



# Survival and Neurologic Outcomes of Out-of-Hospital Cardiac Arrest Patients Who Were Transferred after Return of Spontaneous Circulation for Integrated Post-Cardiac Arrest Syndrome Care: The Another Feasibility of the Cardiac Arrest Center

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It has been proven that safety and efficiency of out-of-hospital cardiac arrest (OHCA) patients is transported to specialized hospitals that have the capability of performing therapeutic hypothermia (TH). However, the outcome of the patients who have been transferred after return of spontaneous circulation (ROSC) has not been well evaluated. We conducted a retrospective observational study between January 2010 to March 2012. There were primary outcomes as good neurofunctional status at 1 month and the secondary outcomes as the survivals at 1 month between Samsung Medical Center (SMC) group and transferred group. A total of 91 patients were enrolled this study. There was no statistical difference between good neurologic outcomes between both groups (38% transferred group vs. 40.6% SMC group,  $P = 0.908$ ). There was no statistical difference in 1 month survival between the 2 groups (66% transferred group vs. 75.6% SMC group,  $P = 0.318$ ). In the univariate and multivariate models, the ROSC to induction time and the induction time had no association with good neurologic outcomes. The good neurologic outcome and survival at 1 month had no significant differences between the 2 groups. This finding suggests the possibility of integrated post-cardiac arrest care for OHCA patients who are transferred from other hospitals after ROSC in the cardiac arrest center.

**Keywords:** Hypothermia Therapy; Heart Arrest; Cardiopulmonary Resuscitation

## INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains as a common public health problem and a leading cause of morbidity and mortality (1). Systematic, post-cardiac arrest care after return of spontaneous circulation (ROSC) can improve the survival and neurologic outcome of OHCA patients (2, 3). In particular, recent studies have demonstrated that therapeutic hypothermia (TH) is an important resuscitation therapy that improves the rate of survival and relieves unfavorable neurological outcomes in cardiac arrest survivors (2, 4). Despite TH being emphasized, the medical community has been slow to adopt TH in the hospital environment (5, 6). This may be due to some barriers, such as a lack of knowledge about TH, financial barriers, and logistic barriers (6, 7). Thus, it is difficult to perform systematic post-cardiac arrest care including TH in all hospitals. Furthermore, the differences in post cardiac arrest mortality between hospitals have been reported (3, 8). In a well-established hospital setting, post resuscitation care including therapeutic hypothermia can improve outcomes among post-cardiac arrest patients (3, 8, 9).

Therefore, it has been suggested that the resuscitation center could provide regional post cardiac-arrest care (9-13). Recently, some studies have proven that the transported distance and time did not affect the outcomes of OHCA patients (10-12). However, these studies have focused on the transport of OHCA patients from the field to the hospital. There was a study to evaluate the outcomes of OHCA patients who have been transported to a well-organized regional center after ROSC (14). This study showed that the outcome of inter-hospital transported patients with pre-transferred cooling did not differ from patients who had directly visited the regional center. However, a delay in the initiation of cooling was associated with an increased risk of death.

Despite pre-transferred TH has potential benefit (14), induction of prehospital TH after ROSC in OHCA is not widely used due to a lack of effective equipment, manpower, and specific guidelines (15). Therefore, most resuscitated patients start TH after their arrival at the hospital (15).

For this reason, we hypothesized that the patients transferred after ROSC would have delayed initiation of cooling, which would produce poor outcome in the transferred patients compared to

directly visited patients. The aim of this study was to evaluate the outcome differences between transferred group and the Samsung Medical Center (SMC) group.

## MATERIALS AND METHODS

We conducted protocol-based therapeutic hypothermia on post cardiac arrest syndrome patients since January 2010. For this study, we collected data retrospectively from the Samsung Medical Center (SMC; A 1,960 bed, university-affiliated, tertiary referral hospital in Seoul, Korea.) hypothermia database of cardiac arrest between January 2010 to March 2012. Samsung Medical Center has been providing care in about 100 cases of OHCA annually directly from the emergency medical service and about 30 cases of transferred OHCA patient after ROSC annually. The primary outcome was the neurologic outcome and the secondary outcome was the survival at 1 month after cardiac arrest.

