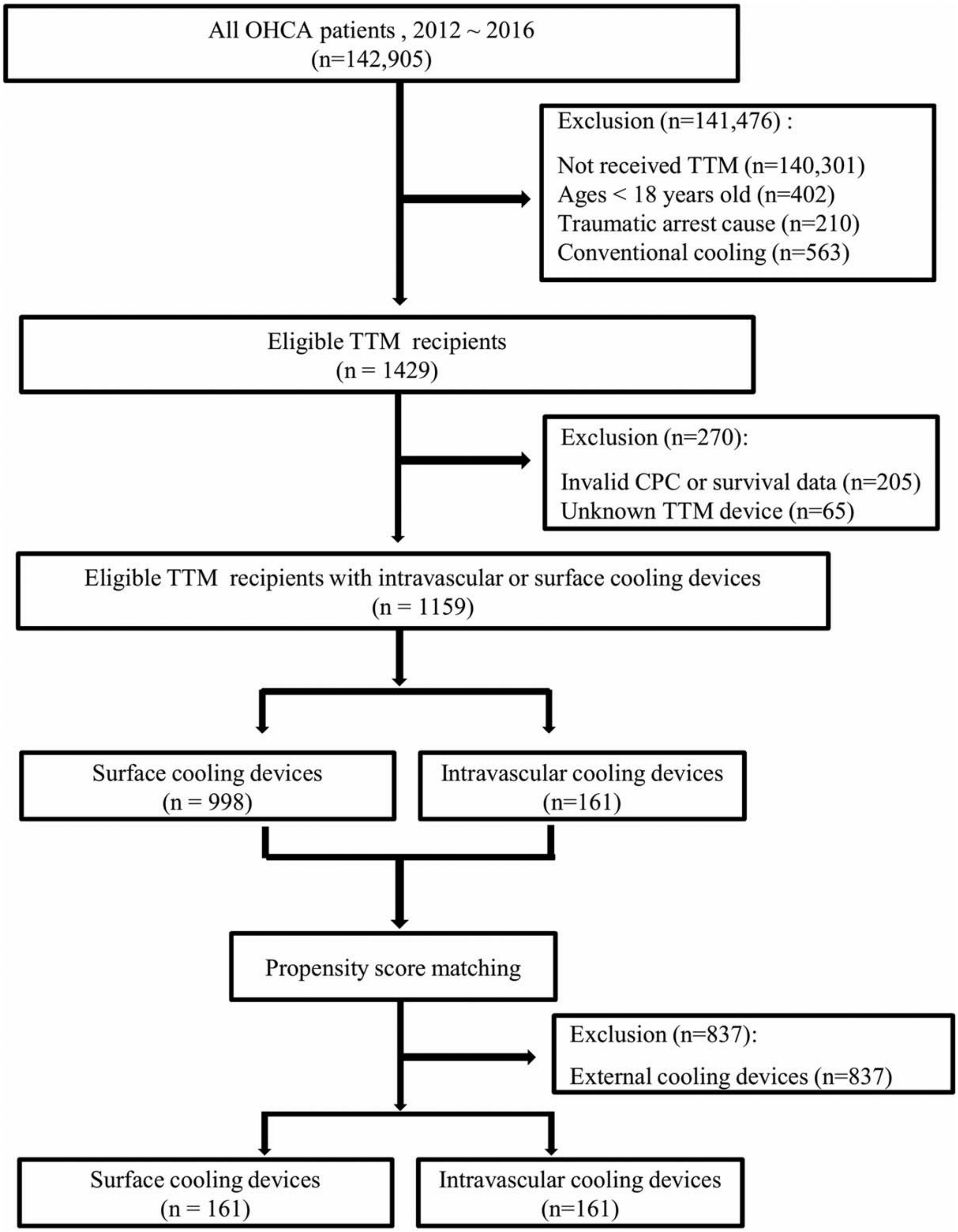

Figure 1. Flow diagram of the study population. CPC = cerebral performance category, OHCA = out-of-hospital cardiac arrest, TTM = targeted temperature management.

In several previous studies, surface cooling has been reported to be less effective than intravascular cooling at achieving and maintaining the target temperature of TTM; however, these studies did not utilize SCDs using temperature feedback control.[14,27–29] The computer-controlled SCDs differ from simple surface cooling by employing a precise temperature feedback-control mechanism. This difference may allow a more rapid induction of cooling and improved control of temperature during maintenance of hypothermia and rewarming than simple surface cooling methods.[18]

Table 1

Baseline characteristics of patients according to cooling devices.

