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Editorial

The crystal ball is filled with CSF

Early biomarkers represent a "crystal ball" that could predict good or bad neurological outcome after cardiac arrest, and could have major implications on post return of spontaneous circulation (ROSC) care. It could help select which patients need an aggressive post-cardiac arrest treatment and those for whom resuscitation is futile. Continuing medical care for patients without any hope for a desirable neurologic outcome could be considered unethical in many situations. It prolongs the suffering of the bereaved family, and can inappropriately divert resource and clinician work load. While having a marker predict a good clinical outcome could help the decision to continue aggressive care.

The ERC guidelines recommended that the earliest time to prognosticate a poor neurologic outcome is 72 h after ROSC, and should be extended longer if the residual effect of sedation and/or paralysis confounds the clinical examination.[1] Several methods have been studied to predict outcomes: prehospital history of the cardiac arrest, clinical exam, biological markers, neuroimaging, advanced vital signs like cerebral oximetry, EEG.[2–6]

For years, we have been looking for a blood-based biomarker to predict neurological prognosis in cardiac arrest survivors. In this edition of Resuscitation, You et al. looked nearer to the brain for the biomarker in the cerebrospinal fluid (CSF).[7] This is not a new idea; in 1980, Vaagenes et al. already studied the changes of CK in CSF post cardiac arrest.[8] However, due to the invasive character of lumbar punctures, few studies have used CSF as a source for protein studies post cardiac arrest.

Release of neuron specific enolase (NSE) in CSF following experimental brain lesions was discovered in the mid 80's and its' use as a prognostic marker for irreversible brain damage in comatose cardiac arrest survivors since the mid 90's.[9,10] The Target Temperature Management (TTM) after Cardiac Arrest trial demonstrated that serum NSE values were strong predictors of poor outcome after out of hospital cardiac arrest.[11] The TTM trial also suggested that 24 h post ROSC was too early to use serum NSE to predict reliable outcomes, and the optimal timing would be at 48 or 72 h. However, as NSE is released from damaged neuron cells into the CSF, and from the CSF into the blood after the blood-brain barrier disruption in the first 24 h after ROSC, NSE could be detectable earlier in the CSF compare to the serum.[12,13] Based on those elements, You et al analyzed the usefulness of NSE in CSF to predict neurological prognosis in cardiac arrest survivors who underwent target temperature management.

They found that an increase in CSF NSE was predictive of a poor neurological outcome as early as day one, while delayed in the serum up to 48–72 h. It is also interesting to note in the figure 2, that for almost every patient, the CSF NSE peak seemed to be achieved on day one. The specificity (up to 100%) and sensitivity (up to 94%) of the CSF NSE were also increase compare to the serum NSE. A value of less than approximately 100 ng/ml is a reasonable predictor of good neurological outcome, while patients with poor neurologic outcome have results mot of frequently $>$ 300 ng/ml. In conclusion, the CSF NSE level is a better and earlier neurological prognosis marker than the serum NSE.

The main limit of this study is the need for a CSF. It seems logical to use CSF and not blood to search for a biomarker of good neurological outcome as CSF is in direct contact with the brain, has a smaller volume than the blood and is not limited by the blood-brain barrier. Lumbar punctures are not part of the usual post cardiac arrest evaluation. Though not complicated to perform, as an LP is an invasive procedure, it is unlikely that it will become standard of care evaluation for post ROSC patient in the near future. There are several other limitations that may limit the generalization of those results. With only 34 patients, the sample size was very limited. A larger study will be necessary. Furthermore, it is also important to note that the patients in the study are younger compared to prior studies with a median age of only 47 years old.

Finally, even if we find a good biological marker to prognosticate neurological outcomes, it is improbable that we would rely upon only one parameter to determine who we should withdraw life-sustaining therapy (WLST) from. It is important to remember that recent studies have demonstrated that we tend to stop post-cardiac care to early.[14] Prognosticating good or bad neurological outcome is a complex decision; it is an art, not an exact science.

Multimodal prognostication rather than a single modality is recommended by the ERC guidelines to improve the quality of predictions and decrease the risk of bias due to a single type of measurement.[1] WLST is a medical, ethical and sociological decision, which varies according to the country and the local culture. In the future, with more definitive research, WLST could be guided by biomarker but must take into account the wishes of the patient and his family. We always need to remember that there is doubt inherent to every prognostication, but with further study, we might find that our "crystal ball" is filled with CSF.

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