INVITED COMMENTARY

Neurological Prognostication Using Electroencephalogram in Adult Veno-arterial Extracorporeal Membrane Oxygenation: Limitations and Recommendations

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Acute brain injuries (ABIs) and neurological complications are associated with an increased morbidity and mortality in patients with veno-arterial extracorporeal membrane oxygenation (V-A ECMO) [1, 2]. However, due to lack of standardized definitions and neuromonitoring protocols for neurological complications in patients with V-A ECMO support, the true prevalence of ABIs is unknown and the detection of ABI is often delayed. As a result, information on neurological prognostication is sparse, especially for persistently comatose V-A ECMO patients.

Electroencephalogram (EEG) is used to neurologically prognosticate patients with clinically significant ABIs with disorders of consciousness [3]. Malignant EEG patterns such as suppression, suppression with periodic discharges, burst-suppression, and nonreactive background in patients after cardiac arrest have been considered as useful prognostic markers for predicting unfavorable neurological outcome in patients after cardiac arrest [4]. Recently, a continuous EEG background, a favorable EEG pattern, if seen as early as at 12 h after cardiac arrest was shown to be associated with favorable neurological outcome [5, 6]. Unfortunately, these studies are typically limited by confounding factors such as sedation,

hypothermia, and a self-fulfilling prophecy with high proportion of patients undergoing withdrawal of life-sustaining therapy (WLST) [7].

In this issue of *Neurocritical Care*, Magalhaes et al. presented their interesting results from a prospective cohort study of adult V-A ECMO patients for refractory cardiogenic shock or cardiac arrest who underwent early 30-min EEG (median 2 days) at a single tertiary center [8]. The authors demonstrated that an early discontinuous and unreactive EEG pattern was associated with an increased mortality at 28 days. They also described that an unreactive EEG in addition to a discontinuous EEG background and a low background frequency (≤ 4 Hz) had a false positive rate of 0% for predicting unfavorable outcome with low sensitivities (8% and 6%, respectively).

Similarly, another prospective observational single-center study of continuous EEG (cEEG) monitoring of comatose ECMO patients (92% V-A ECMO) showed that absence of EEG reactivity with a fair frequency mix predicted unfavorable neurological outcome at discharge [9]. In this study, EEG was monitored for > 24 h, off sedation, and the median time from ECMO cannulation to EEG was 3 days (vs. 30 min, on sedation and median time 2 days in the current study) [9].

EEG studies in patients with ECMO are limited to a few reports and the information presented in the study by Magalhaes et al. [8] adds to our knowledge. The study further underscores the value of EEG monitoring where standard neurological examination is fairly limited. However, several important limitations need to be discussed.

First, caution should be taken regarding early neurological prognostication after ABI. In fact, many

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comatose survivors after cardiac arrest may have delayed awakening [10]. EEG patterns, if evaluated early and continuously after cardiac arrest, often change significantly in the first few days. The results of this study should be considered carefully and not be used to make a premature prognostication decision, especially, when a significant portion of deaths in ECMO is due to WLST (40%), which may lead to a self-fulfilling prophecy.

Secondly, the study includes only six patients with extracorporeal cardiopulmonary resuscitation (ECPR) and the overall mortality was 52% at discharge. This indicates that the study cohort was less critical ill compared to typical V-A ECMO patients. Patients with post-cardiotomy shock or ECPR—two common indications for V-A ECMO—were under-represented in this study. Therefore, the EEG findings in the presented study are not generalizable.

Thirdly, EEG findings are most helpful when neurological diagnoses with neuroimaging data are available, which are lacking in the current study. It is notable that in a series of comatose V-A ECMO patients with cEEG monitoring showing absence of EEG reactivity and a poor neurological exam, 50% had no significant brain injury at the postmortem autopsy to explain the “coma”. This suggests that an “unreactive” EEG may not necessarily be associated with devastating brain injury [11].

Lastly, the degree of sedation and its impact on EEG suppression and reactivity was not controlled, which is particularly important in V-A ECMO population where hepatic and renal dysfunctions are commonly observed.

Despite these limitations, Magalhaes et al. present a large prospective ECMO EEG study with 122 patients, highlighting the importance of standardized EEG monitoring in ECMO population [8]. We suggest further research and societal efforts to improve neurological care in ECMO patients. As the use of ECMO is increasing, it is time for ECMO clinicians to develop standardized and precise definitions for neurological variables, sedation cessation strategy, and a standardized multimodal neuromonitoring protocol [12]. Then, what might a protocol to neurologically monitor ECMO patients look like?

- (1) EEG monitoring for patients with disorder of consciousness off sedation.
 - a. We recommend daily sedation cessation to assess neurological status and a complete sedation cessation by day 3–5 as possible.
 - b. We recommend cEEG rather than routine EEG for a continuous assessment of a potentially evolving or improving brain injury.

- (2) Somatosensory evoked potential for patients with motor Glasgow Coma Scale < 4.
- (3) Daily or intermittent transcranial Doppler ultrasound plus emboli monitoring.
- (4) Continuous cerebral near-infrared spectroscopy monitoring.
- (5) Early and routine CT scan of brain in all ECMO patients.
- (6) Avoidance of early neurological prognostication.

It is important to note that there are limited data on how to utilize these tools in ECMO patients. Further research is warranted to study how to best use each modality to predict neurological injury and outcome. However, given limited intervention options available for ECMO-associated ABIs, we believe this standardized approach will allow for early detection and prevention and is critical for improving neurological outcome.

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