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Clinical paper

# Combination of initial neurologic examination, quantitative brain imaging and electroencephalography to predict outcome after cardiac arrest☆

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ABSTRACT

*Background:* Prognosticating outcome following cardiac arrest is challenging and requires a multimodal approach. We tested the hypothesis that the combination of initial neurologic examination, quantitative analysis of head computed tomography (CT) and continuous EEG (cEEG) improve outcome prediction after cardiac arrest.

*Methods:* Review of consecutive patients receiving head CT within 24 h and cEEG monitoring between April 2010 and May 2013. Initial neurologic examination (Full Outline of UnResponsiveness_Brainstem reflexes (FOUR_B) score and initial Pittsburgh Post-Cardiac Arrest Category (PCAC)), gray matter to white matter attenuation ratio (GWR) on head CT and cEEG patterns were evaluated. The primary outcome was in-hospital mortality.

*Results:* Of 240 subjects, 70 (29%) survived and 22 (9%) had a good neurologic outcome at hospital discharge. Combined determination of GW ratio and malignant cEEG had an incremental predictive value (AUC: 0.776 for mortality and 0.792 for poor neurologic outcome), with 0% false positive rate when compared with either test alone (AUC of GW ratio: 0.683 for mortality and 0.726 for poor outcome, AUC of malignant cEEG: 0.650 for mortality and 0.647 for poor outcome). Addition of FOUR_B or PCAC to this model improved prediction of mortality ($p = 0.014$ for FOUR_B and 0.001 for PCAC) but not of poor outcome ($p = 0.786$ for FOUR_B and 0.099 for PCAC).

*Conclusions:* Combining GWR with cEEG was superior to any individual test for predicting mortality and neurologic outcome. Addition of clinical variables further improved prognostication for mortality but not neurologic outcome. These preliminary data support a multi-modal prognostic workup in this population.



## Introduction

Coma after successful resuscitation from cardiac arrest (CA) is the most common cause of ICU admission, and the main cause of in-hospital mortality is withdrawal of life sustaining treatment for perceived poor neurological prognosis (WLST).[1–4] Targeted temperature management (TTM) is considered standard treatment after CA and can influence sedative drug metabolism and may interfere with accurate prognostication.[5–8] Moreover, WLST is strongly associated with persistent coma. Therefore, strategies for accurate prediction of neurological outcome after CA are critically needed.

Several prognostic tools such as neurologic examination, somatosensory evoked potential (SSEP), serum biomarkers, electroencephalography (EEG), brain computed tomography (CT) and diffusion weighted magnetic resonance imaging (DW-MRI) have been evaluated as predictors of neurological outcome.[9–19] The combination of multiple modalities is recommended because no single test short of physical examination meeting brain death criteria can predict neurologic outcome correctly.[20–22] We previously reported that combining the initial neurologic examination with continuous EEG (cEEG) was superior to any individual test for predicting outcome after CA.[23] Using a multimodal approach can minimize the risk of erroneous prognostication of poor outcome.

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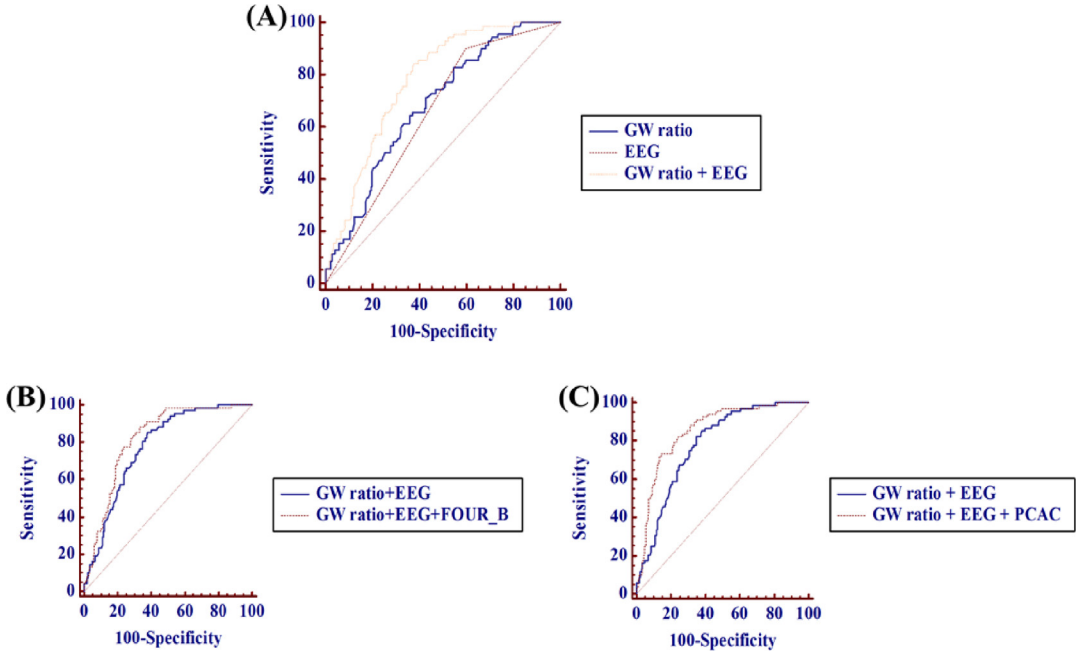


