

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Interhospital transfer in low-volume and high-volume emergency departments and survival outcomes after out-of-hospital cardiac arrest: A nationwide observational study and propensity score-matched analysis



Jeong Ho Park^{a,d}, Seung Chul Lee^{b,d,*}, Sang Do Shin^{a,d}, Kyoung Jun Song^{c,d},
Ki Jeong Hong^{a,d}, Young Sun Ro^{a,d}

^a Department of Emergency Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

^b Department of Emergency Medicine, Dongguk University Ilsan Hospital, Goyang-si, Republic of Korea

^c Department of Emergency Medicine, Seoul National University Boramae Medical Center, Seoul, Republic of Korea

^d Laboratory of Emergency Medical Services, Seoul National University Hospital Biomedical Research Institute, Seoul, Republic of Korea

Abstract

Introduction: Post-resuscitation care of out-of-hospital cardiac arrest (OHCA) patients often involves inter-hospital transfer (IHT). We aimed to determine the association between IHT and outcomes of OHCA.

Methods: This cross-sectional study used data from the nationwide emergency medical services (EMS)-based OHCA registry in Korea. All cases of adult patients with OHCA with a presumed cardiac aetiology and a sustained return of spontaneous circulation (ROSC) at hospitals between 2015 and 2016 were analysed. The primary outcome was a good neurological recovery at discharge, defined as cerebral performance in categories 1 or 2. We compared the primary outcome between a non-IHT group and an IHT group, using a propensity score-matching analysis. All analyses were performed separately by mean annual volume of patients with OHCA initially visiting high-volume emergency departments (HVEDs; >100 OHCA patients) and low-volume emergency departments (LVEDs; ≤100 OHCA patients).

Results: Of 54,779 OHCA patients, 11,632 were included. Of 4477 patients who visited LVEDs initially, 1360 (30%) patients were transferred. Of 7155 patients who visited HVEDs initially, 604 (8%) patients were transferred. In the propensity score-matching analysis, the IHT group was more likely to have good neurological recovery than was the non-IHT group [adjusted odds ratio (OR): 1.34; 95% confidence interval (CI): 1.07–1.67] in LVED visitors, but there was no significant difference of good neurological recovery between the non-IHT group and the IHT group (adjusted OR: 0.84; 95% CI: 0.63–1.13) in HVED visitors.

Conclusion: IHT should be considered when treating OHCA patients in LVEDs.

Keywords: Out-of-hospital cardiac arrest, Patient transfer, Outcomes

* Corresponding author at: Department of Emergency Medicine, Dongguk University Ilsan Hospital, Goyang-si, Republic of Korea.

E-mail addresses: timthe@gmail.com (J.H. Park), emsscl0126@gmail.com, edlee@dumc.or.kr (S.C. Lee), shinsangdo@medimail.co.kr (S.D. Shin), skciva@gmail.com (K.J. Song), emkjhong@gmail.com (K.J. Hong), ro.youngsun@gmail.com (Y.S. Ro).

<https://doi.org/10.1016/j.resuscitation.2019.03.044>

Received 1 December 2018; Received in revised form 7 March 2019; Accepted 27 March 2019

0300-9572/© 2019 Published by Elsevier B.V.

Introduction

Out-of-hospital cardiac arrest (OHCA) poses a significant burden of disease worldwide.^{1–3} Specialised care such as percutaneous coronary intervention (PCI) and extracorporeal membrane oxygenation (ECMO) are often needed to manage the precipitating cause of cardiac arrest. Targeted temperature management is associated with protection against ischemic-reperfusion injury, especially in patients who have a brain injury.^{4,5} Other intensive care modalities, including respiratory care and seizure management, are also emphasised in guidelines to reduce further damage to patients with post-resuscitation care syndrome.⁶

Considerable resources are needed to provide comprehensive post-resuscitation care to OHCA patients. Therefore, low-volume emergency departments (LVEDs) often do not have the capacity to offer comprehensive post-resuscitation care.⁷ In addition, even in high-volume emergency departments (HVEDs), timely post-resuscitation care is not always provided to patients because of transient limitations of resources. Inter-hospital transfer (IHT) is often required to provide comprehensive post-resuscitation care to initial survivors of OHCA.⁸

The association between IHT and outcomes of critically ill patients is controversial.⁹ During transport to other hospitals, adverse events, including re-arrest, might also occur and threaten the survival outcomes of OHCA patients.¹⁰ Therefore, the positive effect of IHT on outcomes of OHCA might be attenuated by the risk of transport.

The effect of IHT on outcomes of OHCA patients might be different for patients who visited LVEDs than for patients who visited to HVEDs. In LVED visitors, risk of IHT might be acceptable because post-resuscitation care could not be provided without IHT in many cases. For HVED visitors, this acceptable threshold for the risk of IHT might be substantially decreased, because post-care might be conducted without IHT.

The aim of this study was to evaluate the effect of IHT on survival outcomes of OHCA, according to the initial visiting ED resuscitation volume.

Methods

Ethics statements

This study was approved by the Institutional Review Board (IRB) of the institutions affiliated with the study investigators, and informed consent was waived (IRB No. 1103-153-357). The study protocol complied with the Declaration of Helsinki.

Study design and setting

This study was a cross-sectional study, using a nationwide, population-based, prospective registry of OHCA in Korea.

Korea has a total population of approximately 50 million in 100,210 km². Korea is composed of 226 administrative counties, of which 82 counties belong to rural areas, according to administrative classification.

