Resuscitation 125 (2018) 56–65

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Cooling methods of targeted temperature management and neurological recovery after out-of-hospital cardiac arrest: A nationwide multicenter multi-level analysis☆

Ki Hong Kim[a], Sang Do Shin[b,*], Kyoung Jun Song[b], Young Sun Ro[c], Yu Jin Kim[d], Ki Jeong Hong[e], Joo Jeong[d], Jeong Ho Park[a], Tae Han Kim[a], So Yeon Kong[c]

[a] Department of Emergency Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[b] Department of Emergency Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
[c] Laboratory of Emergency Medical Services, Seoul National University Hospital Biomedical Research Institute, Seoul, Republic of Korea
[d] Department of Emergency Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea
[e] Department of Emergency Medicine, Seoul National University Boramae Medical Center, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Cooling method
Targeted temperature management
Cardiac arrest
Outcome

ABSTRACT

Objective: The purpose of this study was to determine whether the cooling method used for target temperature management (TTM) was associated with neurological recovery after out-of-hospital cardiac arrest (OHCA).

Methods: From January 2008 to December 2016, adult OHCA patients who survived to hospitalization without any traumatic etiology and who received TTM were included. Patients who did not have information about neurological status at hospital discharge or who did not have information on target temperature management were excluded. Cooling methods were classified into four groups: (1) external device cooling (EDC) using a pad with cooling device, (2) external conventional cooling (ECC) such as ice water, fans, and simple blankets, (3) Intravascular cooling (IVC) using an intravascular cooling catheter, and (4) intracavitary cooling (ICC) using ice water for washing cavitary organ. The outcomes were good cerebral performance scale (CPC) score 1 or 2 and survival to discharge. In multivariate logistic regression analysis, the adjusted odds ratios (AORs) and the 95% confidence intervals (CIs) were calculated (reference = ECC). Finally, we used a GLIMMIX procedure with group-level variables (hospitals) to create a multilevel model for adjusting the clustering factor of patients being treated in the same hospital.

Results: The final analysis included a total of 4246 eligible patients (ECC 1386, EDC 2107, IVC 376, ICC 377). Good neurologic recovery was 20.7% for all (ECC 17.4, EDC 23.1%, IVC 26.9%, and ICC 13.3%, $p < .001$). The survival rate was 46.4% for all (ECC 45.4%, EDC 48.5%, IVC 50.5%, ICC 34.2%, $p < .001$). There were no significant differences (AOR and 95% CI) in the multi-level analysis for good neurological recovery between cooling methods compared with ECC; EDC 1.20 (0.95–1.52), IVC 1.43 (0.90–2.27), and ICC 0.71 (0.46–1.10). The ICC group had a lower survival to discharge rate compared with ECC; EDC 0.97 (0.83–1.15), IVC 0.96 (0.78–1.19), and ICC 0.63 (0.43–0.85).

Conclusion: The cooling methods for TTM did not show any significant difference in neurological recovery in multi-level logistic regression analysis. Only intracavitary cooling resulted in a lower survival to discharge than external surface cooling.

Introduction

Severe neurologic injury after cardiopulmonary resuscitation (CPR) in out-of-hospital cardiac arrest (OHCA) patients has been known to be the most common cause of death [1]. The formation of free radicals and other mediators in the reperfusion phase can cause a neurologic injury cascade [2]. Although several randomized controlled trials attempted and failed to show significant improvement by specific medical interventions [3–5], targeted temperature management (TTM) has shown improvement in outcomes as a neuroprotective treatment in post-

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at https://doi.org/10.1016/j.resuscitation.2018.01.043.

* Corresponding author at: Department of Emergency Medicine, Seoul National University College of Medicine, 101 Daehak-Ro, Jongno-Gu, Seoul 03080, Republic of Korea.
E-mail addresses: emilo@naver.com (K.H. Kim), sdshin@snu.ac.kr (S.D. Shin), skciva@gmail.com (K.J. Song), Ro.youngsun@gmail.com (Y.S. Ro), myda02@gmail.com (Y.J. Kim), emkjhong@gmail.com (K.J. Hong), yukijeje@gmail.com (J. Jeong), timthe@gmail.com (J.H. Park), adoong2001@gmail.com (T.H. Kim), soyeon.Kong@gmail.com (S.Y. Kong).

https://doi.org/10.1016/j.resuscitation.2018.01.043
Received 14 September 2017; Received in revised form 28 January 2018; Accepted 28 January 2018

resuscitation care [6,7].

The potential mechanisms of TTM that improve neurologic outcomes are as follows: a lower cerebral metabolic rate for oxygen, suppression of the chemical reaction associated with reperfusion injury, or activation of anti-apoptotic mechanisms via cooling or control of the temperature using specific methods [8,9]. Those TTM methods were divided into the following four main categories according to the approach to cooling: 1) external conventional cooling (ECC), 2) external device cooling (EDC), 3) intravascular cooling (IVC), and 4) intracavitary (ICC) cooling [10]. ECC, such as crushed ice or an ice bag, have the disadvantage of unintentional cooling below the target temperature, which can have deleterious effects and is less effective in maintaining temperature [11,12]. Maintenance of temperature is difficult and shivering is more common in this method of cooling. [13]. Although IVC showed a similar effect on outcome compared to EDC [14–17], adverse events can occur, such as a catheter-related bloodstream infection, venous thrombosis, and vascular procedure-related complications [16,18]. IVC and EDC methods incorporate more advanced technology and provide easy operation for maintaining temperature; however, these methods are more expensive than conventional cooling methods such as ECC or ICC.