The SMC therapeutic hypothermia protocol was composed of 5 parts - enrollment, induction of hypothermia, maintenance, rewarming, and normothermia. We considered therapeutic hypothermia for all patients of out-of-hospital (OHCA) and in-hospital cardiac arrest (IHCA), who were unresponsive after ROSC regardless of the inter-hospital transfer. The exclusion criteria were as follows: 1) The cause of arrest is sepsis, progression of malignancy, trauma, and hemorrhagic shock; 2) The expected survival time was less than 3 months before the cardiac arrest; 3) The functional performance scale was  $< 3$  (16); 4) Major Operation (head, chest, abdomen and vascular) occurred within 7 days; 5) Over 12 hr have passed after ROSC; 6) A cardiac arrest was not witnessed and the time of occurrence could not be estimated; 7) Intracranial hemorrhage of the brain was observed on non-contrast computerized tomography (CT); and 8) The patient is pregnant.

The following parameters were collected by conventional treatment before induction of hypothermia: mean arterial pressure of 60 mmHg, peripheral oxygen saturation of less than 85%, and coagulopathy (prothrombin time  $> 3$  International normalized ratio [INR], platelet counts  $< 5 \times 10^9/L$ , activated partial thromboplastin time [aPTT]  $< 80$  sec).

The hypothermia induction was started by 4°C cold saline infusion (about 30 mL/kg) for over 30 min. After esophageal temperature probe insertion, we used the commercial temperature regulation system of hydrogel pad (Arctic Sun®; Medivance Corp, Louisville, CO, USA). If the commercial device was not available, we used the conventional methods like the commercial cold blanket, 4°C cold saline bladder irrigation, and traditional ice packs placed on the groin, armpits, around the neck and the head. The target temperature of the induction was 33.5°C. The maintenance lasted for 24 hr. During the maintenance period, the temperature was maintained within  $33 \pm 0.5^\circ\text{C}$ . After the maintenance period, the patient was rewarmed to 36.5°C

with 0.15°C/hr on Arctic Sun® and with less than 0.25°C/hr on cooling blanket. During the period of normothermia, after the temperature had reached 36.5°C, we maintained the temperature at less than 37.5°C until 72 hr after ROSC.

During the hypothermia therapy, we used continuous intravenous midazolam for sedation (start 2 mg/hr; maximum 5 mg/hr), continuous intravenous fentanyl (100 µg/hr) for pain control, and intermittent intravenous pethidine (25 mg; maximum 100 mg/day) for shivering control. The midazolam and fentanyl were tapered during the rewarming period and stopped fully until the normothermia period. The neuromuscular block agents were used based on the decision of the attending physicians.

The hemodynamic optimization was performed based on the early goal-directed therapy (EGDT) for sepsis (17). The hemodynamic optimization target was as follows: central venous pressure (CVP)  $\geq 12$  mmHg, mean arterial pressure (MAP)  $\geq 75$  mmHg, peripheral oxygen saturation (SaO<sub>2</sub>)  $> 94\%$ , and PaCO<sub>2</sub>  $> 40$  mmHg. For targeting, we used dopamine as first line vasopressor (start 10 µg/kg/min; maximum 30 µg/kg/min) and norepinephrine (start 5 µg/min; maximum) as second line. Since then, the use of vasopressin, intra-aortic balloon pump (IABP), or percutaneous cardiopulmonary support (PCPS) device was decided by attending physicians.

If the first electrocardiography (ECG) after ROSC had ST segment elevation or left bundle branch block, or the cause of arrest was suspected to be myocardial infarction, an emergency coronary angiography (CAG) was performed on the patient. The CAG and hypothermia therapy were performed at the same time. Percutaneous coronary intervention (PCI) was performed if required. If the first CAG was normal, a secondary CAG was performed for identification of coronary spasm after the completion of therapeutic hypothermia. SMC emergency CAG protocols regulated door to balloon time within 90 min for MI patients, but not for OHCA patients. Thus, we defined the emergency CAG as within 6 hr after cardiac arrest.

The neurological assessment was conducted 30 days after cardiac arrest in hospitalization or during follow-up for outpatients. We used the cerebral performance category (CPC) score, which grades the level of neurofunctional status after cardiac arrest as follows: CPC 1 is good; CPC 2 is moderate disability; CPC 3 is severe disability; CPC 4 is comatose or vegetative state; and CPC 5 is death (16). If the patients were transferred out to rehabilitation hospitals, we collected the information from his or her attending physicians by phone.

