Current Literature
In Clinical Science

The Role of EEG After Cardiac Arrest and Hypothermia

Continuous EEG in Therapeutic Hypothermia After Cardiac Arrest: Prognostic and Clinical Value.

Crepeau AZ, Rabinstein AA, Fugate JE, Mandrekar J, Wijdicks EF, White RD, Britton JW. *Neurology* 2013;80:339–344.

OBJECTIVES: To determine the prognostic value of an EEG grading scale and clinical outcome of treated seizures detected with continuous EEG (cEEG) during therapeutic hypothermia (TH) and rewarming post cardiac arrest (CA). METHODS: Our cohort study retrospectively reviewed the electronic medical records and cEEGs of all patients undergoing TH after CA under protocol over 2 years. cEEG was initiated during TH and continued until restoration of normothermia (NT). EEGs were graded 1–3 (3 = most severe) using a departmentally developed EEG severity grading scale by 2 authors blinded to clinical outcome. Outcome was measured using the Cerebral Performance Category scale; grades 1–2 were considered a "good" outcome, "3–5" poor. RESULTS: Fifty-four patients were included; 51 remained on cEEG through NT. Nineteen died. EEG severity grading during both TH and NT statistically correlated with outcome (grade 1 = good, grade 3 = poor). Other EEG features correlating with poor outcome included seizures, nonreactive background, and epileptiform discharges. Changes in EEG grade during monitoring did not statistically correlate with outcome. Five patients had seizures; all occurred in patients with grade 3 EEG backgrounds and all had a poor outcome. CONCLUSION: Grades 1 and 3 on our EEG severity grading scale during TH and NT correlated with outcome. Treating seizures did not improve outcome in our cohort.

Commentary

Despite decades of research, the exact role of EEG in predicting and improving outcomes in survivors of cardiac arrest (CA) remains a hot topic of discussion. *Here are the facts:* Since the 1960s, EEG has become an integral part of prognostication after CA (1). In 2002, two randomized clinical trials documented the benefits of mild therapeutic hypothermia (TH) in comatose survivors of CA, improving neurologic outcomes and survival (2). In 2005, the American Heart Association recommended TH as a standard of care (3), and in 2006, the American Academy of Neurology (AAN) formalized outcome prediction in comatose survivors, after cardiopulmonary resuscitation, through practice guidelines (4). So, on the surface, we have an effective treatment and "officially endorsed" guidelines for using various tools, including EEG, in prognostication. *Here is the catch:* despite TH, almost half of patients still do poorly after CA, and all the data driving the AAN guidelines were generated *before* the routine implementation of TH. Yet, many prognostication criteria are potentially affected by TH. A recent prospective study showed a higher rate of false positive rate (FPR) mortality predictions using incomplete recovery of brainstem reflexes (4% FPR), myoclonus (3% FPR), and absent motor response to pain (24% FPR) in the TH population compared with CA survivors from the pre-TH era (0% FPR for all these variables) (5). The door then remains open for work like the study by Crepeau et al., chosen for this commentary, to evaluate the current role of EEG.

Where Do We Stand Now?

First, EEG Findings Remain Highly Predictive of Neurologic Outcome After the Routine Implementation of TH.

The study at hand classifies the "traditional malignant" EEG findings of burst suppression, low-voltage output pattern, alpha/theta coma, focal or generalized seizures, generalized periodic epileptiform discharges, status epilepticus, and background unreactivity into a "grade 3" or "severe" abnormality. Eighty-nine percent of patients with grade 3 abnormality during TH and all those who had it during subsequent normothermia had a poor neurologic outcome (high specificity). Conversely, 76% of patients with a poor outcome had a grade 3 abnormality (high sensitivity). All the patients with mild (grade 1) abnormalities as defined by excessive beta, theta slowing, or anesthetic pattern during TH or normothermia recovered with no to moderate disability. This and other grading systems (1, 6) offer reasonable accuracy but require the clinician to remember the individual classification. An alternate practical approach focuses on the prognostic significance of one critical EEG finding: the extent of background reactivity. In several recent studies (5, 7–9), a nonreactive EEG background was incompatible with good neurologic recovery (100% specificity), regardless of whether it was seen within 12, 24, or 72 hours after CA. The sensitivity of this EEG finding varies from 40% (8) to 81% (5), with an accuracy of 81% (5). Overall, it seems then that—short of applying a comprehensive grading scale—as-

