Hypoxic-ischemic brain injury

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INTRODUCTION — As techniques in resuscitation and artificial life support have improved, clinicians care for an enlarging population of patients with anoxic brain injury. These patients most often have suffered insults such as cardiac arrest, vascular catastrophe, poisoning (such as carbon monoxide intoxication or drug overdose), or head trauma. Many patients expire without recovering awareness, but the evolution of hypothermic treatment for comatose survivors of cardiac arrest has demonstrated the potential to improve neurological morbidity and lessen mortality following anoxic brain injury [1,2].

Progress has also been made in the early identification of patients at greatest risk of poor neurologic outcome, but reliable prediction of good outcomes, with intact memory and independence, has lagged. The evaluation and prognosis of patients with non-traumatic anoxic brain injury are reviewed here.

NOMENCLATURE — Coma is defined as a state of pathologic unconsciousness; patients are unaware of their environment and are unarousable. It is caused by either dysfunction of the reticular activating system above the level of the mid-pons, or dysfunction of both cerebral hemispheres. Physical examination permits localization of the level of central nervous system dysfunction (see 'Clinical assessment' below [3,4]).

Coma must be distinguished from the persistent vegetative state, which is also characterized by unawareness, but in which patients have normal sleep-wake cycles and are arousable. Patients in a coma may progress to a vegetative state, but this may not be associated with an improvement in their overall functional outcome. Both coma and persistent vegetative states must be distinguished from brain death, locked-in syndrome, akinetic mutism, and dementia (table 1) [3,5].

Brain death — Brain death (death by brain criteria) is defined as the irreversible cessation of cerebral and brainstem function. There is no respiratory drive, and thus there are no spontaneous breaths regardless of hypercarbia or hypoxemia. There are no responses arising from the brain (including cranial nerve reflexes and motor responses) to stimuli, although spinal reflexes may persist [6]. One is legally dead in the United States when criteria for brain death have been demonstrated. (See "Diagnosis of brain death".)

In some cases patients who meet brain death criteria may be potential organ donors; issues specific to the management of these individuals are discussed separately. (See "Management of the potential deceased donor".)
Persistent vegetative state — Patients in a persistent vegetative state (PVS) represent a subgroup of patients who suffer severe anoxic brain injury and progress to a state of wakefulness without awareness. PVS may represent a transition between coma and recovery or between coma and death. The term was first used in 1972 and is defined as [3,5,7-10]:

- No evidence of awareness of self or environment and an inability to interact with others
- No evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli
- No evidence of language comprehension or expression
- Intermittent wakefulness manifested by the presence of sleep-wake cycles
- Sufficiently preserved hypothalamic and brainstem autonomic function to permit survival with medical and nursing care
- Bowel and bladder incontinence
- Variably preserved cranial nerve reflexes and spinal reflexes

If a patient remains comatose, the usual outcome is to recovery, PVS, or death within two weeks. On the basis of available clinical data, PVS is judged to be permanent after three months if induced nontraumatically. After three months, recovery is rare and is associated with moderate to severe disability at best. With the use of ancillary testing it is often possible to arrive at reliable prognostic conclusions in much shorter intervals of time following cardiac arrest (see 'Ancillary testing' below).

In patients who continue in PVS, life expectancy is approximately 2 to 5 years, and most patients die from infection of the lungs or urinary tract, multiorgan system failure, sudden death of unknown cause, respiratory failure, or underlying disease. It is estimated that there are 10,000 to 25,000 adult patients in PVS in the United States, generating an estimated annual cost of care of up to 7 billion dollars.

Minimally conscious state — This term has been proposed to describe patients who do not meet criteria for persistent vegetative state [11]. As with PVS, these patients have a severe alteration in consciousness, but demonstrate sleep-wake cycles. In contrast, they may intermittently demonstrate limited interaction with the environment by visually tracking, following simple commands, signaling yes or no (not necessarily accurately), or having intelligible verbalization or restricted purposeful behavior. Data on this group of patients is limited; they are believed to have a somewhat less severe injury and less dire prognosis than patients with PVS [12,13]. However, data on late recovery of patients in minimally conscious state are largely reported in traumatic, rather than anoxic, brain injury [14-16].

