



Original Contribution

Early neurologic examination is not reliable for prognostication in post–cardiac arrest patients who undergo therapeutic hypothermia



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ABSTRACT

Background: Recent advances in post–cardiac arrest (CA) care including therapeutic hypothermia (TH) have improved survival and favorable neurologic outcomes for survivors of CA. Survivors often present with deep coma and lack of brainstem reflexes, which are generally associated with adverse outcomes in many disease processes. Little is known regarding the role of initial emergency department (ED) neurological examination and its potential for prognostication.

Objectives: The purpose of this study is to determine if components of a standardized neurologic examination are reliable prognosticators in patients recently resuscitated from CA. We hypothesize that lack of neurologic function does not reliably predict an adverse outcome and, therefore, should not be used to determine eligibility for TH.

Methods: A standardized neurologic examination was performed in the ED on a prospective, convenience cohort of post-CA patients presenting to a CA resuscitation center who would undergo a comprehensive postarrest care pathway that included TH. Data such as prior sedation or active neuromuscular blockade were documented to evaluate for the presence of possible confounders. Examination findings were then compared with hospital survival and neurologic outcome at discharge as defined by the cerebral performance category (CPC) score as documented in the institutional TH registry.

Results: Forty-nine subjects were enrolled, most of whom presented comatose with a Glasgow Coma Scale of 3 ($n = 41, 83.7\%$). Nineteen subjects (38.8%) had absence of all examination findings, of which 4 of 19 (21.1%) survived to hospital discharge. Of those with at least 1 positive examination finding, 13 of 30 subjects (43.3%) survived to hospital discharge. Subgroup analysis showed that 9 of the 19 patients with absence of brainstem reflexes did not have evidence of active neuromuscular blockade at the time of the examination; 2 of 9 (22.1%) survived to hospital discharge. Eight of these subjects in this group had not received any prior sedation; 1 of 8 (12.5%) survived to hospital discharge. Only 1 of the 17 subjects who survived was discharged with poor neurologic function with a CPC score = 3, whereas all others who survived had good neurologic function, CPC score = 1.

Conclusion: In this cohort of patients treated in a comprehensive postarrest care pathway that included TH, absence of neurologic function on initial ED presentation was not reliable for prognostication. Given these findings, clinicians should refrain from using the initial ED neurological examination to guide the aggressiveness of care or in counseling of family members regarding anticipated outcome.

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1. Background

Despite advances in post–cardiac arrest (CA) care, sudden CA remains a leading cause of death [1,2]. Those who survive to hospital admission suffer significant morbidity and mortality from neurologic injury as part of the post-CA syndrome [2]. Implementation of

aggressive post-CA care protocols, including therapeutic hypothermia (TH), has led to improved neurologic outcomes in survivors of CA [3–5]. In many disease, deep coma is generally associated with adverse outcomes. However, data to support early prognostication following CA is limited. In the absence of these data, clinicians generally apply clinical gestalt and extrapolate knowledge of poor predictors of neurologic outcome from other disease processes to formulate a perceived prognosis of neurologic injury in survivors of CA [6]. Numerous case reports have shown that patients initially perceived as having a poor prognosis go on to survive with a good neurological outcome [7,8]. We believe that

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potential candidates for aggressive care may be excluded from treatment because of perceived futility, supported by a self-fulfilling prophecy [6,9,10]. To our knowledge, there has never been a prospective evaluation of neurologic examination findings shortly after stabilization from CA to determine correlation with neurologic recovery among patients treated with TH.

The purpose of this study was to determine if components of a standard neurologic examination are reliable prognosticators in patients recently resuscitated from CA. We hypothesized that abnormal neurologic findings, including lack of brainstem reflexes, do not confidently predict adverse outcomes and should not be used to determine eligibility for aggressive care including TH.

2. Methods

2.1. Study design

This was a prospective cohort study of patients who survived CA to hospital admission. Patients were enrolled at Carolinas Medical Center Emergency Department (ED) in Charlotte, NC, from October 2012 to October 2013. Comatose patients who presented to the ED and were entered into the Code Cool postarrest clinical pathway that includes TH after resuscitation from CA were eligible for inclusion in this study. The Code Cool protocol at our institution has previously been described in the literature outlining the regionalization of post-CA care [11]. At the time of Code Cool protocol activation, a research team member performed and documented a standardized bedside neurologic examination to assess consciousness, face and extremity motor responses, and brainstem reflexes. These examination findings were then compared with our primary outcomes of survival and neurologic status at hospital discharge using the Cerebral Performance Category (CPC) scoring system [12].

A convenience sample of eligible patients was enrolled by study personnel who performed a standardized, structured neurologic examination. Patients were enrolled after the decision to pursue TH via the “Code Cool” protocol was made by the treating physicians in the ED. The study population included out-of-hospital CA survivors presenting via emergency medical services either from the field or outside hospital transfer as well as patients who achieved return of spontaneous circulation during resuscitation in our ED. Patients suffering CA after hospital admission and patients younger than 18 years were excluded from this study.

