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Continuous electroencephalogram patterns are suggestive of eventual neurologic outcomes in post–cardiac arrest patients treated with therapeutic hypothermia

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ABSTRACT

Introduction: Therapeutic hypothermia (TH) after cardiac arrest (CA) resuscitation is the first therapy proven to increase survival to discharge and neurologic recovery. Methods for neurologic and mortality prognostication after CA resuscitation have been called into question because they were developed based on evidence that was developed prior to the advent of TH. This study examines the relationship between electroencephalogram (EEG) patterns and mortality and neurologic outcomes in post-CA patients undergoing TH.
Methods: Eighty-three of 732 patients who had continuous EEG (cEEG) monitoring during TH were included. Continuous EEG tracings were classified as isoelectric, low voltage, burst suppression, epileptic form, and diffuse slowing. Primary outcomes are survival to discharge and Cerebral Performance Categories (CPCs) at hospital discharge.
Results: Among patients with favorable neurologic outcomes (CPC1 and CPC2), the duration cardiopulmonary resuscitation and time until return of spontaneous circulation were shorter than observed in patients with poorer neurologic outcomes (CPC3, CPC4, and CPC5). The time to target temperature was equivalent among neurologic outcome groups (499.5 minutes vs 431.0 minutes, $P = .09$). Favorable neurologic outcome was associated with initial presentation with ventricular tachycardia or ventricular fibrillation and had cEEG patterns suggestive of diffuse slowing and epileptiform waves.
Discussion: The use of cEEG can provide prognostication information otherwise not obtainable by clinical examination. Specific cEEG patterns predicted probability of mortality for patients according to their initial rhythm of CA as a function of cardiopulmonary resuscitation time.

1. Introduction

Therapeutic hypothermia (TH) in comatose patients after cardiac arrest (CA) resuscitation is the first therapy proven to increase survival to discharge and improved neurologic recovery [1,2]. Prior to the widespread use of TH, prognostication after CA resuscitation was based on the 2006 American Academy of Neurology guidelines for prognosis in comatose survivors after cardiopulmonary resuscitation (CPR). Recently, the reliability of these guidelines has been called into question because they were developed based on evidence prior to the advent of TH and were heavily weighted on the clinical neurologic examination, which can be confounded by the use of sedative and paralytic medication during TH [3]. There is renewed interest in the use of continuous electroencephalogram (cEEG) as an adjunctive prognostic tool in post-CA patients undergoing TH. Furthermore, the optimal goal temperature for TH has not been clearly established with equivalent mortality and neurologic outcomes reported for a goal of 33°C and 36°C [4,5].

The primary goal of this retrospective study is to examine the relationship between EEG patterns and mortality and neurologic outcomes in post-CA patients undergoing TH in an effort to provide more accurate prognostication. The secondary goal is to examine the relationship between clinical outcomes and the time from CA to target cooling temperature.

2. Materials and methods

Approval for this study was obtained from the institutional review board. The study is a single-center retrospective analysis of clinical data collection conducted by investigators blinded to patient outcomes and not involved in clinical care of patients.

The records of patients admitted to the neurologic intensive care unit who underwent cEEG monitoring between April 2010 and December

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2012 were reviewed. A total of 83 charts of consecutive patients were identified who had CA and underwent TH. All post-CA patients who were treated with TH received cEEG monitoring. According to the protocol at this institution, patients with CA, regardless of in-hospital or out-of-hospital arrest or initial cardiac rhythm, with return of spontaneous circulation (ROSC) and sustained unconsciousness were eligible for TH. Sedation was achieved with midazolam infusion at 1 mg/h to maintain a Richmond Agitation Sedation Scale of −2. Shivering was controlled with neuromuscular blockage (cisatricurium 1 μg kg^{-1} min^{-1}). Cooling to a temperature of 32°C to 34°C for at least 24 hours was achieved with a surface cooling device (Arctic Sun Temperature Management System; Medivance, Louisville, Col). Subsequent rewarming was initiated at a rate of 0.2°C per hour. Temperature was measured by indwelling bladder catheters with embedded temperature probes. All patients undergoing TH were monitored according to a standardized institutional protocol with cEEG initiated prior to and during the cooling process, and continued to be monitored until completion of the rewarming phase. Thirty-two channel digital cEEG recordings with digital video recording were acquired (Natus XLTek System, San Carlos, Calif). Full sets of gold-plated electrodes Grass Technologies (Astro-Med Inc, Warwick, RI) were applied using the international 10-20 system for electrode placement. Continuous EEG data were reviewed independently by 2 board-certified neurologists with subspecialty certifications in clinical neurophysiology who were blinded to patient outcomes (J.C. and H.T.). There was no discrepancy between the 2 EEG reviewers on interpretation of the cEEG recordings. Treatment of seizures noted during TH was determined by the Cedars Sinai Neurological Intensive Care service. Continuous EEGs findings were categorized into the following groups: diffuse slowing, epileptiform abnormality, epileptic seizure, burst suppression, low-voltage background, and isoelectric background. The decision to withdraw care was made by the neurointensivist based on clinical grounds and in discussion with the family members. Withdrawal of care decision were universally delayed for at least 48 hours after the completion of rewarming and cessation of any medications that could confound the clinical situation, such as a midazolam infusion. The electroencephalographer did not make any recommendations with regard to withdrawal of care.

