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Clinical paper

Comparison of brain computed tomography and diffusion-weighted magnetic resonance imaging to predict early neurologic outcome before target temperature management comatose cardiac arrest survivors☆

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ABSTRACT

Aim: We previously reported that diffusion-weighted magnetic resonance imaging (DW-MRI) could be used to predict neurologic outcomes before targeted temperature management (TTM) after return of spontaneous circulation (ROSC) from cardiac arrest (CA). We compared the efficacy of brain computed tomography (CT) and DW-MRI to predict neurologic outcome before TTM in comatose cardiac arrest survivors.

Methods: We performed a retrospective study of CA patients treated with TTM. The brain CT and DW-MRI were both obtained before TTM. We analysed the grey matter to white matter ratio (GWR) on the brain CT and the presence of high signal intensity on DW-MRI, alone or in combination, to predict poor neurologic outcome (CPC 3–5).

Results: Of 47 comatose CA patients treated with TTM, 39 patients with brain CT and DW-MRI data were included. Median time from the ROSC to the brain CT and DW-MRI was 90 min (52–150) and 175 min (118–240), respectively. There was no significant difference in predicting poor neurologic outcome between average GWR (area under the curve [AUC] 0.891, sensitivity/specificity 78.8%/100%) and DW-MRI (AUC 0.894, sensitivity/specificity 75.8%/100%) ($p = 0.963$). The combination of average GWR and DW-MRI (AUC 0.939, sensitivity/specificity 87.9%/100%) improved the prediction of poor neurologic outcome rather than each one alone and in other combinations.

Conclusion: Our preliminary finding suggests that DW-MRI is potentially useful for early prediction of neurologic outcome (i.e., before TTM) in CA patients. The combination of GWR on brain CT and that on DW-MRI, rather than on each modality alone, appears to improve the sensitivity for predicting neurologic outcome after ROSC from CA. Large prospective multicenter studies should be conducted to confirm these results.

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Abbreviations: DW-MRI, diffusion weighted magnetic resonance imaging; TTM, targeted temperature management; ROSC, restoration of spontaneous circulation; CA, cardiac arrest; CT, computed tomography; GWR, grey matter to white matter ratio; AUC, arear under curve; CBNUH, Chungbuk National University Hospital; CCAS, comatose cardiac arrest survivors; ICU, intensive care unit; WLST, withdrawal of life-sustaining therapy; ERC, European Resuscitation Council; ADC, apparent diffusion coefficient; HSI, high signal intensity; HU, hounsfield units; BG, basal ganglia; CN, caudate nucleus; P, putamen; T, thalamus; CC, corpus callosum; PIC, posterior limb of internal capsule; CPC, Cerebral Performance Categories; IQR, interquartile range; CI, confidence interval; SSEP, short-latency somatosensory evoked potentials; NSE, neuron-specific enolase; EEG, electroencephalography; aEEG, amplitude-integrated electroencephalography.

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1 Introduction

Target temperature management (TTM) has been shown to improve neurologic outcomes in comatose cardiac arrest survivors (CCAS) and is considered standard treatment [1–5]. However, most CCAS still suffer from the most common causes of serious neurological deficits and require long-term admission to the intensive care units (ICU) [6]. Thus, the current neurologic outcome prediction of CCAS focuses on the end-of-life decision such as the withdrawal of life-sustaining therapy (WLST), but it is a very sensitive and difficult problem due to medical, ethical, and economical reasons.

In 2015, the European Resuscitation Council (ERC) published guidelines to facilitate prognostication of CCAS by various parameters [7]. All prognostic tools are recommended 72 h after cardiac arrest (CA) except for brain CT (within 24 h). However, it is important to have an early prediction of neurologic outcome before TTM after ROSC. In particular, this did not decide to suspend or WLST by predicting neurologic outcome before TTM, but rather to consider medical, economic, and social opportunity costs such as ICU admission. Especially in Korea, the clinics are not permitted to perform WLST unless the patient is considered brain-dead during TTM. Conversely, if it is predicted that a patient has a good neurologic outcome, this may encourage the physicians and families to provide continued life support during the acute stage of post-cardiopulmonary arrest care. In addition, it is not intended to explain the poor neurologic outcome to the family of the CCAS and to deprive the patient of treatment opportunities. Rather, the physician should be able to more precisely predict and explain the patient's neurologic outcome after TTM to the CCAS family to prevent the deterioration of the family-physician relationship, including legal disputes.

