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Does this comatose survivor of cardiac arrest have a poor prognosis?

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Introduction

Most initial out-of-hospital cardiac arrest survivors are comatose and about half die before hospital discharge [1]. Most deaths occur after withdrawal of life-sustaining treatment (WLST) following prognostication of a poor neurological outcome due to presumed severe hypoxic–ischaemic brain injury [2]. Some patients waken shortly after stopping sedation, but for those who remain comatose the outcome is uncertain, and decisions regarding further treatment require a careful prognostic assessment.

Case scenario

A 62-year-old man was resuscitated from a witnessed ventricular fibrillation cardiac arrest preceded by acute chest pain. Return of spontaneous circulation (ROSC) was achieved after about 30 min. On emergency department arrival, he was unconscious with his trachea intubated and lungs ventilated. He had unreactive pupils, and no motor response. A 12-lead electrocardiogram showed acute ST-segment elevation. After primary percutaneous coronary intervention for a left anterior descending artery occlusion, he was admitted to the intensive care unit (ICU). The family were told his chances of survival were uncertain due to a risk of brain injury.

Initial care in the ICU

Targeted temperature management (TTM) was immediately started, maintaining a temperature of 36 °C for 24 h. Fentanyl and propofol were infused to facilitate temperature control. An electroencephalogram (EEG) recorded 4 h after the induction of TTM showed a burst-suppression pattern.

The patient was rewarmed over 4 h and sedation stopped at 32 h after ROSC. At 72 h after ROSC, he was haemodynamically stable but still comatose. His pupils were reactive to light but there was no eye opening or motor response to pain. Short-latency somatosensory evoked potentials (SSEPs) of the median nerve showed a bilaterally present N20 wave of normal amplitude. Serum levels of neuron specific enolase (NSE) were 56 and 41 mcg L^{-1} at 24 and 48 h, respectively. The EEG showed a diffuse, continuous, symmetrical delta pattern with no epileptiform activity. There was variation in both amplitude and frequency of the background EEG rhythm in response to a painful stimulus.

Over the following 2 days, there was no change in the patient's neurological status. He was now febrile with a raised white blood cell count, new infiltrates on a chest radiograph, and worsening oxygenation. The family asked if the patient has any chance of recovery.

Which tests should this patient have, and when?

Neurological prognostication in comatose survivors of cardiac arrest requires a multimodal approach combining clinical and diagnostic tests [3]. Most patients with good outcomes recover consciousness within 72–120 h of arrest [4, 5], and therefore the suggested timing for prognostication is 72 h from ROSC, or later (Fig. 1). Results of earlier prognostic tests, such as status myoclonus and NSE levels, should also be considered at this time point.

A careful clinical neurological examination is the cornerstone of prognostic assessment [6] and it should be performed after major confounders, (e.g. residual sedation, neuromuscular blockade, metabolic derangements) have been excluded. Although absent or extensor motor responses to pain are not specific for predicting a poor neurological outcome [7], they are highly sensitive for identifying those patients who require neurological prognostication.

To prevent the incorrect WLST, the false positive rate (FPR) of any predictor used should be as low as possible. Bilateral absence of either pupillary light reflex or N20 SSEP wave are currently the most robust predictors of poor outcome [FPR <5 % with 95 % confidence interval (CI) <5 %], and should be evaluated first. When, as in this case, these abnormal signs are absent, a set of less reliable predictors should be used. These have a FPR <5 % but wider 95 % CIs, and/or their definition/threshold is inconsistent in prognostication studies. These predictors should be used in combination and include early status myoclonus, high and increasing values of serum NSE, unreactive malignant EEG patterns, and evidence of diffuse hypoxic-ischaemic injury on brain CT or MRI.

NSE thresholds for a 0 % FPR vary between studies [3]. Although the value of 56 mcg L^{-1} in our case is above previously recommended thresholds [8], it is still compatible with neurological recovery in TTM-treated patients [9, 10]. A rising NSE with multiple measurements is more useful than a single NSE value at 24 h [10].

The significance of EEG burst-suppression is modest immediately after ROSC, but increases during the subsequent 24 h [11]. Presence of burst-suppression or status epilepticus and absence of reactivity on EEG after rewarming from TTM all predict a poor neurological outcome [9].

