



Clinical paper

Therapeutic hypothermia and outcomes in paediatric out-of-hospital cardiac arrest: A nationwide observational study[☆]Ikwan Chang^a, Young Ho Kwak^{a,*}, Sang Do Shin^a, Young Sun Ro^b, Eui Jung Lee^a, Ki Ok Ahn^b, Do Kyun Kim^a^a Department of Emergency Medicine, Seoul National University Hospital, Seoul, Republic of Korea^b Laboratory of Emergency Medical Services, Seoul National University Hospital Biomedical Research Institute, Republic of Korea

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ABSTRACT

Objectives: This study aimed to analyse the association between mild therapeutic hypothermia (MTH) and outcomes in paediatric patients who survived out-of-hospital cardiac arrest (OHCA) by using their initial electrocardiogram (ECG) rhythm, which is the key factor used to predict prognosis in paediatric OHCA.

Methods: This cross-sectional observational study utilised the registry of paediatric OHCA patients who survived to admission from 2008 to 2014 in the national OHCA database. MTH was defined as all cooling methods applied after the return of spontaneous circulation. Primary and secondary outcomes were survival to discharge and good neurologic recovery, respectively. Multivariable logistic regression analysis with an interaction term between MTH and the initial ECG at the scene was conducted to calculate adjusted odds ratios (AORs) and 95% confidence intervals (CIs) after adjusting for potential confounders. **Results:** Among the 663 enrolled patients, the rates of survival to discharge and good neurological recovery in the MTH and non-MTH groups were similar, at 48.1% vs. 40.2% ($P=0.17$, AOR 1.05 [0.59–1.88]) and 22.2% vs. 8.7% ($P=0.45$, AOR 1.22 [0.59–2.51]). In the interaction model, the AORs of MTH in shockable rhythm vs. non-shockable rhythm for survival to discharge (AOR 0.62 [0.15–2.52] vs. 1.17 [0.62–2.2]) and good neurological recovery (0.42 [0.12–1.45] vs. 2.22 [0.83–5.98]) were not significantly different.

Conclusion: MTH and the effect of MTH across the initial ECG at the scene were not significantly associated with survival or good neurologic recovery in paediatric OHCA survivors.

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Introduction

Approximately 16,000 children experience out-of-hospital cardiac arrest (OHCA) in the USA every year.¹ The incidence of

Abbreviations: OHCA, out-of-hospital cardiac arrest; MTH, mild therapeutic hypothermia; RCT, randomized clinical trial; ECG, electrocardiogram; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; CDC, Centers for Disease Control and Prevention; FD, fire department; EMS, emergency medical services; ED, emergency department; QMC, quality management control; EMT, emergency medical technician; CPC, cerebral performance category; OR, odds ratio; CI, confidence interval; PICU, paediatric intensive care unit.

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paediatric OHCA is very low, but it is a devastating event. Previous studies have revealed variation in survival to hospital discharge rates ranging from 2 to 27%.^{1–3} The rate of favourable neurologic outcomes in survivors is approximately 24–50%.^{1,2} Poor neurologic outcomes in paediatric OHCA are associated with long-term physical, psychological, and quality of life burdens.^{1,2}

Over the last decade, the effect of mild therapeutic hypothermia (MTH) on patient outcomes after cardiac arrest has been studied. MTH has been reported to have a protective effect on mortality and neurological outcomes in adults.^{4,5} For neonates, a few studies have reported that MTH was associated with good neurological recovery and better survival outcomes. These results were attributed to hypoxic-ischaemic encephalopathy caused by perinatal asphyxia.^{6–8} Beyond the neonatal period, a study reported that MTH in children was associated with increased survival rates following resuscitation.⁹ This study was conducted in a single paediatric ICU and had limited generalizability to other settings. Other studies, however, found that MTH for paediatric OHCA offered no advantages in survival rates or good neurological outcomes.^{10–13}

One randomised clinical trial (RCT) on the effect of MTH in paediatric OHCA was performed in a multicentre setting.¹⁴ The study did not show significant differences in good neurologic outcomes between the MTH and non-MTH groups (20% vs. 12%, $P=0.14$) or in the 1-year survival rates between the groups (38% in the MTH group vs. 29% in the non-MTH group, $P=0.13$).

The initial electrocardiogram (ECG) is the key factor that predicts survival and good neurological recovery in OHCA in both children and adults.¹⁵ Previous studies on the initial ECG and outcomes showed very different proportions of shockable rhythm. In previous studies on MTH and outcomes in paediatric OHCA, the proportions of shockable rhythm varied from 2.3% to 16.5%.^{9–11,13,14} Because shockable rhythm is associated with better outcomes, MTH may not lead to a greater increase in survival rates for patients with shockable rhythm compared to those with non-shockable rhythm, the latter of which is associated with very low survival and is assumed to derive greater benefit from MTH.