The Korean emergency medical services (EMS) system is fire department-based, and the EMS level is intermediate; EMS providers can give cardiopulmonary resuscitation (CPR) with automatic external defibrillation (AED), perform advanced airway management, and give

fluid intravenously. EMS providers cannot declare death in the field. CPR can only be discontinued if return of spontaneous circulation (ROSC) occurs. Therefore, all patients with OHCA are transported to the ED. Patients with OHCA should be transported to the nearest ED according to the national EMS protocol.

There are approximately 546 EDs, and all EDs are designated as level 1, 2, or 3 by the Ministry of Health and Welfare. The ED level designation is based on each ED's capacity and resource measures, such as staffing, equipment, and size of department. Level 1 (n = 20) and level 2 (n = 126) EDs have more resources and better facilities for emergency care and must be covered by an emergency physician 24 h a day. A specialised centre for cardiac arrest is not designated.

The IHT system provides basic services, primarily by ground transportation by hospital ambulances or private EMS agencies. The guideline for IHT was released by the Ministry of Health and Welfare in 2014.⁸ However, it is not mandatory. In the case of critical patients, physicians or nurses might ride the IHT with the patient, but a system for a mobile intensive care unit (ICU) was not adopted, except in the capital city.

Data source

We used the Korean nationwide OHCA registry, which captures all cases of OHCA in the country. The Korean OHCA registry was retrieved from the following four sources: the EMS records for basic ambulance operation information, the EMS CPR registry, the dispatcher CPR registry, and the hospital OHCA registry for hospital care and outcomes. All EMS registries for each patient are linked, using ambulance dispatch numbers in the national fire department's electronic database server and are integrated as a single episode. The medical record reviewers from the Korea Centres for Disease Control and Prevention (KCDC) extract the recorded information on aetiology, hospital care, and outcomes from hospitals. To ensure the quality of the medical record review process, a quality management committee of emergency physicians, epidemiologists, statistical experts, and medical record review experts analyse the data every month while providing feedback to each medical record reviewer. Detailed descriptions of training and quality control of medical record reviewers are described in previous studies.^{11,12}

Study population

Patients with EMS-treated OHCA of presumed cardiac aetiology who were aged 18 years or older and who achieved ROSC in the ED between January 2015 and December 2016 were included. For patients who achieved ROSC before ED arrival, those with sustained spontaneous circulation for 20 min or longer in the ED were included. For patients who achieved ROSC in the ED, any ROSC event was included. Patients were excluded if their episode was witnessed by EMS providers. Patients with missing information on neurologic outcome at the time of discharge were also excluded.

Patients having an arrest of cardiac aetiology were identified by medical record review. Patients were considered to have cardiac aetiology of their OHCA if there was no obvious evidence of noncardiac aetiology such as trauma, drowning, poisoning, burn, and asphyxia.

Outcome measures

The primary outcome was good neurologic recovery at the time of discharge from the hospital, which was defined as having a cerebral

performance category (CPC) score of 1 or 2. The secondary outcome was survival to hospital discharge.

Variables and measurement

Patients were categorised according to the transfer status at the ED of the initially visited hospital: a non-transferred group, who were not transferred from the ED of the initially visited hospitals; or a transferred group, who were transferred to another hospital from the ED of the initially visited hospital. EDs were categorised according to annual resuscitation volume: HVEDs whose annual resuscitation volumes were more than 100, and LVEDs, whose annual mean cardiac arrest patient volume was less or equal to 100. The cut-off volume was defined according to previous studies.¹³

We collected the patients' demographic factors, which included age, gender, and past medical history (diabetes mellitus, hypertension, heart disease, and stroke). We also collected community-EMS factors, which included year of arrest, location of arrest (public, private, and others), bystander witness status (no bystander witness and bystander witness), bystander CPR (no bystander CPR, bystander CPR without dispatcher assistance, and bystander CPR with dispatcher assistance), bystander AED use, bystander defibrillation, initial rhythm (shockable, pulseless electrical activity, and asystole), EMS defibrillation, EMS intravenous (IV) placement, EMS advanced airway management (endotracheal intubation, supra-glottic airway device insertion, and bag-valve ventilation), EMS mechanical CPR device use, EMS response time interval (elapsed time interval from call to EMS arrival at the scene), EMS scene time interval (elapsed time interval from EMS arrival to departure from the scene), and EMS transport time interval (elapsed time interval from departure from the scene to arrival in the ED). Level of ED (levels 1–3) and urbanisation of arrest incident location (categorised into rural, urban, and metropolitan areas, using the administrative classification) were collected. Post-resuscitation care at the first visit to the ED, including PCI, targeted temperature management, and ECMO were also collected.

Statistical analysis

Descriptive analysis was performed to examine the distributions of categorical variables (counts and proportions) and continuous variables (medians and quartiles). The continuous variables were compared using the Wilcoxon rank-sum test, and the categorical variables were compared using the chi-square test.

We compared survival outcomes between the non-transferred group and the transferred group, categorising patients into two groups: patients who visited LVEDs or patients who visited HVEDs. We used both logistic regression analysis for unmatched patients and propensity score-matching analysis to adjust for selection bias when comparing outcomes between the non-transferred group and the transferred group.