Brain CT was the only modality before TTM for comatose survivors after ROSC from CA except the presence of myloclonus; however, this method has low sensitivity and drawbacks of significant deviation depending on the interpreter [7–9]. DW-MRI is a prognostic modality for comatose survivors after ROSC from CA by identifying hypoxic-ischemic brain injury [10,11]. DW-MRI provides a quantitative value for the severity of the brain injury by measurement of the apparent diffusion coefficient (ADC) [12–14]. However, in global ischemia, ADC reduction is delayed and the changes in ADC after CA are not well known. The ERC guidelines recommend ADC-based delayed prognostication to be measured after 3–5 days from ROSC [7]. In our previous study, we performed DW-MRI within 6 h after CA and before TTM, and we analysed the extent of acute global hypoxic-ischemic brain injury [15]. The analysis was performed by scoring 21 brain regions (cortical grey matter and subcortical white matter in the frontal, parietal temporal, and occipital lobes, hippocampus, insular cortex, corpus callosum, deep grey nuclei, cerebellum, and the brain stem) on DW-MRI sequences according to the presence of high signal intensity (HSI) on each brain lesion. As a result, the 'neurologic poor outcome group' showed that scoring of all brain regions was increased after 48 h of ROSC, rather than immediately after ROSC, on DW-MRI. Therefore, we hypothesized that a small volume of HSI on DW-MRI immediately after ROSC may be meaningful in predicting poor neurologic outcome.

Thus, in this study, we compared the prognostic performances of the grey matter to white matter ratio (GWR) on the brain CT and abnormal high signal presence in DW-MRI in CCAS treated with TTM to determine whether the combination of GWR and the presence of abnormal high signal in DW-MRI improves the prognostic performance when compared to either one alone or in other combinations.

2 Methods

2.1 Study design and population

This was a retrospective observational cohort study of adult comatose cardiac arrest survivors treated with TTM at Chungbuk National University Hospital in Cheongju, Korea, between July 2013 and July 2016. This study was approved by the CBNUH Institutional Review Board. We included patients who received both brain CT and DW-MRI before TTM. Exclusion criteria were as follows: age <18 years, traumatic cardiac arrest, interrupted TTM (transfer to another facility or haemodynamic instability) and large artefacts in brain CT or brain DW-MRI.

2.2 TTM protocol

The patients were managed according to our previously published TTM protocol. TTM was induced with ice packs, intravenous cold saline, and two TTM devices: Arctic Sun® Energy Transfer Pads™ (Medivance Corp, Louisville, KY, USA) and Blanketrol® II (Cincinnati Subzero Products, Cincinnati, OH, USA). The target temperature of $33 \pm 0.5\,^{\circ}$C was achieved and maintained for 24 h. Upon completion of the 24-h maintenance phase, active rewarming was attempted at a target rate of 0.25 °C/h to 0.5 °C/h until the body temperature reached 36 °C–36.5 °C. During TTM, the temperature was monitored using a bladder temperature probe. Midazolam and atracurium were used for sedation and shivering control. All patients received standard intensive care according to our institutional intensive care unit protocol.

2.3 Density measurement using brain CT and determining the presence of abnormal high signal using DW-MRI

Our post-cardiac arrest care protocol recommended obtaining a brain CT and DW-MRI before TTM within at least 6 h after the arrest. However, obtaining brain CT or DW-MRI was not mandatory and decisions regarding these tests were at the discretion of the treating physicians or at the agreement of a legal guardian. CT was performed with a 64-channel system (Brilliance CT 64; Philips Medical System, The Netherlands) and MRIs were obtained with a 1.5 T system (Achieva 1.5T; Philips Medical System, The Netherlands). All images were assessed by a board-certified neuro-radiologist (KS Yi). GWR was calculated by a board-certified neuro-radiologist blinded to clinical information and patient outcome. Briefly, Hounsfield units (HU) were recorded at the basal ganglia (BG) level, caudate nucleus (CN), putamen (P), thalamus (T), corpus callosum (CC), and posterior limb of the internal capsule (PIC). The GWR (CN/CC, P/CC, T/CC, CN/PIC, P/PIC, T/PIC, the mean value of 6 zones measured (average), and (CN + P)/(CC + PIC)) were calculated according to previously reported methods [8,9,16,17]. For DW-MRI at the whole-brain axial plane, single-shot spin-echo planar imaging was acquired by applying diffusion-sensitizing gradients along three orthogonal directions with a diffusion weighting factor $b = 1000\,s/mm^2$ and one reference scan with $b = 0$. The section thickness was 5 mm and the section gap was 1 mm. The presence of abnormal HSI in the brain parenchyma was defined by a combination of high DWI and low ADC signal and was distinguished by the same neuroradiologist who did not see the patient information, results, and GWR.

2.4 Outcome

The primary endpoint of this study was neurologic outcome at 6 months after cardiac arrest. The neurologic status of the patients was obtained by assessing the hospital records or directly calling the patient's caregiver. Neurologic outcome was assessed using the

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