Continuous EEG patterns were classified according to previously published literature [6]. Isoelectric cEEG patterns were defined as no visible cEEG. Low-voltage cEEG patterns were defined as cEEG activity less than 20 μV. Burst suppression patterns were defined by the presence of clear increases in amplitude (bursts) followed by intervals with low-voltage activity (suppression). Bursts were required to have cEEG amplitudes of greater than 20 μV. Diffuse slowing patterns were characterized by a dominant frequency less than 8 Hz. Epileptiform patterns included generalized periodic discharges and seizures.

Patients were grouped into survivors and nonsurvivors at discharge. Patients were also analyzed by grouping based on poor versus good neurologic outcomes. Neurologic outcomes were measured at the time of hospital discharge according to the following Glasgow-Pittsburg Cerebral Performance Category (CPC) 5-point scale: (1) a return to normal cerebral function and normal living; (2) cerebral disability but sufficient for independent activities of daily living; (3) severe disability, limited cognition, and inability to carry out independent existence; (4) vegetative state; and (5) death. Cerebral Performance Category scores of 1 or 2 were classified as good outcomes, whereas score of 3, 4, and 5 were considered poor outcomes. Although Glasgow Coma Scale scores were measured, they were not included in the final analysis in an effort to study the isolated prognostic value of cEEG.

For all patients, medical records were reviewed for demographic information and other medical conditions (eg, hypertension and diabetes mellitus), initial cardiac rhythm and etiology of CA, time from CA to the initiation of CPR, CPR time, time from CA to ROSC, time of CA to target temperature, admission time arterial blood gas, admission complete metabolic panel, admission complete blood count, and left ventricular ejection fraction (LVEF) as measured by transthoracic echocardiogram after ROSC.

2.1. Statistical analysis

χ^2 Test and *t* test were used to evaluate bivariate associations for binary and continuous outcome variables. Multivariate stepwise logistic regression was used to assess factors associated with mortality and poor neurologic outcomes. Adjusted odds ratio (OR), 95% confidence intervals (CIs), and *P* values were reported. All analyses used SAS version 9.1 for Windows (SAS Institute Inc, Cary, NC). Predicted probability of mortality as a function of CPR time and 95% CI were calculated using a logistic regression model.

Table 1
Characteristics of 83 CA patients treated with TH between 4/8/2010 and 12/30/2012

	All patients (n = 83)	Deceased patients (n = 49; 59.0%)	Alive patients (n = 34; 41.0%)	*P*
Age (y)				.05
Mean (SD)	62.4 (15.6)	65.0 (15.9)	58.6 (14.4)	
Median (IQR)	64 (52-74)	67 (55-75)	59 (51-69)	
Male (%)	54 (65.1)	35 (71.4)	19 (55.9)	.007
Preexisting conditions				
Diabetes mellitus	29 (34.9)	15 (30.6)	14 (41.2)	.29
Hypertension	45 (54.2)	26 (53.1)	19 (55.9)	.86
Chronic renal failure	20 (24.1)	15 (30.6)	5 (14.7)	.12
Coronary artery disease	29 (34.9)	19 (38.8)	10 (29.4)	.41
End-stage renal disease	17 (20.5)	13 (26.5)	4 (11.8)	.17
Coronary heart failure	20 (24.1)	10 (20.4)	10 (29.4)	.43
LVEF (%)				.17
Mean (SD)	44.5 (19.2)	47.1 (19.2)	40.8 (19.0)	
Median (IQR)	50 (28-60)	50 (30-62)	42.5 (25-56)	
Goal temperature (°C)				.94
Mean (SD)	33.5 (0.6)	33.5 (0.7)	33.4 (0.6)	
Median (IQR)	33 (33-34)	33 (33-34)	33 (33-34)	
Glucose level at admission (mg/dL)				.69
Mean (SD)	240.7 (93.3)	243.4 (98.6)	236.8 (86.4)	
Median (IQR)	252 (178-295)	252 (178-317)	242 (179-289)	
Creatinine level at admission (mg/dL)			.07	
Mean (SD)	2.4 (2.4)	2.7 (2.5)	2.0 (2.2)	
Median (IQR)	1.4 (1.1-2.5)	1.6 (1.1-3.3)	1.3 (1,2)	
pH level at admission				<.0001
Mean (SD)	7.3 (0.2)	7.2 (0.2)	7.4 (0.1)	
Median (IQR)	7.3 (7.2-7.4)	7.2 (7.1-7.3)	7.4 (7.3-7.4)	