In unmatched analyses, univariable and multivariable logistic regression were performed to estimate the association between IHT and outcomes. The multivariable logistic regression model was adjusted for potential confounders, including age, gender, diabetes, hypertension, heart disease, stroke, urbanisation level of incident, place of arrest, bystander witness status, bystander CPR, initial rhythm, prehospital intravenous line placement, prehospital advanced airway management, and EMS response time. In propensity score-matching analyses, we used only pre-transfer variables for calculating

propensity score. We estimated propensity score by fitting a logistic regression model that included age, gender, diabetes, hypertension, heart disease, stroke, urbanisation level of incident, place of arrest, witness status, bystander CPR, initial rhythm, prehospital intravenous line placement, prehospital advanced airway management, and EMS response time. After deriving a propensity score for each patient, one-to-one matching for each patient was performed without replacement for each patient, using a nearest-neighbour matching algorithm with a calliper width no greater than 0.2 times the standard deviation of the logit of the propensity score. Matched patients were compared to assess balance in covariates (i.e., standardised differences for each covariate were <10%).^{14,15} After confirming this, the associations between IHT and outcomes were assessed by constructing a logistic regression model.

A p value <0.05 was considered the level of significance for all analyses. Statistical analyses were performed using R version 3.5.1. (R Project for Statistical Computing; <https://www.r-project.org/>), and the MatchIt package in R (<https://cran.r-project.org/web/packages/MatchIt/index.html>) was used for propensity matching.

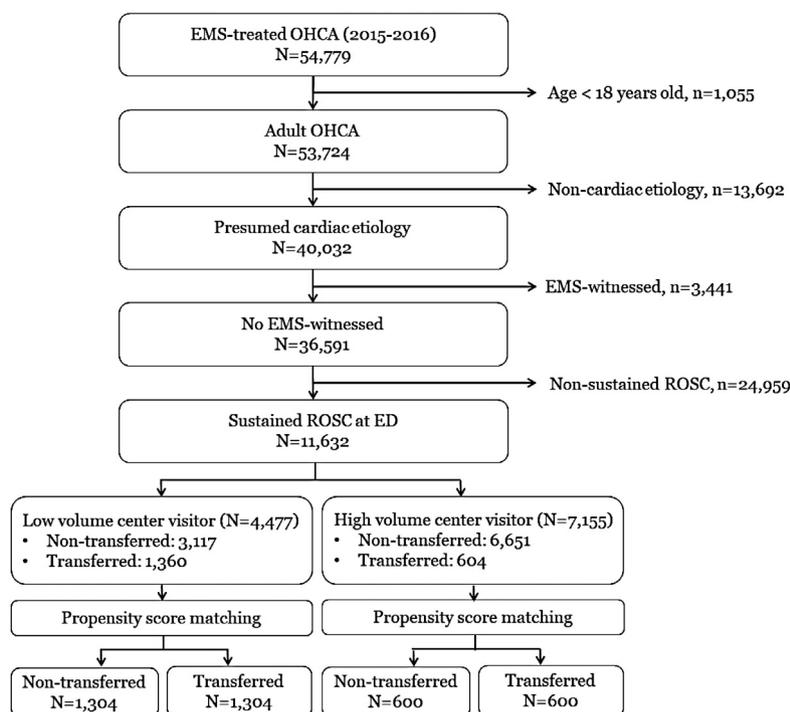
Results

Demographic findings

Among 54,779 EMS-treated patients with OHCA, 11,632 patients were included in the final analysis. We excluded patients who were younger than 18 years of age ($n=1055$), had a non-cardiac aetiology ($n=13,692$), whose arrest was witnessed by EMS ($n=3441$), and who died without ROSC ($n=24,959$). We analysed the cases of 4477 patients who visited LVEDs and 7155 patients who visited HVEDs. Among the LVED visitors, 2608 of 4477 patients were matched. Among the HVED visitors, 1200 of 7155 patients were matched (Fig. 1). An absolute standard mean difference between matched cohorts of all variables was below 0.1 in both LVED visitors and HVED visitors.

The demographic characteristics of unmatched cohorts according to ED resuscitation volume are summarised in Table 1. A total of 1360 (30.4%) LVED patients were transferred, and 604 (8.4%) HVED patients were transferred. Regardless of ED resuscitation volume, the proportion of patients whose age was less than 60 years, the proportion of patients receiving bystander CPR, and the proportion of patients with shockable rhythm were larger in the transferred group than in the non-transferred group. Among the LVED visitors, a total of 275 (8.8%) patients in the non-transferred group had good neurological recovery at discharge, compared with 230 (16.9%) patients in the transferred group. Among the HVED visitors, a total of 1183 (18.1%) patients in the non-transferred group had good neurological recovery at discharge, compared with 100 (16.6%) patients in the transferred group.

The demographic characteristics of matched cohorts according to ED resuscitation volume are summarised in Table 2. There were no significant differences in community, patient, and EMS variables between the non-transferred group and the transferred group in both LVED visitors and HVED visitors. In the LVED visitors, a total of 161 (12.3%) patients in the non-transferred group had good neurological recovery at discharge, compared with 207 (15.9%) patients in the transferred group. Among HVED visitors, a total of 131 (21.8%) patients in the non-transferred group had good neurological recovery at discharge, compared with 100 (16.7%) patients in the transferred group (Table 2).



Abbreviations: EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation.

Fig. 1 – Patient enrolment flow.

Abbreviations: EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation.

