Guideline for neurological prognostication following Cardiac Arrest in Adult patients

University Hospitals of Leicester NHS
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1. Introduction

Severe neurological impairment caused by hypoxic-ischaemic brain injury is common after resuscitation from cardiac arrest. Early identification of patients with no chance of a good neurological recovery will help to avoid inappropriate treatment and provide information for relatives.

Brain injury is the dominant cause of death for cardiac arrest patients who are admitted to an intensive care unit, and the majority of patients die after withdrawal of life sustaining therapy (WLST) based on a presumed poor neurologic outcome. It is therefore imperative that neurological prognostication is based on the most accurate and up-to-date medical research and knowledge. This guideline aims to standardize neurological prognostication across critical care within UHL and is based on the advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine on “Prognostication in comatose survivors of cardiac arrest” published in 2014.

The majority of patients who are admitted to the ICU following cardiac arrest are unconscious. Patients who improve their level of consciousness after withdrawal of sedative and analgesic substances usually have a good outcome. For those who remain in coma, the prognosis becomes gradually worse with increasing time from the insult. Prognostication is indicated in any patient with prolonged coma after resuscitation and is the most difficult component of the critical care management of these patients. Prognostication involves thorough clinical examination combined with neurophysiologic and neuroradiologic investigations to estimate the extent of brain injury. Patients post cardiac arrest admitted to critical care in UHL will usually undergo targeted temperature management (i.e. core temperature aim of 36^0C for 36 hours and ≤ 37.5^0C for 36-72hours post ROSC) but a minority may still be treated with therapeutic hypothermia (TH) (i.e. core temperature $32\text{-}34^0$C for initial 24 hours and ≤ 37.5^0C for 24-72hours post ROSC). In certain patients, senior clinicians may deem temperature management is not indicated to allow neuroprognostication to be undertaken as early as possible. This guideline is written to cover all treatment groups.

Daily sedation holds must be undertaken to allow neurological examination including GCS, motor response to pain, pupillary and corneal reflexes.

Flowchart for neurological prognostication is presented on page 5

2. Scope

This guideline is relevant to all medical and nursing staff involved in patient care on Adult Critical Care Units at University Hospitals of Leicester NHS Trust.
This guideline applies to all adult patients who remain comatose following Return of Spontaneous Circulation (ROSC) and should be read in conjunction with the Guideline for the Targeted Temperature Management of Adult patients following Cardiac Arrest.

3. Guideline Standards and Procedures

Timing of prognostication

Following global post-anoxic injury, the brain will make a gradual recovery. Brainstem reflexes return first, then the motor response to pain and, finally, cortical activity and consciousness. This process is completed within 72 h from arrest. Consequently, in the absence of residual sedation, 72 h after ROSC seems to be a suitable time for prognostication to begin.

For the vast majority of patients treated with targeted temperature management as per UHL Guideline for the Targeted Temperature Management of Adult patients post Cardiac Arrest, prognostication can be reliably **started** at 72 hours post return of spontaneous circulation (ROSC). Sedative and neuromuscular medications may have an extended duration of action in any patient treated with therapeutic hypothermia (TH) and in those patients neurological prognostication cannot be undertaken until 72 hours **post rewarming** to normothermia.

Excluding other causes of coma

Before decisive assessment is performed, it is imperative that major confounders are excluded. Apart from sedation and neuromuscular blockade, these include hypothermia, severe hypotension, hypoglycaemia, and metabolic and respiratory derangements. Sedatives and neuromuscular blocking drugs should be suspended long enough to avoid interference with clinical examination. Short-acting drugs such as propofol +/- remifentanil are preferred sedatives whenever possible. When residual sedation/paralysis is suspected, consider using antidotes to reverse the effects of these drugs. Be careful if using flumazenil to reverse the effects of benzodiazepines, since this drug may lower the seizure threshold.

Clinical examination

Ocular reflexes:

Bilateral absence of pupillary light reflex immediately after recovery of spontaneous circulation (ROSC) has a very limited value in predicting poor outcome. Conversely, at 72 h from ROSC a bilaterally absent pupillary light reflex predicts poor outcome both in TH-treated and in non-TH-treated patients. A bilaterally absent corneal reflex is slightly less specific than the pupillary reflex for prediction of poor outcome.