### The data collection

SMC hypothermia database contained the following hypothermia treatment information using standardized case forms following the Utstein style (18): Initial tympanic temperature at induction, initial esophageal temperature, induction time, target temperature time, cooling method, and sequential organ fail-

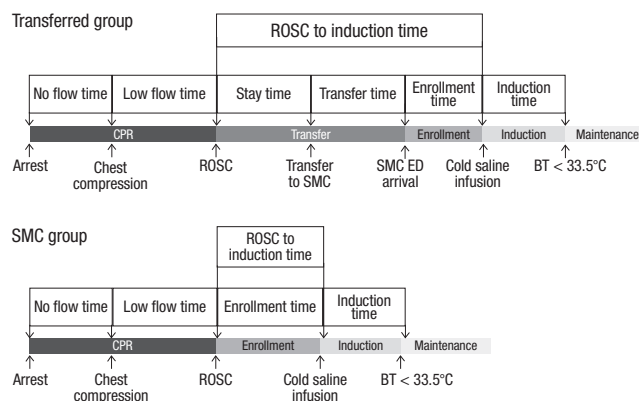
ure assessment (SOFA) score, except glows coma scale at the hypothermia induction. We defined the respective organ failure as each SOFA score of greater than 2 (19). The data was recorded by the attending physician primarily and was reviewed by one faculty in the Department of Emergency Medicine. In addition to the database, we reviewed the transfer-records of the patients to gather information associated with inter-hospital transfer.

We defined time variables related to the inter-hospital transfer and therapeutic hypothermia as follows: time in-hospital; from ROSC to start transfer to SMC; Transfer time; from start transfer to arrival SMC emergency department (ED); enrollment time, from ED arrival to start cold saline infusion in transferred patients; from ROSC to start cold saline infusion in non-transferred patients; induction time, from cold saline infusion to time of core temperature below 33.5°C; ROSC to induction time, from ROSC to cold saline infusion (Fig. 1). We defined the primary outcome as good neurofunctional status of CPC 1 or 2 at 1 month, and the secondary outcomes as the survival at 1 month between the non-transferred group and transferred group.

**Statistical analysis**

To compare both groups, we used the chi-square test for nominal variable, *t*-test for continuous variable with normal distribution, and the Wilcoxon rank-sum test for continuous variables without normal distribution. In addition, we used the log-rank test for survival of both groups. To analyze the relationships between initial tympanic temperature and the ROSC to induction time, we used the linear regression model. To analyze the relationships between the ROSC to induction time, the induction time and good neurologic outcomes, we categorized the time variables to quartile format and used multivariable logistic model with the Hosmer- Lemeshow goodness-of-fit test.

For statistical analysis, we used STATA 11.0 (StataCorp, College Station, TX, USA) and considered *P* value of less than 0.05



**Fig. 1.** Diagram of defined time variables for both groups. CPR, Cardiopulmonary resuscitation; ROSC, Return of spontaneous circulation; ED, Emergency department; SMC, Samsung medical center; BT, Body temperature.

as statistically significant difference. In this study, we described the nominal data as number of case with percentage, the continuous variable with normal distribution as mean ± standard deviation, the continuous variable without normal distribution as a median with an inter quartile range, and the odds ratio as odds ratio with a 95% confidence interval.

**Ethics statement**

The study protocol was reviewed and approved by the institutional review board of Samsung Medical Center (IRB No. 2012-05-013-001). Informed consent was waived by the board.

**RESULTS**

During the study period, therapeutic hypothermia was performed on a total of 107 patients. Among these, 15 IHCA patients were excluded. In addition, one patient transferred after the hypothermia induction was excluded. Finally, a total of 91 patients were enrolled in this study; 41 patients (SMC group) visited SMC directly after their cardiac arrest, and 50 patients (transferred group) were transferred from other hospitals to SMC after ROSC.

**Table 1.** Basic characteristics of both groups

Parameters	Transferred group (n = 50)	SMC group (n = 41)	<i>P</i> value
Age (yr)	48.9 ± 16.9	54.6 ± 17.6	0.113
Gender male (%)	28 (56.0)	27 (65.9)	0.339
Underlying disease			
Hypertension (%)	13 (26.0)	8 (19.5)	0.465
Diabetics (%)	4 (8.0)	6 (14.6)	0.314
Heart disease (%)	5 (10.0)	6 (14.6)	0.500
Chronic liver disease (%)	0 (0.0)	1 (2.4)	0.267
Chronic renal disease (%)	2 (4.0)	3 (7.3)	0.490
Malignancy (%)	4 (8.0)	5 (12.2)	0.505
Organ failure rate			
Heart (%)	31 (62.0)	29 (70.7)	0.382
Lung (%)	27 (54.0)	27 (65.8)	0.252
Liver (%)	1 (2.0)	0 (0)	0.363
Kidney (%)	5 (10.0)	5 (12.2)	0.739
Coagulation (%)	2 (4.6)	3 (7.9)	0.527
SOFA score (median)	5 (IQR 2-7)	6 (IQR 3-7)	0.314
Arrest cause (%)			0.485
Cardiac	34 (68.0)	29 (70.7)	
Respiratory	16 (32.0)	11 (26.8)	
Other	0 (0)	1 (2.4)	
Bystander CPR (%)	16 (32.0)	17 (41.4)	0.350
AED apply (%)	24 (68.0)	27 (65.8)	0.828
AED shock (%)	21 (42.0)	17 (41.5)	0.888
No-flow time (min)	10.6 ± 9.8	8.7 ± 8.6	0.192
Low-flow time (min)	26.3 ± 15.7	25.1 ± 21.0	0.758
BLS time (min)	10.8 ± 8.27	12.6 ± 8.96	0.324
ACLS time (min)	13.7 ± 14.0	14.3 ± 18.7	0.851
Initial rhythms (%)			0.883
VF	21 (42.0)	19 (46.3)	
PEA	16 (32.0)	13 (31.7)	
Asystole	13 (26.0)	9 (21.9)	

