Epilepsy Currents
2019, Vol. 19(1) 24-26

DOI: 10.1177/1535759718822037
journals.sagepub.com/home/epi
SAGE

Continuous EEG Monitoring—The Neurologist's Crystal Ball

Time to Epileptiform Activity and EEG Background Recovery Are Independent Predictors After Cardiac Arrest

Westhall E, Rose I, Rundgren M, Bro-Jeppesen J, Kjaergaard J, Hassager C, Lindehammar H, Horn J, Ullen S, Nielsen N, Friberg H, Cronberg T. *Clin Neurophysiol*. 2018;129:1660-1668. doi:10.1016/j.clinph.2018.05.016

Objective: To investigate the temporal development of electroencephalogram (EEG) and prognosis. Methods: Prospective observational substudy of the Target Temperature Management trial. Six sites performed simplified continuous EEG monitoring (cEEG) on comatose patients after cardiac arrest, blinded to treating physicians. We determined time points of recovery of a normal-voltage continuous background activity and the appearance of an epileptiform EEG, defined as abundant epileptiform discharges, periodic/rhythmic discharges, or electrographic seizure activity. Results: One hundred thirty-four patients were included, of which 65 had a good outcome. Early recovery of continuous background activity (within 24 hours) occurred in 72 patients and predicted good outcome since 55 (76%) had good outcome, increasing the odds for a good outcome 7 times compared to a late background recovery. Early appearance of an epileptiform EEG occurred in 38 patients and 34 (89%) had a poor outcome, increasing the odds for a poor outcome 6 times compared to a late debut. The time to background recovery and the time to epileptiform activity were highly associated with outcome and levels of neuron-specific enolase. Multiple regression analysis showed that both variables were independent predictors. Conclusions: Time to epileptiform activity and background recovery are independent prognostic indicators. SIGNIFICANCE: Patients with early background recovery combined with late appearance of epileptiform activity may have a good outcome.

Commentary

Neurologists are frequently called upon to prognosticate the outcome of a patient after cardiac arrest (CA). The need for such prognostication cannot be overstated: families are anxious to know whether their loved one will get better; care teams are eager to decide how "aggressive" their treatment approach should be; and hospitals, insurance providers, and the community at large is concerned about escalating health-care costs in the final days of life. Moreover, the prognosis is being demanded earlier and earlier despite institution of many therapeutic measures in recent years that may improve survivability.

The American Academy of Neurology published a Practice Parameter on predicting outcome in survivors of CA in 2006.[1] Absent pupillary light responses or corneal reflexes; extensor posturing or no response to pain; myoclonus status epilepticus (SE); absent cortical waveforms (N20) of median nerve somatosensory evoked potentials; and serum neuron-specific enolase levels >33 μg/L were thought to be reliable predictors of poor outcome 3 days after CA. The Practice Parameter also noted that an electroencephalogram (EEG) showing generalized suppression (≤20 μV), burst-suppression pattern with generalized epileptiform activity, and generalized periodic discharges were highly, but not invariably, associated with poor outcome. However, at the time this Practice Parameter was published, therapeutic hypothermia (TH) was not routinely used and descriptions of EEG patterns seen in critically ill patients were not standardized. With the increasing use of TH, availability of continuous EEG monitoring (cEEG) and better definition of EEG terminology, a reappraisal of the role of EEG in prognostication is necessary.