CLINICAL ASSESSMENT

Clinical setting — A thorough history from the patient's family members or health care providers is essential to the assessment, although in some cases it may be impossible to obtain. The time and pace of onset, history of drug and medication use, prodromal symptoms, and the duration of resuscitation and presumed cerebral hypoxia assist in determining both the etiology and the prognosis of a given patient's condition [17]. However, none of these factors is sufficiently reliable to differentiate those with poor outcomes (no greater than PVS) from those patients who regain awareness.
The circumstances of cardiopulmonary resuscitation (CPR) can affect prognosis after a cardiac arrest in terms of both survival and quality of life. In one study of out of hospital cardiac arrest, 44 percent of patients receiving CPR survived initially, 30 percent were alive at 24 hours, 13 percent at one month, and only 6 percent were alive after 6 months. The duration of CPR significantly correlated with outcome; no patient who required more than 15 minutes of CPR survived more than 6 weeks [18]. (See "Outcome of sudden cardiac arrest".)

In other studies, variables such as age >70, stroke or renal failure prior to admission, fever within the first 48 hours, and recent congestive heart failure were associated with a poor prognosis; in contrast, factors such as a witnessed arrest and an initial rhythm of ventricular fibrillation (VF) or tachycardia have correlated with a better prognosis [17,19,20].

**Prognosis based on clinical findings** — Some features of the physical and neurological examinations are helpful in determining prognosis (table 2 and table 3) [18,21,22]. (See "The detailed neurologic examination in adults" and "Stupor and coma in adults", section on the Neurologic examination.)

Physical assessment should include documentation of:

- Presence or absence of spontaneous movements
- Response to voice, light touch, and painful stimuli
- Pupillary size and response to light
- Other cranial nerve function, including corneal and oculovestibular (caloric) reflexes
- Respiratory pattern (spontaneous, ataxic, etc)

A number of clinical series and systematic reviews have assessed the utility of specific clinical findings in predicting outcome from anoxic brain injury. A Glasgow Coma Scale (GCS) score (table 4) of ≤4 within the first 48 hours has been associated with poor outcome (death, persistent coma) [23,24]. In other series, absent corneal or pupillary light reflexes at 24 hours and absent motor responses at 24 or 72 hours have also been associated with poor prognosis (severe neurologic disability or death) [17,21].

For making decisions regarding withdrawal of life support, statistically significant associations are inadequate. Two systematic reviews have concluded that two clinical criteria have been found to be 100 percent specific for poor outcome [17,25]:

- Absent or extensor motor response on day three
- Absent pupillary or corneal reflexes on day three

The use of medications can confound these assessments: eg, anticholinergics used in resuscitation or sedative, paralytic agents used after arrest. Similarly, acute metabolic derangements, especially acute renal or liver failure or shock, may impair the predictive ability of these findings. The use of induced hypothermia may also impact test reliability (see 'Induced hypothermia' below). In these patients, ancillary testing may be helpful (see 'Ancillary testing' below).

**Myoclonic status epilepticus** — Persistent bilaterally synchronous myoclonus in the face, limbs, and axial musculature is usually associated with in-hospital death or poor outcome, even in patients with intact brainstem reflexes or some motor response [26-28].
In a postmortem study, myoclonic status epilepticus (MSE) was associated with severe ischemic brain, brainstem, and spinal cord damage, a pattern that is distinct from the neuropathology of status epilepticus [29].

However, increasing evidence suggests that the presence of MSE has insufficient negative prognostic power when considered in isolation. Cases with good recovery have been reported in patients with MSE in whom circulatory arrest was secondary to respiratory failure [17,30-32]. In some of these, accumulation of sedative agents could have been confounders, and in others, the myoclonus was not clearly generalized and persistent, and may have been sporadic. One systematic review of three series which examined MSE as a prognostic factor found that it did not have sufficient predictive ability for poor outcome [21], while another concluded that in the setting of primary circulatory arrest, MSE within the first day reliably identifies patients with a poor neurologic outcome [17]. In another case series, the authors report functional recovery in six patients with MSE; all had received hypothermia treatment and had intact brainstem function at 36 hours, reactive background activity on EEG, and intact cortical responses on SSEP [33]. In addition, two of four patients with only EEG evidence of MSE recovered, while 23 of 24 patients with electroclinical MSE did not awaken. Thus, the presence of MSE should be considered in the context of other clinical features in making decisions to withdraw or maintain care.

Myoclonic seizures may respond to valproate or clonazepam [34]. Given the overall poor prognosis associated with MSE following primary cardiac arrest, it does not seem justified to resort to general anesthesia to stop the seizures. Stopping the myoclonus does not improve the dismal outcome.