SOFA, sequential organ failure assessment; CPR, cardiopulmonary resuscitation; AED, automated external defibrillator; BLS, basic life support; ACLS, advanced cardiac life support; VF, ventricular fibrillation; PEA, pulseless electrical activity.

**Table 2.** Therapeutic hypothermia and treatment process of both groups

Therapy process	Transferred group (n = 50)	SMC group (n = 41)	P value
Initial tympanic temperature at induction (°C)	36.0 ± 1.4	35.1 ± 1.0	< 0.001
Cooling method			0.527
Hydrogel pad	36 (72.0)	27 (65.8)	
Conventional method	14 (34.2)	14 (28.0)	
ROSC to induction time (median, min)	220 (IQR 139-336)	72 (IQR 43-100)	< 0.001
Stay time (median, min)	77 (IQR 31-176)		
Transfer time (median, min)	24 (IQR 17-54)		
Enrollment time (median, min)	75 (IQR 24-110)	72 (IQR 43-100)	0.986
Induction time (min)	195.9 ± 101.5	168.1 ± 111.8	0.212
Emergency CAG	22 (44.0)	20 (48.8)	0.649
> 50% of stenosis	7 (14.0)	9 (21.9)	0.746
Spasm	7 (14.0)	9 (21.9)	
< 50% stenosis and no spasm	2 (4.9)	4 (6.6)	
IABP	2 (4.9)	1 (2.0)	0.443
PCPS	1 (2.0)	6 (15.6)	0.024
Status epilepticus in EEG	11 (22.0)	14 (34.2)	0.197

ROSC, Return of spontaneous circulation; IQR, Interquartile range; CAG, Coronary angiography; IABP, Intra-aortic balloon pump; PCPS, Percutaneous cardiopulmonary support; EEG, Electroencephalography.

**Table 3.** Primary and secondary outcomes of both groups

Outcomes	Transferred group (n = 50)	SMC group (n = 41)	P value
CPC score at 1 month (%)			0.908
1 or 2	19 (38.0)	17 (40.6)	
3	4 (8.0)	6 (14.6)	
4	11 (22.0)	6 (14.6)	
5	16 (32.0)	11 (26.8)	
Survival at 1 month (%)	33 (66.0)	31 (75.6)	0.318

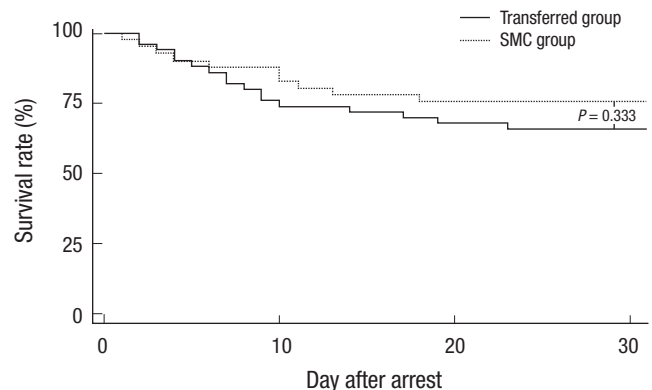
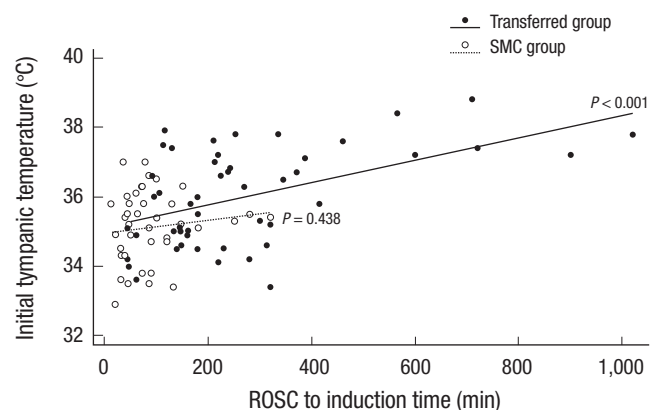
CPC, cerebral performance category.

