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Clinical Paper

Efficacy of diffusion-weighted magnetic resonance imaging performed before therapeutic hypothermia in predicting clinical outcome in comatose cardiopulmonary arrest survivors

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ABSTRACT

Aim of the study: To develop a clinically relevant and qualitative brain magnetic resonance imaging (MRI) scoring system for acute stage comatose cardiac arrest patients.
Methods: Consecutive comatose post-cardiopulmonary arrest patients were prospectively enrolled. Routine brain MRI sequences were scored by two independent and blinded experts. Predefined brain regions were qualitatively scored on diffusion-weighted imaging (DWI) sequences according to the severity of the abnormality on a scale from 0 to 4. The mean score provided by the raters determined poor outcome defined under the Cerebral Performance Categories 3, 4, or 5. DWI scans were repeated after therapeutic hypothermia (TH). The same qualitative scoring system was applied and results were compared to the initial scores.
Results: Out of 24 recruited patients, 19 with brain MRI scans were included. Of the 19 included patients, seven showed a good outcome at hospital discharge and 12 patients showed poor neurologic outcome. Median time from the arrest to the initial DWI was 166 min (IQR 114–240 min). At 100% specificity, the overall, cortex, and cortex plus deep grey nuclei scores predicted poor patient outcome with a sensitivity of 91.7–100% (95% CI). Follow-up DWI scans after TH showed worse results than initial scans.
Conclusion: A qualitative MRI scoring system effectively assessed the severity of hypoxic-ischaemic brain injury following cardiopulmonary arrest. The scoring system may provide useful prognostic information in comatose cardiopulmonary arrest patients.

1. Introduction

Improvements in intensive care medicine have led to increased bed ridden vegetative states and severe neurological deficits in cardiopulmonary arrested survivors (CPAS). In the past, only 10–30% of comatose CPAS demonstrated functional recovery.[1] However, these percentages improved with increasing use of therapeutic hypothermia (TH).[2,3] Post-cardiopulmonary arrest brain injury is a common cause of morbidity and mortality. Despite the use of TH, 45–70% of cardiac arrest victims still experience severe neurological deficits due to anoxic reperfusion cerebral injury.[4,5] Conversely, premature withdrawal of life support from patients who may have a chance of functional recovery represents an ethical dilemma. Thus, early and accurate identification of patients who will not likely recover is an important healthcare issue.

Many studies have focused on early identification of comatose CPAS expected not to regain consciousness.[6–8] Historically, the most specific early predictors for poor outcome after cardiopulmonary arrest include the following: absence of brain stem or extensor reflexes, absence of motor response at post-arrest day 3, absence of cortical responses by somatosensory evoked potentials (SSEP) at 24 h post arrest, serum neuron specific enolase (NSE) levels >33 μg/L in the first 3 days, and early myoclonic status epilepticus.[9] These predictors have substantive limitations, a low sensitivity for poor outcome, and may not be valid in patients treated with hypothermia.[10] The first limitation in the predictors is that they identify only a subset of poor-outcome patients with high specificity. Second, neurological examinations and results of

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Brain regions			Scoring system
Supratentorial	Cortex	Frontal lobe	0 = normal
		Parietal lobe	1 = possibly abnormal
		Temporal lobe	2 = abnormal, mild
		Occipital lobe	3 = abnormal, moderate
		Insula	4 = abnormal, severe
		Hippocampus	
	Deep grey nuclei	Caudate	
		Putamen	
		Globus pallidus	
		Thalamus	
	White matter	Frontal lobe	
		Parietal lobe	
		Temporal lobe	
		Occipital lobe	
		Corpus callosum	
Infratentorial	Brainstem	Midbrain	
		Pons	
		Medulla	
	Cerebellum	Cortex	
		White matter	
		Dentate nuclei	

Fig. 1. The 21 scored brain regions and DWI scoring system.

electroencephalography may be difficult to interpret in the presence of sedative agents or metabolic derangements. Third, serum markers are potentially susceptible to false-positive test results and are not yet readily available in many hospitals.[9,11] Several studies have reported brain magnetic resonance imaging (MRI) as a useful tool in imaging comatose CPAS.[12–24] Typically, the presence of extensive and severe cortical signal abnormalities on MRI is associated with poor outcome.[12–15,18–22] MRI offers the advantage of providing an objective measure of cerebral injury and may be particularly useful in patients who have received sedative agents. Furthermore, the method is useful in patients who have metabolic derangements that render neurological examinations unreliable and patients treated with TH.

Recent developments in brain imaging through MRI include diffusion-weighted MRI (DWI). DWI is a novel, fast (10 min), and potentially powerful marker of early global ischaemic brain injury.[21] Additionally, patient monitoring devices are available during DWI. Preliminary studies have shown widespread abnormalities detected by DWI in poor-outcome patients at 1 week post-cardiac arrest.[21] However, obtaining a brain MRI in critically ill patients with potential cardiac instability is challenging. We used a clinically applicable brain MRI scoring system that is qualitative and has potential for broad use and application. This is an important tool for facilities without access to qualitative MRI analysis or technically inadequate scanners. This qualitative MRI scoring system has been described in previous studies as a tool to predict outcome following perinatal asphyxia.[24–27] The overall aim of this study was to determine the feasibility and prognostic utility of DWI before TH in comatose CPAS in a prospective study.

2. Methods

2.1. Study design and population

Consecutive CPAS who remained comatose after successful resuscitation were prospectively enrolled over a 2-year period at Chungbuk National University Hospital, a university-affiliated 600-bed hospital in Chungju, Korea, from March 2012 to March 2014. Patients were enrolled if they met the following inclusion criteria: ≥16 years of age, status post resuscitation for in- or out-of-hospital cardiac arrest, and persistent coma defined as the inability to open eyes to voice and inability to follow commands. The study was approved by the institutional review board, and written consent from a legally authorized representative was required for study participation. Clinical parameters were obtained in a prospective and standardized fashion at predefined time points. Neurological examinations (including a Glasgow Coma Scale score and an assessment of brainstem function) were performed daily during the first 3 days and at 1 and 2 weeks after cardiopulmonary arrest.

Functional outcomes were determined by the Cerebral Performance Categories (CPC) at discharge. The first MRI examinations were conducted before TH within at least 6 h. Additional MRI examinations were conducted within the first week after the arrest if the treating physicians agreed the patient could safely undergo MRI after TH. Reasons for patients not undergoing an MRI and adverse events during patient transport to or from the MRI suite and during imaging acquisition were documented.

2.2. Therapeutic hypothermia protocol

In all patients, TH was applied according to a written TH protocol. TH was induced with ice packs, intravenous cold saline, and cooling devices (Blanketrol II, Cincinnati Subzero Products, Cincinnati, USA; Artic Sun Energy Transfer Pads, Medivance Corp, Louisville, USA; COOLGARD 3000 Thermal Regulation System, Alsius Corporation, Irvine, USA). The target temperature of $33 \pm 0.5\,^{\circ}C$ was maintained for 24 h. Upon completion of the TH maintenance phase, patients were rewarmed to 36.5 °C at a rate of 0.25–0.5 $^{\circ}C\,h^{-1}$. During TH, 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. Magnetic resonance imaging and scoring

All patients with technically adequate brain DWIs obtained before TH within at least 6 h after the arrest are included in this study. MRIs were obtained with a 1.5 T system (Achieva 1.5 T; Philips Medical System, The Netherlands). For DWI, 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 $b = 1000\,s/mm^2$ plus one reference scan with $b = 0$. The section thickness was 5 mm and