Association Between EEG Patterns and Serum Neurofilament Light After Cardiac Arrest

A Post Hoc Analysis of the TTM Trial

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Study Question
Is there an association between highly malignant patterns on EEG and serum neurofilament light (NfL) levels in patients in a coma after cardiac arrest?

What Is Known and What This Paper Adds
Recent guidelines list highly malignant EEG patterns as predictors of poor neurologic outcome in patients who survive a cardiac arrest. Studies for prediction of neurologic outcome often permit clinical decision-making based on the results from the same examinations, raising the possibility of self-fulfilling prophecies. NfL is a measure of the extent of brain injury and may serve as a surrogate marker for neurologic outcome, reducing this potential. This study’s results show that benign, malignant, and highly malignant EEG patterns are associated with serum NfL levels.

Methods
This post hoc analysis of the Target Temperature Management After Out-of-Hospital Cardiac Arrest trial (TTM-trial) included 262 unconscious patients examined with both EEG and serum NfL. Routine EEGs were prospectively performed after the temperature intervention ≥36 hours postarrest. Patients who awoke or died prior to 36 hours postarrest were excluded. EEG experts blinded to clinical information classified EEG background, the amount of discharges, and highly malignant EEG patterns according to the standardized American Clinical Neurophysiology Society terminology. Prospectively collected serum samples were analyzed for NfL after trial completion using an ultrasensitive Simoa assay. The highest available concentration at 48 or 72 hours postarrest was used.

Results and Study Limitations
Patients with highly malignant EEG patterns had 2.9 times higher (95% CI 1.4–6.1) NfL levels than patients with malignant patterns and NfL levels were 13 times higher (95% CI 6.5–26.2) in patients with malignant patterns than those with benign patterns. Both background and the amount of discharges were independently associated with NfL levels (p < 0.001), but the EEG background had a stronger association with NfL levels (R² = 0.30 and R² = 0.10, respectively). EEG patterns >36 hours after cardiac arrest reflect the extent of brain injury as measured by NfL in serum. Limitations of this study include the late timing of examination and the single timepoint of examination. We cannot exclude occurrence of electrographic seizures, potentially affecting NfL levels, not detected by routine EEG.

Registration, Study Funding, and Competing Interests
This study was registered at ClinicalTrials.gov (ID NCT01020916). This study was funded by governmental institutions, national institutions, and private foundations. Some authors report receiving consulting fees and speaking fees from several drug and biotech companies or additional commercial interests. Go to Neurology.org/N for full disclosures.
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