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Response to "Categorization of post-cardiac arrest patients according to the pattern of amplitude-integrated electroencephalography after return of spontaneous circulation"

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See related research by Sugiyama et al., https://ccforum.biomedcentral.com/articles/10.1186/s13054-018-2138-2

We read with great interest the recent article by Sugiyama et al. [1], "Categorization of post-cardiac arrest patients according to the pattern of amplitude-integrated electroencephalography after return of spontaneous circulation." However, we have some concerns in regards to their study conclusion. The authors claimed that they can successfully categorize patient's neurological prognoses according to their pattern of electroencephalography (EEG) during the early post-cardiac arrest period, which could be used as a potential guide to customize post-cardiac arrest care for each patient.

Early studies have shown that reductions in core temperature during therapeutic hypothermia (TH) cause vaso-constriction and shivering, which result in skin breakdown, infection, and increased oxygen consumption [2]. To prevent the above observed complications, anesthetics and sedatives were administered during TH in adult and pediatric patients after cardiac arrest (CA).

EEG has exhibited a direct reflection of the effects of sedatives and anesthetics on patients and offers unique guidance on the adequacy of anesthesia [3]. Under such circumstances, an important question is raised: the EEG may not reflect the patient's true neurological status during the phase of mild TH with sedative and anesthetic intervention after CA.

The EEG pattern could be inadvertently altered by sedatives and anesthetics, and not be the native representation of patient brain function during the interventional period of mild TH. In addition, it is still debatable how to precisely titrate the depth of sedation during TH for patients after CA. Furthermore, the pharmacokinetics of sedative regimens may be altered under mild hypothermia and result in prolonged systemic clearance of anesthetic agents. There may be accumulative effects of sedatives for CA patients who have undergone TH, which leads to delay in awakening, extending the duration of mechanical ventilation and other subsequent complications [4]. Mild TH plus the cumulative effect of sedatives could have a significant impact on the activity of brain function; one would suspect that the predictive value of the EEG could be obscured [5]. Therefore, when sedatives and anesthetics are given to patients during TH after CA, the EEG is not consistent and its predictive value becomes questionable.

From the discussion above, the current study by Sugiyama et al. did not provide convincing evidence that the EEG pattern has reliable value in predicting a patient's neurological prognosis when influenced by hypothermia and sedative agents. We suggest that further study is necessary to elucidate the relationship between EEG and neurological outcome after CA.

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Authors' response

Kazuhiro Sugiyama

We would like to thank Dr. Li and colleagues for their letter.

They comment on the influence of sedatives during target temperature management (TTM) on EEG. However, the administration of sedatives during TTM is currently required for any prognostic study after cardiac arrest, and many studies have reported the usefulness of continuous EEG in this field [6, 7].

Our study showed that post-cardiac arrest patients could be categorized according to their neurological prognosis using the recovery time to continuous normal voltage and the presence of burst suppression in amplitude-integrated EEG (aEEG) monitoring. In our study, 0.05–0.1 mg/kg/h midazolam was used for sedation and a muscle relaxant was used to control shivering. In another study by Oh et al. evaluating the pattern of aEEG in post cardiac patients, 0.04–0.2 mg/kg/h midazolam and a muscle relaxant were also administered [8]. The cut-off for continuous normal voltage (CNV) recovery time for predicting good neurological outcome was around 24 h in both studies [8, 9]. Furthermore, although the prolonged sedation caused by accumulation of medication could affect the CNV recovery time, a recovery time of more than 36 h predicted poor neurological outcomes in both studies. In the sedation protocol with the administration of this dose of midazolam and a muscle relaxant, the categorization suggested in our study could contribute to precise prognostication and determination of the severity of hypoxic encephalopathy.

However, as Dr. Li pointed out, the sedation protocol during TTM remained undetermined. If propofol or a higher dose of midazolam is used for sedation during TTM, the CNV recovery time might be affected. To our knowledge, no prior study evaluated the difference in CNV recovery time among different sedatives in post-cardiac arrest patients. Furthermore, the meaning of burst suppression might be different between midazolam and propofol. As we discussed in the article, burst suppression can be induced by propofol, and might lose its meaning as a predictor of neurological prognosis in a sedation protocol using propofol.

We believe it is worth investigating whether the categorization in our study can predict prognosis in post-cardiac patients with good accuracy using different sedation protocols during TTM.

Authors' contributions

JL participated in the sequence alignment and drafted the manuscript, and NTL, GYP conceived of the study and participated in its design and coordination. All authors read and approved the final manuscript.

Competing interests

The authors all declare that they have no competing interests.

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