Main analyses

Table 3 describes the results of the logistic regression analyses among the unmatched cohorts by ED resuscitation volume. Among LVED visitors, patients in the transferred group showed significantly better outcomes than patients in the non-transferred group (adjusted OR: 1.42; 95%CI: 1.11–1.82 for good neurological recovery and adjusted OR: 1.89; 95%CI: 1.56–2.28 for survival to discharge). There was no significant difference of outcomes between the non-transferred group and the transferred group among HVED visitors (adjusted OR: 0.75; 95%CI: 0.56–1.01 for good neurological recovery and adjusted OR: 0.85; 95%CI: 0.67–1.09 for survival to discharge).

Table 4 shows the results of outcome comparison between the non-transferred group and the transferred group, following propensity-score matching by ED resuscitation volume. Among LVED visitors, patients in the transferred group showed significantly better outcomes than patients in the non-transferred group (adjusted OR: 1.34; 95%CI: 1.07–1.67 for good neurological recovery and adjusted OR: 1.55; 95%CI: 1.30–1.86 for survival to discharge). Among HVED visitors, there was no statistically significant difference of outcomes between the non-transferred group and the transferred group for survival outcomes (adjusted OR: 0.84; 95%CI: 0.63–1.13 for good neurological recovery and adjusted OR: 0.94; 95%CI: 0.73–1.22 for survival to discharge).

Discussion

We found that more than 16% of OHCA patients experienced IHT. We also found the different associations between IHT and outcomes of

OHCA patients according to initially visited ED resuscitation volume. IHT increased the frequency of good neurological recovery and survival to discharge after OHCA in LVED visitors. However, IHT was not significantly associated with better outcomes in OHCA patients among HVED visitors.

Comprehensive post-resuscitation care is important to initial survivors of OHCA.⁶ However, EDs with LVs of OHCA patients could easily not be equipped with the full resources necessary for comprehensive post-resuscitation care, because of cost-effectiveness and quality control of that kind of specialised care. Even in HVEDs, limitation of resources might occur, preventing early post-resuscitation care to patients.¹⁶ Because post-resuscitation care also occurs in ICUs, limitation of ICUs could also contribute to preventing those patients from receiving full post-resuscitation care. Therefore, IHT is often needed to provide post-resuscitation care to OHCA patients. However, IHT might be risky in critically ill patients.⁹ During transport to another hospital, interruption of monitoring and insufficient supply of oxygen or drugs might occur and threaten the outcomes of OHCA patients.⁸ Previous studies have estimated the incidence of some type of re-arrest at 38.0% to 79.0% in OHCA patients.^{10,17,18} Therefore, a careful decision about IHT is important for OHCA patients. Because we found that IHT of LVED visitors may help to increase the more favourable outcomes of OHCA patients, this factor should be taken seriously in clinical decisions for patients in LVEDs.

The effect of IHT on OHCA patients is difficult to assess, because it only occurred for selected patients. Patients who are not expected to survive should not be transferred in most cases, and clinicians might tend to decide in favour of IHT for patients whose condition appeared to indicate a more favourable outcome. We also found that transferred

Table 1 – Baseline characteristics of unmatched patients according to the ED resuscitation volume.