Variable	Total (N=1159)	Surface cooling (N=998)	Intravascular cooling (N=161)	*P*
Age, y	56 (45–66)	56 (45–67)	54 (47–63)	.18
Male	903 (77.9%)	772 (77.4%)	131 (81.4%)	.30
Metropolitan	1014 (87.5%)	874 (87.6%)	140 (87.0%)	.92
Cardiac origin	1118 (96.5%)	960 (96.2%)	158 (98.1%)	.31
Public place	352 (30.4%)	298 (29.9%)	54 (33.5%)	.39
Witnessed cardiac arrest	888 (76.6%)	776 (77.8%)	112 (69.6%)	.02
Bystander CPR	431 (37.2%)	367 (36.8%)	64 (39.8%)	.52
Prehospital ROSC	488 (42.1%)	419 (42.0%)	69 (42.9%)	.90
Initial shockable rhythm	557 (48.1%)	477 (47.8%)	80 (49.7%)	.71
PCI	216 (18.6%)	170 (17.0%)	46 (28.6%)	<.01
Mechanical CPR	36 (3.1%)	35 (3.5%)	1 (0.6%)	.08
ECMO	42 (3.6%)	37 (3.7%)	5 (3.1%)	.87
Survival to hospital discharge	1042 (89.9%)	892 (89.4%)	150 (93.2%)	.18
Good neurologic outcome	594 (51.3%)	503 (50.4%)	91 (56.5%)	.17

CPR=cardiopulmonary resuscitation, ECMO=extracorporeal membrane oxygenation, PCI=percutaneous coronary intervention, ROSC=return of spontaneous circulation.

Table 2

Baseline characteristics of patients according to cooling devices after propensity score matching.

Variable	Total (N=322)	Surface cooling (N=161)	Intravascular cooling (N=161)	*P*
Age, y	56 (47–66)	57 (48–66)	54 (47–63)	.11
Male	255 (79.2%)	124 (77.0%)	131 (81.4%)	.41
Metropolitan	283 (87.9%)	143 (88.8%)	140 (87.0%)	.73
Cardiac origin	313 (97.2%)	155 (96.3%)	158 (98.1%)	.50
Public place	106 (32.9%)	52 (32.3%)	54 (33.5%)	.90
Witnessed cardiac arrest	224 (69.6%)	112 (69.6%)	112 (69.6%)	1.00
Bystander CPR	123 (38.2%)	59 (36.6%)	64 (39.8%)	.64
Prehospital ROSC	145 (45.0%)	76 (47.2%)	69 (42.9%)	.50
Initial shockable rhythm	159 (49.4%)	79 (49.1%)	80 (49.7%)	1.00
PCI	92 (28.6%)	46 (28.6%)	46 (28.6%)	1.00
Mechanical CPR	4 (1.2%)	3 (1.9%)	1 (0.6%)	.62
ECMO	13 (4.0%)	8 (5.0%)	5 (3.1%)	.57
Survival to hospital discharge	294 (91.3%)	144 (89.4%)	150 (93.2%)	.32
Good neurologic outcome	177 (55.0%)	86 (53.4%)	91 (56.5%)	.65

CPR=cardiopulmonary resuscitation, ECMO=extracorporeal membrane oxygenation, PCI=percutaneous coronary intervention, ROSC=return of spontaneous circulation.

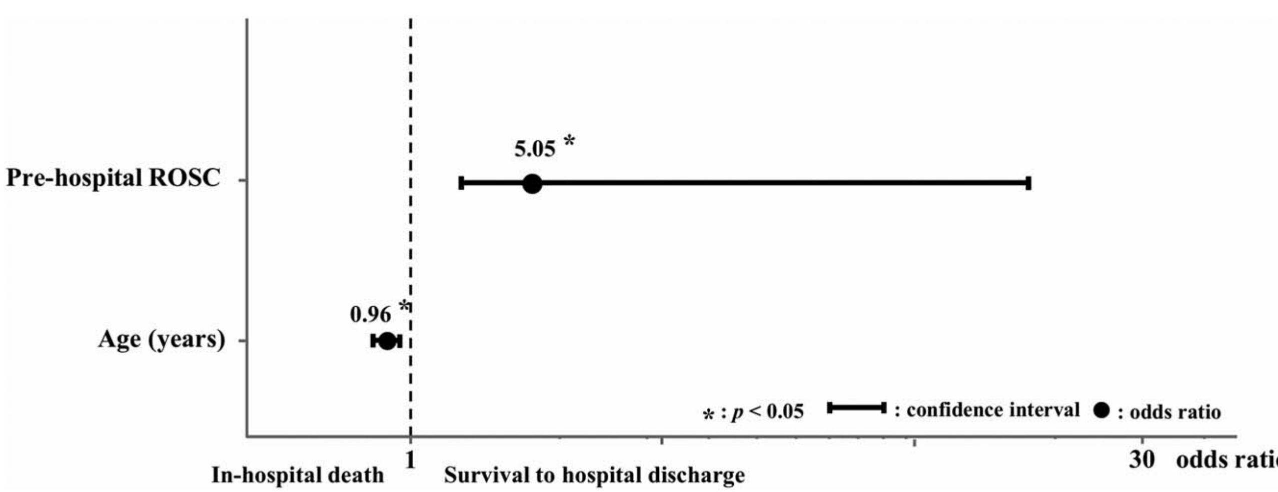

Figure 2. Independent predictors of survival to hospital discharge of targeted temperature management patients in out-of-hospital cardiac arrest. ROSC=return of spontaneous circulation.