There were no statistical differences in age, gender, underlying disease, and cause of arrest between both groups. The no-flow time of transferred group was slightly longer than that of SMC group. However, there was no statistically significant difference (Table 1). The individual organ failure rate had no significant difference between both groups. In addition, the total SOFA score except for GCS had no significant difference (Table 1).

The ROSC to induction time of transferred group was longer than that of the SMC group with statistical significance. However, there was no difference in enrollment time between both groups. The initial tympanic temperature at induction of the transferred group was higher with statistical significance than that of SMC group. The induction time of the transferred group was longer than that of the SMC group. However, it was not statistically significant (Table 2). The emergency CAG rate and CAG results were similar in both groups. The application of PCPS was greater in the SMC group (Table 2).

There was no statistical difference in good neurologic outcomes between the two groups (38% in transferred group vs. 40.6% in SMC group) (Table 3). The 1 month survivals had no statistical difference in the Log rank test in both groups ( $P = 0.333$ ) (Fig. 2).

The linear regression model showed that the initial tympanic temperature was positively associated with ROSC to induction

**Fig. 2.** The Kaplan-Meier survival curve of both groups. The log rank test in both groups ( $P = 0.333$ ).**Fig. 3.** Scatter plot of patient initial body temperature for both groups. (Transferred group, standardized beta coefficients 0.49,  $P < 0.001$  vs. SMC group, standardized beta coefficients 0.12,  $P = 0.438$ ).

time in transferred group (standardized beta coefficients 0.49,  $P < 0.001$ ). However in SMC group, there was no statistical correlation (standardized beta coefficients 0.12,  $P = 0.438$ ) (Fig. 3).

**Table 4.** Odds ratio of good neurologic outcomes in a logistic regression model

Variables	CPC 1 or 2 (No.)	Univariate model	Multivariate model
Age		0.98 (0.95-1.00)	0.93 (0.89-0.99)
Gender			
Male (n = 55)	24	Ref.	Ref.
Female (n = 36)	12	1.54 (0.64-3.71)	1.13 (0.26-4.76)
No flow time		0.85 (0.78-0.92)	0.85 (0.74-0.97)
Low flow time		0.98 (0.95-1.00)	0.93 (0.89-0.97)
AED shock			
No (n = 54)	12	Ref.	Ref.
Yes (n = 37)	24	6.46 (2.54-16.39)	1.99 (0.31-12.8)
Shockable rhythm			
No (n = 51)	11	Ref.	Ref.
Yes (n = 40)	25	6.06 (2.40-15.27)	2.64 (0.44-15.6)
Arrest cause			
Cardiac (n = 63)	35	Ref.	Ref.
Respiratory (n = 27)	1	0.04 (0.00-0.24)	0.03 (0.00-0.56)
Other (9/1)	0	-	-
ROSC to induction time			
< 63 (n = 23)	10	Ref.	Ref.
64-132 (n = 23)	9	0.83 (0.26-2.71)	1.16 (0.17-7.95)
133-250 (n = 23)	8	0.69 (0.21-2.27)	1.03 (0.17-6.13)
> 251 (n = 22)	9	0.90 (0.27-2.94)	2.91 (0.37-22.51)
Induction time			
< 100 (n = 23)	8	Ref.	Ref.
101-170 (n = 23)	8	1 (0.29-3.36)	0.12 (0.01-1.26)
171-250 (n = 23)	12	2.01 (0.62-6.69)	0.34 (0.04-2.77)
> 251 (n = 22)	8	1.07 (0.31-3.63)	0.12 (0.01-1.23)

CPC, cerebral performance category; AED, automated external defibrillator; ROSC, return of spontaneous circulation.

In the univariate model, the ROSC to induction time and the induction time had no association with the good neurologic outcome. In addition, we made adjustments in the multivariate model for the following variables: age, gender, no-flow time, low-flow time, AED shock, initial rhythms, and cause of arrest. There was no statistical association between these variables (Table 4).

