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Clinical paper

Relationship between ventricular characteristics on brain computed tomography and 6-month neurologic outcome in cardiac arrest survivors who underwent targeted temperature management☆

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ABSTRACT

Aim of the study: Brain swelling after cardiac arrest may affect the ventricles. We aimed to investigate the prognostic performance of ventricular characteristics on brain computed tomography (CT) in cardiac arrest survivors who underwent targeted temperature management (TTM).

Methods: This retrospective cohort study included adult comatose cardiac arrest survivors who underwent brain CT scan within 24 h after resuscitation and underwent TTM from 2014 to 2016. The ventricular areas (lateral, third, and fourth ventricle), distances between the anterior horns of the lateral ventricle (LV) and the posterior horns of the LV, and maximal internal diameter of the skull were measured. Grey-to-white matter ratio (GWR), Evans' index, and relative LV area were calculated. The primary outcome was a 6-month neurologic outcome.

Results: Of 258 patients, 176 (68.2%) had an unfavourable neurologic outcome. GWR, LV area, third ventricle area, distance between the anterior horns of the LV, distance between the posterior horns of the LV, Evans' index, and relative LV area were different between neurologic outcome groups. Evans' index (0.683; 95% confidence interval [CI], 0.623–0.739) and relative LV area (0.670; 95% CI, 0.609–0.727) had higher value of area under the curve than the other ventricular characteristics and showed prognostic performance comparable with GWR (0.600; 95% CI, 0.538–0.661). All ventricular characteristics and GWR were not independently associated with neurologic outcome after adjusting for covariates.

Conclusion: Ventricular characteristics on brain CT were associated with 6 months neurologic outcome in cardiac arrest survivors. Ventricular characteristics were objective measures that had comparable prognostic performance with GWR.

Introduction

Despite the advancement in post-cardiac arrest care [1–3], survival to hospital discharge of cardiac arrest remains approximately 12% [4]. Withdrawal of life sustaining therapy based on perceived neurologic prognosis is a major cause of death after cardiac arrest [5,6]. To improve the proper prognostication of cardiac arrest survivors, a multimodal approach to prognostication is recommended [7,8]. Each of the prognostic tools has limitations in use and interpretation. Among the available prognostic tools, brain computed tomography (CT) is widely used and easy to obtain even in post-cardiac arrest patients. Furthermore, brain CT should be standard in patients who achieved restoration of spontaneous circulation (ROSC) to evaluate the neurologic aetiology of cardiac arrest and exclude the contraindication for targeted temperature management (TTM).

The loss of differentiation between grey and white matter which represents brain swelling on brain CT was proven to be an ominous sign in cardiac arrest survivors [9–13]. Grey-to-white matter ratio (GWR) was suggested to be a useful prognosticator irrespective of TTM [9–12]. However, guidelines recommended the use of GWR as a prognostic tool with caution, because thresholds of GWR for prediction of unfavourable outcome varied and the calculation methods for GWR were inconsistent

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across studies [14]. Ventricular size is another objective tool that corresponds to brain swelling. Lower quantitative measures of ventricular size on brain CT were associated with brain swelling in benign intracranial hypertension [15]. In addition, the difference in third ventricular size between ante-mortem CT and post-mortem CT reflected brain swelling [16]. Ventricular characteristics including area, width, and distance between ventricles are other quantitative measurements on brain CT besides GWR and can be easily measured. However, to our knowledge, the relationship between ventricular characteristics and neurologic outcome in cardiac arrest survivors has not been investigated.

We hypothesised that brain swelling after cardiac arrest would affect the ventricular characteristics differently according to neurologic outcomes; thereby, ventricular characteristics can be used as prognostic tools in cardiac arrest survivors. Hence, we aimed to investigate the prognostic performance of ventricular characteristics on brain CT in cardiac arrest survivors treated with TTM.

Methods

Study design and population

This was a retrospective observational study using prospectively collected data of adult comatose cardiac arrest survivors treated with TTM at Chonnam National University Hospital in Gwangju, Korea, from January 2014 to December 2016. This study was approved by the Institutional Review Board of Chonnam National University Hospital (CNUH-2018-048).

Cardiac arrest patients over 18 years of age who underwent brain CT and were treated with TTM were included in the study. Patients (1) with pre-arrest cognitive impairment, (2) who did not undergo brain CT, (3) who underwent brain CT more than 24 h after ROSC, (4) with pseudo-subarachnoid haemorrhage (SAH) on brain CT, or (5) with extracorporeal membrane oxygenation applied during post-cardiac arrest care were excluded from the study.