Characteristics	Low volume (n = 4477)		P	High volume (n = 7155)		P
	Non-transferred (n = 3117)	Transferred (n = 1360)		Non-transferred (n = 6651)	Transferred (n = 604)	
Year			0.397			0.383
2015	1548 (49.7%)	656 (48.2%)		3175 (48.5%)	281 (46.5%)	
2016	1569 (50.3%)	704 (51.8%)		3376 (51.5%)	323 (53.5%)	
Community urbanisation			<0.001			<0.001
Metropolitan	1731 (55.5%)	534 (39.3%)		5093 (77.7%)	346 (57.3%)	
Rural	394 (12.6%)	345 (25.4%)		171 (2.6%)	25 (4.1%)	
Urban	992 (31.8%)	481 (35.4%)		1287 (19.6%)	233 (38.6%)	
Age, mean (SD) [years]	69.1 (14.9)	63.3 (15.1)	<0.001	65.4 (15.5)	64.7 (15.6)	0.315
Age group			<0.001			0.278
18–60 years	822 (26.4%)	555 (40.8%)		2341 (35.7%)	235 (38.9%)	
61–79 years	1461 (46.9%)	601 (44.2%)		2882 (44.0%)	249 (41.2%)	
80+ years	834 (26.8%)	204 (15.0%)		1328 (20.3%)	120 (19.9%)	
Male gender	2027 (65.0%)	926 (68.1%)	0.051	4436 (67.7%)	395 (65.4%)	0.263
Pre-arrest comorbidities						
DM	740 (23.7%)	247 (18.2%)	<0.001	1,705 (26.0%)	129 (21.4%)	0.014
HTN	1114 (35.7%)	338 (24.9%)	<0.001	2,632 (40.2%)	185 (30.6%)	<0.001
Heart	529 (17.0%)	217 (16.0%)	0.427	1277 (19.5%)	134 (22.2%)	0.124
Stroke	302 (9.7%)	66 (4.9%)	<0.001	552 (8.4%)	46 (7.6%)	0.541
Place of arrest			<0.001			0.114
Public	688 (22.1%)	490 (36.0%)		1720 (26.3%)	180 (29.8%)	
Private	2382 (76.4%)	844 (62.1%)		4705 (71.8%)	416 (68.9%)	
Others	47 (1.5%)	26 (1.9%)		126 (1.9%)	8 (1.3%)	
Witnessed by bystanders	1722 (55.2%)	837 (61.5%)	<0.001	4003 (61.1%)	385 (63.7%)	0.219
Bystander CPR			<0.001			0.757
No bystander CPR	1273 (40.8%)	486 (35.7%)		2511 (38.3%)	223 (36.9%)	
Bystander CPR without dispatcher assistance	305 (9.8%)	175 (12.9%)		800 (12.2%)	73 (12.1%)	
Bystander CPR with dispatcher assistance	1539 (49.4%)	699 (51.4%)		3240 (49.5%)	308 (51.0%)	
Bystander AED use	84 (2.7%)	29 (2.1%)	0.317	201 (3.1%)	25 (4.1%)	0.187
Bystander defibrillation	18 (0.6%)	11 (0.8%)	0.493	65 (1.0%)	7 (1.2%)	0.857
Initial rhythm			<0.001			0.020
Shockable	558 (17.9%)	401 (29.5%)		1617 (24.7%)	165 (27.3%)	
PEA	441 (14.1%)	161 (11.8%)		1078 (16.5%)	118 (19.5%)	
Asystole	2118 (67.9%)	798 (58.7%)		3856 (58.9%)	321 (53.1%)	
EMS defibrillation	963 (30.9%)	555 (40.8%)	<0.001	2562 (39.1%)	238 (39.4%)	0.921
EMS IV placement	872 (28.0%)	325 (23.9%)	0.005	2,200 (33.6%)	148 (24.5%)	<0.001
EMS advanced airway management			0.001			0.001
Endotracheal intubation	249 (8.0%)	98 (7.2%)		631 (9.6%)	50 (8.3%)	
Supraglottic airway	1024 (32.9%)	379 (27.9%)		2658 (40.6%)	205 (33.9%)	
Bag valve ventilation	1844 (59.2%)	883 (64.9%)		3262 (49.8%)	349 (57.8%)	
EMS mechanical CPR device use	30 (1.0%)	9 (0.7%)	0.412	184 (2.8%)	14 (2.3%)	0.566
EMS time interval						
Response time, median (IQR), [min]	7.0 (5.0–9.0)	7.0 (5.0–9.0)	0.491	6.0 (5.0–8.0)	6.0 (5.0–8.0)	0.178
On-scene time, median (IQR), [min]	11.0 (8.0–15.0)	11.0 (8.0–15.0)	0.001	12.0 (9.0–16.0)	11.0 (8.0–15.0)	<0.001
Transport time, median (IQR), [min]	6.0 (4.0–9.0)	5.0 (3.0–9.0)	<0.001	6.0 (4.0–9.0)	6.0 (4.0–10.0)	0.739
ED level			<0.001			
Level 1	173 (5.6%)	10 (0.7%)		1923 (29.4%)	95 (15.7%)	<0.001
Level 2	1413 (45.3%)	295 (21.7%)		4470 (68.2%)	435 (72.0%)	
Level 3	1531 (49.1%)	1055 (77.6%)		158 (2.4%)	74 (12.3%)	
Post-resuscitation management						
PCI	179 (5.7%)	3 (0.2%)	<0.001	725 (11.1%)	4 (0.7%)	<0.001
Targeted temperature management	66 (2.1%)	1 (0.1%)	<0.001	775 (11.8%)	6 (1.0%)	<0.001
ECMO	18 (0.6%)	0 (0.0%)	0.011	227 (3.5%)	1 (0.2%)	<0.001
Clinical outcomes						
Survival to discharge	483 (15.5%)	406 (29.9%)	<0.001	1757 (26.8%)	160 (26.5%)	0.899
Good neurological recovery	275 (8.8%)	230 (16.9%)	<0.001	1183 (18.1%)	100 (16.6%)	0.387

Abbreviations: ED, emergency department; DM, diabetes mellitus; HTN, hypertension; CPR, cardiopulmonary resuscitation; AED, automatic external defibrillation; PEA, pulseless electrical activity; PCI, percutaneous coronary intervention; ECMO, extracorporeal membrane oxygenation.

Table 2 – Baseline characteristics of matched patients according to the ED resuscitation volume.