Motor response to pain

In non-TH-treated patients an absent or extensor motor response to pain, corresponding to a motor score 1 or 2 of the Glasgow Coma Scale (M ≤ 2) at 72 h from ROSC has a high sensitivity for prediction of poor outcome. Similar results are observed in TH-treated patients. Like the corneal reflex, the motor response can be suppressed by the effects of sedatives or neuromuscular blocking drugs.

Myoclonus and status myoclonus

Myoclonus is a clinical phenomenon consisting of sudden, brief, involuntary jerks caused by muscular contractions or inhibitions. A prolonged period of continuous and generalised myoclonic jerks is commonly described as status myoclonus. There is no definitive consensus on the duration or frequency of myoclonic jerks required to qualify as

status myoclonus, however in prognostication studies in comatose survivors of cardiac arrest the minimum reported duration is 30 min. The names and definitions used for status myoclonus vary among those studies. Terms like status myoclonus, myoclonic status, generalised status myoclonicus, and myoclonus (or myoclonic) status epilepticus have been used interchangeably. In post-anoxic comatose patients clinical myoclonus is only inconsistently associated with epileptiform activity on EEG.

In comatose survivors of cardiac arrest treated with TH, the presence of myoclonic jerks (not status myoclonus) within 72 h from ROSC is not consistently associated with poor outcome. A status myoclonus starting within 48 h from ROSC was consistently associated with a poor outcome in prognostication studies made in non-TH-treated patients and is also highly predictive in TH-treated patients. However, several case reports of good neurological recovery despite an early-onset, prolonged and generalised myoclonus have been published. In some of these cases myoclonus persisted after awakening and evolved into a chronic action myoclonus (Lance-Adams syndrome). In others it disappeared with recovery of consciousness. The exact time when recovery of consciousness occurred in these cases may have been masked by the myoclonus itself and by on-going sedation. Evaluating patients with post-arrest status myoclonus off sedation whenever possible; in those patients, EEG recording can be useful to identify EEG signs of awareness and reactivity and to reveal a coexistent epileptiform activity. A reactive EEG background with myoclonic status may confer a better prognosis whereas a non-reactive EEG background and myoclonus is consistently associated with a poor prognosis.

Neurophysiology Investigations

Somatosensory Evoked Potentials (SSEPs)

Bilateral absence of SSEP N20 wave

In non-TH-treated post-arrest comatose patients, bilateral absence of the N20 wave of short-latency somatosensory evoked potentials (SSEPs) predicts death or vegetative state as early as 24 h from ROSC and it remains predictive during the following 48 h with a consistent sensitivity. In TH-treated patients, a bilaterally absent N20 wave accurately predicts poor outcome both during TH and after rewarming (at 72 h from ROSC).
SSEP are only indicated if the GCS motor score is ≤3.

Electroencephalogram (EEG)

Ideally EEG examination should be done off sedation. Combining a non-reactive EEG with a malignant EEG pattern is more predictive of a poor prognosis than a single malignant pattern alone.

Absence of EEG reactivity:

In TH-treated patients, absence of EEG background reactivity (e.g. to suction stimulus) during TH is almost invariably associated with poor outcome while after rewarming at 48–72 h from ROSC it predicts a poor outcome.

Malignant EEG patterns

1) **Status epilepticus**:

In TH-treated patients, the presence of status epilepticus (SE) refractory to 2 anti-epileptic drugs (AEDs), i.e. a prolonged epileptiform activity, during TH or immediately after rewarming is almost invariably followed by poor outcome

2) **Burst suppression pattern**
3) **Supressed background with or without periodic discharges**

EEG background continuity is commonly categorised as continuous, discontinuous, burst suppression (50-99% suppression periods) or suppression (>99% activity <10µV amplitude). Whilst a suppressed EEG is relatively common and transient at 24 hours post ROSC, persistent suppressed patterns at ≥72 h from ROSC are less common and associated with a poor outcome.

Neuroradiology Investigations

Use of brain CT and MRI for prognosticating poor outcome after cardiac arrest should only be in combination with other predictors.

Brain CT

Brain CT is often performed in resuscitated comatose patients, mainly to exclude further causes of coma e.g. subarachnoid haemorrhage. The main CT finding of global anoxic-ischaemic cerebral insult following cardiac arrest is cerebral oedema, which appears as a reduction in the depth of cerebral sulci (sulcal effacement) and an attenuation of the grey matter/white matter due to a decreased density of grey matter. The presence of this pattern on brain CT performed immediately after resuscitation predicted poor outcome.