ANCILLARY TESTING — Several tests have been studied in the period after anoxic injury; these are often helpful at arriving at an earlier prognostic determination than would be possible with clinical testing alone.

Somatosensory evoked potentials — Somatosensory evoked potentials (SSEPs) are the averaged electrical responses in the central nervous system to somatosensory stimulation. Bilateral absence of the N20 component of the SSEP with median nerve stimulation at the wrist in the first week (usually between 24 and 72 hours) from the arrest has a pooled likelihood ratio of 12.0 (95% CI of 5.3 to 26.6) and a false positive rate of zero percent for an outcome no better than PVS [17,25,27,35-39]. Repeated testing should be considered when the N20 responses are present in the first two to three days from the cardiac arrest, as they may later disappear. (See "Clinical neurophysiology", section on 'Somatosensory evoked potentials'.)

In a multicenter cohort, the interobserver agreement of SSEP interpretation in patients with hypoxic ischemic coma was only moderate [40]. Noise level strongly influenced interobserver disagreement. Despite this finding, an absent N20 was still 100 percent predictive of a dismal outcome, ie, no better than persistent coma [39].

The presence of the N20 responses, however, does not assure a good outcome. About one-half of patients with a preserved N20 response on SSEP testing still die without recovering consciousness [17]. Although some studies have suggested that the presence or absence of the long latency response, N70, on SSEP can add to the prognostic ability of SSEP in this group of patients [41], a multicenter cohort study did not confirm this finding [39].

Induced hypothermia may slow conduction velocities and alter the predictive ability of SSEP
findings in patients with anoxic brain injury [17,42]. One study found that bilaterally absent N20 responses remains predictive of poor outcome; a confirmatory study is planned [43]. (See 'Induced hypothermia' below.)

The clinical operating characteristics of other evoked potentials (brainstem, auditory, visual, middle latency, and event-related) have not been adequately evaluated. SSEPs are the best validated and most reliable of the ancillary tests currently available for clinical use.

**Electroencephalography** — The clinical value of the electroencephalogram (EEG) is unclear in the assessment of prognosis of anoxic brain injury because investigators have used different classification systems and variable intervals of recordings after resuscitation. Furthermore, the EEG is susceptible to subjective interpretation, the effects of sedative drugs, metabolic disturbances, and sepsis, which can invalidate the results. (See "Clinical neurophysiology", section on 'Electroencephalogram'.)

EEG categories can be crudely classified into malignant and benign/types. The former includes complete or near complete suppression, burst-suppression, generalized periodic complexes and the alpha-theta pattern. In one series, these malignant EEG findings were associated with a higher mortality (91 versus 54 percent) compared with those who did not have these findings [44]. Of these findings, complete, generalized suppression (<20 microvolts) is the most specific for poor outcome; other patterns are less reliable for prognosis [17,36,45]. The presence of variability and reactivity are relatively favorable features for recovery of awareness.

An EEG can also be helpful to evaluate for the possibility of status epilepticus, which may be clinically suppressed by sedation or neuromuscular junction blockade, medications sometimes used to control shivering in induced-hypothermia therapy [46]. Severe brain injury may also cause an electroclinical dissociation.

**Biochemistry** — The predictive value of several chemical tests including neuron-specific enolase (NSE), the glial S-100 protein, creatine kinase, and lactate in blood and cerebrospinal fluid (CSF) has been evaluated after anoxic brain injury in a number of studies [47-52]. Smaller studies have also examined the utility of CSF adenylosuccinate, lactate dehydrogenase, acid phosphatase, and glutathione concentrations predicting neurologic outcome [53]. A meta-analysis of all reported biochemical tests in blood and CSF concluded that the combined results were not sufficiently predictive for clinical use [25,54].

Subsequent studies have confirmed that markedly elevated serum levels of NSE and S-100 are associated with poor outcomes, but cut-off values vary among series [27,54-57]. A prospective study of 407 consecutive patients after cardiopulmonary resuscitation used cut-off values derived from a previous meta-analysis [27,54]. In this study, NSE >33 mcg/L was found to perform similarly to SSEP as a test of poor outcome with zero percent false-positive rate and a positive likelihood ratio of 23 (95% CI: 2-357) [54]. When combined with SSEP, the prevalence of an abnormal test result (either NSE or SSEP) was extended from 45 to 66 percent.

