



Poor neurologic outcomes after cardiac arrest; a spectrum with individual implications*



Keywords:

Cardiac arrest
Neuroprognostication
Self-fulfilling prophecy
Hypoxic–ischemic encephalopathy
Heart arrest
Outcomes assessment

Dear Sir,

We read the case report published by Becker et al. of a cardiac arrest (CA) survivor who had a late neurological recovery despite poor prognostic markers [1]. While we agree that this is a fascinating case which highlights the complexity of neurological recovery and the shortcomings of current neuroprognostication practices in hypoxic–ischemic encephalopathy (HIE), we disagree that this was a “miss in prognostication.”

On admission, prior to sedation, the patient was noted to withdraw from pain, suggesting a less severe initial insult [2]. At 48 h, he had absent vestibular–ocular, gag, and corneal reflexes; however, pupillary reactivity re-emerged. Absence of brainstem reflexes at 48 h combined with motor GCS ≤ 2 after rewarming has been shown to predict Cerebral Performance Category scores (CPC) 3–5 with a positive predictive value of 100%. However, the studies pooled in this meta-analysis were contaminated by withdrawal of life-sustaining therapies (WLST) and subjected to a self-fulfilling prophecy bias [3]. While absent pupillary light reflexes predict poor outcome, this finding within 72 h from CA has lower specificity if therapeutic hypothermia is employed [3]. Recently published international guidelines have updated the recommendations regarding timing of neurological assessments and recommended caution when interpreting early examination findings, underscoring that absence of good neurological function at 48–72 h does *not* rule out subsequent awakening [4–6]. Additionally, the reported patient had post-anoxic status epilepticus, which is associated with a high mortality. However, 3–7% of patients may regain consciousness once this is treated, particularly in the setting of a reactive and continuous encephalographic (EEG) background [8–10]. Nonetheless, the presence of brainstem reflexes, N20 peaks on somatosensory evoked potentials, and preserved reactivity are helpful in identifying survivors with a potential to regain consciousness, but not necessarily regain independence [8]. Based on the above findings, predicting a poor prognosis (CPC 3–5) would be consistent with current national and international guidelines [4,6,11,12]. It would be a “miss in prognostication” if this patient had not only regained consciousness, but also become independent with daily living activities (CPC 1–2). Although a CPC score was not assigned in the reported case, he would likely be classified as CPC 3 given the extent

of cognitive deficits, traditionally considered a poor outcome in the CA literature. The natural history of HIE, unexposed to WLST, is unknown. Landmark CA studies suggest a bimodal distribution of outcomes with the highest proportion of patients falling into extremes: CPC 1 and CPC 5. Likely due to perceived poor neurological prognosis and subsequent WLST, there are relatively few cases achieving a CPC 3, a broad category of deficits with varying severity, often reported as less than 10% of survivors [13]. There is no clear consensus among practitioners regarding the clinical significance of CPC 3 other than awakening as demonstrated by a survey of European Society of Intensive Care Medicine members: 58% of survey respondents defined poor outcome as CPC category 3–5, while 39% used CPC category 4–5 [14]. We also must recognize that patients' families may have a similar divergence regarding what degree of clinical recovery is acceptable. It is conceivable that an elderly patient may accept some loss of independence, while a younger patient may find this unacceptable. The CPC score provides only a broad outcome measure, however, a novel extended approach, the CPC-E, explores performance over 10 functional domains and, if used in further prospective CA studies, holds promise in providing more detailed functional outcomes [15].

This case also highlights the potential for late recovery, beyond the 3–11-day range seen in the “late awakeners” group, which occurs more often in survivors of older age, those with renal impairment, and those treated with therapeutic hypothermia [16–18]. Early WLST due to perceived poor neurological outcomes often limits the evaluation of late recovery. Moreover, we do not fully understand the significance of prolonged sedation and anesthetic use in the setting of hypothermia; this certainly had some impact in the clinical course of this case.

