The Spectrum of Neurological Recovery

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Abstract

The equivalence of brain death with death is largely, although not universally accepted. Patients may have suffered insults such as cardiac arrest, vascular catastrophe, poisoning, or head trauma. Early identification of patients at greatest risk of poor neurologic outcome and management in the appropriate critical care setting is the key to maximizing neurological recovery. Recent technological advances and neuroimaging have made it possible to predict neurological reversibility with great accuracy. Significant improvements in therapy such as hypothermia, will improve outcomes in neurological catastrophies, particularly in anoxic-ischemic encephalopathy. The clinical spectrum and diagnostic criteria of minimally conscious and vegetative states is reviewed. The current understanding of the differences in prognosis and prediction of meaningful cognitive and functional recovery in each neurological state is described. Establishing an understanding of the ethical principles that guide medical decisions in clinical practice related to different neurological states is evolving into a new field called neuroethics.

Key words: Brain death, minimally conscious state, coma, persistent vegetative state, hypoxic-ischemic brain injury, functional MRI, hypothermia protocol, neuron-specific enolase.

Introduction

Death is an irreversible, biological event that consists of permanent cessation of the critical functions of the organism as a whole. It requires the loss of integrated function of various organ systems. Death of the brain therefore qualifies as death, as the brain is essential for integrating critical functions of the body. The equivalence of brain death with death is largely, although not universally, accepted. Patients may have suffered insults such as cardiac arrest, vascular catastrophe, poisoning, or head trauma. Early identification of patients at greatest risk of poor neurologic outcome and management in the appropriate critical care setting is the key to maximizing neurological recovery. Evaluation and prognostication is based on a good history, physical examination, and neuroimaging. Recent functional medical resonance imaging (FMRI) has been proven to be of great prognostic value in predicting reversibility of neurological damage. The discussion of goals of care is based on prognosis and recovery of neurological function.[1,2]

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Coma

Coma is defined as a state of pathologic unconsciousness where the patient is unaware of his or her surroundings and is unarousable. Dysfunction of the reticular activating system (RAS) above mid pons level or dysfunction of both cerebral hemispheres is generally responsible for a comatose state. Physical examination allows localization of the level of central nervous system dysfunction.[3]

Brain Death

Brain death is a result of irreversible cessation of cerebral and brainstem function. Absence of respiratory drive is seen, and no responses arising from the brain to stimuli (including cranial nerve reflexes and motor responses) are noted. Spinal reflexes may persist. In the United States, one is declared legally dead when criteria for brain death have been demonstrated. These patients may be potential candidates for organ donation. Clinical prerequisites for brain death include clinical or neuroimaging evidence of an acute central nervous system catastrophe that is compatible with the clinical diagnosis of brain death (cause should be known). Exclusion of complicating medical conditions such as severe metabolic derangement, hypoxia, and severe hypothermia is essential. There should be no drug intoxication or poisoning that may confound the clinical assessment. The core temperature should be greater than 32 degrees Celsius or 90 degrees Fahrenheit. Neurological examination reveals absent cerebral and brainstem function, as evidenced by coma; absent motor response; absent pupillary light reflex, absent corneal reflex; absent jaw-jerk reflex; absent gag-reflex; absent cough with tracheal suctioning; and absent sucking and rooting reflexes. The apnea test should be positive. Most states require two apnea tests performed four hours apart as confirmation of brain death.

Hypoxic-ischemic Brain Injury

Cardiac arrest, experienced by approximately 450,000 Americans annually, has a very poor survival rate.[4] Some patients who initially survive cardiopulmonary resuscitation (CPR) remain comatose, demonstrating obvious impairments in consciousness and neurologic function. This syndrome, called anoxic-ischemic encephalopathy (AIE), also known as anoxic brain injury or hypoxic-ischemic coma, can result in outcomes ranging from full recovery to permanent unconsciousness to death.

Neurologic Outcome

A challenge in interpreting the literature on AIE is the use of variable or imprecise definitions of a "poor neurologic outcome." The American Academy of Neurology practice parameter paper defines poor outcome as death, persistent unconsciousness (such as a vegetative state), or severe disability requiring full nursing care after six months.[5]

Predictors of Neurologic Outcome

A review of the current literature[2-4] reveals that data obtained by careful neurologic examination, electrophysiologic studies, and biochemical markers are most predictive of outcome. Other factors not strongly predictive of outcome include age, sex, cause of arrest, type of arrhythmia, total arrest time, duration of CPR, geographic location of arrest, elevated body temperature, elevated intracranial pressure, concurrent respiratory failure, and brain imaging findings. It is important to note that these criteria are applied to patients while they are not receiving any medication, such as high-dose barbiturates, that would significantly confound their neurologic examination. In all cases, a specialist's neurologic examination and input are advised.