**Neuroimaging** — Computed tomography (CT) and magnetic resonance imaging (MRI) contribute little to the assessment of the anoxic patient unless stroke, bleeding, or trauma is suspected. In contrast, there is a strong correlation between MRI findings and long-term outcome infants suffering hypoxic ischemic encephalopathy [58]. (See "Clinical features, diagnosis, and treatment of neonatal encephalopathy", section on 'Neuroimaging.
predictors'.

In the future, larger studies may find a role for standard MRI as well as functional neuroimaging, such as positron emission tomography (PET) and functional MRI (fMRI), in the prognostic assessment of adults with anoxic-ischemic brain injury [59,60]. As an example, two case series have used diffusion-weighted MRI to identify a threshold volume of brain with reduced apparent diffusion coefficient that aids the clinical examination in distinguishing between poor and relatively good outcomes [61,62]. fMRI studies examining auditory and visual processing also show promise in their ability to demonstrate awareness and thereby potentially distinguish patients in different prognostic categories [63,64]. However, the performance and interpretation of these studies remains complex, and their use remains investigational [3].

**MANAGEMENT** — Supportive and preventive care remains the mainstay of therapy in all forms of anoxic brain injury [7,8,65]. Efforts should be focused upon providing adequate nutritional support, reducing the potential for nosocomial infection, and providing adequate prophylaxis against venous thromboembolism and gastric stress ulceration. (See "Prevention of venous thromboembolic disease in surgical patients" and "Stress ulcer prophylaxis in the intensive care unit".)

**Induced hypothermia** — The induction of mild to moderate hypothermia (chill therapy) to a target temperature 32 to 34°C for 24 hours improves the neurologic outcome of patients successfully resuscitated after cardiac arrest, even when the patient remains comatose following resuscitation [1,2,66,67]. This was demonstrated in two randomized trials; both enrolled only patients with ventricular fibrillation (VF) as the initial cardiac rhythm and who had return of spontaneous circulation:

- The first trial randomly assigned 275 patients who had spontaneous circulation restored within 60 minutes of the arrest to therapeutic hypothermia or conventional therapy and normothermia [1]. At six months, patients treated with hypothermia were significantly more likely to have a favorable neurologic outcome with a good recovery or only moderate disability (55 versus 39 percent for normothermia, risk ratio 1.4) and a lower mortality (41 versus 56 percent, risk ratio 0.74).

- The second trial evaluated a more select group of 77 patients who remained unconscious after resuscitation [2]. Those randomly assigned to treatment with hypothermia were significantly more likely to have a good outcome and be discharged to home or a rehabilitation facility (49 versus 26 percent for normothermia). After adjusting for age and time from arrest to return of spontaneous circulation, hypothermia was associated with a significantly better outcome compared with normothermia (odds ratio 5.25).

Only 13 to 19 percent of patients with out-of-hospital cardiac arrest fulfill both major inclusion criteria for these trials: VF as the initial cardiac rhythm and restoration of spontaneous circulation [68].

Other smaller randomized trials, as well as observational series, suggest that induced hypothermia is likely to be of benefit after cardiac arrest in somewhat broader patient populations [69-71]. Two meta-analyses that combined these trials with the other trials described above concluded that induced hypothermia improves short-term neurologic
recovery and survival in patients resuscitated from [72,73]:

- Out of hospital cardiac arrest
- Cardiac arrest of presumed cardiac origin
- Cardiac arrest with VF/VT as the presenting rhythm

The value of this approach in early survivors of cardiac arrest in other situations has not been rigorously assessed.

We recommend using the following hypothermic protocol for patients who meet the above outlined criteria [1,2]:

- Endotracheal intubation and mechanical ventilation are continued.
- Sedation is maintained and shivering prevented using a combination of a short-acting sedative and a neuromuscular blocking agent.
- Temperature is monitored either by central venous access or a bladder temperature probe.
- A cooling blanket or external ice packs are used to lower temperature to 32 to 34°C.
- This is maintained for 24 hours, followed by rewarming passively or using warming blankets.

Several case series suggest endovascular cooling using cold intravenous fluids is feasible and effective, and does not increase risk for adverse outcomes [74-78]. We use external cooling, in part, because it can be implemented more quickly than endovascular cooling which requires a central line.

