

# Continuous evaluation of neurological prognosis after cardiac arrest

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Post-resuscitation care has changed in the last decade, and outcome after cardiac arrest has improved, thanks to several combined measures. Induced hypothermia has shown a treatment benefit in two randomized trials, but some doubts remain. General care has improved, including the use of emergency coronary intervention. Assessment of neurological function and prognosis in comatose cardiac arrest patient is challenging, especially when treated with hypothermia. In this review, we evaluate the recent literature and discuss the available evidence for prognostication after cardiac arrest in the era of temperature management. Relevant literature was identified searching PubMed and reading published papers in the field, but no standardized search strategy was used. The complexity of predicting outcome after cardiac arrest and induced hypothermia is recognized in the literature, and no single test can predict a poor prognosis with absolute certainty. A clinical neurological examination is still the gold standard, but the results need careful interpretation because many patients are affected by sedatives and by hypothermia. Common adjuncts include neurophysiol-

ogy, brain imaging and biomarkers, and a multimodal strategy is generally recommended. Current guidelines for prediction of outcome after cardiac arrest and induced hypothermia are not sufficient. Based on our expert opinion, we suggest a multimodal approach with a *continuous evaluation* of prognosis based on repeated neurological examinations and electroencephalography. Somatosensory-evoked potential is an established method to help determine a poor outcome and is recommended, whereas biomarkers and magnetic resonance imaging are promising adjuncts. We recommend that a decisive evaluation of prognosis is performed at 72 h after normothermia or later in a patient free of sedative and analgetic drugs.

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**T**HE 2010 International Liaison Committee on Resuscitation guidelines on prognostication after cardiac arrest<sup>1</sup> state that there is inadequate evidence for specific recommendations on prediction of outcome in hypothermia-treated cardiac arrest patients. Hence, the practice parameters for outcome prediction, formulated in 2006 by the American Academy of Neurology (AAN),<sup>2</sup> need to be reevaluated because they are based on treatment algorithms prior to the introduction of temperature management and the more active care that followed.<sup>3,4</sup> Induced hypothermia has been implemented in a majority of Scandinavian hospitals as recommended<sup>5</sup> and implicates prolonged intensive care with consequent sedation and intermittent muscle paralysis.

Previous recommendations emphasized 72 h after cardiac arrest as the optimal time for evaluation of neurological prognosis because the specificity for several clinical indicators of a poor prognosis reached 100% at this time.<sup>2,6,7</sup> In fact, only a minority of patients in coma at 48–72 h after cardiac arrest ever regained consciousness,<sup>6,8</sup> and the 72-h time point was considered safe. This has changed after the introduction of hypothermia and the recurring reports of false predictions of outcome at 72 h after cardiac arrest and delayed recovery from coma.<sup>9–14</sup> This failure of established prognostic parameters may be caused by sedation and reduced turnover of drugs because of the intervention,<sup>15–17</sup> but a direct effect on the brain by hypothermia, affecting awakening and recovery, cannot be excluded.

Most authors agree that delaying the time for prognostication and a subsequent decision on level of care beyond 72 h after cardiac arrest is mandated in patients treated with hypothermia,<sup>10,14,18,19</sup> which is also suggested in the present guidelines.<sup>1</sup> Moreover, to reduce the risk of a false prediction, a multimodal strategy is recommended,<sup>10,14,18–20</sup> where a neurological examination is combined with other prognostic methods (neurophysiology, biomarkers, neuroimaging). A solid basis for a decision on level of care is of uttermost importance because withdrawal of active care will lead to rapid deterioration and death in most patients. Therefore, new methods need to be tested in large, high-quality prospective trials to secure safe and evidence-based routines.

In this review, we will discuss the available evidence and present our opinion on how prognostication after cardiac arrest in hypothermia-treated patients may be performed, emphasizing the need of a multimodal strategy and a *continuous evaluation* of cerebral function in the intensive care unit (ICU). Relevant literature was identified searching PubMed and reading published papers in the field, but no standardized search strategy was used. We will conclude with hands-on recommendations based on the current guidelines, recent reports and our own experience.

