

Neurological Prognosis after Cardiac Arrest Guideline

I. Associated Guidelines and Appendices

1. Therapeutic Hypothermia after Cardiac Arrest
2. Hypothermia after Cardiac Arrest Algorithm

II. Rationale

General Considerations

The precision of neurological prognosis in patients with coma after cardiac arrest is limited. The goal of bedside neurological examination and ancillary testing is to differentiate between a poor versus favorable chance of a good neurological outcome. Studies to date have identified strong predictors of *poor* prognosis. However, the remaining individuals have an indeterminate prognosis.

Neuroprognosis without therapeutic hypothermia

Anoxic brain damage is the major complication of cardiac arrest that strongly influences recovery. The only available therapy to improve neurological recovery is mild therapeutic hypothermia (32-34°C), and every effort should be made to institute therapy in patients who qualify.^{1,2} For patients who are not treated with therapeutic hypothermia, neurological examination and ancillary test findings can identify patients with poor neurological prognosis (see below).³

Neuroprognosis after therapeutic hypothermia

Recent studies suggest that therapeutic hypothermia alters the specificity of most prognostic indicators, including neurological exam findings, the presence of myoclonic status epilepticus, and SSEPs findings. Consequently neurological prognostication is more challenging in patients treated with therapeutic hypothermia. For specific details, refer to Table 1 in the appendix for how therapeutic hypothermia may alter the rate of false positive prediction for poor outcome.

III. Patient Selection

1. In- or out-of-hospital VF, asystolic, or PEA cardiac arrest requiring CPR and with return of spontaneous circulation, with or without therapeutic hypothermia.
2. Patients who are comatose after ROSC.
3. Adults age ≥ 18 years old. The relevance of these guidelines to pediatric patients is not known.
4. The Stroke/ICU consult Service (beeper 20202) should be consulted to facilitate the determination of neurological prognosis.

IV. Definitions of Neurological Outcome

Various definitions of good and poor neurological outcome have been used in the literature. However, a commonly used definition is based on Cerebral Performance Category (CPC) Scale

score at 3-6 months after discharge,⁸ where "Good outcome" = CPC 1-2, and "Poor outcome" = CPC 3-5.

“Good outcome” often indicates independence in daily living, whereas “Poor outcome” implies dependence on others for daily living. CPC scores are defined as follows:

Good Outcome:

- **CPC 1.** Mild deficits. Able to work. May have mild neurologic/psychologic deficits.
- **CPC 2.** Moderate deficits. Capable of independent activities of daily life. Able to work in sheltered environment.

Poor Outcome:

- **CPC 3.** Severe deficits. Conscious but dependent on others for daily support. Ranges from ambulatory state to severe dementia or paralysis.
- **CPC 4.** Coma or vegetative state.
- **CPC 5.** Brain death: apnea, areflexia, EEG silence, etc.

V. Recommended Approach to Prognosis

The following clinical examination and ancillary tests can be considered. A decision guiding prognosis frequently requires a synthesis of test results, put into the context of the individual patient.

Neurological examination:

Findings with particular prognostic significance include pupillary responses, corneal reflexes, oculocephalic reflexes, and to a lesser extent motor responses.

| | <u>No Hypothermia</u> | <u>Therapeutic Hypothermia</u> |
|---------------------------|------------------------------|---|
| Timing of Neuro Exam | Day 3 or Day 7 | Day 5 or Day 9 |
| Neuro exam findings: | | |
| No motor response to pain | Poor prognosis | indeterminate |
| No pupillary reflex | Poor Prognosis | Poor prognosis (but ~4% false positive rate) |
| No corneal reflex | Poor Prognosis | Poor prognosis (but ~4% false positive rate) |
| No oculocephalic reflex | Poor Prognosis | Poor prognosis (but ~4% false positive rate) |

Rare cases of recovery have been reported for nearly all negative prognostic signs. **Concordance of exam findings, in conjunction with ancillary testing, is essential.**

Continuous EEG monitoring:

Continuous EEG monitoring (cEEG) can provide prognostic information and detect seizures. The main focus of cEEG monitoring in the comatose cardiac arrest patient is for *prognosis* rather than real-time seizure detection. For patients undergoing therapeutic hypothermia, cEEG can be used during cooling. If cEEG is started during the cooling phase, it should generally continue for approximately 24 hours after reaching normothermia, to allow evaluation of trends (e.g. toward normal vs. deterioration) in background activity.

The presence of seizures or status epilepticus, sporadic or periodic epileptiform discharges, diffuse voltage attenuation, and burst suppression, lack of EEG reactivity to external stimulation, and alpha or delta coma patterns are signs of poor prognosis. However, no single feature is sufficiently specific to be used in isolation.

Patients found to have seizures on EEG should be treated with anticonvulsants, targeting seizure control. Patients found to have status epilepticus on EEG should be considered for treatment with IV antiepileptic drugs targeting electrographic burst suppression for at least 24 hours. It is not known whether anti-epileptic therapy in the setting of anoxic brain injury alters outcome.

- cEEG monitoring is recommended for prognostic utility.
- Detection and treatment of seizures or status epilepticus can be considered for ≤ 24 hours, however, it is not known whether seizure suppression alters outcome after anoxic brain injury.