The effect of induced-hypothermia therapy on the prognostic utility of clinical examination findings and ancillary testing (such as SSEP) has not been systematically studied and may not apply in this setting [17,42]. As an example, one study found that loss of motor responses better than extension on day three was not prognostically reliable in this setting, while absent pupillary and corneal reflexes on day 3 remained predictive of no recovery [79]. However, with a sufficient time interval (more than 24 hours) following return to normothermia and reversal of neuromuscular blockade, the more robust of these assessments are likely to be applicable. (See 'Clinical assessment' above.)

Family counseling — Family members of patients with severe neurologic injuries should be kept well informed about prognosis. They should be informed that patients in a coma are thought to experience no pain because there is no sense of awareness of self or environment, despite what may appear as grimaces, crying, or other expressions of discomfort. The perception of pain and suffering are conscious experiences governed by the cerebral cortex, while the expression of pain may be elicited at any level of the nervous system, including the motor/behavioral, endocrinologic, and autonomic responses that may occur as reflexes in the absence of consciousness.

Decision making regarding withdrawal of various levels of treatment is dependent on accurate prognostication. Once this is established, the autonomy of the patient is of prime concern and the level of care can be decided (see "Ethics in the intensive care unit: Informed consent; withholding and withdrawal of life support; and requests for futile therapies" and "Ethical issues near the end of life").

**SUMMARY AND RECOMMENDATIONS** — Resuscitation from cardiac arrest or other cardiopulmonary catastrophe may be complicated by hypoxic ischemic brain injury.
Obtundation or coma are frequent early on, followed by recovery or evolution to brain death or persistent vegetative state.

- We recommend induced hypothermia with a target temperature of 32 to 34 °C for 24 hours for patients who are unconscious after successful resuscitation from an out-of-hospital cardiac arrest, cardiac arrest of presumed cardiac origin, and cardiac arrest with VF/VT as the presenting rhythm (Grade 1A). (See 'Induced hypothermia' above.)

- Certain clinical criteria have been demonstrated to be reliable in identifying individuals with a very poor prognosis. Absent pupillary or corneal reflexes, or absent or only extensor motor responses at three days after cardiac arrest are invariably associated with a poor outcome. (See 'Clinical assessment' above.)

- A serum enolase level >33 mcg/L or bilaterally absent somatosensory evoked responses bilaterally at 24 to 72 hours may be useful to identify those with a poor prognosis. While very specific, these signs are not very sensitive for poor neurologic outcome. (See 'Ancillary testing' above.)

- Potential confounding factors in the clinical assessment of patients in anoxic coma include acute metabolic derangements (eg, renal failure, liver failure, shock), the administration of sedative or neuromuscular agents, and induced-hypothermia therapy.

- If no negative prognostic criteria apply, the patient should continue to be supported until a more definitive prognosis can be reached.

- Regular information sessions with substitute decision maker(s) and family are advisable.

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REFERENCES


73. Cheung, KW, Green, RS, Magee, KD. Systematic review of randomized controlled trials of therapeutic hypothermia as a neuroprotectant in post cardiac arrest patients. CJEM 2006; 8:329.


GRAPHICS
### Characteristics of the persistent vegetative state and related conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Self-awareness</th>
<th>Sleep-wake cycles</th>
<th>Experience of suffering</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent vegetative state</td>
<td>Absent</td>
<td>Intact</td>
<td>No</td>
<td>Depends upon cause</td>
</tr>
<tr>
<td>Coma</td>
<td>Absent</td>
<td>Absent</td>
<td>No</td>
<td>Usually recovery, persistent vegetative state or death in 2 to 4 weeks</td>
</tr>
<tr>
<td>Brain death</td>
<td>Absent</td>
<td>Absent</td>
<td>No</td>
<td>No recovery</td>
</tr>
<tr>
<td>Locked-in syndrome</td>
<td>Present</td>
<td>Intact</td>
<td>Yes</td>
<td>Recovery unlikely, persistent quadriplegia with prolonged survival possible</td>
</tr>
<tr>
<td>Akinetic mutism</td>
<td>Present</td>
<td>Intact</td>
<td>Yes</td>
<td>Recovery very unlikely (depends on cause)</td>
</tr>
<tr>
<td>Dementia</td>
<td>Present but lost in late stages</td>
<td>Intact</td>
<td>Yes, but lost in late stages</td>
<td>Irreversible (ultimate outcome depends on cause)</td>
</tr>
</tbody>
</table>