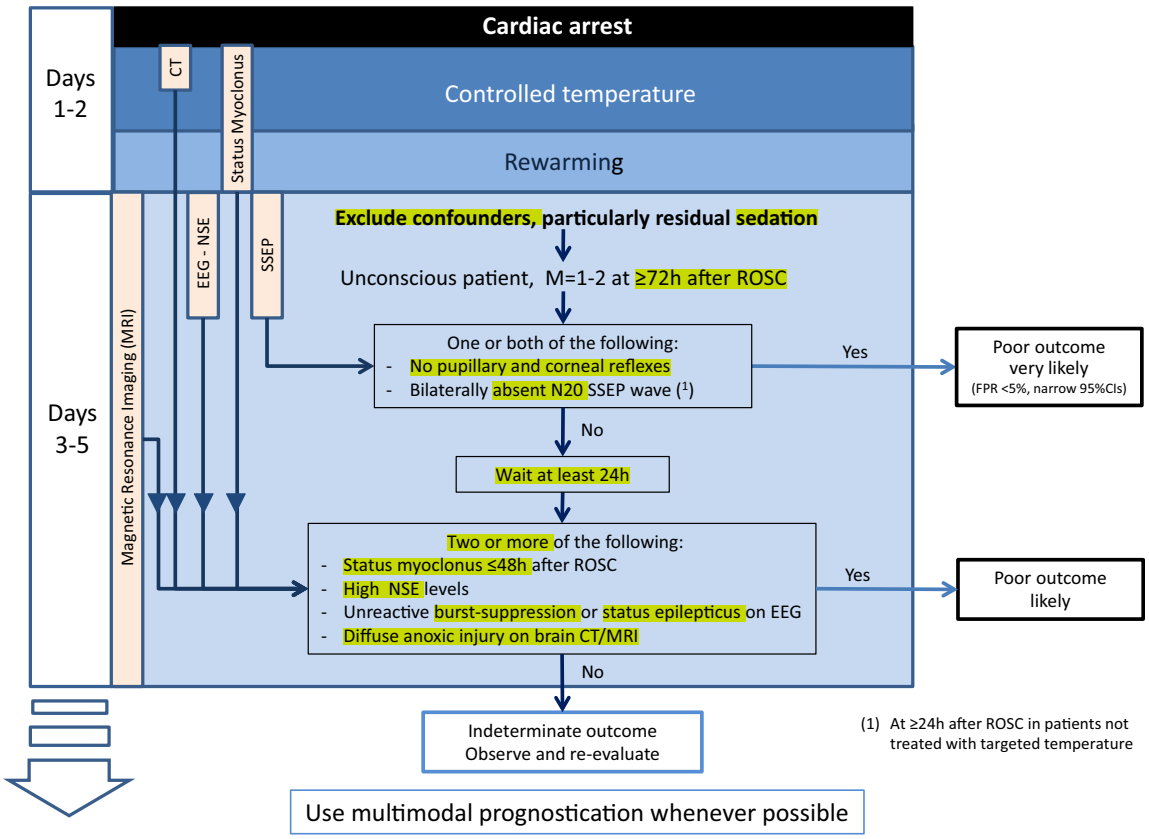

Fig. 1 Suggested prognostication algorithm. The algorithm is entered ≥72 h after ROSC if, after the exclusion of confounders, the patient remains unconscious with no or only extensor motor response to pain. The absence of pupillary and corneal reflexes and/or bilaterally absent N20 SSEP wave indicates that a poor outcome is very likely. If neither of these features is present, wait at least 24 h before reassessing. If two or more of the less robust predictors are present, poor outcome is likely. If none of these criteria are met, consider continuing to observe and re-evaluate. (From [3])

What happened to our patient?

In our patient, both the most robust predictors or the combination of less robust predictors of poor outcome are absent and recovery cannot be excluded [5] as the outcome is indeterminate (Fig. 1). After discussion with the patient's family, a decision to continue treatment was taken.

The patient had a ventilator-associated pneumonia treated with antibiotics and mechanical ventilation. Further sedation with propofol and fentanyl infusion was required on day 5 to enable adequate ventilation and oxygenation with controlled mechanical ventilation. After a sedation-hold on day 7, he started opening his eyes spontaneously, did not obey commands, and withdrew both arms and grimaced after a painful stimulus. On day 11, he was obeying verbal commands, weaned from ventilation and extubated. On day 15, he was ready for transfer to a rehabilitation facility. He was home at 30 days and now at 6 months he is independent, complains of fatigue and has a minor memory deficit.

Conclusions

We recommend a multimodal approach based on clinical examination and diagnostic tests for reliable prognostication after cardiac arrest to prevent the incorrect WLST for presumed irreversible brain injury. Bilaterally absent N20 SSEP wave or pupillary reflexes are the most accurate predictors. Less accurate predictors include unreactive malignant EEG patterns, high and increasing serum NSE values, early myoclonus, and signs of diffuse hypoxic–ischaemic injury on brain CT or MRI. Most survivors of cardiac arrest waken 3–5 days after ROSC but some patients have a delayed recovery. When the outcome is uncertain, clinicians should always consider a further period of observation.

Compliance with ethical standards

Conflicts of interest All the authors have co-authored the ERC-ESICM Advisory Statement on Prognostication in Comatose Survivors of Cardiac Arrest.

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