Clinical paper

Correlation between initial serum levels of lactate after return of spontaneous circulation and survival and neurological outcomes in patients who undergo therapeutic hypothermia after cardiac arrest ☆

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ABSTRACT

Objectives: We analysed the relationship between serum levels of lactate within 1 h of return of spontaneous circulation (ROSC) and survival and neurological outcomes in patients who underwent therapeutic hypothermia (TH).

Methods: This was a multi-centre retrospective and observational study that examined data from the first Korean Hypothermia Network (KORHN) registry from 2007 to 2012. The inclusion criteria were out-of-hospital cardiac arrest (OHCA) and examination of serum levels of lactate within 1 h after ROSC, taken from KORHN registry data. The primary endpoint was survival outcome at hospital discharge, and the secondary endpoint was poor neurological outcome (Cerebral Performance Category, CPC, 3–5) at hospital discharge. Initial lactate levels and other variables collected within 1 h of ROSC were analysed via multivariable logistic regression.

Results: Data from 930 cardiac arrest patients who underwent TH were collected from the KORHN registry. In a total of 443 patients, serum levels of lactate were examined within 1 h of ROSC. In-hospital mortality was 289/443 (65.24%), and 347/443 (78.33%) of the patients had CPCs of 3–5 upon hospital discharge. The odds ratios of lactate levels for CPC and in-hospital mortality were 1.072 (95% confidence interval (CI) 1.026–1.121) and 1.087 (95% CI = 1.031–1.147), respectively, based on multivariate ordinal logistic regression analyses.

Conclusion: High levels of lactate in serum measured within 1 h of ROSC are associated with hospital mortality and high CPC scores in cardiac arrest patients treated with TH.

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1. Introduction

Therapeutic hypothermia (TH) has improved the survival and neurological outcomes of patients who survive cardiac arrest [1,2]. The therapy is commonly used for comatose survivors with cardiac arrest as part of a series of survival treatments for cardiopulmonary resuscitation [3]. During TH, physicians need to be aware of the neurological and survival outcomes of comatose patients. Thus, several studies have been performed to develop tools to predict the neurological prognosis and survival outcomes. However, no single effective method for the prediction of outcome has been found. Several biological markers, such as the S-100B protein and neuron-specific enolase, have been demonstrated to be useful, and electroencephalography and neuroimaging, including brain computed tomography and magnetic resonance imaging, have been used by physicians to predict neurological outcomes [4–12]. However, these methods require serial check-ups and longer times to determine results.

An effective method for predicting survival and neurological outcomes that can be applied early on in the treatment process would be useful for planning treatment strategies for post-cardiac arrest care. However, there is a lack of objective data on such patients collected within 1 h after return of spontaneous circulation (ROSC) in the emergency department (ED). Such data would comprise pre-hospital data, including data from emergency medical service (EMS); initial laboratory findings taken after ROSC; and the results of physical and neurological examinations performed in the ED. Serum lactate levels are one of these initial laboratory findings. Early and effective clearance of serum lactate (i.e., lower levels) are associated with lower mortality in patients with many critical illnesses, including sepsis and severe trauma [13–18]. For cardiac arrest survivors, the relationships between clearance of serum lactate and neurological and survival outcomes have been studied [19–23]. However, few studies have addressed the potential relationship between initial serum levels of lactate and outcomes in patients who have been treated with TH. Thus, in this study, we evaluated whether initial levels of lactate in the serum at ROSC were correlated with neurological and survival outcomes of patients undergoing TH.

2. Methods

2.1. Registry data collection

This was a multi-centre, retrospective, observational, registry-based study that used data from the first Korean Hypothermia Network (KORHN) registry. KORHN, a multi-centre clinical research consortium for TH in South Korea, was organised in 2011, and a multi-centre retrospective, registry project was performed in 2012. The KORHN investigators collected data regarding post-cardiac arrest TH in 24 teaching hospitals around South Korea from 2007 to 2012. The institutional review board of each institution approved the study protocol before data collection. The need for informed consent was waived because of the retrospective nature of the study.

Adults (≥18 years) who suffered out-of-hospital cardiac arrest (OHCA), treated with TH after ROSC achieved pre-hospital and in the ED, were included in the study. Traumatic cardiac arrest patients were excluded. In a case report form, standard definitions of 87 variables and an investigator manual were developed from a literature review and consensus of the study investigators. The registry data were collected from manual medical charts or electronic medical record reviews. Data collected in each hospital were verified for completeness by the site's principal investigator, and were recorded on a web-based data registration system

(http://starcrf.com) by the clinical research coordinator. A data manager and three clinical research associates regularly monitored and reviewed data quality. The site's principal investigators or clinical research coordinators could be contacted through the query function in the system or directly by phone to clarify any questions about the data.

2.2. Data collection

Data that could be collected within 1 h after ROSC were used. The inclusion criteria from the KORHN registry data were OHCA and examination of serum levels of lactate within 1 h after ROSC (Fig. 1). Specifically, the data were demographics (gender, age), cause of arrest, pre-hospital resuscitation variables (witness, bystander CPR, ECG rhythm in EMS, pre-hospital time), in-hospital resuscitation variables (ECG rhythm at ED arrival, amount of injected epinephrine, hospital resuscitation time), neurological examination after ROSC (corneal reflex, light reflex, myoclonus), serum levels of lactate within 1 h after ROSC, and neurological and survival outcomes at discharge.

2.3. Outcome measures

The primary endpoint of the study was survival outcome at hospital discharge. A secondary endpoint was poor neurological outcome at hospital discharge, defined as a Cerebral Performance Category (CPC) of 3–5. CPC 3 indicates severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. It ranges from an ambulatory state to severe dementia or paralysis. CPC 4 indicates a coma or a vegetative state: any degree of coma without the presence of brain death criteria. Unawareness, even if appears awake (vegetative states) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. CPC 5 indicates cerebral unresponsiveness, indicates brain death: apnoea, areflexia, EEG silence.

2.4. Statistical analysis

Baseline descriptive characteristics of the subjects are presented with basic statistical analyses including means and standard deviations (SDs) for continuous variables, and numbers and percentages for categorical variables. Patient data were analysed according to survival and neurological outcomes at hospital discharge. Univariate and multivariate linear regression were used to evaluate the relationship between lactate levels and variables before hospital arrival. To compare lactate levels and neurological outcomes (CPC scores) as continuous variables, ordinal univariate and multivariate logistic regressions were used. All of the parameters were included in the multivariable logistic analysis to determine independent predictors for neurologic outcomes. Binary univariate and multivariate logistic regression analyses were used to estimate correlations between lactate levels and poor neurological outcome. CPC scores of 3, 4, and 5 were considered to be poor neurological outcomes.

For correlation between lactate levels and mortality, binary univariate and multivariate logistic regression analyses were used. Odds ratios (ORs) and 95% confidence intervals (CIs) are reported as estimates of variability and effect size. p-Values ≤0.05 were considered statistically significant. p-Values were corrected for multiple comparisons and within-method comparisons using the Holm–Bonferroni method. All of the statistical analyses were performed using the SPSS (ver. 20.0 for Windows; Chicago, IL) and SAS (SAS Institute, Cary, NC) software.