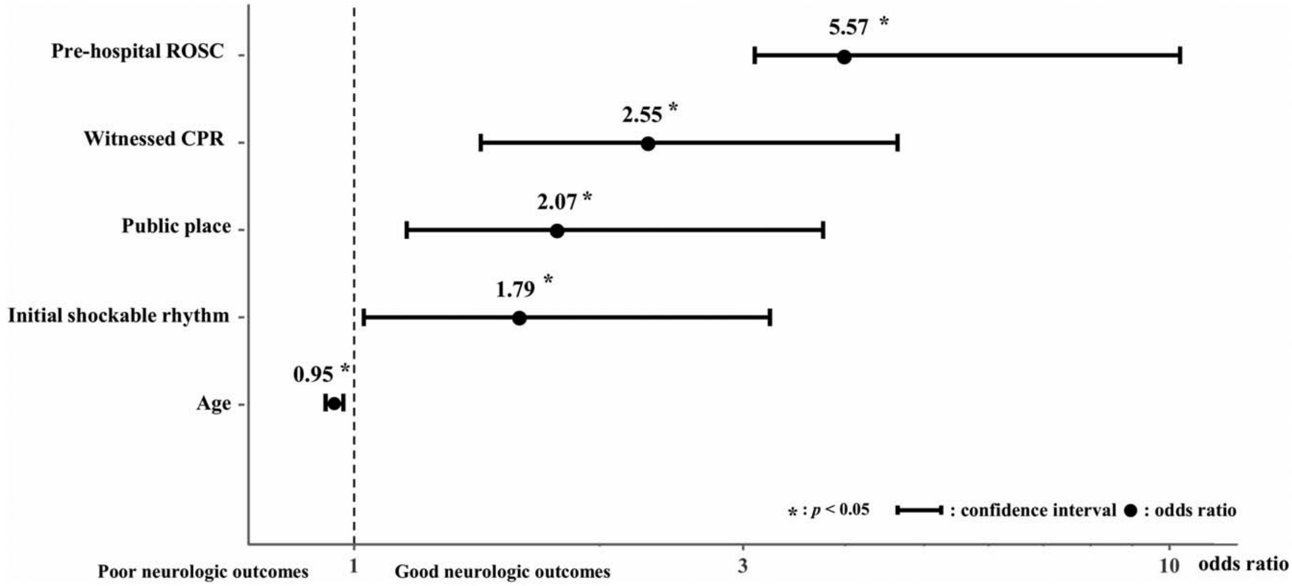

Figure 3. Independent predictors of good neurologic outcome of targeted temperature management patients in out-of-hospital cardiac arrest. CPR = cardiopulmonary resuscitation, ROSC = return of spontaneous circulation.

Because of the requirement of a central venous line, ICDs are more time consuming than SCDs in the application of TTM and have been reported to cause thrombosis, insertion-related bleeding, or infection. In contrast, SCDs may be associated with shivering and skin injury.[30] Considering these mechanical and adverse properties between ICD and SCD, we performed this study to identify the clinical efficacy of ICD compared with SCD.

Table 3

Multivariate analysis for survival to hospital discharge and good neurological outcomes in elderly and nonelderly subgroup.

	OR (95% CI)	*P*
Survival to hospital discharge		
Nonelderly group (age ≤65 y, n=241)		
Cardiac origin	0.38 (0.01–9.77)	.55
Public place	13.27 (0.51–344.94)	.11
Prehospital ROSC	9.20 (0.98–86.53)	.05
Initial shockable rhythm	9.45 (0.96–93.08)	.05
Mechanical CPR	0.07 (0.00–1.99)	.11
Elderly group (age >65 y, n=81)		
Witnessed CPR	7.54 (1.80–31.51)	<.01
Prehospital ROSC	14.55 (1.62–130.86)	.01
Intravascular cooling devices*	4.10 (0.90–18.76)	.06
Good neurologic outcome		
Nonelderly group (age ≤65 y, n=241)		
Metropolitan	0.40 (0.14–1.16)	.09
Cardiac origin	12.62 (0.58–273.37)	.10
Public place	3.17 (1.58–6.39)	<.01
Witnessed CPR	3.14 (1.61–6.13)	<.01
Prehospital ROSC	7.18 (3.51–14.67)	<.01
Initial shockable rhythm	2.17 (1.11–4.24)	.02
Elderly group (age >65 y, n=81)		
Witnessed CPR	3.24 (0.84–12.48)	.08
Bystander CPR	2.99 (0.84–10.70)	.09
Pre-hospital ROSC	9.41 (2.80–31.57)	<.01
ECMO	16.23 (0.68–388.21)	.08
Intravascular cooling devices*	3.97 (1.19–13.23)	.02

Model of multivariate logistic regression analysis is stepwise backward elimination. CI = confidence interval, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal membrane oxygenation, OR = odds ratio, ROSC = return of spontaneous circulation.
* Compared with surface cooling devices.

