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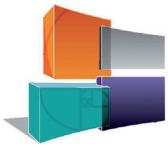

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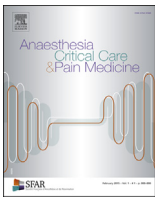

Original article

# Neuron specific enolase and Glasgow motor score remain useful tools for assessing neurological prognosis after out-of-hospital cardiac arrest treated with therapeutic hypothermia

Claire Roger [a,*], Ludovic Palmier [a], Benjamin Louart [a], Nicolas Molinari [b], Pierre-Geraud Claret [a], Jean-Emmanuel de la Coussaye [a], Jean-Yves Lefrant [a], Laurent Muller [a]

[a] Department of anaesthesiology, emergency and critical care medicine, Nîmes university hospital, place du Pr.-Debré, 30029 Nîmes cedex 9, France
[b] UMR 729 MISTEA, department of biostatistics, Montpellier university hospital, avenue Gaston-Giraud, 34093 Montpellier, France

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ABSTRACT

*Aim of the study:* Identifying clinical, electrophysiological and biological predictors for 6-month neurological outcome in survivors at day 3 after cardiac arrest (CA) treated with therapeutic hypothermia (TH).
*Methods:* We conducted a retrospective cohort study of adults comatose after out-of hospital CA treated with TH. All data were collected from medical charts and laboratory files.
*Results:* Between January 2010 and March 2013, among the 130 analysed CA survivors, 27 (21%) had a good neurological outcome at 6 months and 103 (79%) had a poor neurological outcome, including 98 deaths. The Glasgow coma score motor response (GCS-M), pupillary reflexes and Neuron Specific Enolase (NSE) were the three best predictors of neurological outcome ($P < 0.0001$). The area under the Receiver Operating Characteristic curve for NSE was 0.92 [0.84–0.99].
*Conclusion:* NSE values, GCS-M scores and pupillary reflexes are the best predictors of poor 6-month outcome after out-of-hospital CA treated with TH. Of these, NSE values have the best-isolated prognostic performance when above 28.8 μg/L.


## 1. Introduction

Cardiac arrest (CA) management remains challenging. As fewer than 20% of patients survive to hospital discharge, early prognostication of functional outcome requires accurate prediction [1]. Outcomes for survivors depend on initial CA conditions (cause, duration and severity of ischemic injury) that may lead to post-cardiac arrest syndrome, associated with high mortality. Hypoxic-ischemic encephalopathy is one major cause of poor outcomes following CA. Indeed, most survivors remain comatose or in a vegetative state, leading to decisions to withdraw life support. Thus, the American Academy of Neurology proposed a decision algorithm for use in prognostication of comatose survivors published in 2006 [2]. Before the widespread use of TH, predictor factors of neurological outcome were: serum neuron-specific enolase (NSE), N20 somatosensory-evoked potentials (SSEP), status epilepticus, pupil and corneal reflexes and the Glasgow coma score motor response (GCS-M). Therapeutic hypothermia (TH) is recommended in the management of CA [3–5] and has been associated with improved outcome after ventricular fibrillation out-of-hospital cardiac arrest (OHCA) [6]. However, mild therapeutic hypothermia (33 °C) does not appear to provide any benefit in cardiac arrest survivors compared to normothermia (36 °C) [7]. One explanation is that TH may

*Abbreviations:* OHCA, Out-of-hospital cardiac arrest; TH, Therapeutic hypothermia; GCS-M, Glasgow coma score motor response; CPC, Cerebral performance category; NSE, Neuron specific enolase; SSEP, Somatosensory-evoked potentials; ICU, Intensive care unit; ROC curve, Receiver Operating Characteristic curve; EEG, Electro-encephalogram; EoL, End-of-life.

* Corresponding author. Tel.: +33 4 66 68 30 50; fax: +33 4 66 68 38 41.
*E-mail addresses:* claire.roger@chu-nimes.fr (C. Roger), lpalmier@hotmail.fr (L. Palmier), benjamin.louart@chu-nimes.fr (B. Louart), nicolas.molinari@inserm.fr (N. Molinari), pierre.geraud.claret@chu-nimes.fr (P.-G. Claret), jean.emmanuel.delacoussaye@chu-nimes.fr (J.-E. de la Coussaye), jean.yves.lefrant@chu-nimes.fr (J.-Y. Lefrant), laurent.muller@chu-nimes.fr (L. Muller).

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interfere with clinical examination and electrophysiological predictors (EEG, SSEP), making prognostication of functional outcome more difficult [8–10]. The use of sedative drugs and muscle paralysis during TH is another cause for delayed neurological assessment and prognostication [11–13]. In addition, the NSE cutoff values for predicting poor neurological outcome are not well defined and can also be influenced by TH [2,10,14,15]. The present study aims at identifying clinical, electrophysiological and biological predictors of 6-month neurological outcome in survivors at day 3 after CA treated by TH.