## Natural course of neurological recovery after cardiac arrest

The severity of the initial insult decides the natural course and timeline of recovery after cardiac arrest and depends on several factors, the main one being the *no-flow time*, defined as the time of cardiac arrest without cardiopulmonary resuscitation (CPR). The *low-flow time* is the time with on-going CPR, either by bystanders or by medical personnel. A third factor of importance is the *quality of CPR*, including depth and rate of compressions and the CPR fraction, defined as time with ongoing CPR (as opposed to hands-off time).<sup>21</sup> Other factors such as age, cause of arrest (asphyxia vs. cardiac cause) and comorbidities in individual patients may also affect the severity of the brain injury.

Soon after cardiac arrest, most brain functions succumb. When perfusion and pressure are reinstated with consequent delivery of oxygen, brain functions recover in an orderly fashion.<sup>22</sup> First, primitive brain-stem functions return, such as spontaneous breathing and brain-stem reflexes. This is followed by return of activity in the deep structures of the brain<sup>23</sup> and eventually a recovery of cortical

activity and consciousness.<sup>22</sup> Because the brain stem is less sensitive to circulatory arrest than the brain cortex, at least partial recovery of brain-stem functions is common during the first hours to day(s) after cardiac arrest, also in patients with severe anoxic injury and poor prognosis for awakening. Hence, if ventilation is supported, nutrition is supplied, and complications are treated, the severely brain-injured cardiac arrest survivor may develop a chronic vegetative state, a condition rarely seen in most countries<sup>3,24</sup> probably because of current protocols for withdrawal of care.<sup>2,25,26</sup>

## Clinical neurological examination

The clinical neurological examination is still the gold standard to assess prognosis after cardiac arrest, but it needs careful interpretation because many patients are affected by sedatives and possibly by hypothermia.<sup>15,16</sup> Already on arrival in the emergency room, the level of consciousness may be associated with the final outcome,<sup>3,12</sup> but even deep coma including absence of pupillary and corneal reflexes at admission does not exclude a final good outcome.<sup>6,27</sup>

The bedside neurological examination of the comatose cardiac arrest survivor is based on: (1) observation of seizures and spontaneous movements, (2) determination of coma depth and (3) testing of brain-stem reflexes. Seizures are most often myoclonic and discussed separately and in more detail later in this review. The most widely used coma-level scale is the Glasgow Coma Scale, originally developed for head injury.<sup>28</sup> In reality, the two first parts, concerning verbal response and eye opening is of less importance after cardiac arrest mainly because a patient with any verbal or eye response (other than by reflex) has a less pronounced coma and consequently a favorable prognosis. In contrast, the motor response to pain has been the most widely used prognostic test, and an absence of or extensor response to pain has been considered a reliable predictor of poor outcome on day 3 after cardiac arrest, with a positive likelihood ratio 16.8 [95% confidence intervals (CIs) 3.4–84.1] and a false-positive rate (FPR) of 0% (95% CI 0–6.7).<sup>29</sup> After the introduction of hypothermia, a good outcome despite an absence of or extensor response to pain at 72 h has been described,<sup>9,12,13</sup> with a reported FPR of 10% (95% CI 6–16) in a recently published study.<sup>30</sup> This may be explained by lingering effects of sedation,<sup>16</sup> and a consequence is that motor response to pain no longer can constitute

the foundation of a poor prognosis statement in hypothermia-treated patients.<sup>19</sup>

We routinely test pupillary light responses and corneal reflexes, which are the best studied brain-stem reflexes<sup>27,29</sup> but also the gag/cough response and the oculovestibular reflex (Doll's eye). When response to the latter is absent or indeterminate, a caloric test with ice-cold water is performed. Several studies on hypothermia-treated patients have confirmed that a bilateral loss of corneal or pupillary reflexes at 72 h after arrest are useful predictors of poor outcome.<sup>9,12,31</sup> In the study from Bouwes and coworkers,<sup>30</sup> the FPR for an absent corneal reflex was 4% (95% CI 1–13), and for an absent pupillary reflex, the FPR was 1% (95% CI 0–7). However, reactivity of constricted pupils as well as the corneal reflex may be difficult to assess, and it is vital that effects of lingering sedation is excluded.