TTM protocol

Comatose cardiac arrest survivors were treated with TTM in accordance with the guidelines. TTM was performed according to our written protocol. A target temperature of either 33 °C or 36 °C was maintained for 24 h using either feedback-controlled endovascular catheters (Thermoguard, ZOLL Medical Corporation, Chelmsford, MA, USA) or surface cooling devices (Blanketrol® II; Cincinnati Subzero Products, Cincinnati, OH, USA; Artic Sun® Energy Transfer Pads™; Medivance Corp, Louisville, CO, USA). The temperature was monitored using an oesophageal probe. Upon completion of the TTM maintenance phase, patients were rewarmed at a rate of 0.25 °C–0.5 °C per hour. All patients undergoing TTM received continuous intravenous midazolam and remifentanil (or fentanyl). A neuromuscular blocking agent was administered to control shivering on an as-needed basis. All other aspects of patient management were at the discretion of the treating physicians. Patients were not eligible for TTM if they had an intracranial haemorrhage, active bleeding, known terminal illness, or a poor pre-arrest neurologic status (cerebral performance category [CPC] scale ≥ 4).

Care after targeted temperature management

Supportive care continued in patients who remained comatose after TTM, unless withdrawal of life sustaining therapy was determined. Patients who required persistent supportive care were transferred to another hospital or rehabilitation facility to provide long-term care. Withdrawal of life sustaining therapy can be performed only in the patients who are pronounced brain dead or are impending death. Adhering to the agreement of the patient's family, organ donation was performed in the brain dead. A persistent vegetative state that lasts over 6 months can be judged by the hospital ethics committee in order to withdraw the life sustaining therapy. Even after withdrawal of life sustaining therapy, basic medical support including nutritional support, oxygen, and antibiotics was provided.

Data collection and measurements

The following data were obtained from hospital records: age, sex, comorbidities, first monitored rhythm, aetiology of cardiac arrest, location of cardiac arrest, presence of a witness on collapse, bystander cardiopulmonary resuscitation (CPR), adrenaline dose used during CPR, time to ROSC, Glasgow Coma Scale (GCS) after ROSC, serum lactate and glucose after ROSC, PaO_2 and $PaCO_2$ after ROSC, time from ROSC to TTM, sequential organ failure assessment (SOFA) score within the first 24 h after admission [17], time from ROSC to brain CT, brain CT findings, and neurologic outcome at 6 months after cardiac arrest.

One investigator who was blinded to the outcome reviewed patients' brain CT results using M-View control system version 5.4 (Marosis Infinity, Republic of Korea) to measure the variables (Supplemental Fig. S1). The Hounsfield units (HUs) of putamen and corpus callosum were measured and GWR was calculated. Circular regions of measurement (9.4 mm^2) were placed over the putamen and corpus callosum bilaterally, and the average attenuations were recorded in HU. The ventricular areas (lateral, third, and fourth ventricle) and distances between both anterior horns and both posterior horns of the lateral ventricle (LV) were measured. Measurement of the LV was performed at the level that showed the maximal size of the LV. Measurement of the third ventricle was performed at the level where the HU of basal ganglia was measured. Measurement of the fourth ventricle was performed at the level that showed the maximal size of the fourth ventricle around the cerebellar peduncle. The maximal internal diameter of the skull was measured at the level where the measurements of the LV were performed. Evans' index was calculated as the distance between the anterior horns of the LV divided by the maximal internal diameter of the skull [18]. We also calculated the relative LV area by measuring the LV area divided by the maximal internal diameter of the skull.

Neurologic outcome was assessed using the CPC scale 6 months after cardiac arrest via phone interview and recorded as CPC 1 (good performance), CPC 2 (moderate disability), CPC 3 (severe disability), CPC 4 (vegetative state), or CPC 5 (brain death or death) [19]. The primary outcome was an unfavourable neurologic outcome, defined as CPC 3–5.

Statistical analysis

Categorical variables were presented as frequencies and percentages. Comparisons of categorical variables were performed using χ^2 or Fisher's exact tests, as appropriate. Continuous variables were presented as means with standard deviation or median values with interquartile ranges according to normality test. The Mann–Whitney U test or independent t-test was conducted for comparisons of continuous variables, as appropriate. We examined the receiver operating characteristics (ROC) curves to examine the performances of the variables for prediction of unfavourable neurologic outcome. We calculated the sensitivity, specificity, positive predictive value, negative predictive value, and area under ROC curve (AUC). ROC analyses were additionally performed in stratified groups (patients with cardiac aetiology and those with non-cardiac aetiology). Multivariate logistic regression analysis was performed to select the covariates. All variables with $p < 0.2$ in the univariate analyses were included in the multivariate regression model (Supplemental Table S1). Backward selection was used to obtain the final model. Age, shockable rhythm, cardiac aetiology, time to ROSC, and GCS after ROSC were selected as covariates (Supplemental Table S1). We used a multivariate logistic