Somatosensory Evoked Potentials:

SSEPs should be performed greater than 48 hours after cardiac arrest, or 48 hours post-rewarming if the patient underwent induced hypothermia.

- Bilateral absence of N20 is specific for poor prognosis, with or without hypothermia.

Serum Biomarkers:

Neuron-specific enolase (NSE), typically sent 1-3 days after arrest or after rewarming is routinely recommended. No definitive cutoff value has been validated, and the influence of therapeutic hypothermia on NSE level is not known.

- Serum biomarkers are not recommended for prognosis.

Neuroimaging:

Head CT at 48 hours post-arrest or 48 hours post-rewarming can identify patients with poor prognosis if there is widespread hypodensity.

Brain MRI can be considered after day 3, although the utility for prognosis is not firmly established.

- Head CT or brain MRI can be used after day 3 (no hypothermia) or day 5 (if therapeutic hypothermia was used). Emerging evidence suggests these modalities can be useful to detect some patients with poor prognosis.

VI. Summary

The decision to proceed with or withdraw supportive care requires careful consideration. Often, the prognosis for neurological recovery is indeterminate, but may be influenced by patient specific factors such as age, comorbidities, and the prior wishes of the patient along with prognostic data obtained through testing described above. When in doubt about prognosis, particularly in younger patients, consider allowing more time.

VII. Appendix

As an aid, estimates of the false positive rates of the most commonly prognostic indicators are summarized in Table 1. Using these indicators *in combination* is essential to reducing the false positive rates of individual indicators. One published scheme for combining many of these indicators to predict a *poor* neurological prognosis is given in Table 2.⁴

Table 1. False Positive Rates of Univariate Predictors of Poor Neurological Outcome[‡] After Cardiac Arrest, With and Without Therapeutic Hypothermia

| Predictor | Timing | FPR: No TH | FPR: TH |
|---|-----------|---------------------------|---------------------------|
| Non-VF Cardiac arrest | | | 15 (6-30)% ⁴ |
| ROSC >25 min | | | 24 (13-40)% ⁴ |
| Low voltage [‡] EEG – early on | Before TH | | 47 (35-60)% ⁵ |
| Low voltage [‡] EEG – upon rewarming | Day 1* | | 5 (2-14)% ⁵ |
| Discontinuous EEG (burst suppression pattern) | Day 1* | | 7 (2-23)% ⁵ |
| Epileptiform activity on first EEG [‡] | Day 1-3 | | 9 (2-21)% ⁴ |
| Unreactive EEG background | Day 1-3* | | 7 (1-18)% ⁴ |
| Early myoclonus | Day 1* | 0 (0-8.8)% ³ | 3 (0-11)% ⁴ |
| Bilaterally absent N20 on SSEP | Day 1-3* | 0.7 (0-3.7)% ³ | 0 (0-8)% ⁴ |
| Serum Neuron-specific Enolase (NSE) > 33µg/L | Day 1-3* | 0 (0-3)% ³ | 11 (4-27)% |
| Absent or Extensor only motor response to pain | Day 3* | 0 (0-3)% ³ | 24 (14-39)% ⁴ |
| ≥1 brainstem reflexes absent (pupillary, oculocephalic, corneal) | Day 3* | 0 (0-3)% ³ | 4 (1-15)% ⁴ |
| Head CT diffuse hypodensity + GCS ≤8 | Day 1-3* | 0 (0-48)% ⁶ | 0 (0-27)% ⁶ |
| MRI: Any diffusion restriction | Day 1-3* | 54 (26-80)% ^{#7} | 54 (26-80)% ^{#7} |
| [‡] Poor neurological outcome = death, unconsciousness, or severe disability at >1 month [*] Assessed after rewarming and discontinuation of sedation. [‡] 'Seizure activity' = epileptiform discharges of any kind (e.g. spikes, lateralized periodic discharges (PLEDs) or generalized epileptiform discharges (GPEDs)) or electrographic seizures; "Low voltage" = <10µv (but not | | | |

meeting criteria for electrocerebral silence);
 #Patients who did and did not undergo TH were analyzed as one group.

Table 2: Improved prediction of poor outcomes by combining prognostic indicators

| Prognostic value of <u>A COMBINATION OF AT LEAST TWO</u> of the following negative findings (measured after completion of re-warming following TH, between 36-72 hours post cardiac arrest) | | |
|--|------------------------------|--|
| <ul style="list-style-type: none"> • Bilaterally Absent SSEP • Unreactive EEG Background • Early Myoclonus • Incomplete Recovery of Brainstem Reflexes | | |
| Prediction: | In-Hospital Mortality | Poor 3-6 Month Neurological Outcome |
| Sensitivity (95% CI) | 79 (67-88) % | 62 (51-72) % |
| False Positive Rate (95% CI) | 0 (0-8) % | 0 (0-14)% |
| PPV (95% CI) | 100 (93-100) % | 100 (93-100) % |
| NPV (95% CI) | 76 (63-86) % | 44 (31-58) % |
| <p><i>Statistics are based on outcomes in 111 comatose survivors of cardiac arrest treated with TH. Poor outcome: defined as severe disability/dependency, coma, or death.</i></p> | | |

VIII. References

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IX. Authoring Information

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