A new study by Westhall and colleagues reports on cEEG data in 134 patients enrolled in the Targeted Temperature Management (TTM) trial. They found that recovery of continuous normal voltage (>20 μV) EEG activity at 24 hours after CA was associated with a good outcome in 55 of 72 patients (positive predictive value [PPV] of 76%). If continuous normal background appeared between 36 and 60 hours, 21 of 31 patients had a poor outcome (PPV of 68%). Appearance of epileptiform activity (including abundant epileptiform discharges, periodic or rhythmic discharges, electrographic seizures or SE) within 24 hours was associated with poor outcome, seen in 34 of 38 patients with this pattern (PPV of 89%). If the epileptiform activity occurred after 24 hours, patients were less likely to have a poor outcome (16 of 28 patients, PPV 57%). The background activity and presence of epileptiform activity were independent predictors of outcome. The degree of hypothermia did not affect these findings.This study provides a unique perspective as it evaluated a subgroup of patients enrolled in a larger prospective, controlled trial that randomized unconscious patients with out of hospital CA of presumed cardiac cause to 33°C versus 36°C control temperature and reported no differences in mortality or neurocognitive function (Nielsen et al, 2013.]. Continuous EEG monitoring was obtained, but its interpretation was not provided to the clinicians caring for the patients and consequently was not used to determine whether withdrawal of life-sustaining therapy (WLST) should be instituted. Rather, WLST was based on predetermined criteria that did not include EEG results. In many previous studies, clinicians were not blinded to EEG interpretation, leading to concerns that the EEG results were a "self-fulfilling prophecy." The EEGs were analyzed in predetermined time intervals up to 60 hours following CA and interpretations followed standardized criteria and nomenclature proposed by the American Clinical Neurophysiology Society.[2] This allowed reporting of evolving findings in a reliable and reproducible manner. This study, however, evaluated only 134 of the 939 patients enrolled in the TTM trial. Only 6 of the sites participated in this sub study of the TTM trial, and of these, 2 sites had no prior experience with cEEG. Most patients were enrolled from the 4 sites that had experience. In all sites, a limited 6-channel EEG was used for cEEG. The authors also note that while they tried to withhold results of the EEG from the treating clinicians, sometimes technical problems or clinical convulsions made it challenging to do so. In addition, the analyses performed in the paper were only designed to investigate the prognostic relation between development of background and epileptiform activity, rather than to establish reliable outcome predictors. While these limitations are important to note, this study helps update our knowledge on how to use cEEG in prognosticating outcome in patients with CA undergoing TH.

Previous studies have also noted similar findings. Many EEG findings can be very helpful in accurate prognostication even in the TH era:

- Suppressed or very low-amplitude (<20 μV) EEG 24 hours after CA has consistently been associated with poor prognosis, with many studies demonstrating a false positive rate of 0%.[3-6]
- Epileptiform activity, including spikes, periodic discharges, electrographic seizures, stimulus-induced rhythmic, periodic, or ictal-appearing discharges, and SE, has traditionally been associated with poor outcomes.[7,8] The study by Westhall and colleagues also supports this view. This is particularly the case if the seizures arise from a burst-suppression background.[9] However, some patients being treated with TH that have electrographic seizures have had a favorable outcome.[4,10] This is more likely if the seizures arise from an EEG background that is continuous and reactive.
- Burst-suppression pattern is often associated with poor outcome.[3,5,11] It is most reliable as a predictor of poor outcome when it occurs after return to normothermia.[4] While undergoing TH, some patients may have a burst-suppression pattern that improves upon rewarming. The initial 500 ms of the bursts may provide a clue; if the start of the bursts is similar ("identical bursts"), the pattern is more likely to be associated with poor outcome regardless of whether it occurs during or after TH.[12]
- Nonreactive EEG is very often associated with poor outcome, but for this finding to be most reliable, it should be checked after rewarming.[3-5] During TH, some patients may have a nonreactive EEG, only to improve with normothermia.[4] Studies typically do not describe how reactivity testing was performed, however.
- Alpha and theta coma patterns are associated with poor outcomes.[13] These patterns are often associated with a nonreactive EEG. Non classical alpha coma patterns that do not have an anteriorly dominant, nonreactive alpha frequency may not have the same unfavorable prognosis.[14]
- Spindle coma and rhythmic delta activity when seen in comatose patients after CA has a more favorable prognosis, with poor outcomes occurring in 23% and 43% of patients, respectively.[13]
- Continuous background EEG activity (>20 μV) in the first 24 hours after CA is associated with a favorable outcome.[11,15]

Prognosticating the outcome of coma after CA is a remarkable responsibility. The consequences of an inaccurate prediction are severe, especially if an inappropriately unfavorable prognosis is given. Despite the use of TH, EEG, and especially cEEG remain very useful tools to aid in prognostication. Advances in quantitative EEG analysis are likely to enhance the value of this important test. However, this is only one of several tools at the disposal of the neurologist when looking into the crystal ball and trying to predict the future; the neurologic exam and other ancillary tests also remain very helpful in this important endeavor.