## DISCUSSION

In this study, we demonstrated that there were no significant differences in hospital mortality and neurologic outcome between the patients transferred from other hospital after ROSC and the non-transferred patients in OHCA. Furthermore, this study provided additional evidence that inter-hospital transfer for TH in OHCA patient after ROSC can be achieved in the real world.

Recent studies have evaluated the patients with ROSC or without ROSC transported to the specialized hospitals, which had large volume and were well-organized for post resuscitation care that could improve the patients' survival rate (10, 12, 20) and neurologic outcome (9). The results emphasized that transportation interval or distance did not appear to influence on the outcome in OHCA patients. These studies suggested the efficiency and feasibility of transporting patients from the field to

a specialized hospital (9-12, 20).

However, there are few studies on inter-hospital transport system for TH patients. We evaluated distance and transport interval between the referring hospital and SMC. Mean transferred distance was  $39.1 \pm 45.7$  km (4.1-227.0 km) and median transfer time was 24 (IQR 17-54) min. Transfer time and distance were shorter than the other studies (14). This might have been induced by geographical difference and the differential distribution of the transferred hospital. To clearly demonstrate the effect of inter-hospital transfer distance and time in OHCA, further study will be needed.

Application of PCPS was significantly higher in SMC group. PCPS has been reported that difficult procedures were required and that affording specialized staff was costly (21). Therefore, it is difficult to apply PCPS in all hospitals, and these barriers induced difference in application of PCPS between both groups. Also, this procedure was applied in refractory cardiac arrest (22). Although initial SOFA score and other factors did not differ significantly between transferred group and SMC group, it is possible that patients of transferred group were more stable than patients of SMC group. This problem could have effected on the number of PCPS insertion.

We found that the initial body temperature was significantly higher in transferred group than in SMC group. We presumed that patients in transferred group, who were transported from other hospitals, were not initiated with TH. On the other hand, we applied TH protocol as soon as possible to comatose survivors of OHCA. So, the body temperature of the transferred group was higher than the SMC group. Mooney et al. also reported that there was no difference in survival and neurologic outcome between transferred group and not-transferred group (14). However, this study started TH during transferring to the receiving hospital. So, it is difficult to evaluate the effect of initiating or not initiating TH during inter-hospital transport. Providing education about TH and post-resuscitation care could improve the outcomes of OHCA (13, 14). However, if referral hospital could not perform TH, our data could provide the evidence for suggesting the possibility of inter-hospital transport without pre-hospital TH, which was performed before arriving at the receiving hospital.

The benefits of early initiation of TH have been proved in animal models (23, 24). The studies in humans have been controversial for early induction time of TH. Wolff et al. (25) recommended prompt achievement of core temperature by endovascular cooling for improved neurologic outcomes. Another study demonstrated the association between time to cooling and mortality. They have been proved that 1 hr delay in time to cooling could increase 20% in risk of death (13). On the other hand, early initiation of therapeutic hypothermia after cardiac arrest could increase mortality (26). Nielsen et al. (27) showed that there was no association between time of initiation of TH and neurologic

outcomes. Our studies agreed on this result. Although transferred group took more times to initiate TH, we could not find any difference in neurologic outcome between transferred group and SMC group.

In addition, we analyzed this time interval. The time interval from ROSC to induction time of TH consisted of staying time at the other hospital, transfer time, and enrollment time. Therefore, median interval from ROSC to induction time of TH was significantly longer in transferred group. However, there were no difference in enrollment time in both groups, and this enrollment time was similar or shorter than other studies (13, 27).

Hartke et al. (28) studied feasibility of transporting post-cardiac arrest patients to other hospital, by evaluating the rate of re-arrest and the rate of critical events. They used highly trained critical care transport teams (CCTT) for transporting post-cardiac arrest patients. They showed that repeat cardiac arrest occurred infrequently, and the most critical events occurred during the first 60 min via CCTT. Because our study patients were transported from referral hospital to SMC by emergency medical technicians (EMTs) or doctors of the other hospitals, we do not have detailed information on critical events and re-arrest during the transport. However, we were able to obtain major information about the patients, from EMTs or doctors of referral hospitals. To our knowledge, there were no patients who died during the transport to the SMC. However, it might still be possible that some patients were transferred to the other hospital due to cardiac arrest or death during the transfer. More investigations may be needed on the safety of inter-hospital transport of OHCA patients.

