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Clinical paper

A multicentre observational study of inter-hospital transfer for post-resuscitation care after out-of-hospital cardiac arrest☆

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ABSTRACT

Aim: To provide therapeutic hypothermia (TH) to survivors after out-of-hospital cardiac arrest (OHCA), inter-hospital transfers (IHT) are frequently required. The safety of IHT remains controversial. The aim of this study was to investigate whether the effect of TH on brain recovery after OHCA differs between IHT and direct arrival groups.

Methods: We identified patients with OHCA of presumed cardiac aetiology who were resuscitated by emergency medical services and experienced return-of-spontaneous circulation in 27 hospitals between January and December 2014. The main exposure variables were TH and IHT. The primary endpoint was discharge with good neurological recovery. We compared outcomes between the TH and non-TH groups using multivariable logistic regression with an interaction term between TH and IHT, after adjusting for potential confounders.

Results: Among 1616 patients, 576 patients were included in the final analyses. Neurologic recovery was better in the TH group (46.2%) than in the non-TH group (20.1%) (adjusted odds ratio [aOR] 2.03 [95% confidence interval (CI) 1.24–3.33]). In the interaction model for the outcome of good neurological recovery, the aOR for TH was 2.82 (95% CI 1.59–5.01) in the direct transfer group vs. 0.76 (95% CI 0.29–2.01) in the IHT group. The measure of interaction on the multiplicative scale in this model was also statistically significant (OR 0.27 [95% CI 0.07–0.83]; p = 0.02).

Conclusion: IHT modified the effect of TH on neurological recovery for survivors of OHCA. TH is significantly less beneficial for good neurological recovery in patients who arrive via IHT than for those who arrive directly.

Introduction

Several studies have reported beneficial effects of post-resuscitation care, including therapeutic hypothermia (TH), on neurologic recovery for patients with out-of-hospital cardiac arrest (OHCA),[1–3] and the 2010 resuscitation and CPR guidelines from the American Heart Association included active and comprehensive post-resuscitation care in the 5th link in the chain of survival for patients with OHCA.[4] Therefore, active and comprehensive post-resuscitation care is a required sophisticated capacity for critical care and represents a considerable resource requirement for hospitals. Not all hospitals that receive patients with OHCA have the capacity for post-resuscitation care, including TH. Inter-hospital transfer (IHT) is often required to provide active and comprehensive post-resuscitation care to survivors of OHCA.

In studies describing the introduction of an IHT protocol for regionalized cardiac arrest care, IHT for patients with OHCA who underwent TH was not significantly associated with the outcome.[5,6] However, IHT has been suggested as risky for unstable patients, such as patients with OHCA after they have been

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resuscitated.[7,8] During transport to other facilities, interrupted monitoring and insufficient supply of oxygen or drugs, even temporarily, might occur and threaten neurologic recovery.

Previously successful adoptions of an IHT protocol to provide TH to patients with OHCA were likely the result of a pre-existing regional system for care of ST-elevation myocardial infarction and well controlled quality of care during transfer in a single-center study.[5] Therefore, we questioned the safety of IHT in different settings and populations. The aim of this study was to compare the effect of TH on neurologic recovery after OHCA between IHT and direct arrival at the hospital.

Methods

Study setting

In Korea, the standardized incidence and survival rates of emergency medical service (EMS)-assessed OHCAs in 2010 were reportedly 46.8 per 100,000 person-years and 3.6%, respectively.[9] Nationally, 8.3% of patients who survived at admission underwent TH.[10] A center for cardiac arrest care is not available; instead, patients with OHCA should be transported to the nearest hospital that is considered to be at a higher level than the local emergency facility, according to the pre-hospital care and transport protocol.

The IHT system provides basic services primarily by ground transportation via private EMS agencies or hospital ambulances. The guideline for IHT was released by the Ministry of Health & Welfare in 2014.[11] For critical patients, physician or nurses might staff the IHT, but a system for a mobile intensive care unit was not adopted.