By Aatif M. Husain

References

1. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S; Quality Standards Subcommittee of the American Academy of N. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;67(2):203-210.
2. Hirsch LJ, LaRoche SM, Gaspard N, et al. American clinical neurophysiology society's standardized critical care EEG terminology: 2012 version. *J Clin Neurophysiol*. 2013;30(1):1-27.
3. Golan E, Barrett K, Alali AS, et al. Predicting neurologic outcome after targeted temperature management for cardiac arrest:

systematic review and meta-analysis. *Crit Care Med*. 2014;42(8): 1919-1930.
4. Sandroni C, Cavallaro F, Callaway CW, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: a systematic review and meta-analysis. Part 2: patients treated with therapeutic hypothermia. *Resuscitation*. 2013; 84(10):1324-1338.
5. Sivaraju A, Gilmore EJ, Wira CR, et al. Prognostication of post-cardiac arrest coma: early clinical and electroencephalographic predictors of outcome. *Intensive Care Med*. 2015;41(7):1264-1272.
6. Soholm H, Kjaer TW, Kjaergaard J, et al. Prognostic value of electroencephalography (EEG) after out-of-hospital cardiac arrest in successfully resuscitated patients used in daily clinical practice. *Resuscitation*. 2014;85(11):1580-1585.
7. Crepeau AZ, Rabinstein AA, Fugate JE, et al. Continuous EEG in therapeutic hypothermia after cardiac arrest: prognostic and clinical value. *Neurology*. 2013;80(4):339-344.
8. Rossetti AO, Carrera E, Oddo M. Early EEG correlates of neuronal injury after brain anoxia. *Neurology*. 2012;78(11):796-802.
9. Rundgren M, Westhall E, Cronberg T, Rosen I, Friberg H. Continuous amplitude-integrated electroencephalogram predicts outcome in hypothermia-treated cardiac arrest patients. *Crit Care Med*. 2010;38(9):1838-1844.
10. Legriel S, Hilly-Ginoux J, Resche-Rigon M, et al. Prognostic value of electrographic postanoxic status epilepticus in comatose cardiac-arrest survivors in the therapeutic hypothermia era. *Resuscitation*. 2013;84(3):343-350.
11. Cronberg T, Brizzi M, Liedholm LJ, et al. Neurological prognostication after cardiac arrest—recommendations from the Swedish Resuscitation Council. *Resuscitation*. 2013;84(7): 867-872.
12. Hofmeijer J, Tjepkema-Cloostermans MC, van Putten MJ. Burst-suppression with identical bursts: a distinct EEG pattern with poor outcome in postanoxic coma. *Clin Neurophysiol*. 2014;125(5): 947-954.
13. Muhlhofer W, Szaflarski JP. Prognostic value of EEG in patients after cardiac arrest—an updated review. *Curr Neurol Neurosci Rep*. 2018;18(4):16.
14. Berkhoff M, Donati F, Bassetti C. Postanoxic alpha (theta) coma: a reappraisal of its prognostic significance. *Clin Neurophysiol*. 2000;111(2):297-304.
15. Cloostermans MC, van Meulen FB, Eertman CJ, Hom HW, van Putten MJ. Continuous electroencephalography monitoring for early prediction of neurological outcome in postanoxic patients after cardiac arrest: a prospective cohort study. *Crit Care Med*. 2012;40(10):2867-2875.