It was included in the algorithm of the AAN guidelines<sup>2</sup> that absence of all brain-stem reflexes at any time should prompt a testing for brain death. In our experience, in the small fraction of patients who eventually were declared brain dead, it was common that some brain-stem function recovered only to be lost again with the generalized brain swelling heralding the complete cessation of intracranial circulation (Dragancea I, unpublished observation). Brain death diagnosis should be made with caution in cardiac arrest patients, especially when hypothermia has been applied, as highlighted in a recent report.<sup>32</sup> Because of the inherent complexity, we do recommend ancillary tests to confirm cessation of cortical activity [electroencephalography (EEG), somatosensory evoked potentials (SSEPs)] and a generalized brain infarction [computed tomography (CT), magnetic resonance imaging (MRI)] in order to support the clinical brain death examination after cardiac arrest. If in doubt, a four-vessel contrast-enhanced angiography should be done to confirm cessation of intracranial circulation, which is in accordance with current legislation in many countries.

## Neurophysiology

EEG has been used for decades to diagnose seizure activity and as an aid in predicting outcome in the comatose patient after cardiac arrest. The limitations of EEG include that a single, conventional EEG is a snapshot of what is going on in the brain during a limited time (usually 20–30 min) and that EEG activity is affected by sedatives. Recent guidelines recommend that EEG is performed early after cardiac

arrest and that continuous EEG monitoring should be considered for patients treated with induced hypothermia.<sup>1</sup>

Continuous EEG monitoring is common in the neonatal ICU,<sup>33</sup> increasingly used in the neuro-ICU,<sup>34</sup> but is yet uncommon in the adult general ICU.<sup>35</sup> One reason is its complexity and the need of certain skills. Instead, a simplified EEG montage with a limited number of raw EEG curves, in combination with an amplitude integrated EEG (aEEG) trend curve, may be used (Fig. 1) and has become standard practice in many neonatal ICUs. Our group has shown that simplified EEG/aEEG is feasible and of clinical value in the adult, comatose cardiac arrest patient as well.<sup>36,37</sup> Because cardiac arrest leads to a global hypoxic, ischemic injury, two hemispheric leads should be sufficient to give relevant bedside information on the recovery or deterioration of cortical activity. If needed, the simplified EEG/aEEG can be combined with a conventional EEG to test for EEG-reactivity to external stimuli (sound, pain) and to verify malignant patterns. The obvious application for continuous EEG monitoring is seizure detection in the sedated, paralyzed patient in whom clinical seizures may be concealed. Second, relevant monitoring of anticonvulsive treatment mandates continuous EEG monitoring. Third, we have shown that the change and evolution of EEG patterns using simplified EEG/aEEG-monitoring can predict good as well as poor outcome in cardiac arrest patients,<sup>37</sup> with a positive predictive value for a good outcome of 0.87 (95% CI 0.76–0.94) if a continuous pattern is present at normothermia and a negative predictive value for a good outcome of 0.91 (95% CI 0.76–0.98) for all other patterns at normothermia.