We found that short no-flow time (adjusted OR, 0.85; 95% CI, 0.74-0.97) and short low-flow time (adjusted OR, 0.93; 95% CI, 0.89-0.97) could improve the neurologic outcome. This result was consistent with past studies (9, 14, 27). Recent study found that the survival group had longer time to target temperature than the non-survival group (29). On the other hand, shortening the delay from ROSC to hypothermic target temperature may significantly improve survival (30); and this issue is still being debated. We did not find any correlation between ROSC to induction time or induction time and good neurologic outcome. These results should be interpreted with caution, because early start of TH is important and the physiological processes of neuroprotection effect of early initiation of cooling have been proven by previous studies (2, 13, 23, 24, 30). Therefore, we could not interpret our results as evidence of relationship between delayed cooling and good neurologic outcome. However, we could suggest that the neurologic outcome of the transferred patients, who were referred from the hospital where TH was impossible, was no different compared to non-transferred patients. It is important that post cardiac arrest patients need TH transfer to resuscitation center for improving neurologic outcome.

This observational study has several limitations. First, this is a

single-centered study in Korea. The inter-hospital transport system in Korea is under rapid development, but TH has not been widely adopted in Korean medical environment. Therefore, difference in geographical characteristics, hospital settings, and hospital transport system might be difficult to be compared with other institutions. Second, our study was retrospective observational study, so selection bias could have influenced the significance of our results. As mentioned above, the number of PCPS insertions was higher in SMC group. Also, we could not include patients who died or had cardiac arrest during transferring to SMC. These factors might have been influenced as selection bias in the result. In addition, we were unable to fully adjust for the effects of unobserved biases. Additionally, the small study population might have affected our result.

The hypothermia inductions of transferred patients after ROSC were delayed compared with that of directly visited patients. The good neurologic outcome and survival at 1 month had no significant differences between both groups. This finding suggests the possibility of integrated post-cardiac arrest care for OHCA patients who are transferred from other hospitals after ROSC in the cardiac arrest center.

## DISCLOSURE

The authors have no conflicts of interest to disclose.

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## REFERENCES

1. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, Rea T, Lowe R, Brown T, Dreyer J, et al. *Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA 2008; 300: 1423-31.*
2. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Böttiger BW, Callaway C, Clark RS, Geocadin RG, Jauch EC, et al. *Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: a Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke. Resuscitation 2008; 79: 350-79.*
3. Carr BG, Kahn JM, Merchant RM, Kramer AA, Neumar RW. *Inter-hospital variability in post-cardiac arrest mortality. Resuscitation 2009; 80:*