Characteristics	Low volume (n = 2608)			High volume (n = 1200)		
	Non-transferred (n = 1304)	Transferred (n = 1304)	P	Non-transferred (n = 600)	Transferred (n = 600)	P
Year			0.845			1
2015	641 (49.2%)	635 (48.7%)		278 (46.3%)	279 (46.5%)	
2016	663 (50.8%)	669 (51.3%)		322 (53.7%)	321 (53.5%)	
Community urbanisation			0.329			0.950
Metropolitan	566 (43.4%)	530 (40.6%)		347 (57.8%)	346 (57.7%)	
Rural	281 (21.5%)	303 (23.2%)		19 (3.2%)	21 (3.5%)	
Urban	457 (35.0%)	471 (36.1%)		234 (39.0%)	233 (38.8%)	
Age, mean (SD) [years]	64.5 (15.9)	63.9 (14.8)	0.358	64.9 (16.6)	64.7 (15.6)	0.821
Age group			0.125			0.430
18–60 years	497 (38.1%)	512 (39.3%)		234 (39.0%)	235 (39.2%)	
61–79 years	566 (43.4%)	590 (45.2%)		232 (38.7%)	248 (41.3%)	
80+ years	241 (18.5%)	202 (15.5%)		134 (22.3%)	117 (19.5%)	
Male gender	873 (66.9%)	887 (68.0%)	0.587	411 (68.5%)	393 (65.5%)	0.297
Pre-arrest comorbidities						
DM	246 (18.9%)	242 (18.6%)	0.88	109 (18.2%)	128 (21.3%)	0.192
HTN	331 (25.4%)	332 (25.5%)	1	200 (33.3%)	184 (30.7%)	0.353
Heart	218 (16.7%)	212 (16.3%)	0.792	122 (20.3%)	133 (22.2%)	0.480
Stroke	62 (4.8%)	66 (5.1%)	0.786	49 (8.2%)	46 (7.7%)	0.831
Place of arrest			0.595			0.378
Public	433 (33.2%)	444 (34.0%)		169 (28.2%)	180 (30.0%)	
Private	840 (64.4%)	836 (64.1%)		427 (71.2%)	412 (68.7%)	
Others	31 (2.4%)	24 (1.8%)		4 (0.7%)	8 (1.3%)	
Witnessed by bystanders	801 (61.4%)	791 (60.7%)	0.718	390 (65.0%)	382 (63.7%)	0.673
Bystander CPR			0.127			0.891
No bystander CPR	516 (39.6%)	472 (36.2%)		229 (38.2%)	221 (36.8%)	
Bystander CPR without dispatcher assistance	143 (11.0%)	167 (12.8%)		72 (12.0%)	73 (12.2%)	
Bystander CPR with dispatcher assistance	645 (49.5%)	665 (51.0%)		299 (49.8%)	306 (51.0%)	
Bystander AED use	44 (3.4%)	29 (2.2%)	0.097	11 (1.8%)	25 (4.2%)	0.028
Bystander defibrillation	10 (0.8%)	11 (0.8%)	1	4 (0.7%)	7 (1.2%)	0.545
Initial rhythm			0.409			0.633
Shockable	334 (25.6%)	359 (27.5%)		164 (27.3%)	165 (27.5%)	
PEA	151 (11.6%)	159 (12.2%)		131 (21.8%)	118 (19.7%)	
Asystole	819 (62.8%)	786 (60.3%)		305 (50.8%)	317 (52.8%)	
EMS defibrillation	507 (38.9%)	513 (39.3%)	0.841	255 (42.5%)	238 (39.7%)	0.348
EMS IV placement	320 (24.5%)	318 (24.4%)	0.964	139 (23.2%)	146 (24.3%)	0.684
EMS advanced airway management			0.932			0.503
Endotracheal intubation	92 (7.1%)	93 (7.1%)		39 (6.5%)	49 (8.2%)	
Supraglottic airway	366 (28.1%)	374 (28.7%)		214 (35.7%)	204 (34.0%)	
Bag valve ventilation	846 (64.9%)	837 (64.2%)		347 (57.8%)	347 (57.8%)	
EMS mechanical CPR device use	11 (0.8%)	8 (0.6%)	0.645	11 (1.8%)	14 (2.3%)	0.686
EMS time interval						
Response time, median (IQR), [min]	7.0 (5.0–9.0)	7.0 (5.0–9.0)	0.443	6.0 (5.0–8.0)	6.0 (5.0–8.0)	0.966
On-scene time, median (IQR), [min]	11.0 (8.0–15.0)	11.0 (8.0–15.0)	0.584	11.0 (8.0–15.0)	11.0 (8.0–15.0)	0.444
Transport time, median (IQR), [min]	6.0 (4.0–10.0)	5.0 (3.0–8.0)	<0.001	6.0 (4.0–10.0)	6.0 (4.0–10.0)	0.814
ED level			<0.001			<0.001
Level 1	66 (5.1%)	10 (0.8%)		171 (28.5%)	92 (15.3%)	
Level 2	598 (45.9%)	292 (22.4%)		411 (68.5%)	434 (72.3%)	
Level 3	640 (49.1%)	1002 (76.8%)		18 (3.0%)	74 (12.3%)	
Post-resuscitation management						
PCI	94 (7.2%)	3 (0.2%)	<0.001	62 (10.3%)	4 (0.7%)	<0.001
Targeted temperature management	32 (2.5%)	1 (0.1%)	<0.001	60 (10.0%)	5 (0.8%)	<0.001
ECMO	10 (0.8%)	0 (0.0%)	0.004	21 (3.5%)	1 (0.2%)	<0.001
Clinical outcomes						
Survival to discharge	269 (20.6%)	375 (28.8%)	<0.001	181 (30.2%)	160 (26.7%)	0.201
Good neurological recovery	161 (12.3%)	207 (15.9%)	0.011	131 (21.8%)	100 (16.7%)	0.028

Abbreviations: ED, emergency department; DM, diabetes mellitus; HTN, hypertension; CPR, cardiopulmonary resuscitation; AED, automatic external defibrillation; PEA, pulseless electrical activity; PCI, percutaneous coronary intervention; ECMO, extracorporeal membrane oxygenation.

Table 3 – Univariable and multivariable analyses of clinical outcomes in unmatched cohorts by ED resuscitation volume.