## 2. Methods

### 2.1. Studied population

According to French Law (Law 88-1138 relative to Biomedical Research dated 20 December 1988, modified on 9 August 2004), this non-interventional study did not require informed signed consent from patients. After Institutional Review Board approval (No. 14/01-01), a retrospective chart review was conducted on all adult CA survivors admitted to the Nîmes University Hospital intensive care unit (ICU) between January 2010 and March 2013. Our inclusion criteria included adult patients (≥ 18 years) successfully resuscitated following OHCA and admitted to ICUs. In-hospital cardiac arrest patients and patients who died before ICU admission were excluded.

### 2.2. Standard care

All patients were monitored and treated according to recommended clinical standards [4,5]. The local protocol (Fig. 1) for comatose survivors of CA admitted to the ICU consisted in cooling until body temperature reached 32°–34 °C using surface cooling. Therapeutic hypothermia was maintained for 24 hours, patients were sedated with propofol and remifentanil until passive rewarming reached 36 °C. If patients presented shivering, cisatracurium was added. The sedative drugs were stopped at normothermia in order to assess neurological status.

### 2.3. Data collection

The following data were recorded: demographic data, cardiac arrest circumstances, neurological examination at days 3 and 7 including corneal and pupillary reflexes, GCS-M, status epilepticus, electro-encephalogram (EEG) and SSEP data. Biological data including NSE levels between day 2 and day 3 were collected.

### 2.4. Neurological outcome assessment

Neurological functional status was assessed using the Cerebral Performance Category (CPC) 5-item scale. Neurological status was retrospectively assessed at 6 months: a CPC of 1 or 2 was defined as good neurological outcome and a CPC of 3 to 5 was defined as poor

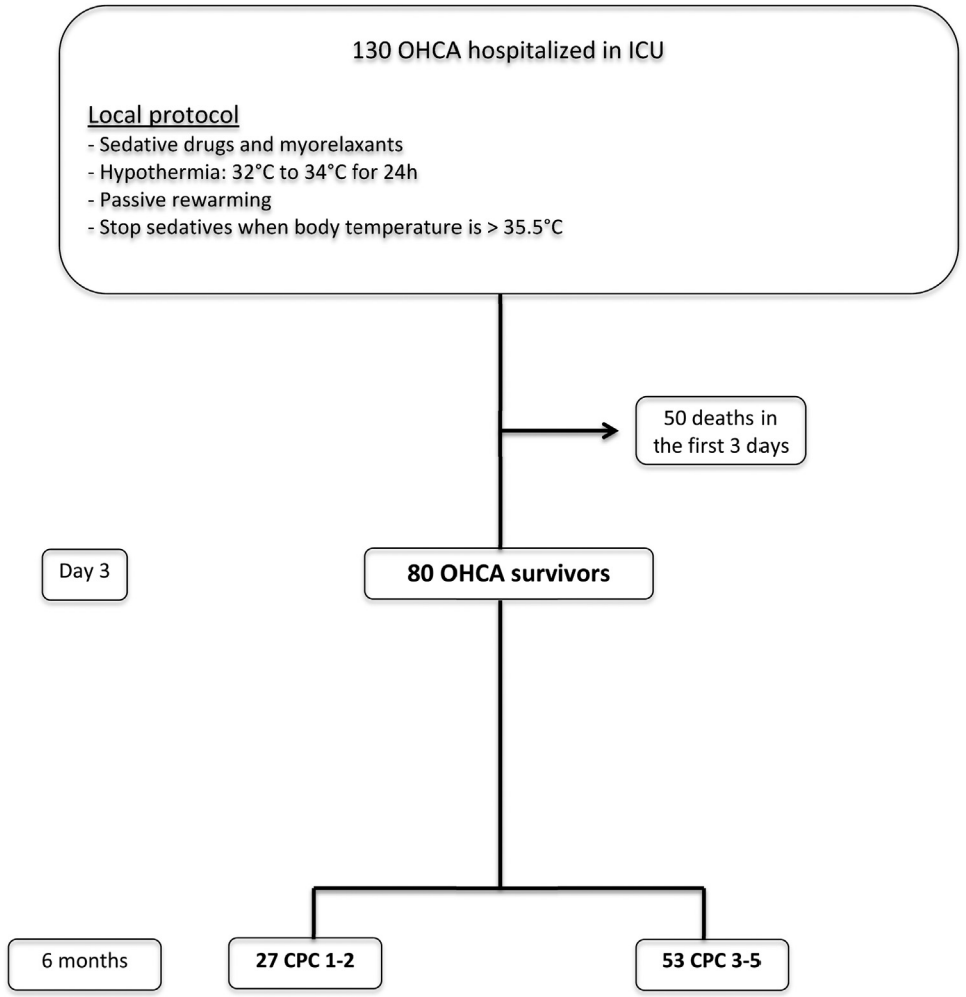


**Fig. 1.** Flow chart. OHCA: out-of-hospital cardiac arrest; ICU: intensive care unit; CPC: cerebral performance category.