MRI

Advantages of MRI over brain CT include a better definition and a high sensitivity for identifying ischaemic brain injury. MRI can reveal extensive changes when results of other predictors such as SSEP or ocular reflexes are normal, however its use can be problematic in the most clinically unstable patients and some patients may not be able to undergo MRI due to MRI-incompatible cardiac stents, pacemakers etc. The presence of extensive reduction in diffusion at 2-5days post ROSC predicts a poor outcome.

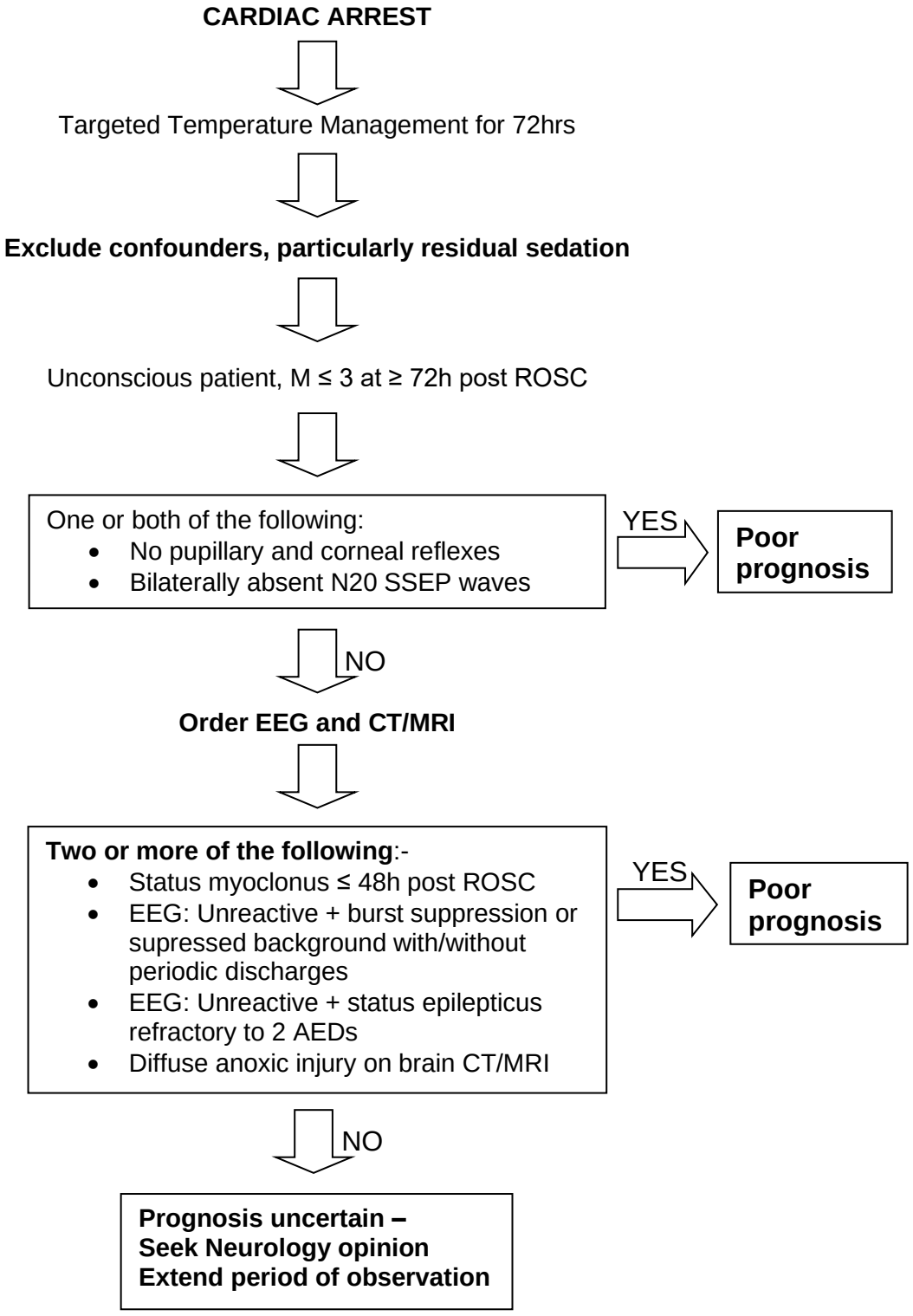
Biomarkers

Neurone-specific enolase (NSE) is a protein biomarker released following injury to neurons. Blood values of NSE post cardiac arrest are likely to correlate with the extent of anoxic-ischaemic neurological and the severity of neurological outcome. High levels of NSE predict a poor neurological prognosis but the cut-off value is not as yet clearly defined. NSE levels are not currently available in UHL within a suitable timeframe to aid prognostication.