SSEP is incorporated in prognostication guidelines and seems to keep its position in the era of temperature control seemingly less affected by temperature and the use of sedation. Prior to the introduction of induced hypothermia, a large systematic review evaluated bilateral absence of N20 potentials during the first week after cardiac arrest and found an FPR of 0% (95% CI 0–2.0).<sup>29</sup> In hypothermia-treated patients, a bilateral loss of N20 potentials at normothermia still seems to be a reliable prognostic measure<sup>13</sup> with an FPR of 0% (95% CI 0–18),<sup>30</sup> but there are rare reports of the opposite,<sup>11</sup> and interobserver variability also exists.<sup>38</sup> Moreover, the SSEP results were not blinded in the study by Bouwes,<sup>30</sup> and a lack of N20 potentials resulted in withdrawal of care in 79% of cases because of a *perceived* poor outcome, which may have affected the results.

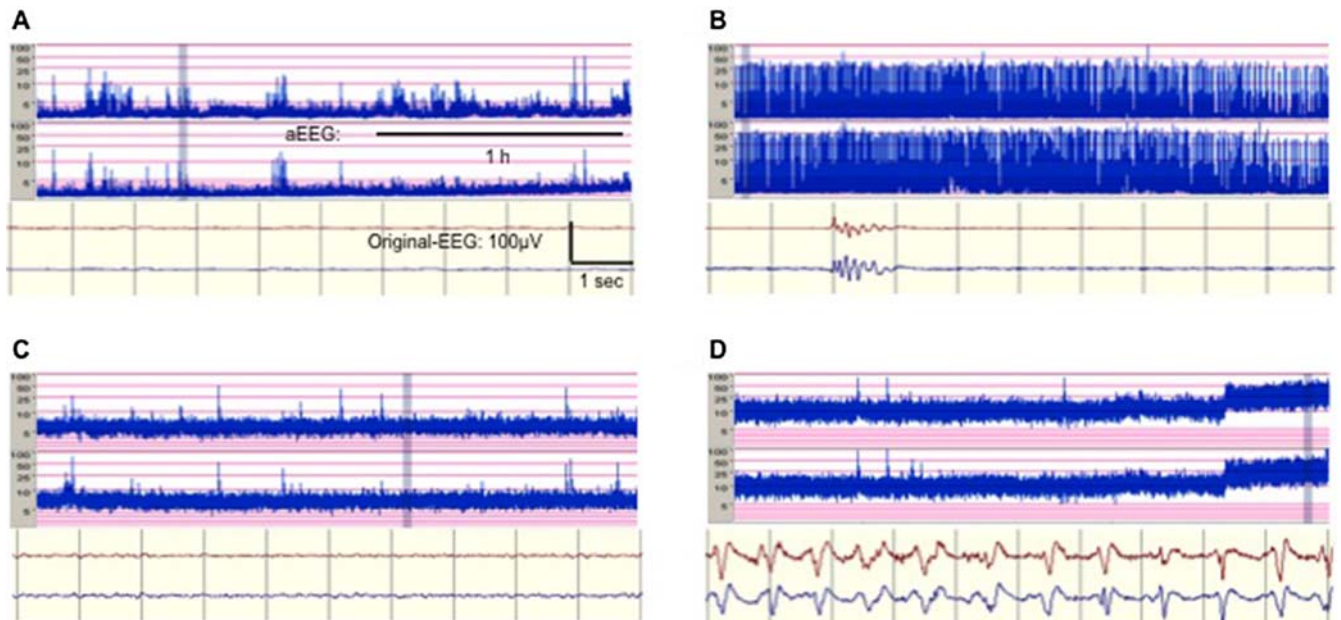


Fig. 1. A simplified electroencephalogram (EEG) with two original EEG curves (lower panel), in combination with an amplitude integrated EEG (aEEG) trend curve (upper panel). Four dominating EEG patterns after cardiac arrest are shown: (A) flat, (B) suppression-burst, (C) continuous and (D) electrographic status epilepticus.

Hence, there are concerns of a self-fulfilling prophecy, and future studies need to address this further. SSEP is sensitive to muscle artifacts and relaxation should be used liberally during testing. As for the brain-stem reflexes, sensitivity to predict poor outcome using SSEP is low (< 50%), which limits its usefulness in clinical practice. We use SSEP as a confirmatory test when a poor prognosis is indicated from clinical findings, biomarkers and EEG results.

