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Is Neurologic Prognostication After Hypothermia Ready for Primetime?

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Since the introduction of mild induced hypothermia as a neuroprotective measure in patients after cardiac arrest (CA), there have been numerous questions regarding the validity of previously established prognostication methods (1–3). The concern has been: if hypothermia can improve neurologic outcomes, then perhaps by using older prognostication markers, we have been underestimating the recovery potential of hypothermia-treated patients. An obvious and grave consequence would be misleading the patient's family members to withdraw care prematurely. Fortunately, several studies published over the past few years have attempted to clarify the validity of early and long-term prognostication markers in patients treated with hypothermia (4–8).

In this edition of *Critical Care Medicine*, Hsu *et al* adds to the growing body of literature that examines predictors of prognosis in cardiac arrest patients treated with therapeutic hypothermia (9). In their study of patients treated with targeted temperature management (TTM) of 33 to 34°C after cardiac arrest, the authors reported that good Cerebral Performance Category (CPC) scores at hospital discharge predicted longer patient survival. Their study included out-of-hospital and in-hospital post-cardiac arrest patients with both

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groups demonstrating similar correlations between CPC scores and long-term survival. The important and noteworthy feature of this study is the fact that they looked exclusively at patients treated with hypothermia. This significantly highlights the importance of the research focus on hypothermia and also explains the slightly low sample size as only a fraction of post-cardiac arrest patients are treated with TTM (24.1%, 140/582 in this study) (9). Other studies correlating CPC with long-term survival after cardiac arrest included a mix of patients treated with and without TTM, introducing uncertainty regarding the validity of their results in cooled patients (10, 11). Accounting for the differences in sample size between the studies, the strong correlation between CPC score at discharge and long-term survival was similar in the present study compared to the previous ones. One may not find this similarity between patients treated with or without hypothermia surprising, especially given the recently published large trial that showed no significant benefit of a protocol of mild hypothermia over anti-pyrexia (12).

Interestingly, the study by Phelps et al (10), which included a large proportion of patients not treated with TTM (75.3%), had a lower percentage of patients at discharge with CPC score 3 or 4. Though no explanation of the difference is offered by Hsu et al, one possibility is the selection bias of patients treated with TTM. That is, TTM is usually only instituted in patients who remain comatose after resuscitation from a cardiac arrest, thereby selecting out patients with mild to moderate initial cerebral injury.

The present study's choice of using the CPC score as the prognostic marker has its advantages as well as drawbacks (9). The CPC score has been widely used in the cardiac arrest literature, and is relatively easy to estimate and interpret, though typically as an outcome measure (however intermediate) rather than a prognostic marker. The straightforwardness of the scale also makes it simple for family members to understand the meaning of each category. However, the authors' exclusive use of chart review by one of three abstractors (without the evaluation of inter-rater reliability) as the method for ascertaining CPC scores at hospital discharge calls into question the accuracy of the assigned scores. Additionally, the CPC score is a very broad measure of global function and best used as a measure of outcome. It does not address specific deficits useful for predicting functional outcomes (such as language, memory, or ambulatory function) that other more comprehensive scales assess (13). Most neurologists/intensivists may not wait until discharge to talk with families about prognosis, thus earlier tests and markers should be the focus in future researches.

Perhaps more important than the length of a patient's life, quality has become a key determinant of decisions regarding life-sustaining measures. Essential to every family discussion about prognosis is not only the likelihood of survival, but also an estimate of what that life will look like. One limitation of the study by Hsu et al (9) is that the only outcome measure was the length of survival after hospital discharge. It would have been very interesting and informative to see if there were changes in the CPC scores of the patients over time. In particular, do patients with anoxic brain injury that are discharged from the hospital in an unconscious state (CPC 4) remain so for the rest of their lives? Did some regain consciousness? These are questions that families and loved-ones would very much like answers to when making decisions about ongoing care. The authors do recognize

this limitation and hope to address this with future studies incorporating neurocognitive tests (9).

It has been twelve years since the publication of the sentinel papers showing benefit to treating comatose survivors of cardiac arrest with mild hypothermia (1, 2). Though the adoption of the practice has been slow and not without controversy, more and more patients are treated with TTM. Previously, we may have been hesitant to render prognoses on cardiac arrest survivors that have been cooled. Now, with growing data and literature on the subject, we may finally be ready to discuss prognoses in these patients with some confidence.

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