Anoxic-Ischemic Brain Injury

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KEYWORDS

• Prognostication • Cardiac arrest • Anoxic-ischemic brain injury • Coma

KEY POINTS

- Information should be taken from multiple different tests, all based on clinical context, for the estimation of neurologic prognosis after cardiac arrest. Decisions should not be made on one test alone.
- Poor neurologic outcomes are expected in comatose patients after cardiac arrest if there are absent pupillary light responses or corneal reflexes, extensor or absent motor response, or myoclonus status epilepticus.
- Sedative and analgesic medications can eliminate the corneal reflexes and motor responses. Oftentimes more than 72 hours is needed to wait for the effects of these drugs to wear off.
- Somatosensory evoked potentials are useful to predict prognosis, but only if there are absent bilateral N20 (cortical) responses, which portends a poor outcome. The presence of N20s is not useful in prognostication.
- Status epilepticus that is present during active cooling protocols is often refractory to treatment and portends a poor prognosis. Discrete electrographic seizures that arise during rewarming, normothermia, or from a continuous EEG background should be treated.

INTRODUCTION

Each year in the United States, more than 350,000 cardiac arrests occur. Cardiac arrest is often instantaneous, occurring with no or little warning signs. Despite recent advances in cardiopulmonary resuscitation (CPR) (eg, increasing availability of automated external defibrillators; emphasis on high-quality, uninterrupted chest compressions), cardiac arrest is frequently lethal. Almost 90% of US patients with out-of-hospital cardiac arrest treated by emergency medical services die. Of those who do survive to hospital admission, overall mortality may be declining,[1] but still reaches 60% to 70%, and anoxic-ischemic brain injury is the most common cause of death in these patients.[2,3]

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Anoxic-ischemic brain injury is one of the most feared and devastating complications of cardiac arrest. Consciousness is lost within seconds to minutes because of insufficient cerebral blood flow (CBF) in the midst of complete hemodynamic collapse. If adequate circulation is restored promptly, neurons and glial cells may be saved, but time is critical because cerebral oxygen stores are lost within 20 seconds and glucose and adenosine triphosphate stores are depleted in only 5 minutes. "Anoxia" refers to a complete lack of oxygen delivery (eg, complete cessation of blood flow during cardiac arrest); "hypoxia" describes what may occur during periods of decreased oxygen delivery but with some degree of continuous blood flow. Hypoxic-ischemic brain injury, which is less clearly understood than anoxic-ischemic injury, is usually caused by severe hypoxemia (eg, asphyxia) or respiratory arrest.

PATHOPHYSIOLOGY

In contrast to most acute brain pathologies, anoxia induces a global brain injury. The extent of neuronal and glial damage is largely related to the duration of interrupted CBF. Brain cells become ischemic as CBF drops below levels needed to sustain brain metabolism. During a cardiac arrest, the decrease in CBF is uniform throughout the brain, but the damage to individual cells is not, because neuronal vulnerability is variable among different areas of the brain.[4] The regions most susceptible are found in the CA1 sector of the hippocampus, the basal ganglia (caudate nucleus and putamen), the cerebellar Purkinje cells, and the neocortex. Cortical necrosis is known as laminar necrosis in pathologic terms. The vulnerability of these particular brain areas may be explained by the presence of excitatory neurotransmitter receptors or the high metabolic demands of neurons in these regions. Two main modes of ischemic cell death exist: necrosis and apoptosis. Dying neurons can exhibit characteristics of both pathways. Another mechanism of neuronal and glial damage in anoxic-ischemic brain injury is "excitatory" brain injury. An efflux of glutamate (an excitatory neurotransmitter) increases intracellular calcium, which causes cellular injury by the activation of catabolic enzymes and endonucleases and also may produce free reactive oxygen species.[4] Subsequently, cytokines that lead to proinflammatory states (eg, tumor necrosis factor-α, interleukin-1β and -6) are also released and may further exaggerate cellular damage.

In addition to these mechanisms of ischemia and cellular death, research has discovered an additional phenomenon called "no reflow" that can potentially cause further brain injury in the post–cardiac arrest patient. This describes substantial microcirculatory perfusion deficits that exist after circulation is restored. Coagulation may occur within these reperfusion zones, with intravascular fibrin formation and microthrombosis.

One of the important questions regarding anoxic-ischemic brain injury is whether the degree of brain injury is modifiable, and if so, whether there is an optimal time period during which action must be taken. Is the damage to the brain permanent at the time of cardiac arrest, or are there detrimental processes at work that might be attenuated or even reversed? The concept of "neuroprotection" has garnered much research interest but unfortunately many candidates have fallen short in the clinical world. Induced hypothermia had been considered by many to be the only beneficial neuroprotectant, but even this has recently come under scrutiny.

CLINICAL MANAGEMENT

The most immediate threat following resuscitation from cardiac arrest is cardiovascular collapse. Interventions to optimize blood pressure and maintain systemic perfusion