**Fig. 1.** Comparison of ROC curve for predicting mortality.
(A) AUC for GW ratio: 0.683, for malignant cEEG: 0.650, for combining GW ratio and malignant cEEG: 0.776 ($p < 0.001$, $p < 0.001$, respectively) (B) AUC for adding FOUR_B: 0.820 ($p = 0.014$) (C) AUC for adding PCAC: 0.855 ($p = 0.001$).

We hypothesized that the combination of initial neurologic examination, quantitative analysis of brain CT and cEEG can improve outcome prediction after CA. We performed a retrospective analysis of data to test whether the combination of initial brain stem reflex examination evaluated using Full Outline of UnResponsiveness Brainstem (FOUR_B) score or Pittsburgh Cardiac Arrest Category (PCAC), quantitative analysis of head CT calculated by gray matter to white matter attenuation ratio (GWR) and cEEG was superior to either test alone for predicting outcome after CA.

## Methods

### *Study design and setting*

We conducted a retrospective analysis of prospectively collected data from a single urban teaching hospital between April 2010 and May 2013. This study was approved by the University of Pittsburgh Institutional Review Board. We included patients who received both head CT scan within 24 h and cEEG monitoring. All patients receive serial clinical examinations as part of clinical care. Exclusion criteria were as follows: age <18 yrs, traumatic cardiac arrest, history of cerebrovascular accident, intravenous contrast in brain CT and large artifacts in brain CT.

The patients were managed according to our previously published post-cardiac arrest care protocols.[13,23,24] Briefly, TTM at 33 °C was induced with rapid infusion of 30 cc/kg of 4 °C saline and thermostatically controlled surface cooling devices (Gaymar Industries, Orchard Park, NY; Arctic Sun, Bard Medical Division, Louisville CO) and maintained for 24 h. Intravascular cooling is rarely employed after cardiac arrest in our cohort. Propofol was infused to suppress shivering, or midazolam was infused in cases of hypotension. Neuromuscular paralysis was used often during induction period and rarely used during maintenance and rewarming period.

### *Methods of measurement*

Initial neurologic examination was routinely assessed using FOUR score and PCAC within the first 6 h of resuscitation and without sedation and paralysis by one of the post-cardiac arrest service physicians. The FOUR score is composed of Motor, Brainstem, Respiratory and Eye responses. Each domain has a 0–4 score and a higher score indicates greater function. As previously reported, we used the FOUR_B score to stratify patients into three groups; FOUR_B = 0–1, FOUR_B = 2 and FOUR_B = 4.[23] We also quantified severity of post-arrest illness using the validated Pittsburgh Cardiac Arrest Category system, where: (I) awake, (II) coma (not following commands but intact brainstem responses) + mild cardiopulmonary dysfunction (SOFA cardiac + respiratory score <4), (III) coma + moderate-severe cardiopulmonary dysfunction (SOFA cardiac + respiratory score ≥4), and (IV) coma without brainstem reflexes.[3,25]

Our hospital implemented 22-channel digital cEEG recordings for the first 48 h after resuscitation from CA as standard monitoring for all comatose post-cardiac arrest patients in August 2009.[13] cEEGs were interpreted during patient care by board certified neurologists, and malignant patterns were defined as follows: nonconvulsive status epilepticus (NCSE), convulsive status epilepticus (CSE), myoclonic status epilepticus (MSE) and generalized periodic epileptiform discharges (GPEDs). The definition of each malignant pattern has been described previously.[13] Myoclonic status epilepticus was characterized as the presence of myoclonic jerks or facial movements associated with GPEDs or with the bursts in a burst suppression pattern. The presence of reactivity and continuous background was not always provided in the clinical interpretation and was not included in the report of the EEG for this study. Patients with malignant EEG patterns are treated with a bolus of lorazepam followed by levetiracetam and valproic acid. Phenytoin is employed next, followed by either a continuous infusion of midazolam or phenobarbital for refractory cases.

Baseline brain CT scanning in patients presenting comatose after resuscitation is a part of standard care in our hospital. CT scans were obtained on a GE Light Speed VCT scanner (GE Healthcare, Little Chalfont, UK) with 5 mm slices at the time of emergency department admission. GWR was calculated by an investigator blinded to clinical information as previously reported.[17] Briefly, Hounsfield Units (HU) were recorded at the basal ganglia level;