Strong indicators of poor outcome (false positive rates of 0% based on current literature) include the following:

- Absent pupillary light reflexes 24 hours after CPR, or 72 hours after CPR for those who initially had intact pupillary light reflexes.
- Absent corneal reflexes 72 hours post-CPR.
- Short-latency somatosensory evoked potentials (SSEP, an electrophysiologic study): bilateral absence of the N20 potentials on SSEP of the median nerve in AIE patients greater than 24 hours post-CPR.
- Neuron-specific enolase (NSE, a blood test): serum NSE > 33 mcg/L on day 1 to 3. While this biomarker is promising, it has not been studied in large trials, nor is the assay itself standardized, so its current clinical role remains undefined.[5-7]

Moderate predictors of poor outcomes (all predict a poor outcome, but not as invariably as the above factors based on current literature):

- Clinical exam findings: no spontaneous eye

movements or absent oculocephalic reflexes at 72 hours postarrest; no, or extensor-only, motor response to painful stimuli at 72 hours.
- Electroencephalogram findings: certain findings can be strongly associated with poor outcomes but are highly subject to institutional/technician variability. Myoclonic status epilepticus within one day of cardiac arrest is the most predictive of a poor outcome.[5]

The majority of the evidence for prognosis in the comatose patient after CPR predates the widespread use of therapeutic hypothermia in patients after cardiac arrest. It remains unclear how this intervention will change prognostication.[8] While the above factors will likely still indicate poor prognosis, the timing of when the evaluations should be done, as well as if they will predict a uniformly poor outcome is uncertain. One European study advises that patients have an initial neurological assessment as soon as possible, but that the second assessment occurs no earlier than 48-72 hours after resumption of normothermia. Zandbergen et al suggest that serum NSE >33 mcg/L occurring while the patient is hypothermic still accurately predicts consistently poor outcomes.[7] Initial data on the predictive value of SSEPs in patients who underwent hypothermia confirmed that bilateral absent N20 responses is highly predictive of a poor outcome. There has been a case report of a single patient with absent N20 responses who made a full recovery, highlighting the importance of ongoing investigation into the impact of the hypothermia protocol on the prognosis of AIE.

In conclusion, recent technological advances and neuroimaging have made it possible to predict neurological reversibility with great accuracy. Significant improvements in therapy such as hypothermia will improve outcomes of neurological catastrophes, particularly in anoxic-ischemic encephalopathy.

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Question from the audience:

With my background is in nanotechnology and in talking about persistent vegetative state and minimally conscious states and thinking about new technologies, one of the things that came to mind was K. Eric Drexler's book The Engines of Creation[a] and the proponents of nanotechnology accepted by the Foresight Institute, which talks about cryonics and the idea of the emerging neuroremediation technologies. We talked a little about deep brain stimulation (DBS).[b] Roy Bakay, for example, at Emory University also developed a chip and worked with a radio transmitter that allowed a totally paralyzed patient to communicate.[c] So, how do we reconcile these issues, how far do we go? Will we ever in your opinion accept the idea of cryonics or accept the new and emerging technologies? I think it was Rabbi Davidson who said that it does not matter to what extent, but if there is any hope of saving a life that process should be allowed and permitted.[d] Please comment on any of that.

Dr. Mir's Response: If we take this question in the context of an ethical perspective, one can say that, if nanotechnology, deep brain stimulation, and all other new techniques, which are very advanced and expensive, can save a life, they should be used because for individuals of most religious backgrounds. Life should be preserved at all costs. But if you look at it from a public health perspective and wearing a public policy hat, one can say that, if the cost of saving one life is going to be a few hundred million dollars, would we do that or would we screen for breast or cervical cancer or HIV and save "x" number of lives for the same cost? I am not saying that we are a country of rationing. Absolutely, not. But clearly we need to have clinical guidelines about what is the value of this person to the family, what is the value to society, and what can we enhance in this person's life by adding all the good things that technology has to offer. By the same token, we have to be very cost conscious. We cannot take experimental therapies and implement them on patients. For example, the hypothermic therapy I talked about is extremely inexpensive. It entails ice packs and intravenous fluids that are stored in the freezer at a certain temperature. Yet, its benefit to the majority of intensive care unit patients is profound. That is why it is being adopted universally. Nanotechnology, stem cell transplant, brain regenerating, and using growth factors that would help all look great. Clearly, we are not at the level where this is standard clinical practice. We are not there yet, and I do not think we will be there for a while.

Editor's Notes

a Drexler KE. Engines of Creation 2.0. http://e-drexler.com/p/06/00/EOC_Cover.html

b National Institute of Neurological Disorders and Stroke. National Institutes of Health. NINDS deep brain stimulation for Parkinson's disease information page. http://www.ninds.nih.gov/disorders/deep_brain_stimulation/deep_brain_stimulation.htm [Updated 2011-Aug-16; Accessed 2011-Oct-27]

c Baker S. The rise of the cyborgs. Discover. 2008 Oct. http://discovermagazine.com/2008/oct/26-rise-of-the-cyborgs/

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