Brainstem death

A small fraction of cardiac arrest patients develops a total brain infarction with massive oedema leading to herniation and complete loss of brain stem function. If brainstem death is suspected with bilateral pupillary dilatation and apnoea formal testing to diagnose death by neurological criteria should be undertaken in line with UHL's Guideline for the Diagnosis of Death in Adult Critical Care.

Flowchart for neurological prognostication



The above provides a framework to aid in neurological prognostication based upon the most current medical evidence and expert opinion. The decision to discontinue active treatment and switch to comfort care and palliation in any patient should ideally be a multidisciplinary decision in the best interest of the patient decided with the assent of their next of kin.

The decision ultimately lies with the intensive care consultant in charge of their care.

4. Education and Training

Guideline to be available to all staff working within critical care at UHL, with forms readily accessible for printing

Junior and senior medical and nursing staff to be informed of current guidelines within critical care and where to access the relevant information at local induction.

5. Monitoring and Audit Criteria

Element to be Monitored	Lead	Method	Frequency	Reporting arrangements
Compliance	Local audit leads for ICU	Snapshot audit	2 yearly	To local consultant meeting Q&S board for assurance

6. Supporting References

1. Nolan JP, Laver SR, Welch CA, et al. Outcome following admission to UK intensive care units after cardiac arrest: a secondary analysis of the ICNARC Case Mix Programme Database. *Anaesthesia* 2007; 61207-16.

2. Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. *Intensive Care Med* 2004; 30:2126-8.

3. Bernard SA et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002; Feb 21;346(8):557-63.

4. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med*. 2002; Feb 21;346(8):549-56.

5. TTM Trial Investigators. Nielson N, Wetterslev J, Cronberg T et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest*. N Engl J Med.* 2013;369(23):2197.

6. Therapeutic Hypothermia After Cardiac Arrest: An Advisory Statement by the Advanced Life Support Task Force of the International Liason Committee on Resuscitation. *Circulation* 2003;108:118-21.

7. Standards for the Management of Patients After Cardiac Arrest. Standards and Guidelines. The Intensive Care Society, Standards document, October 2008.

8. Sandroni, Cariou 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. Resuscitation 85 (2014) 1779–1789 http://dx.doi.org/10.1016/j.resuscitation.2014.08.011

9. Cronberg, Hornet al. A structured approach to neurologic prognostication in clinical cardiac arrest trials. Scand J Trauma, Resuscitation and Emerg Med 2013, 21:45 http://www.sjtrem.com/content/21/1/45

10. Blondin and Greer. Neurologic Prognosis in Cardiac Arrest Patients Treated With Therapeutic Hypothermia. *The Neurologist* 2011;17:241–248

11. Gold, Puertas et al. Awakening after cardiac arrest and post resuscitation hypothermia: Are we pulling the plug too early? *Resuscitation*. 85(2); 211–214 http://dx.doi.org/10.1016/j.resuscitation.2013.10.030

12. Nolan, J.P., Sandroni, C., Böttiger, B.W. et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care. Intensive Care Med 47, 369–421 (2021). https://doi.org/10.1007/s00134-021-06368-4

7. Key Words

Neurological prognosis following cardiac arrest

Myoclonic status

Cardiac arrest care

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Dr Caroline Sampson Consultant in ICM and Anaesthesia	**Lead Committee or Executive Lead** **ITU Head of Service**
Date of Next Review by Approval Committee:	**Details of Changes made during review:** 1. Sentence added to the introduction clarifying that in some patient groups senior clinicians may deem that neither TTM or TH is indicated. 2. SSEP section updated: SSEPs are only indicated if the GCS motor score is ≤3 3. Malignant EEG patterns updated to add status epilepticus (SE) refractory to 2 anti-epileptic drugs (AEDs) and supressed background with/without periodic discharges. Explanation of supressed EEG updated. 4. Paragraph prior to flowchart removed as felt to be repetitive 5. Flowchart updated to Unconscious patient, M ≤ 3 (in line with European resuscitation council and ESICM guidelines 2021) 6. Flowchart updated to add supressed background with/without periodic discharges as malignant EEG 7. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care reference added