	Non-transferred n/N (%)	Transferred n/N (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^a
Low volume				
Good neurological recovery	275/3117 (8.8%)	230/1360 (16.9%)	2.10 (1.74–2.54)	1.42 (1.11–1.82)
Survival to discharge	483/3117 (15.5%)	406/1360 (29.9%)	2.32 (1.99–2.70)	1.89 (1.56–2.28)
High volume				
Good neurological recovery	1183/6,551 (18.1%)	100/604 (16.6%)	0.90 (0.72–1.13)	0.75 (0.56–1.01)
Survival to discharge	1757/6,551 (26.8%)	160/604 (26.5%)	0.98 (0.81–1.19)	0.85 (0.67–1.09)
Abbreviations: ED, emergency department.				
^a Adjusted variables: Age, gender, year of visit, urbanisation level of incident, place of arrest, witness status, bystander CPR, initial rhythm, prehospital advanced airway management, and response time.				

Table 4 – Logistic regression analyses of clinical outcomes in propensity score-matched cohorts by the ED resuscitation volume.

	Non-transferred n/N (%)	Transferred n/N (%)	OR (95% CI)
Low volume			
Good neurological recovery	161/1304 (12.3%)	207/1304 (15.9%)	1.34 (1.07–1.67)
Survival to discharge	269/1304 (20.6%)	375/1304 (28.8%)	1.55 (1.30–1.86)
High volume			
Good neurological recovery	115/600 (19.2%)	100/600 (16.7%)	0.84 (0.63–1.13)
Survival to discharge	167/600 (27.8%)	160/600 (26.7%)	0.94 (0.73–1.22)
Abbreviations: ED, emergency department.			

patients were younger, more likely to have a witnessed arrest, and to have more shockable rhythm than non-transferred patients. To minimise those selection biases, propensity score-matching analysis was conducted in this study; we could then compare non-transferred patients and transferred patients with similar probabilities of IHT.

The different situations of IHT across EDs were another problem when estimating the effect of IHT on survival outcomes of OHCA patients. Expected care and clinical courses if patients were not transferred when initially visiting an ED could be substantially different across EDs. The LVEDs might not be able to provide post-resuscitation care without IHT because of an absolute shortage of resources. However, IHT might be only one option for management of patients in HVEDs. If we evaluated mixed cases, the effect of IHT might be attenuated, especially among LVED visitors. We conducted separate analyses according to ED resuscitation volume to address the issue.

Previous studies reported successful regionalisation for OHCA in some areas.^{19–21} Those studies evaluated the outcomes of patients who directly visited cardiac arrest receiving centres by EMS. Therefore, the effectiveness of the EMS bypass protocol, rather than IHT, was evaluated in those studies. Regionalisation systems integrating EMS bypass and IHT of OHCA patients might increase favourable outcomes among OHCA patients. Because we found that IHT could increase favourable outcomes for OHCA patients who visited LVEDs, a traditional centralised regionalisation network might still be valid for OHCA patients.²² A careful decision about inter-hospital transport and efforts to reduce risk of IHT is also needed in regionalisation of OHCA patients.²³

We believe our results have important clinical implications for planning a regionalisation system for OHCA patients. Because all hospitals do not always have post-resuscitation facilities, IHT should be integrated into the regionalisation system for OHCA patients. If a patient first visits the

hospital without post-resuscitation care facilities, the patient can receive effective post-resuscitation care through IHT. Further investigations are needed to establish the regionalisation of OHCA care that emphasises the IHT and specialised team for safe transfer.

Limitations

This study has several limitations. First, in-depth information about the resource availability for post-resuscitation care in each hospital and main reason of the transfer for each patient could not be captured. Although we found that post-resuscitation care, including PCI, targeted temperature management, and ECMO, were conducted more often in HVEDs than in LVEDs, there might also be other reasons for transfer for post-resuscitation care in each patient. Second, detailed post-resuscitation care at the hospital the patient was transferred to could not be captured. Therefore, we could not assess which component of post-resuscitation care could contribute to the effects of IHT on the outcomes of OHCA patients. Third, we might not have fully eliminated the selection bias of IHT. However, in our propensity score-matched cohort, both groups showed a well-balanced distribution of demographics and most confounders. Fourth and last, this study was an observational study, not a randomised controlled trial. There may be significant potential biases that were not controlled.

Conclusion

Among OHCA patients who visited LVEDs initially, IHT was associated with improved outcomes. However, among the patients who visited HVEDs initially, IHT was not associated with better outcomes.

Author contributions

Drs Park and Lee had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Park, Lee, Shin, and Song.

Acquisition, analysis, or interpretation of data: Park, Lee, Shin, Ro, and Hong.

Drafting of the manuscript: Park, Lee, Shin, and Ro.

Critical revision of the manuscript for important intellectual content: Park, Lee, and Shin.

Statistical analysis: Park, Lee, Shin, and Ro.

Obtained funding: Shin.

Administrative, technical, or material support: Park, Lee, Shin, Song, and Hong.

Study supervision: Lee, Shin, Song, Hong, and Ro.

Manuscript approval: All authors.

Conflict of interest

The authors have nothing to declare regarding conflict of interest.

Acknowledgments

This study was financially supported by the Research Program funded by the Korea Centers for Disease Control and Prevention.