The data collection form and standardized examination used in this study were formulated with the guidance of attending emergency medicine physicians, a critical care physician, and a neurologist using established practice parameters from the American Academy of Neurology [13] to provide a comprehensive and objective neurologic assessment. The included examination components have been used in brain death testing and have been well studied in prognostication research of CA survivors [14–16]. Before data collection, all research team members were educated on performance of the examination components and individually performed the standardized neurologic examination on a test patient to ensure reproducibility among research members. The data collection form included screening for possible confounding variables such as the presence of neuromuscular blockade (NMB), sedative hypnotic agents, and core temperature at the time of examination. Examination components included whether or not the patient was breathing spontaneously; motor response to painful stimuli; the presence or absence of myoclonus; and evaluation of brainstem function, including pupillary, corneal, gag, cough, oculocephalic, and oculovestibular reflexes. In addition, Glasgow Coma Scale (GCS) and FOUR (Full Outline of UnResponsiveness) scores [17] were calculated for each patient. Before performing the examination, a train-of-4 (TOF) monitor was used to document muscle twitches to determine the absence or presence of NMB. Patients who were in a hard cervical collar at the time of examination did not undergo oculocephalic testing

but instead received oculovestibular testing. Patients who were not in a cervical collar first had their oculocephalic reflex tested and, if this was negative, then had oculovestibular reflex testing performed.

Clinical data, including arrest and treatment variables, complications, and outcomes, were prospectively collected on patients with the use of a previously established prospective registry that includes a preformatted standard data collection tool using the Utstein criteria [18]. This study was approved by the Institutional Review and Privacy Board at Carolinas Medical Center.

2.2. Statistical analysis

Outcomes were obtained from the TH registry maintained at our institution. The primary outcome measured was survival to hospital discharge with a secondary outcome of neurologic performance at time of discharge. Neurologic performance was measured and recorded using the CPC score, with scores of 1–2 representing a good neurologic outcome, 3–4 representing poor neurologic outcomes, and 5 representing death.

This is a descriptive study. Means, confidence intervals (CIs), counts, and percentages were calculated. SAS (Cary, NC), version 9.3, was used for all analyses.

3. Results

A convenience sample of 49 subjects was enrolled from a total population of 129 postarrest patients who received TH during the investigation period. Our sample was representative of the entire Code Cool population during this time with regard to age, initial rhythm, survival, and neurologic outcome (Table 1). The mean age was 54.9 ± 16 years; 36 (73.5%) were men and 13 (26.5%) were women. Average core temperature at the time of examination was 35.0°C (median = 35.1°C), with active cooling initiated in 34 subjects (69.4%). The most common presenting arrest rhythm was asystole ($n = 17$, 34.7%) followed by pulseless electrical activity ($n = 16$, 32.7%), ventricular fibrillation ($n = 8$, 16.3%), and ventricular tachycardia ($n = 7$, 14.3%). In 1 patient (2%), the presenting arrest rhythm was unknown. At the time of the examination, 22 subjects (44.9%) had previously received sedation, 19 (38.8%) had evidence of active NMB, and 34 (69.4%) were actively being cooled. Overall, 17 patients (34.7%; 95% CI, 22%–50%) survived to hospital discharge. Of those surviving to hospital discharge, 16 (94.1%; 95% CI, 71%–100%) had a favorable neurologic outcome with a CPC score of 1, whereas only 1 subject (5.9%) who survived to hospital discharge had a poor neurologic outcome with a CPC of 3.

A majority of patients had absent pupillary ($n = 37$, 75.5%), corneal ($n = 41$, 83.7%), gag ($n = 40$, 81.6%), oculocephalic ($n = 32$, 65.3%), or oculovestibular ($n = 40$, 81.6%) reflexes (Table 2). Oculocephalic reflex testing was not performed in 10 subjects (20.4%) because they presented in a cervical collar, whereas 8 subjects (16.3%) did not have oculovestibular reflex testing performed because either they had a presence of an oculocephalic reflex ($n = 7$, 14.3%) or the test was inadvertently omitted ($n = 1$, 2.0%). Twenty-six subjects (53.1%) were found to be breathing spontaneously. Only 1 subject (2.0%) had evidence of seizure or myoclonus at the time of their neurologic examination.

The predominate GCS was 3 ($n = 41$, 83.7%). Similarly, the most common total FOUR score was 0 ($n = 25$, 51.0%). A breakdown of the individual components of these scores and their prevalence among study participants is listed in Table 3.

The only examination finding that demonstrated statistically significant survival was the presence of a gag reflex, where 6 of 9 (66.7%, 95% CI, 29.9%–92.5%) of subjects with a gag reflex survived to hospital discharge, whereas only 11 of 40 (27.5%, 95% CI, 14.6%–43.9%) without a gag reflex survived ($P = .049$). However, all isolated examination components demonstrated clinically significant survival of 21.7%–35.4% in the absence of a positive finding (Table 1). The 2 coma scales also demonstrated clinically significant survival at the lowest scores possible (Table 3). In subjects who had GCS of 3, 14 of 41 (34.1%, 95% CI,

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