- 30-4.
4. Polderman KH. *Hypothermia and neurological outcome after cardiac arrest: state of the art. Eur J Anaesthesiol Suppl* 2008; 42: 23-30.
  5. Abella BS, Rhee JW, Huang KN, Vanden Hoek TL, Becker LB. *Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey. Resuscitation* 2005; 64: 181-6.
  6. Merchant RM, Soar J, Skrifvars MB, Silfvast T, Edelson DP, Ahmad F, Huang KN, Khan M, Vanden Hoek TL, Becker LB, et al. *Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. Crit Care Med* 2006; 34: 1935-40.
  7. Mechem CC, Goodloe JM, Richmond NJ, Kaufman BJ, Pepe PE; U.S. Metropolitan Municipalities EMS Medical Directors Consortium. *Resuscitation center designation: recommendations for emergency medical services practices. Prehosp Emerg Care* 2010; 14: 51-61.
  8. Carr BG, Goyal M, Band RA, Gaieski DF, Abella BS, Merchant RM, Branas CC, Becker LB, Neumar RW. *A national analysis of the relationship between hospital factors and post-cardiac arrest mortality. Intensive Care Med* 2009; 35: 505-11.
  9. Kajino K, Iwami T, Daya M, Nishiuchi T, Hayashi Y, Kitamura T, Irisawa T, Sakai T, Kuwagata Y, Hiraide A, et al. *Impact of transport to critical care medical centers on outcomes after out-of-hospital cardiac arrest. Resuscitation* 2010; 81: 549-54.
  10. Davis DP, Fisher R, Aguilar S, Metz M, Ochs G, McCallum-Brown L, Ramanujam P, Buono C, Vilke GM, Chan TC, et al. *The feasibility of a regional cardiac arrest receiving system. Resuscitation* 2007; 74: 44-51.
  11. Spaite DW, Bobrow BJ, Vadeboncoeur TF, Chikani V, Clark L, Mullins T, Sanders AB. *The impact of prehospital transport interval on survival in out-of-hospital cardiac arrest: implications for regionalization of post-resuscitation care. Resuscitation* 2008; 79: 61-6.
  12. Cudnik MT, Schmicker RH, Vaillancourt C, Newgard CD, Christenson JM, Davis DP, Lowe RA; ROC Investigators. *A geospatial assessment of transport distance and survival to discharge in out of hospital cardiac arrest patients: implications for resuscitation centers. Resuscitation* 2010; 81: 518-23.
  13. Nichol G, Aufderheide TP, Eigel B, Neumar RW, Lurie KG, Bufalino VJ, Callaway CW, Menon V, Bass RR, Abella BS, et al. *Regional systems of care for out-of-hospital cardiac arrest: a policy statement from the American Heart Association. Circulation* 2010; 121: 709-29.
  14. Mooney MR, Unger BT, Boland LL, Burke MN, Kebed KY, Graham KJ, Henry TD, Katsiyannis WT, Satterlee PA, Sendelbach S, et al. *Therapeutic hypothermia after out-of-hospital cardiac arrest: evaluation of a regional system to increase access to cooling. Circulation* 2011; 124: 206-14.
  15. Taccone FS, Donadello K, Beumier M, Scolletta S. *When, where and how to initiate hypothermia after adult cardiac arrest. Minerva Anestesiol* 2011; 77: 927-33.
  16. Jennett B, Bond M. *Assessment of outcome after severe brain damage. Lancet* 1975; 1: 480-4.
  17. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, et al. *Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med* 2008; 36: 296-327.
  18. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J. *Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). Circulation* 2004; 110: 3385-97.
  19. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S. *Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study: working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med* 1998; 26: 1793-800.
  20. Cha WC, Lee SC, Shin SD, Song KJ, Sung AJ, Hwang SS. *Regionalisation of out-of-hospital cardiac arrest care for patients without prehospital return of spontaneous circulation. Resuscitation* 2012; 83: 1338-42.
  21. Arlt M, Philipp A, Zimmermann M, Voelkel S, Amann M, Bein T, Müller T, Foltan M, Schmid C, Graf B, et al. *Emergency use of extracorporeal membrane oxygenation in cardiopulmonary failure. Artif Organs* 2009; 33: 696-703.
  22. Avalli L, Maggioni E, Formica F, Redaelli G, Migliari M, Scanziani M, Celotti S, Coppo A, Caruso R, Ristagno G, et al. *Favourable survival of in-hospital compared to out-of-hospital refractory cardiac arrest patients treated with extracorporeal membrane oxygenation: an Italian tertiary care centre experience. Resuscitation* 2012; 83: 579-83.
  23. Zhao D, Abella BS, Beiser DG, Alvarado JP, Wang H, Hamann KJ, Hoek TL, Becker LB. *Intra-arrest cooling with delayed reperfusion yields higher survival than earlier normothermic resuscitation in a mouse model of cardiac arrest. Resuscitation* 2008; 77: 242-9.
  24. Kuboyama K, Safar P, Radovsky A, Tisherman SA, Stezoski SW, Alexander H. *Delay in cooling negates the beneficial effect of mild resuscitative cerebral hypothermia after cardiac arrest in dogs: a prospective, randomized study. Crit Care Med* 1993; 21: 1348-58.
  25. Wolff B, Machill K, Schumacher D, Schulzki I, Werner D. *Early achievement of mild therapeutic hypothermia and the neurologic outcome after cardiac arrest. Int J Cardiol* 2009; 133: 223-8.
  26. Italian Cooling Experience (ICE) Study Group. *Early- versus late-initiation of therapeutic hypothermia after cardiac arrest: preliminary observations from the experience of 17 Italian intensive care units. Resuscitation* 2012; 83: 823-8.
  27. Nielsen N, Hovdenes J, Nilsson F, Rubertsson S, Ståmmet P, Sunde K, Valsson F, Wanscher M, Friberg H; Hypothermia Network. *Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. Acta Anaesthesiol Scand* 2009; 53: 926-34.
  28. Hartke A, Mumma BE, Rittenberger JC, Callaway CW, Guyette FX. *Incidence of re-arrest and critical events during prolonged transport of post-cardiac arrest patients. Resuscitation* 2010; 81: 938-42.
  29. Benz-Woerner J, Delodder F, Benz R, Cueni-Villoz N, Feihl F, Rossetti AO, Liaudet L, Oddo M. *Body temperature regulation and outcome after cardiac arrest and therapeutic hypothermia. Resuscitation* 2012; 83: 338-42.
  30. Howes D, Ohley W, Dorian P, Klock C, Freedman R, Schock R, Krizanac D, Holzer M. *Rapid induction of therapeutic hypothermia using convective-immersion surface cooling: safety, efficacy and outcomes. Resuscitation* 2010; 81: 388-92.