# Clinical parameters associated with an unfavorable prognosis

<table>
<thead>
<tr>
<th>Clinical parameters</th>
<th>Unfavorable prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of anoxia</td>
<td>&gt;8-10 minutes</td>
</tr>
<tr>
<td>Duration of CPR</td>
<td>&gt;30 minutes</td>
</tr>
<tr>
<td>Pupillary light reaction</td>
<td>Absent on day 3</td>
</tr>
<tr>
<td>Motor response to pain</td>
<td>Absent on day 3</td>
</tr>
<tr>
<td>Brainstem reflexes</td>
<td>Absent</td>
</tr>
<tr>
<td>Blood glucose on admission</td>
<td>&gt;300 mg/dL</td>
</tr>
<tr>
<td>Glasgow coma score on day 3</td>
<td>&lt;5</td>
</tr>
<tr>
<td>GPCS on day 3</td>
<td>&lt;22</td>
</tr>
</tbody>
</table>
### Significance of physical findings in coma following cardiac arrest

<table>
<thead>
<tr>
<th>Patients with virtually no chance of regaining independence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial examination</strong></td>
</tr>
<tr>
<td>No pupillary light reflex</td>
</tr>
<tr>
<td><strong>One day</strong></td>
</tr>
<tr>
<td>Motor response no better than flexor and spontaneous eye</td>
</tr>
<tr>
<td>movements neither orienting nor roving conjugate</td>
</tr>
<tr>
<td><strong>Three days</strong></td>
</tr>
<tr>
<td>Motor response no better than flexor, no spontaneous eye</td>
</tr>
<tr>
<td>opening</td>
</tr>
<tr>
<td><strong>One week</strong></td>
</tr>
<tr>
<td>Motor response not obeying commands and spontaneous eye</td>
</tr>
<tr>
<td>movements neither orienting nor roving conjugate.</td>
</tr>
<tr>
<td><strong>Two weeks</strong></td>
</tr>
<tr>
<td>Oculocephalic response not normal, not obeying commands,</td>
</tr>
<tr>
<td>no spontaneous eye opening, eye opening not improved at</td>
</tr>
<tr>
<td>least 2 grades from initial examination</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients with best chance of regaining independence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial examination</strong></td>
</tr>
<tr>
<td>Pupillary light reflexes present and motor response flexor</td>
</tr>
<tr>
<td>or extensor. Spontaneous eye movements roving conjugate or</td>
</tr>
<tr>
<td>orienting</td>
</tr>
<tr>
<td><strong>One day</strong></td>
</tr>
<tr>
<td>Motor response withdrawal or better and eye opening</td>
</tr>
<tr>
<td>improved at least 2 grades</td>
</tr>
<tr>
<td><strong>Three day</strong></td>
</tr>
<tr>
<td>Motor response withdrawal or better and spontaneous eye</td>
</tr>
<tr>
<td>movements normal</td>
</tr>
<tr>
<td><strong>One week</strong></td>
</tr>
<tr>
<td>Motor response obeying commands</td>
</tr>
<tr>
<td><strong>Two weeks</strong></td>
</tr>
<tr>
<td>Normal oculocephalic response</td>
</tr>
</tbody>
</table>
### Glasgow coma scale

<table>
<thead>
<tr>
<th>Eye opening</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>Response to verbal command</td>
<td>3</td>
</tr>
<tr>
<td>Response to pain</td>
<td>2</td>
</tr>
<tr>
<td>No eye opening</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best verbal response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oriented</td>
<td>5</td>
</tr>
<tr>
<td>Confused</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>Incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>No verbal response</td>
<td>1</td>
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</table>

<table>
<thead>
<tr>
<th>Best motor response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Obeys commands</td>
<td>6</td>
</tr>
<tr>
<td>Localizing response to pain</td>
<td>5</td>
</tr>
<tr>
<td>Withdrawal response to pain</td>
<td>4</td>
</tr>
<tr>
<td>Flexion to pain</td>
<td>3</td>
</tr>
<tr>
<td>Extension to pain</td>
<td>2</td>
</tr>
<tr>
<td>No motor response</td>
<td>1</td>
</tr>
</tbody>
</table>

The GCS is scored between 3 and 15, 3 being the worst, and 15 the best. It is composed of three parameters: best eye response (E), best verbal response (V), and best motor response (M). The components of the GCS should be recorded individually; for example, E2V3M4 results in a GCS score of 9. A score of 13 or higher correlates with mild brain injury; a score of 9 to 12 correlates with moderate injury; and a score of 8 or less represents severe brain injury.