Few studies have compared the effects of the four different types of cooling methods on outcomes. We hypothesized that the cooling methods for TTM are associated with outcomes after OHCA. This study aimed to compare the effect among the four cooling method groups for TTM on neurological outcomes after OHCA.

Methods

The study was approved by the Institutional Review Board at the research site, and the Korea Center for Disease Control and Prevention (CDC) approved the use of the data in this study.

Study design and setting

The study is a cross-sectional analysis using a nationwide OHCA registry. The study was performed in Korea, which has a population of 50 million people. Single-tiered and government-based emergency medical services (basic-to-intermediate level) are supported by 17 provincial fire departments with a total of 1400 ambulance stations. Emergency medical technicians provide basic life support and the use of an automatic defibrillator for OHCA patients in the field and transport all patients to the emergency department (ED) with continuous CPR if the patient is not resuscitated. Most advanced life support methods are limited, and only advanced airway management and intravenous fluid resuscitation under direct medical supervision are allowed. Prehospital intervention for hypothermia or TTM is not allowed in the study setting.

There are three levels of EDs that are designated by the national government and categorized by the emergency care resources and functional requirements. There are 20 level 1 EDs that provide 24-h/365-day emergency care by emergency specialists, 110 level 2 EDs that are served by emergency physicians, and 270 level 3 EDs that are staffed by general physicians. EDs usually provide a full range of advanced care and emergency procedures such as primary coronary intervention, pacemaker insertion, and other critical procedures. Most TTM procedures are performed after admission to the intensive care unit where the intensivists, emergency specialists, and neurologists are providing TTM.

The guidelines (2010) for CPR and TTM are not standardized among hospitals; however, they are accepted by the national academic societies. These recommendations and guidelines are modified and adapted to hospital protocol according to the physicians' preference. Therefore, the TTM methods, devices, and protocols are different among institutions or physicians but still adhere to the international guidelines. Until 2015, the target temperature for hypothermia was 32–34 °C, and the maintenance of management varies between protocols according to 2010 guidelines [19,20].

Data source

We used the Korean OHCA registry (KOHCAR), which was developed and supported by the Korea Centers for Disease Control and Prevention (CDC) and collaborates with the National Fire Department [21]. The KOHCAR is a population-based, EMS-assessed OHCA registry and retrospective patient cohort. Indexed cases are extracted from the EMS database (dispatch registry, EMS run sheet, and EMS CPR registry), followed by a medical record review for hospital care, and outcomes are provided by medical record reviewers of the Korea CDC. The KOCHAR has information on individual and socioeconomic factors, EMS operational factors, Utstein factors, ED care and hospital procedures, and outcomes at discharge. EMS data variables are recorded by EMTs on the basis of the EMS variable data dictionary. Data quality is maintained by regular education and feedback by designated medical directors who are responsible for the EMS CPR registry review. All medical directors are required to visit the fire department and provide a weekly review for all OHCA cases. All data collection by the Korea CDC for medical record review for hospital care and outcomes occurs through an electronic data collection system. Approximately 15 medical record reviewers visit all EDs and hospitals where the OHCA patients are transported and review the cases for treatment and outcomes. All of the items are defined in the medical record review guidelines, which are developed by the project quality management committee (QMC). All medical record reviewers are trained by the QMC prior to joining the project. When they are not able to objectively define a coding element, reviewers consult an emergency medicine physician in the QMC. A monthly quality assurance meeting encourages the reviewers to meet the standard data collection protocol. They receive feedback regarding the internal validity of their collected data.

Study population

Adult OHCA patients aged 18 years or older who received TTM after spontaneous circulation recovery (ROSC) as a result of CPR in EMS or ED from January 2008 to December 2016 were included in the study. Patients who did not have information about neurological status at hospital discharge or who did not have information on target temperature management were excluded.

Variables

Information on TTM was obtained from medical record review. TTM was defined as a case receiving therapeutic hypothermia after ROSC using various methods such as external cooling or internal cooling. The definition of TTM includes patients who receive cooling of body temperature regardless of cooling technique, regardless of the cooling interval to the target temperature, and regardless of success of achievement of the desired temperature. Cooling methods were categorized into four main groups.

Existing conventional cooling (ECC) is defined as the use of a cooling blanket, a water jet pan, or an underarm ice pack. External device cooling (EDC) can be performed using specific device such as Arctic Sun® (Medivance Corp, Louisville, KY, USA), GAYMAR (Gaymar Industries, Orchard Park, NY, USA), Blanketrol III (Cincinnati Sub-Zero Products, Cincinnati, OH, USA), or EMCOOLS Flex.Pad™ (EMCOOLS, Vienna, Austria). Intravascular cooling (IVC) refers to the insertion of an intravascular catheter into a large vessel. Finally, intracavitary cooling (ICC) refers stomach cooling using a nasogastric tube, bladder cooling using a foley catheter, and cavitary cooling by inserting a percutaneous catheter into the abdominal cavity or pleural cavity. If there were duplicated methods to control the temperature, the last method used was defined as the TTM procedure category in the case.

Information on individual factors including event year, age, gender,