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Clinical paper

Better prognostic value with combined optic nerve sheath diameter and grey-to-white matter ratio on initial brain computed tomography in post-cardiac arrest patients☆

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ABSTRACT

Aim: We aimed to evaluate the prognostic value of optic nerve sheath diameter (ONSD) and grey-to-white matter (GWR) either alone or in combination in patients treated with targeted temperature management (TTM) after cardiac arrest (CA).

Methods: We conducted a retrospective single centre study of post cardiac arrest patients treated with TTM. ONSD and GWR on brain computed tomography (CT) was measured by two emergency physicians. We analysed the prognostic performance and cut offs of GWR and ONSD, singly and in combination in predicting poor neurologic outcome (CPC 3–5).

Results: Of the 119 patients studied, 74 patients showed poor outcome. The combination of ONSD and GWR significantly ($p = 0.002$) improved prognostic performance (AUROC 0.67, 95% CI: 0.58–0.76, $p < 0.001$) in predicting poor neurologic outcomes rather than each ONSD (AUROC 0.59, 95% CI: 0.50–0.68, $p = 0.08$) or GWR (AUROC 0.65, 95% CI: 0.56–0.74, $p = 0.002$) alone. A combined cut off of 'GWR and ONSD (1.16 and 4.9)' and 'GWR or ONSD (1.13 or 6.5)' improved the sensitivity for predicting poor outcome while maintaining high specificity compared to GWR alone.

Conclusion: The combination of ONSD and GWR yielded improved prognostic value for predicting poor neurologic outcomes in post cardiac arrest patients treated with TTM.

Introduction

Ischemia-reperfusion cerebral injury significantly contributes to mortality and may reduce the quality of life in many cardiac arrest survivors.[1–3] Post cardiac arrest care and temperature management has been emphasized as an effective therapy for neuroprotection in these patients.[4] Neurologic prognostication is needed to guide targeted treatment interventions according to severity and to provide information to treating physicians. Although many prognostic factors including neurologic exams, electrophysiological tests (electroencephalography, somatosensory evoked potential),[5,6] serum markers such as neuron-specific enolase (NSE)[7] have been studied, most are predictive of outcomes only after 72 h of post-cardiac-arrest.[8] Therefore, earlier prediction of neurologic outcomes is of importance in the setting of post-cardiac arrest care for guiding treatment strategies.

Many patients generally undergo initial brain computed tomography (CT) scanning post cardiac arrest to evaluate brain haemorrhage or infarction before admission to the intensive care unit (ICU). Several recent studies have focused on the early prediction of neurologic outcomes using the grey-to-white matter ratio (GWR) on initial brain CT in cardiac arrest survivors treated with TTM.[9–11] The obliteration of grey and white matter decreases values of the grey-to-white matter ratio, leading to the presumption that the patient has brain oedema and will have a poor outcome. These studies showed various prognostic performances with various cut-offs[12] and some studies combined prognostic factors so as to enhance the performance.[9,13]

We assessed the optic nerve sheath diameter (ONSD), which is known to correlate with increased intracranial pressure (IICP)[14–16]

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and is easily measured on brain CT, and sought to determine whether it can improve our ability to predict poor prognosis in post cardiac arrest patients when combined with GWR. The optic nerve sheath is easily assessed as a part of the brain meninges[17] and it is known to be a good predictor of mortality in patient with traumatic brain injuries.[15] Hypoxic brain injury during cardiac arrest and delayed hyperemia after return of spontaneous circulation (ROSC) may result in increased intracranial pressure and brain swelling, which can be associated with poor neurologic outcomes.[18] There was previously one study of GWR and ONSD on post cardiac arrest patients. However, 40 out of 91 of the patients underwent temperature management and had various initial Glasgow coma scale (GCS) scores in this study by Kim et al.[19] Therefore, this is the first study to evaluate the prognostic value of ONSD and GWR either alone and combined in a homogeneous group of comatose patients treated with TTM after cardiac arrest.

Methods

This study was approved by the Institutional Review Board of Samsung Medical Centre (SMC-2015-01-065-001). Consent forms were waived due to the retrospective design.

Study design and population

This was a retrospective single-centre observational cohort study using medical records of patients who had been treated with TTM following cardiac arrest in an urban tertiary care hospital, Samsung Medical Center in Seoul, Korea from October 2009 to December 2013. Resuscitated cardiac arrest patients who were comatose after ROSC and underwent TTM were included. Patients under 18 or over 75 years of age, with families that refused further treatment, who had brain haemorrhage on initial brain CT, patients with high bleeding risk or with a traumatic cause of arrest did not undergo TTM. The exclusion criteria for this study were (1) TTM interrupted due to hemodynamic instability or family refusing further treatment, (2) brain CT not obtained, (3) brain CT obtained more than 6 h after ROSC, (4) brain CT too poor in quality to measure the ONSD or GWR, and (5) other apparent brain parenchymal disease or ophthalmic disease that would affect the GWR and ONSD.

