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INVITED COMMENTARY

Neuroprognostication Under ECMO After Cardiac Arrest: Impossible is Nothing!

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Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is increasingly used to treat patients with refractory cardiac arrest (i.e., extracorporeal cardiopulmonary resuscitation) or postcardiac arrest refractory shock. Postresuscitation care guidelines from 2021 recommend the use of a multimodal prognostication algorithm including clinical examination, electrophysiology, biomarkers, and imaging. This algorithm should be proposed for all patients who remain comatose with a Glasgow motor score of ≤ 3 at ≥ 72 h after the return of spontaneous circulation in the absence of common confounders, such as residual sedation and hypothermia [1]. Whether this algorithm is applicable to patients with extracorporeal cardiopulmonary resuscitation or patients with postcardiac arrest shock treated with VA-ECMO is questionable. Multimodal prognostication is a complex task in this setting, as most patients receive sedation for several days, making early clinical evaluation difficult. Electroencephalography (EEG) and somatosensory evoked potential (SSEP) studies appear feasible, but their diagnostic performances to predict outcome in patients with cardiac arrest have not been thoroughly investigated [2–6]. Elevated serum levels of neuron-specific enolase (NSE), a blood biomarker of neuronal injury, are associated with poor outcomes in patients treated with VA-ECMO [7–9]. However, VA-ECMO is associated with significant hemolysis, which may confound the performance profile of NSE in the acute phase. Finally, magnetic resonance studies to diagnose hypoxic-ischemic brain injury are contraindicated because of the metallic nature of the ECMO device.

In a single-center study published in the journal, Ben-Hamouda et al. [10] report diagnostic performances of routinely used predictors of poor neurological outcome after cardiac arrest in adult patients treated with VA-ECMO. By using a multimodal approach on the basis of the most recent international recommendations, the authors carefully evaluated 50 consecutive adult patients treated with VA-ECMO. Values obtained in the VA-ECMO population were compared with those of 397 patients with cardiac arrest treated without VA-ECMO.

The criterion for poor functional outcome at 3 months was a Cerebral Performance Category score of 3 to 5, indicating severe disability or death. Withdrawal of life-sustaining therapies was decided in the presence of at least two common predictors of poor outcome among clinical findings (loss of brainstem reflexes, myoclonus), EEG (repetitive epileptiform discharges, lack of reactivity), and SSEP studies (bilateral loss of N20 waves).

Compared with patients not treated with ECMO, patients treated with ECMO were younger, with a longer time to return of circulation and a worse functional outcome at 3 months. Clinical features (i.e., absent pupillary responses, early myoclonus) and electrophysiological patterns (unreactive and/or discontinuous EEG background, bilateral absence of SSEP) associated with poor outcome were comparable between the two groups. By contrast, NSE levels within 48 h were significantly higher in patients treated with ECMO, as compared with those of patients not treated with ECMO.

The presence of any two of the poor outcome criteria from the 2021 postresuscitation care guidelines (i.e., no pupillary reflex at 72 h, myoclonus, bilaterally absent SSEP, highly malignant EEG within 36–72 h, and/or NSE > 60 µg/l within 48 h) showed a high specificity (i.e., a low false positive rate) for the prediction of poor

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outcome at 3 months in the whole population (specificity 99.4%), in patients treated with ECMO (specificity 100%), and in patients not treated with ECMO (specificity 99.3%). However, the heterogenous performance of the different poor outcome indicators deserves further consideration. First, the specificity of the two clinical parameters (i.e., absent pupillary reflex and myoclonus) was not excellent, especially for patients treated with ECMO (< 93%), highlighting the limits of qualitative clinical evaluation for outcome prediction in this setting. Second, the sensitivities of EEG and SSEP criteria were low, especially for patients treated with ECMO, confirming the importance of a multimodal approach for prognosticating these patients. Finally, among all indicators, an NSE > 60 µg/l within 48 h had the best performance profile for the prediction of poor outcome, with a specificity > 98% and a relatively high sensitivity. Interestingly, the authors observed similar predictive performances of NSE between patients treated with ECMO and patients not treated with ECMO, with areas under the receiver operating characteristic curve of 0.787 and 0.824, respectively.