### Myoclonus and electrographic status epilepticus

Myoclonus is the brief and involuntary twitching of a muscle or group of muscles. It may be physiological but is more often a sign of a metabolic, structural or pharmacological influence on the brain. Spontaneous or stimulus-induced myoclonus is common following cardiac arrest but is often masked by sedatives that are part of most hypothermia protocols.<sup>39</sup> Occasional myoclonic jerks has little prognostic value. When myoclonus is generalized (both face and limbs) and starts during the first day after cardiac arrest, it is often combined with a burst-suppression pattern on the EEG and is a sign of severe cortical injury and poor prognosis.<sup>40,41</sup> There are recent reports that early myoclonus no longer

has 100% specificity for poor outcome in hypothermia-treated cardiac arrest patients,<sup>42,43</sup> but it should still be considered a grave sign. Additional tests are needed, and a malignant EEG pattern and an absence of cortical SSEP responses after the patient has been rewarmed will usually confirm the poor prognosis. It has also been described that survivors after cardiac arrest secondary to respiratory failure and hypoxia may have a good outcome despite early generalized myoclonus.<sup>44</sup> These patients may also develop an action-induced myoclonus days to weeks after the arrest, which may become chronic,<sup>45,46</sup> in contrast with the early generalized myoclonus, which usually subsides during the first days.

Electrographic status epilepticus (ESE) following cardiac arrest, or post-anoxic ESE, has been defined as repetitive epileptic discharges during at least 30 min and with a frequency of > 1 Hz.<sup>37</sup> However, no international consensus on the definition of post-anoxic ESE exists. It has been debated whether post-anoxic ESE is a genuine epileptic condition or merely a hallmark of a severely injured brain without treatment potential.<sup>41</sup> The majority of patients who develop ESE after cardiac arrest have clinical seizures,<sup>37</sup> which are mainly myoclonic, sometimes tonic-clonic, and typically suppressed by propofol.<sup>39</sup>

Following the introduction of hypothermia, there are several reports of patients surviving post-anoxic ESE with good neurological outcome,<sup>37,43,47,48</sup> and it has been suggested, but not shown, that aggressive antiepileptic treatment improves outcome. Electrographic indicators of a favorable outcome include a return of a continuous EEG background pattern before the start of ESE<sup>37</sup> and a reactive EEG background during ESE.<sup>13,49</sup> Our experience is that seizure activity is difficult to suppress with conventional antiepileptic agents alone, why a combination with sedative agents, often for a prolonged time, may be needed in this subset of patients.

We regard post-anoxic ESE as an epileptic condition, superimposed and secondary to an underlying encephalopathy, and we believe that a potential treatment effect depends on the extent of brain damage. Patients with severe brain damage may develop ESE early, whereas patients with less severe damage may develop ESE during or after rewarming, as sedation is reduced.<sup>37</sup> We speculate that ESE itself might contribute or even be the sole cause of prolonged coma.<sup>10</sup> Additional means of quantifying the burden of brain damage, such as serial measurements of neuron-specific enolase (NSE), SSEP and MRI of the brain, are therefore of importance. In the absence of other signs of brain damage in a comatose patient, we recommend prolonged observation, EEG monitoring and seizure suppression with sedative agents.

## Biomarkers

Biomarkers are quantifiable biologic markers that can be collected and measured in different fluid compartments, most often blood. The best studied biomarkers after cardiac arrest are NSE and S-100B, of which NSE has been incorporated in guidelines stating that a value  $> 33 \mu\text{mol/l}$  is a reliable predictor of a poor outcome.<sup>2</sup> These guidelines were based on studies prior to the era of temperature control, and some recent studies have questioned the value of NSE for prognostication in hypothermia-treated patients,<sup>50,51</sup> whereas other studies support its use.<sup>52,53</sup> One explanation to these diverse results may be differences in laboratory methods and a lack of standardization. Also, hemolysis should be carefully controlled because it generates false high NSE values.