Study design and participants

This study was a secondary analysis of data from a prospective observational study using the Cardiac Arrest Pursuit Trial with Unique Registration and Epidemiologic Surveillance (CAPTURES) project database in Korea. The CAPTURES project was a prospective hospital-based patient cohort study conducted from January to December 2014 in 27 emergency departments that volunteered to participate; the CAPTURES project included patients for whom resuscitation was attempted by the EMS (EMS-treated OHCA) and who had a presumed cardiac aetiology. In this study, the IHT group included patients who transferred from other hospitals to one of the 27 participating EDs. There was no predefined protocol nor incentive to transfer patients to one of the 27 EDs. The project excluded patients who had a terminal illness, were under hospice care, were pregnant, lived alone or were homeless without a reliable information source, and had a 'Do Not Resuscitate' card. Detailed information and data quality management processes for the CAPTURES program have been described previously.[12]

The present study limited the sample to subjects who achieved return of spontaneous circulation (ROSC). We excluded patients whose time from collapse to ROSC was >60 min, who underwent TH in referring hospitals, or whose neurologic outcome at discharge was unknown.

The study was approved by all Institutional Review Boards of the participating study institutes, and the need for informed consent was waived (IRB number; H-1401-090-550).

Data collection and variables

The registry included patient socio-demographic, EMS, and emergency department information using the Utstein template. Patient demographics, circumstances of the OHCA, EMS response time (time interval from EMS call to ambulance arrival at the scene), EMS scene time (time interval from arrival to departure from the scene), EMS transport time (time interval from departure from the scene to arrival at the first visiting ED), patient outcomes, post-resuscitation care and process, route to the hospital, and elapsed time for the IHT process were collected. The place of ROSC (prehospital, referring hospital, or receiving hospital) and the exact time at which ROSC achieved was recorded. For patients who underwent TH, the first cooling time was also collected. The primary exposure was TH, which included all kinds of cooling methods. The route to the hospital (direct visit or IHT) was also considered an exposure variable. The primary outcome was good neurologic recovery (Cerebral Performance 1 or 2) at discharge.[13]

Statistical analysis

Demographic findings and outcomes based on TH and IHT are described. Continuous data are reported as mean and standard deviation or median and interquartile range; categorical variables are reported as counts and percentages. Multivariable logistic regression analysis was conducted to estimate the effect of TH on good neurological recovery, and the adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated after adjusting for the potential risk factors, such as Utstein co-variables (age, sex, witness status, pre-hospital defibrillation, location of event [public vs. private], bystander CPR, EMS response time, EMS scene time, EMS transport time, and prehospital electrocardiogram rhythm [shockable vs. non-shockable]) and comorbidities (hypertension and diabetes) as covariates.[14] Interactions between IHT and TH for the effect on neurologic recovery were tested to compare the effect size of TH, adjusting for the same co-variables.

Additionally, we wanted to evaluate whether the time intervals of the patient's clinical course varied by route of arrival in patients who underwent TH. The times from collapse to the first compression (no flow time), from first compression to ROSC (low flow time), from ROSC to first cooling, and from collapse to first cooling were compared between the direct visit and IHT groups using Mann–Whitney U tests. Also, within the TH group, the process of care was compared based on good neurological recovery using Mann–Whitney U tests.

Two-sided tests were conducted, and $p < 0.05$ was considered statistically significant. Data management and statistical analyses were performed with R, version 3.24 (available at http://www.r-project.org).

Results

Of the total 1616 patients with EMS-treated OHCA and presumed cardiac aetiology in the CAPTURES program, 581 (35.9%) patients achieved ROSC within 60 min. After excluding 2 patients who underwent TH before transfer and 3 patients with unknown outcome information, 576 (35.6%) cases were analyzed (Fig. 1).

Table 1 provides the patient characteristics based on TH. TH was performed for 31.6% of the patients. Significant differences in patient demographics and pre-hospital and hospital emergency care were present based on TH. Of those who underwent TH, 31.3% arrived by IHT, compared with 16.2% of those who did not undergo TH ($p < 0.01$). The TH group showed better outcomes than the non-TH group: 46.2% vs. 20.1%, good neurological recovery ($p < 0.01$).

The median time interval from ROSC to cooling was 177 min (interquartile range [IQR] 101–275) in the TH group. Within the TH group, those who arrived via IHT had a longer median time from ROSC to cooling than the direct visit group (209.0 [149.0–357.0] vs. 154.0 [91.5–255.0] min; $p < 0.01$; Fig. 2). However, there was no significant difference between the median time from ROSC to cooling