However, whether MTH has different effect sizes according to the initial ECG rhythm, such as shockable versus non-shockable, is not clear. The current study aimed to test the association between MTH and outcomes in paediatric OHCA according to initial ECG rhythm using an interaction analysis.^{16,17}

Methods

This study was approved by the institutional review board of the relevant institution and by the Korea Centres for Disease Control and Prevention (CDC). Informed consent was waived because we used the database without obtaining identification or private information.

Study design and data source

This study utilised a cross-sectional design using the national OHCA database. The database has been constructed since 2006 via collaboration between the national fire department (FD) and the Korea CDC of the government of the Republic of Korea. Primary data were obtained from multiple sources including emergency medical services (EMS) run sheets, the EMS cardiac arrest registry, and retrospective medical records.^{16,17}

The data of the EMS cardiac arrest registry, which are recorded immediately after EMS providers transport OHCA patients, are stored in the national FD electronic server. Every case is routinely reviewed by county FD medical directors for data quality. The national FD has a central quality management committee, that is, tasked with the monthly monitoring of a strong and in-depth quality management programme for the EMS cardiac arrest registry.

Hospital registries of care and outcomes collect data regarding emergency department (ED) resuscitation care, comorbidities, post-resuscitation care and time variables. All such data are collected by trained medical record reviewers employed by the Korea CDC. The reviewers visit all hospitals and collect information on the basis of data dictionaries, they then input the information into the Korea CDC data server. The quality control of these data and medical record reviews is performed by the Data Quality Management Control (QMC) team.^{16,17}

Study setting

The Korean EMS is a single-tiered, government-operated system that provides a basic life support ambulance service run.^{16,17} Emergency medical technicians (EMTs) can conduct CPR on paediatric and adult OHCA patients both at the scene and during transport by using automatic external defibrillation and advanced airway management under direct medical control.¹⁸ The EMS CPR protocol followed the recommendations of the 2005 and 2010 international

guidelines and accepted the recommendations on the basis of the Korean EMS service level. However, EMTs cannot declare death at the scene and are mandated to transport OHCA patients to the ED while providing CPR during ambulance transport. Further, EMTs are not allowed to provide epinephrine or advanced life support medication to OHCA patients, following the EMS Act.¹⁹

EDs are classified into three levels according to resources and functional requirements by the national health department of the government; level 1 EDs (regional emergency medical centre, $n=20$) and level 2 EDs (local emergency medical centre, $n=110$) provide more and better emergency services by using emergency physicians for 24 h and 7 d a week. However, level 3 EDs (local emergency medical facility, $n=310$) have fewer resources and facilities than do other EDs and thus provide basic emergency care by using general physicians. Most forms of post-resuscitation care are available at level 1 or 2 EDs, which have a higher level of care than level 3 EDs do. All of these facilities participate in the national ED performance evaluation programme and undergo service level re-designation every year.^{16,20} The post-resuscitation care programme has been accepted by hospital physicians on the basis of academic recommendations and the limitation of resources for both adults and children.

The paediatric ED system in the study setting is different from the general ED system (Levels 1, 2, 3). Paediatric EDs have been designated as independent EDs in a hospital with general ED since 2013 based on different designation criteria (facility, human resource, and equipment), but in 2014, the number was not sufficient ($n=12$) to cover all paediatric OHCA cases. General EDs usually have a paediatric care zone or bay to provide more specialised emergency care. Both paediatric and general EDs follow the same CPR guidelines for neonatal, infant, and child CPR.^{21,22}

Study population

Of all EMS-assessed OHCA patients from January 1, 2008 to December 31, 2014, patients who survived to admission and were 18 years of age or younger, regardless of the cause (presumed cardiac or non-cardiac origin), were included. Patients were excluded if they had unknown neurological status at hospital discharge or if they had an alert mental status after resuscitation at the ED.

Data variables

MTH was defined as a case in which patients received therapeutic hypothermia (core temperature 32–34 °C) after recovering spontaneous circulation (ROSC) by using a method such as external cooling (water, fanning, or ice padding), internal cooling (gastric lavage, bladder cooling, or intravascular cooling using a catheter) or mixed cooling.²⁰ Although the target temperature should be between 32 and 34 °C, and the minimum duration of hypothermia should be at least 12 h, we considered a case to be part of the hypothermia-treated group if the hospital attempted the procedure regardless of either the duration or the withdrawal of the procedure due to death during induced hypothermia.²⁰ However hospitals selected and provided the MTH method according to physicians' preference on the basis of international academic guidelines rather than a standard care protocol.^{16,17,20}

We collected all potential confounders, which are known as Utstein risk factors (Tables 1 and 2).²³ We defined ventricular fibrillation/ventricular tachycardia as shockable rhythm and bradycardia without pulse, pulseless electrical activity, and asystole as non-shockable rhythm.²³ In addition, we included the following covariates: comorbidities including lung disease and heart disease¹⁴; level of ED (levels 1–3) according to ED capacity; and location of ROSC (i.e., pre-hospital or ED).

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