In a large, prospective study from the Netherlands,<sup>30</sup> NSE at 48 h was measured in 310 patients; 99 had a value  $> 33 \mu\text{mol/l}$ , of whom 10 had a good outcome, resulting in a FPR of 7% (95% CI 4–12). It

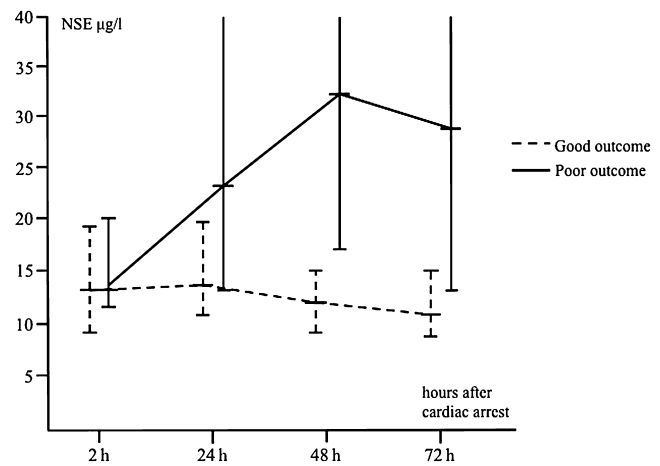


Fig. 2. Neuron-specific enolase (NSE) in peripheral blood in patients treated with hypothermia after cardiac arrest; typical release curves in the good and the poor outcome groups are shown. Values are median and interquartile range.

may be that trends, for example the 24- to 48-h trend for NSE,<sup>52,53</sup> are more useful to study than single values, but this was not addressed in the Dutch study. In our hands, NSE is a useful prognostic tool with typical release curves in the good and the poor outcome groups (Fig. 2). Today, the NSE analysis has been incorporated in modern laboratory equipment and may be available as a routine test. A single high NSE should be interpreted with care, whereas repeated low NSE values in a comatose patient should alert the physician that a potentially treatable condition may exist. This was illustrated in a recent study,<sup>10</sup> where a late debut of ESE seemed to be the sole cause of prolonged coma in some patients, while other signs of brain injury, including elevated NSE, were lacking.

Like NSE, S-100B has been extensively studied, and some authors prefer this biomarker for neurological prognostication,<sup>54–56</sup> but its role is less established. Other potentially interesting biomarkers include tau,<sup>57</sup> glial fibrillary acidic protein,<sup>58</sup> neurofilaments,<sup>59</sup> organ-specific micro-RNAs<sup>60</sup> and more. More high-quality trials evaluating biomarkers after cardiac arrest are needed before any biomarker can be incorporated in common guidelines and reach general use.

## Imaging

An early CT of the brain is commonly used to rule out an unexpected intracerebral cause of coma in patients who remain unconscious after cardiac arrest. We encourage the expansion of this examina-

tion to include the cervical spine if trauma is suspected after encountering two patients with high cervical fractures as an explanation for tetraplegia after cardiac arrest (Cronberg T, unpublished observation). Both our patients were elderly men, and both regained consciousness and higher functions. A CT scan of the brain has also been used as an early predictor of neurological outcome.<sup>61–66</sup> A loss of distinction between gray and white matter, indicating cerebral edema, is associated with a lower likelihood for a good outcome. However, current guidelines state that there is insufficient data to support CT imaging as a prognostic instrument.<sup>1</sup>

Brain MRI is a better tool than CT to visualize post-anoxic brain injury after cardiac arrest<sup>67–70</sup> and may be of value as a prognostic adjunct. Wijman and coworkers recently showed<sup>71</sup> that diffusion-weighted imaging MRI changes were region- and time-dependent, providing relevant prognostic information 2–5 days after cardiac arrest. At this late time, other prognostic information is already at hand, which limits the clinical usefulness of this rather cumbersome investigation. In selected patients, an MRI without signs of extensive brain injury may motivate prolonged and active treatment. As a prognostic tool after cardiac arrest, routine brain MRI, like CT, needs further evaluation before it can be incorporated into clinical guidelines.