In multivariate logistic analysis, there was no significant difference in hospital survival and neurological outcome between the 2 cooling device groups. However, the notable finding of our study was the relationship of age to both survival to hospital discharge and good neurological outcomes after TTM. Our study showed that age was inversely associated with both survival to hospital discharge and good neurological outcome through multivariate logistic regression analysis. In a previous study on the effect of age on outcome of TTM, Look et al[31] reported that age, duration from collapse to sustained ROSC, and rebound hyperthermia were significant factors associated with survival. Oh et al and Winther et al[32,33] reported negative prognostic effect of age on neurological outcome of TTM.

Therefore, we categorized TTM recipients by age groups (elderly [age >65 years] versus nonelderly [age ≤65 years]) to compare prognostic difference between ICD and SCD according to the age groups,[24,25] and additionally, we evaluate prognostic factors on survival to hospital discharge and good neurological outcomes in both elderly and nonelderly groups. In the elderly subgroup, TTM recipients using ICD had a significantly better neurological outcome than TTM recipients with SCD. The reason for this is unclear. However, the favorable effect of ICD on neurological outcomes may be related to more precise temperature control with ICD than SCD. The mechanism of action of ICD is the direct heat exchange between catheter and blood, resulting in a rapid transfer of cold blood throughout the body, whereas SCD depends on relatively slow conduction of coldness mainly through the tissue itself.[15] Because of this difference in the cooling mechanism, temperature fluctuations were present greater degree in SCD compared to ICD during the maintenance phase. Nielsen et al reported that precise temperature control may be important because fluctuations in core temperature could lead to intermittent brain hyperthermia.[4,9,34] Furthermore, neurological function and neural plasticity of the brain diminished with increasing age.[35] Therefore, we assumed that more accurate temperature control with ICD may contribute to better neurological outcome in elderly TTM recipients. Moreover, we found other prognostic factors associated with good outcome in the elderly TTM recipients. Our multivariate analysis suggested that witnessed CPR and prehospital ROSC were significant factors associated with survival to hospital discharge, and prehospital ROSC was identified as a prognostic factor favoring good neurological outcome. Prolonged CPR duration is related to cerebral damage and low probability of ROSC.[36] Hence, prehospital ROSC could contribute to good neurological outcomes of TTM recipients by the decrease in brain damage before TTM treatment.

5. Limitations

This study has several limitations. First, our study has a potential of reporting bias and selection bias because this study was not randomized and was a retrospective observational study. Although we attempted to reduce confounding using propensity score matching, there was still a risk of bias because our study was a retrospective, registry-based multicenter study. Therefore, the results of this study should be cautiously interpreted. Second, we could not assess long-term survival and neurological outcome after hospital discharge. In addition to survival, the CPC score measured at hospital discharge could have changed up after hospital discharge.[37,38] Therefore, the survival and neurological outcomes of TTM recipients could be different if the CPC score and survival were followed up and measured after hospital discharge. Third, we did not evaluate potential confounders such as underlying disease, hemodynamic status, laboratory findings, and mental status before TTM treatment because data on such confounders were not included in the registry. These factors could affect survival and neurological outcomes in addition to the choice of cooling devices. Therefore, the results of our study should be confirmed through well-designed studies that include additional variables related to patient's status and TTM.

Fourth, target temperature and maintenance time for TTM were not provided from the raw data of OHCAS in this study. However, all TTM protocols in the South Korea have been adhering to the international 2010 to 2015 American Heart Association guidelines (target temperature: 32°C ~36°C, maintenance time: 12~24 hours).[39,40] Therefore, the TTM guideline change from 2010 to 2015 might affect the outcomes of patients.

Finally, generalization of this study results to other countries is uncertain. The study was performed on the data of the South Korea EMS system. The findings of this study may not be similar to other study settings or other countries with different EMS and medical systems. For more generalizable findings, further data from other races or countries are required.

6. Conclusions

In the overall-matched patients, there were no significant differences in neurological outcomes and survival to hospital discharge between SCDs and ICDs. In our analysis of age subgroups, the use of ICDs may have favorable effect on the neurological outcome compared with surface cooling devices for elderly TTM patients after OHCA.

Author contributions

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