Targeted temperature management (TTM) protocol

All patients received standard TTM and intensive care according to our institutional ICU protocol. TTM was induced with intravenous cold saline or cooling devices (Artic Sun® Energy Transfer Pads TM, Medivance Corp., Louisville, USA). The target temperature of 33 °C was maintained for 24 h with rewarming to 36.5 °C at a rate of 0.15 °C /h and was monitored using an esophageal temperature probe. Sedatives and analgesics were used during TTM and patients received standard care according to our hypothermia protocol as described previously.[20] A spot EEG was performed during TTM as soon as possible. When seizure was suspected either clinically or through EEG, anti-epileptic medications were started. All patients that received TTM was documented in our hypothermia database.

Data collection

We reviewed data from a prospectively documented hypothermia database including Utstein-style data, temperature management data and the Glasgow-Pittsburgh Cerebral Performance Categories (CPC) at one month after ROSC of both in-hospital and out-of-hospital cardiac arrest patients treated with temperature management. The following data were retrospectively collected from the database: age, gender, presence of a witness of collapse, bystander CPR, first monitored rhythm, etiology of cardiac arrest, time from collapse to CPR that was defined as no flow time, time from CPR to ROSC that was defined as low flow time, SOFA score and one month neurologic outcome. Time from ROSC to obtaining the brain CT was retrospectively determined from electronical medical records.

Measurement of ONSD and GWR on CT scan

Two emergency physicians blinded to the patient outcome retrospectively reviewed the brain CT on the picture archiving and communication system (PACS) radiology workstation (Centricity Enterprise, GE). ONSD was measured at a distance of 3 mm behind the sclera at both the patient's left and right eye.[15] We measured the average hounsfield units (HU) of circular regions of interest ($10.0\,mm^2$–$15\,mm^2$) on each side of the basal ganglia, centrum semiovale and high cortical level. The caudate nucleus (CN) putamen (PU), posterior limb of internal capsule (PLIC) and corpus callosum(CC) was measured for the basal ganglia, and the grey and white matter from the medial cortex was measured at the centrum semiovale (MC1, MW1) and high cortical level (MC2, MW2). The GWR for the basal ganglia (GWR-BG= (CN + PU)/(PLIC + CC)), for the cerebrum (GWR-CE = (MC1 + MC2)/(MW1 + MW2)) and the average of the two (GWR-AV = (GWR-BG + GWR-CE)/2) were calculated as previously described[10,21](Fig. 1).

Statistical analysis

The intra- and inter-observer variabilities were evaluated for two physicians and were calculated by analysis of GWR and ONSD measures. Continuous variables were reported as the median with interquartile range (IQR) or mean and standard deviation (SD) depending on normal distribution. The Mann–Whitney *U*-test or two-tailed *t* test was conducted for comparisons of continuous variables. Categorical variables are presented as frequencies and percentages and comparisons were done using the chi-square test or Fisher's exact test. Receiver operating characteristic (ROC) curves were plotted to determine the performance of ONSD, GWR and combined ONSD and GWR in predicting neurologic outcomes. The ROC curves were calculated and compared by the DeLong method. Cut-off values with high specificity were calculated for predicting poor neurologic outcome. Data were analysed using Stata software, version 13 (Stata Corp. LP, TX, USA) and SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

Characteristics of study subjects

Of the 188 post cardiac arrest patients who were admitted to the ICU for temperature management, CT was not performed in 38 patients, CT was delayed over 6 h in 23 patients and the quality of CT was suboptimal for analysis in eight patients. Ultimately, a total of 119 patients were analysed (Fig. 2). Baseline characteristics are shown in Table 1. A total of 74 patients (62.2%) resulted in CPC 3–5 at one month after cardiac arrest. The median time from ROSC to brain CT did not differ between the outcome groups (55.5 min (35.5–121.5) vs. 63 min (39–125), $p = 0.73$).

ONSD and GWR on brain CT

The mean ONSD was not significantly different between the outcome groups (5.6 ± 0.5 mm vs. 5.8 ± 0.6 mm, $p = 0.05$). However GWR at the basal ganglia (GWR-BG) (1.26 ± 0.71 vs. 1.21 ± 0.10, $p = 0.002$), GWR at the cerebrum (GWR-CE) (1.21 ± 0.005 vs. 1.17 ± 0.08, $p = 0.02$) and the average of the two GWR values (GWR-AV) (1.23 ± 0.05 vs. 1.19 ± 0.08, $p = 0.002$) was significantly lower