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Prognostication following cardiac arrest: do we have our patients' safety in mind?

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This practice of prognostication in post cardiac arrest (PCA) patients has grave importance particularly in the era where resources are limited and cost-containment is emphasized. Prior to the introduction of therapeutic hypothermia in comatose survivors of cardiac arrest, a clinical practice guideline advocates for 72 hours post arrest as an acceptable time cut-off for prognostication of neurological recovery.¹ The introduction of therapeutic hypothermia (TH) shifted the paradigm as it improved outcomes and increased attention to the post-arrest care. TH has also renewed the interest in prognostication.² Hence, developing validated prognostic tools and establishing the optimal timing and predictive accuracy of tests used in response to the changes to outcomes that TH has caused is one of the most pressing research needs in post resuscitation care.³

In this issue of Critical Care Medicine, *Golan and colleagues* present a meta-analysis on predicting neurological outcome following TH post cardiac arrest that included 20 studies with 1845 patients.⁴ Measures of poor neurological outcome were Glasgow outcome score (GOS) of 1-3 or Glasgow-Pittsburgh cerebral performance categories (CPC) score of 3-5. The study assessed several validated tests such as clinical tests, electroencephalogram, somatosensory evoked potentials (SSEP), neuroimaging and serum biomarkers such as neuron specific enolase and Tau. The authors concluded that bilateral absence of pupillary reflexes more than 24 hours after return of spontaneous circulation was the best predictor of outcomes with a false positive rate (FPR) of 0.02 (95% CI: 0.01-0.06), while bilateral absence of corneal reflexes was the second best predictor (FPR of 0.04, 95% CI: 0.01-0.09).

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Somatosensory evoked potentials accurately prognosticated neurological recovery especially when performed in the first week post arrest (FPR 0.03, 95% CI: 0.01-0.07). Notably, the authors cautioned that the specificity of available tests improved when these were performed beyond 72 hours. Furthermore, they warned that clinicians should use caution with these predictors as they carry the inherent risk of becoming self-fulfilling.

Several meta-analysis on this topic have been published^{5,6}, but some of the strengths of the *Golan and colleagues* study include the comprehensive inclusion of relevant observational, retrospective and prospective studies, along with formal appraisal of the quality of evidence. One of the highlights of this study is the standardized approach with regard to timing of the tests. In contrast, the meta-analysis by Sandroni and colleagues examined the role of different tests at different time points making its application in clinical practice less feasible.⁵ Moreover, *Golan and colleagues* included predictors of neurological outcome within the first 14 days, as opposed to 7 days by Sandroni and colleagues,⁵ to minimize the confounding effect of sedation and paralytics. Another meta-analysis by Kamps and colleagues that included 10 studies also reported similar findings regarding the diagnostic accuracy of pupillary reflexes and somatosensory potentials when performed within 72 hours.⁶ Despite the similarities in the sensitivity analyses, the study by *Golan and colleagues* had narrower confidence intervals due to the inclusion of more studies and correspondingly a larger sample size. As we compare the three meta-analyses, all three studies provide some serious caution regarding their observations and recommendations.

Critical evaluation of published literature on neuro-prognostication raises a few noteworthy questions. Firstly, on timing, are we justified in using the 72-hour cut-off for arriving at a prognosis in patients treated with TH? A recent study of 194 patients reported that the time to awakening after PCA was variable and often longer than 72 hours.⁷ As *Golan and colleagues* cautioned us that the specificity of test increased beyond 72 hours, and with early prognostication of poor outcome at 72 hours resulting in withdrawal of life sustaining therapies and death, what is the patient safety implication of this practice? Second, on study design, the lack of blinding in the vast majority of the prognostication studies support the idea that self-fulfilling prophecy is common in this area. How many patients are actually harmed by self-fulfilling prophecy? It is rather intriguing to find that blinding, which is considered quintessential in randomized clinical trials on drugs and interventions, is not the norm in prognostication studies. Self-fulfilling prophecy can have a significant negative impact on our ability to fully appreciate the effects of treatments and interventions⁸, and withdrawal of life sustaining therapies has a profound confounding effect on the predictive value of the tests and overall PCA mortality.^{9,10} Third, earmarking the 3 or 6-month follow-up as standard for long-term outcomes particularly in the context of recent evidence suggesting a more prolonged recovery following PCA.¹¹ Fourth, are the measures of outcome currently in vogue like CPC or GOS, truly the best surrogates of neurological recovery in these patients? Studies have shown CPC to correlate poorly with quality of life, while GOS is an inadequate measure of cognitive outcomes.¹²⁻¹⁵

Despite these limitations, we commend the *Golan and Colleagues* on performing this meta-analysis on a very important yet complex topic. As this study tries to show that simple bedside clinical tests and somatosensory potentials have a high neuro-prognostic predictive

ability, mostly when performed after 72 hours following cardiac arrest, we need to ponder on our motivations for prognostication. A few years before the introduction of TH, the Institutes of Medicine published the report on a comprehensive strategy by which government, health care providers, industry, and consumers can reduce preventable medical errors.¹⁶ This report brought heightened awareness on patient safety as a paradigm shifter that affected the practice of medicine in general and critical care medicine in particular. As we juxtapose the two paradigm shifters of TH and patient safety in the practice of early prognostication, is there anything we can do to keep these patients safer? How many patients are potentially affected by early prognostication? Considering that there are over 400,000 cardiac arrests in the USA per year¹⁵, and while the mortality seems to be trending downward^{17,18}, majority of PCA survivors are comatose for variable periods of time initially, and hence susceptible to early prognostication which may result in withdrawal of life sustaining therapies. As we try to address the limitations of existing prognostication practices by designing studies with better study design, newer and better prognostic tests, and more comprehensive battery of functional and neurocognitive outcome measures, are we subjecting our patients to unsafe early prognostication practices in our pursuit to possibly minimize suffering and conserve valuable resources? With all the limitations and cautions related to early prognostication, the time has come that we approach prognostication with our patients' safety in mind.

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