### When to assess patients in persistent coma

Our view is that the formerly accepted 72-h time point for evaluation of prognosis is no longer valid for patients who have received induced hypothermia after cardiac arrest.<sup>10,18,19,70</sup> Within the Lund Coma Study, we decided to postpone a decision on level of care until 72 h *after normothermia* in hypothermia-treated patients.<sup>10</sup> We found that 6 of 34 patients with persisting coma at 4–5 days after arrest eventually regained consciousness and that four were alive at 6 months, supporting a delayed assessment. Future studies will clarify which time point is optimal and lay the foundation for recommendations. Until we know more, we suggest that a written protocol for withdrawal of active care is used and that a decisive neurological assessment is done at 72 h after normothermia or later. This strategy has also been decided in a large ongoing trial, the target temperature management after out-of-hospital cardiac arrest trial (TTM-trial) (ClinicalTrials.gov NCT01020916).<sup>26</sup>

### Recommendations

Neurological prognostication following cardiac arrest serves two main purposes. Early information can be used to inform relatives that there is hope for recovery or that tests indicate that the prognosis is poor. At a later time point, the prognostic information may be that the best possible outcome is a vegetative state, supporting the physician to make a decision to withdraw supportive treatment.

The Swedish Resuscitation Council recently appointed a study group to write national recommendations for prognostication after cardiac arrest, as has already been done in the Netherlands (<http://www.neurologie.nl/publiek/beroepsinformatie/richtlijnen/nvn-richtlijnen/>). Based on the present review and our expert opinion, we recommend that caution and patience should be emphasized while caring for the cardiac arrest patient with prolonged coma in the ICU. This includes a prolonged observation time and a strategy using several methods in parallel to optimize the assessment of the comatose patient. A neurological examination should be performed regularly and at least once daily. We recommend that brain cortical function is monitored, optimally with a simplified EEG/aEEG trend monitor, during the ICU stay until awakening or until a decision on level of care is made. If this cannot be performed, a minimum would be that at least one conventional EEG is performed in patients remaining in coma, soon after normothermia. In selected patients, an early CT scanning (< 24 h) should be performed to rule out secondary brain injury (trauma, bleeding), whereas MRI is recommended in selected patients with prolonged coma at a later time (48–108 h) to visualize brain ischemia. We also suggest that serial NSE measurements are analyzed and taken into account. SSEP, when available, should be performed in patients remaining in coma. A decision on level of care should, with few exceptions, not be performed earlier than 72 h after normothermia (4–5 days after cardiac arrest) and in a patient who is not affected by sedative and analgetic drugs. Regarding ESE after cardiac arrest, we want to emphasize that special considerations should be made for the small group of comatose patients with a late debut of ESE and no other signs of extensive brain injury, i.e., a reactive EEG background pattern, a normal SSEP, low NSE values and an MRI<sup>10,13</sup> without extensive signal abnormalities. We judge that this subgroup of potentially treatable patients should be targeted in coming prospective trials.

Table 1

Criteria allowing withdrawal of active care in patients with persisting coma after cardiac arrest, according to the TTM trial\*.

- 1 Ethical reasons (at any time).
- 2 The patient is brain dead because of cerebral herniation.
- 3 The patient develops severe myoclonus status† in the first 24 h after admission and has a bilateral absence of N20 peaks on median nerve SSEP after rewarming.
- 4 At 72 h after normothermia, the patient is in persisting coma with a Glasgow Motor Score 1–2 and has bilateral absence of N20 peaks on median nerve SSEP.
- 5 At 72 h after normothermia, the patient is in persisting coma with a Glasgow Motor Score 1–2 and has a treatment refractory status epilepticus.‡
- 6 Patients in persisting coma with a Glasgow Motor Score 1–2 at 72 h after normothermia and with no improvements 1–2 days later.