The authors should be commended for reporting the comparison of several established indicators of poor outcome after cardiac arrest between patients treated with ECMO and patients not treated with ECMO. Although the results of the study suggest that the 2021 recommended algorithm is applicable to patients treated with ECMO, several points should be borne in mind. The study had limitations inherent to a single-center design. Neuroimaging was not used routinely, and therefore neuroimaging studies could not be integrated into the algorithm. Moreover, in the absence of adjusted analyses, it is not known to what extent imbalances for age and time to return of circulation observed between patients treated with ECMO and patients not treated with ECMO impacted the study results.

In conclusion, a systematic multidisciplinary approach is required in patients with cardiac arrest treated with VA-ECMO, not only to avoid continuing futile and expensive therapies when poor neurological outcomes are likely but also to avoid inappropriate withdrawal of life-sustaining therapies in patients who may otherwise have a chance of achieving neurological recovery [11, 12]. The current study provides new insights in the field and suggests that electrophysiological parameters and serum NSE may be of special interest in patients treated with VA-ECMO. Future research should focus on gathering prospective, multicenter, observational data from high-volume ECMO centers. Prognostication algorithms should be a priori defined, and decisions to withdraw life-sustaining therapies should be protocolized. New outcome parameters should be developed by using a quantitative approach, and results should not be communicated to caregivers before the end of the study to avoid the self-fulfilling prophecy. Apart from functional outcome assessments, core outcome measurements including data on cognitive function and quality of life at 3 or 6 months may provide critical information on neurological recovery in survivors [13].

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References

1. Nolan JP, Sandroni C, Böttiger BW, et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med. 2021;47(4):369–421.
2. Sinnah F, Dalloz M-A, Magalhaes E, et al. Early electroencephalography findings in cardiogenic shock patients treated by venoarterial extracorporeal membrane oxygenation. Crit Care Med. 2018;46(5):e389–94.
3. Magalhaes E, Reuter J, Wanono R, et al. Early EEG for prognostication under venoarterial extracorporeal membrane oxygenation. Neurocrit Care. 2020;33(3):688–94.
4. Peluso L, Rechichi S, Franchi F, et al. Electroencephalographic features in patients undergoing extracorporeal membrane oxygenation. Crit Care. 2020;24(1):629.
5. Cho S-M, Ziai W, Mayasi Y, et al. Noninvasive neurological monitoring in extracorporeal membrane oxygenation. ASAIO J. 2020;66(4):388–93.
6. Cho S-M, Choi CW, Whitman G, et al. Neurophysiological findings and brain injury pattern in patients on ECMO. Clin EEG Neurosci. 2019. https://doi.org/10.1177/1550059419892757.
7. Floerchinger B, Philipp A, Camboni D, et al. NSE serum levels in extracorporeal life support patients-relevance for neurological outcome? Resuscitation. 2017;121:166–71.
8. Schrage B, Rübsamen N, Becher PM, et al. Neuron-specific-enolase as a predictor of the neurologic outcome after cardiopulmonary resuscitation in patients on ECMO. Resuscitation. 2019;136:14–20.
9. Reuter J, Peoch K, Bouadma L, et al. Neuron-specific enolase levels in adults under venoarterial extracorporeal membrane oxygenation. Crit Care Explor. 2020;2(10):e0239.
10. Ben-Hamouda N, Ltaief Z, Kirsch M, et al. Neuroprognostication under ECMO after cardiac arrest, are classical tools still performant? Neurocrit Care. 2022. https://doi.org/10.1007/s12028-022-01516-0.
11. Sonneville R, Schmidt M. Extracorporeal cardiopulmonary resuscitation for adults with refractory out-of-hospital cardiac arrest: towards better neurological outcomes. Circulation. 2020;141(11):887–90.
12. Cho S-M, Ritzl EK. Neurological prognostication using electroencephalogram in adult veno-arterial extracorporeal membrane oxygenation: limitations and recommendations. Neurocrit Care. 2020;33(3):652–4.
13. Geocadin RG, Callaway CW, Fink EL, et al. Standards for studies of neurological prognostication in comatose survivors of cardiac arrest: a scientific statement from the American Heart Association. Circulation. 2019;140(9):e517–42.