In summary, our current prognostication practices differentiate between two groups, those who will regain independence (CPC 1–2) and those who will die or remain severely disabled (CPC 3–5). This case highlights our knowledge gaps and the importance of using a functional outcome assessment (CPC-E) in order to determine those who can make a meaningful recovery. Knowledge of the natural history of CA recovery, untainted by WLST, is crucial to understand each patient's trajectory, and to accurately counsel family members.

Funding

None.

Acknowledgments

Dr. Rachel Beekman reports no disclosures.

Dr. David M. Greer serves as Editor-in-Chief of *Seminars in Neurology* and has received compensation for medical-legal consultation.

Dr. Carolina B. Maciel reports no disclosures.

References

- [1] Becker DA, et al. A major miss in prognostication after cardiac arrest: burst suppression and brain healing. *Epilepsy Behav Case Rep* 2017;7:1–5.

* Letter to the Editor regarding: “A major miss in prognostication after cardiac arrest: Burst suppression and brain healing”.

- [2] Rossetti AO, et al. Electroencephalography predicts poor and good outcomes after cardiac arrest: a two-center study. *Crit Care Med* 2017.
- [3] Sandroni C, et al. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: a systematic review and meta-analysis. Part 2: patients treated with therapeutic hypothermia. *Resuscitation* 2013;84(10):1324–38.
- [4] Taccone FS, et al. Neuroprognostication after adult cardiac arrest treated with targeted temperature management: task force for Belgian recommendations. *Acta Neurol Belg* 2017.
- [5] Sandroni C, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. *Intensive Care Med* 2014;40(12):1816–31.
- [6] Callaway CW, et al. Part 8: post-cardiac arrest care: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132(18 Suppl. 2):S465–82.
- [7] Sandroni C, D'Arrigo S. Neurologic prognostication: neurologic examination and current guidelines. *Semin Neurol* 2017;37(1):40–7.
- [8] Rossetti AO, et al. Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia. *Neurology* 2009;72(8):744–9.
- [9] Backman S, et al. Electroencephalographic characteristics of status epilepticus after cardiac arrest. *Clin Neurophysiol* 2017.
- [10] Rossetti AO, et al. Status epilepticus: an independent outcome predictor after cerebral anoxia. *Neurology* 2007;69(3):255–60.
- [11] Wijdicks EF, et al. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2006;67(2):203–10.
- [12] Nolan JP, et al. European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care. *Intensive Care Med* 2015.
- [13] Nielsen N, et al. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med* 2013;369(23):2197–206.
- [14] Friberg H, et al. Survey on current practices for neurological prognostication after cardiac arrest. *Resuscitation* 2015;90:158–62.
- [15] Balouris SA, et al. Development and validation of the Cerebral Performance Categories-Extended (CPC-E). *Resuscitation* 2015;94:98–105.
- [16] Gold B, et al. Awakening after cardiac arrest and post resuscitation hypothermia: are we pulling the plug too early? *Resuscitation* 2014;85(2):211–4.
- [17] Paul M, et al. Delayed awakening after cardiac arrest: prevalence and risk factors in the Parisian registry. *Intensive Care Med* 2016.
- [18] Zanyk-McLean K, et al. Time to awakening is often delayed in patients who receive targeted temperature management after cardiac arrest. *Ther Hypothermia Temp Manag* 2016.

Rachel Beekman

Department of Neurology, Yale School of Medicine, New Haven, CT 06510, United States

Corresponding author at: Yale School of Medicine, 15 York Street, P.O. Box 208018, New Haven, CT 06520, United States.
E-mail address: Rachel.Beekman@yale.edu.

David M. Greer

Department of Neurology, Boston University School of Medicine, Boston, MA 02118, United States

Carolina B. Maciel

Department of Neurology, UF-Health Shands Hospital, University of Florida College of Medicine, Gainesville, FL 32611, United States

21 June 2017

Available online 7 September 2017