\*Target temperature management after cardiac arrest. (Clinical-Trials.gov NCT01020916).

†Generalized myoclonic convulsions in face and extremities for 30 min or longer.

‡Unresponsive to active treatment with sedatives and antiepileptics for at least 24 h.

SSEP, somatosensory evoked potentials.

The ongoing TTM-trial randomizes comatose patients after out-of-hospital cardiac arrest to two controlled target temperatures, 33°C vs. 36°C. In this study, we have a common protocol with pre-defined criteria for discontinuation of care in order to limit early withdrawal and to minimize bias (Table 1). Furthermore, all use of sedative and analgetic drugs is registered.

## Conclusion

Current guidelines for prediction of outcome after cardiac arrest and induced hypothermia are not sufficient, and there is a need for prospective evaluation of prognostic factors in large patient cohorts with clear defined criteria for discontinuation of care. Based on our expert opinion, we suggest a novel multimodal approach of *continuous evaluation of prognosis* in all hypothermia-treated cardiac arrest patients (Table 2). This includes daily neurological examinations and, whenever possible, continuous monitoring of cortical activity, preferably using a simplified EEG/aEEG trend monitor. If no such monitor is at hand, at least one conventional EEG should be performed in all comatose patients early after normothermia in order to rule out potentially treatable ESE. Brain imaging should be used liberally; CT scanning may be performed early (< 24 h) to rule out secondary brain injury (trauma, bleeding), whereas MRI may be used in patients with prolonged coma to visualize an

Table 2

Continuous evaluation of neurological prognosis, suggested investigations.

Investigation	When	Reference(s)	Priority
Clinical neurological examination	Daily	2, 12, 30	1
Neurophysiology			
continuous EEG*	Continuously	1, 35, 37	2
conventional EEG†	36–72 h	1, 43	1
SSEP‡	48–108 h	2, 30	2
Biomarkers§			
Neuron-specific enolase	24 + 48 h	30, 52, 53	2
Brain imaging¶			
CT scanning	< 24 h	65, 66	1
MRI	48–108 h	71	2

h is hours after cardiac arrest.

Late MRI to visualize the extent of post-anoxic brain injury.

Priority 1: the investigation should be available. Priority 2: availability is recommended.

\*Preferably simplified EEG/aEEG-monitoring.

†If continuous, EEG is not used. Perform earlier if suspected clinical seizures.

‡In comatose patients.

§Repeated samples.

¶Early CT to exclude intracerebral cause of coma other than post-anoxic injury.

CT, computed tomography; EEG, electroencephalography; aEEG, amplitude integrated EEG; MRI, magnetic resonance imaging; SSEP, somatosensory evoked potentials.

ischemic injury at a later time (48–108 h). SSEP, when available, should be performed in all patients with prolonged coma (48–108 h). Serial NSE (24 + 48 h) is recommended as an adjunct and as a part of a continuous assessment. We conclude that centers responsible for high-quality post-cardiac arrest care need to have access to at least CT scanning and EEG, while access to MRI, SSEP and NSE is recommended but optional (Table 2). We recommend that a decisive evaluation on prognostication and a decision on level of care are done at 72 h after normothermia or later in a patient free of sedative and analgetic drugs.

*Conflict of interest:* Hans Friberg is on the speaker’s bureau of CareFusion, Inc.® Carefusion, Inc.® supports the trial ‘Prognostic value of EEG after cardiac arrest in TH and non-TH patients’ with Nicolet™ Monitors. Niklas Nielsen is the chief investigator of the TTM trial.

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