REFERENCES

- Grasner JT, Lefering R, Koster RW, et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: A prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. *Resuscitation* 2016;105:188–95, doi:http://dx.doi.org/10.1016/j.resuscitation.2016.06.004.
- Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: Systematic review of 67 prospective studies. *Resuscitation* 2010;81:1479–87, doi:http://dx.doi.org/10.1016/j.resuscitation.2010.08.006.
- Myat A, Song KJ, Rea T. Out-of-hospital cardiac arrest: current concepts. *Lancet* 2018;391:970–9, doi:http://dx.doi.org/10.1016/S0140-6736(18)30472-0.
- Perman SM, Goyal M, Neumar RW, Topjian AA, Gaieski DF. Clinical applications of targeted temperature management. *Chest* 2014;145:386–93, doi:http://dx.doi.org/10.1378/chest.12-3025.
- Lampe JW, Becker LB. State of the art in therapeutic hypothermia. *Annu Rev Med* 2011;62:79–93, doi:http://dx.doi.org/10.1146/annurev-med-052009-150512.
- Callaway CW, Donnino MW, Fink EL, et al. Part 8: Post-Cardiac Arrest Care: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2015;132:S465–82, doi:http://dx.doi.org/10.1161/CIR.0000000000000262.
- Park CJ, Shin SD, Park CB, et al. Association between Case Volume of Cardiopulmonary Resuscitation and Implementation of Therapeutic Hypothermia. *J Korean Soc Emerg Med* 2011;22:423–30.
- Park JH, Ahn KO, Shin SD, et al. A multicentre observational study of inter-hospital transfer for post-resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2016;108:34–9, doi:http://dx.doi.org/10.1016/j.resuscitation.2016.08.025.
- Hill AD, Vingilis E, Martin CM, Hartford K, Speechley KN. Interhospital transfer of critically ill patients: demographic and outcomes comparison with nontransferred intensive care unit patients. *J Crit Care* 2007;22:290–5, doi:http://dx.doi.org/10.1016/j.jccr.2007.06.002.
- Salcido DD, Stephenson AM, Condle JP, Callaway CW, Menegazzi JJ. Incidence of rearrest after return of spontaneous circulation in out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2010;14:413–8, doi:http://dx.doi.org/10.3109/10903127.2010.497902.
- Ro YS, Shin SD, Lee YJ, et al. Effect of Dispatcher-Assisted Cardiopulmonary Resuscitation Program and Location of Out-of-Hospital Cardiac Arrest on Survival and Neurologic Outcome. *Ann Emerg Med* 2017;69:52–61.e1, doi:http://dx.doi.org/10.1016/j.annemergmed.2016.07.028.
- Ro YS, Shin SD, Song KJ, et al. A trend in epidemiology and outcomes of out-of-hospital cardiac arrest by urbanization level: a nationwide observational study from 2006 to 2010 in South Korea. *Resuscitation* 2013;84:547–57, doi:http://dx.doi.org/10.1016/j.resuscitation.2012.12.020.
- Schober A, Sterz F, Laggner AN, et al. Admission of out-of-hospital cardiac arrest victims to a high volume cardiac arrest center is linked to improved outcome. *Resuscitation* 2016;106:42–8, doi:http://dx.doi.org/10.1016/j.resuscitation.2016.06.021.
- Chan PS, Berg RA, Tang Y, Curtis LH, Spertus JA. American Heart Association's Get With the Guidelines-Resuscitation I. Association Between Therapeutic Hypothermia and Survival After In-Hospital Cardiac Arrest. *JAMA* 2016;316:1375–82, doi:http://dx.doi.org/10.1001/jama.2016.14380.
- Normand ST, Landrum MB, Guadagnoli E, et al. Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: a matched analysis using propensity scores. *J Clin Epidemiol* 2001;54:387–98.
- Chalfin DB, Trzeciak S, Likourezos A, Baumann BM, Dellinger RP, group D-Es. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. *Crit Care Med* 2007;35:1477–83, doi:http://dx.doi.org/10.1097/01.CCM.0000266585.74905.5A.
- White RD, Russell JK. Refibrillation, resuscitation and survival in out-of-hospital sudden cardiac arrest victims treated with biphasic automated external defibrillators. *Resuscitation* 2002;55:17–23.
- van Alem AP, Post J, Koster RW. VF recurrence: characteristics and patient outcome in out-of-hospital cardiac arrest. *Resuscitation* 2003;59:181–8.
- Davis DP, Fisher R, Aguilar S, et al. The feasibility of a regional cardiac arrest receiving system. *Resuscitation* 2007;74:44–51, doi:http://dx.doi.org/10.1016/j.resuscitation.2006.11.009.
- Kajino K, Iwami T, Daya M, et al. Impact of transport to critical care medical centers on outcomes after out-of-hospital cardiac arrest. *Resuscitation* 2010;81:549–54, doi:http://dx.doi.org/10.1016/j.resuscitation.2010.02.008.
- Spaite DW, Bobrow BJ, Stolz U, et al. Statewide regionalization of postarrest care for out-of-hospital cardiac arrest: association with survival and neurologic outcome. *Ann Emerg Med* 2014;64:496–506.e1, doi:http://dx.doi.org/10.1016/j.annemergmed.2014.05.028.
- Glickman SW, Kit Delgado M, Hirshon JM, et al. Defining and measuring successful emergency care networks: a research agenda. *Acad Emerg Med* 2010;17:1297–305, doi:http://dx.doi.org/10.1111/j.1553-2712.2010.00930.x.
- Dunn MJ, Gwinnutt CL, Gray AJ. Critical care in the emergency department: patient transfer. *Emerg Med J* 2007;24:40–4, doi:http://dx.doi.org/10.1136/emj.2006.042044.