



PREDICTION OF OUTCOME IN COMATOSE SURVIVORS AFTER CARDIOPULMONARY RESUSCITATION

This is a summary of the American Academy of Neurology (AAN) evidence-based guideline reviewing all available evidence on the prognostic value of the clinical examination and ancillary investigations (electrophysiologic, biochemical, and radiologic) for poor outcome in comatose survivors after cardiopulmonary resuscitation. Poor outcome is defined as death, unconsciousness after one month, or unconsciousness or severe disability after six months.

Please refer to the full guideline for detailed findings and supporting evidence at www.aan.com.

RECOMMENDATIONS FOR THE PROGNOSTIC VALUE OF THE CLINICAL EXAMINATION

Strong (Level A) evidence	Features of the neurologic examination: Glasgow Coma Scale (GCS) score; Motor part of the GCS; Brainstem reflexes (pupillary light reflexes, corneal reflexes and eye movements)	The prognosis is invariably poor in comatose patients with absent pupillary or corneal reflexes, or absent or extensor motor responses three days after cardiac arrest (Level A).
Good (Level B) evidence	Presence of seizures or myoclonus status epilepticus (defined as spontaneous, repetitive, unrelenting, generalized multifocal myoclonus involving the face, limbs, and axial musculature in comatose patients)	Patients with myoclonus status epilepticus within the first day after a primary circulatory arrest have a poor prognosis (Level B).
Good (Level B) evidence	Circumstances surrounding CPR: Anoxia time; Duration of CPR; Cause of the cardiac arrest (cardiac vs. noncardiac); Type of cardiac arrhythmia	Prognosis cannot be based on the circumstances of CPR (Level B).
Weak (Level C) evidence	Elevated body temperature	Prognosis cannot be based on elevated body temperature alone (Level C).

RECOMMENDATIONS FOR THE PROGNOSTIC VALUE OF ELECTROPHYSIOLOGIC STUDIES

Good (Level B) evidence	Somatosensory evoked potential (SSEPs)	The assessment of poor prognosis can be guided by the presence of bilaterally absent cortical SSEPs (N20 response) within one to three days (Level B).
Weak (Level C) evidence	EEG and evoked/event-related potential (EP) studies	Burst suppression or generalized epileptiform discharges on EEG predicted poor outcomes but with insufficient prognostic accuracy (Level C).

RECOMMENDATIONS FOR THE PROGNOSTIC VALUE OF BIOCHEMICAL MARKERS

Good (Level B) evidence	Serum neuron-specific enolase (NSE)	Serum NSE levels >33 µg/L at days one to three post-CPR accurately predict poor outcome (Level B).
Insufficient (Level U) evidence	Serum S100; Creatine kinase brain isoenzyme (CKBB)	There are inadequate data to support or refute the prognostic value of other serum and CSF biochemical markers (Level U).
Insufficient (Level U) evidence	Intracranial pressure; Brain oxygenation	There are inadequate data to support or refute the prognostic value of ICP monitoring (Level U).

RECOMMENDATIONS FOR THE PROGNOSTIC VALUE OF RADIOLOGIC STUDIES

Insufficient (Level U) evidence	Neuroimaging studies: CT; MRI; PET	There are inadequate data to support or refute whether neuroimaging is indicative of poor outcome (Level U).
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Confounding factors

Some factors may confound the reliability of the clinical exam and ancillary tests. Major confounders could include the use or prior use of sedatives or neuromuscular blocking agents, induced hypothermia therapy, presence of organ failure (e.g., acute renal or liver failure) or shock (e.g., cardiogenic shock requiring inotropes). However, studies in comatose patients have not systematically addressed the role of these confounders in neurologic assessment.

COMA DECISION ALGORITHM

Exclude major confounders

No brain stem reflexes at any time (pupil, cornea, oculocephalic, cough)	▶ Yes	Brain death testing	▶ No	Indeterminate outcome	
-or-					
Day 1: Myoclonus status epilepticus	▶ Yes	Poor outcome	FPR* 0% (0-8.8)	▶ No	Indeterminate outcome
-or-					
Day 1-3: Serum NSE* >33 ug/L**	▶ Yes	Poor outcome	FPR 0% (0-3)	▶ No	Indeterminate outcome
-or-					
Day 3: Absent pupil or corneal reflexes; extensor or absent motor response	▶ Yes	Poor outcome	FPR 0% (0-3)	▶ No	Indeterminate outcome
-or-					
Day 1-3: SSEP* absent N20 responses**	▶ Yes	Poor outcome	FPR 0.7% (0-3.7)	▶ No	Indeterminate outcome

Decision algorithm for use in prognostication of comatose survivors after CPR. The numbers in parentheses are exact 95% confidence intervals. The confounding factors potentially could diminish prognostic accuracy of this algorithm. *NSE = neuron-specific enolase; SSEP = somatosensory evoked potential; FPR = false positive rate. ** These tests may not be available on a timely basis. Serum NSE testing may not be sufficiently standardized.

Communication with family and further decision making

The complexity of evaluation and various options of decision making require neurologic professional expertise. More than one scheduled meeting with the family is generally required to facilitate a trusting relationship. The neurologist can explain that the prognosis is largely based on clinical examination with some help from laboratory tests. In a conversation with the family, the neurologist may further articulate that the chance of error is very small. When a poor outcome is anticipated, the need for life supportive care (mechanical ventilation, use of vasopressors or inotropic agents to hemodynamically stabilize the patient) must be discussed. Fully informed and more certain, the family or proxy is allowed to rethink resuscitation orders or even to adjust the level of care to comfort measures only. However, these decisions should be made after best interpretation of advance directives or the previously voiced wishes of the patient.

This guideline summary is evidence-based. The AAN uses the following definitions for the level of recommendation and classification of evidence. **Class I:** Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: a) primary outcome (s) is/are clearly defined, b) exclusion/inclusion criteria are clearly defined, c) adequate accounting for drop-outs and cross-overs with numbers sufficiently low to have minimal potential for bias, d) relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences OR a statistical, population-based sample of patients studied at a uniform point of time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations. **Class II:** Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a RCT in a representative population that lacks one criterion a-d OR a statistical, non-referral-clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations. **Class III:** All other controlled trials including well-defined natural history controls or patients serving as own controls in a representative population, where outcome assessment is independently assessed or independently derived by objective outcome measurement * Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data) OR a sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation by someone other than the treating physician. **Class IV:** Evidence from uncontrolled studies, case series, case reports, or expert opinion.

Recommendation Level: "Level" refers to the strength of the practice recommendation based on the reviewed literature. **Level A**=Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.) **Level B**=Probably effective, ineffective, or harmful for the given condition in the specified population (Level B rating requires at least one Class I study or at least two consistent Class II studies.) **Level C**=Possibly effective, ineffective, or harmful for the given condition in the specified population (Level C rating requires at least one Class II study or two consistent Class III studies.) **Level U**=Data inadequate or conflicting; given current knowledge, treatment is unproven.

This is an educational service of the American Academy of Neurology. It is designed to provide members with evidence-based guideline recommendations to assist with decision-making in patient care. It is based on an assessment of current scientific and clinical information, and is not intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on the circumstances involved. Physicians are encouraged to carefully review the full AAN guidelines so they understand all recommendations associated with care of these patients.



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