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sessing background EEG reactivity is a very useful and valid prognostication tool, regardless of core temperature and sedation levels. Work to quantify and characterize the value of using EEG severity grading scales as opposed to relying on individual findings (such as EEG reactivity) would be helpful.

Second, EEG Alone Is Insufficient to Adequately Predict Neurologic Outcome.

In Crepeau et al., as shown previously (5, 7–10), an unacceptably high number of survivors would be missed if EEG classification were used as the sole prognostic tool. Incorporating additional clinical and electrophysiological indicators improves the accuracy of assessment (4). In a recent prospective study (5), the best prediction of poor long-term neurologic outcome in survivors of CA treated with TH (100% specificity, 100% positive predictive value) was accomplished with the presence of any two of the following four independent outcome predictors: 1) nonreactive EEG background, 2) incomplete recovery of brainstem reflexes, 3) bilaterally absent Somatosensory Evoked Potentials (SSEP)s, and 4) myoclonus. For this sick patient population, a multidisciplinary and conservative approach seems justifiable.

Where Do We Go From Here?

The first obvious question is: Do we really need continuous video-EEG (c-EEG) for prognostication in *all* CA survivors treated with TH, or can this practice be tailored to particular patient populations, at particular times? Even though EEG patterns changed in up to 25% of patients in Crepeau et al., this change would have had a prognostic implication (into or out of a grade 1 or 3 severity degree) in only 16%. In continuous EEG studies of TH patients, prognostication was related to the presence or absence of specific EEG characteristics at specific time points, rather than findings throughout the entirety of the record: for example, outcome was good in all patients with a continuous EEG pattern 12 hours post resuscitation, and poor in all patients with iso-electric or low-voltage EEG 24 hours post resuscitation (8). Most studies do in fact concur that even when EEG changes occur in this patient population, the evolution is over several hours to days, so the question of whether continuous recording is necessary naturally poses itself. Could the same clinical information be derived from periodic EEG recordings? In an evolving landscape of healthcare delivery, proving the superiority of a more-expensive and labor-intensive technique falls upon us. In this context, superiority would be defined as "added value" and "advanced performance" in improving patient outcomes, and not simply a higher rate of detecting findings of questionable clinical implications on patient care.

The second question is tightly linked to the above c-EEG discussion and relates to the significance of seizures in CA survivors treated with TH. In Crepeau et al., all patients with seizures died, although seizures were successfully controlled in more than 80% of the cases. Similarly, seven out of eight TH patients with seizures died in another study (9). The two common features that unite these seizure-related mortalities are that 1) seizures started *during* the hypothermia phase, and 2) seizures emerged out of a nonreactive EEG background. In fact, survivors of postanoxic seizures typically have their first seizures during the rewarming or late phases of hypothermia (7) and have preserved background reactivity. Considering that hypothermia itself carries some neuroprotective effects (2, 3, 5, 7, 9), one could hypothesize that seizures *during* TH are simply a reflection of the severity of the underlying insult, better reflected by the background EEG activity; so detecting these seizures—and possibly even treating them—does not necessarily alter prognosis. For patients then with a nonreactive background or seizures during the TH phase, the exact role of further prolonging cEEG remains unclear. Later seizures, starting during or after rewarming, especially when arising from a reactive EEG background, represent a different category where treatment may actually make a difference. Confirming the distinction between these two "seizure categories," clarifying the role of c-EEG in this setting (to detect subclinical seizures), and documenting the outcome implications of treating seizures are all questions needing further research.

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