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Prognosis and Therapy after Cardiac Arrest-Induced Coma

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Cases in which a family must make difficult, life-and-death decisions for a loved one are always complicated—both for the decision makers and for the medical team. Family members, often coming to the situation with inaccurate or unrealistic views about what modern medicine can achieve, struggle to understand unfamiliar and frightening medical concepts, all the while dealing with guilt, stress, and grief. Members of the health care team frequently find themselves navigating potentially volatile family dynamics while attempting to do their best for a patient who is caught in a medical gray area.

The role of a neurologist in these circumstances is to provide as much prognostic information as possible to help guide the decisions of both the family and the medical team. Timely, accurate information can be the key to avoiding misunderstandings and anxiety and to promoting a decision with which everyone is comfortable. A neurologist assesses the situation by examining the patient, initially and over time, for behaviors and reflexes that suggest or portend consciousness and other higher brain functions and uses that information to prognosticate the patient's medical course.

Consciousness and Coma

Consciousness is defined as an "awareness of self and environment," although the boundaries of consciousness and how to definitively determine its presence are still debated in the neuroscientific, bioethical, and philosophical communities [1]. *Coma* is defined as "unarousable unresponsiveness," or "the absence of any psychologically understandable response to external stimulus or inner need" [1, 2]. Given the ambiguity of these definitions and the difficulty in determining consciousness, many physicians avoid using these terms altogether and instead describe the patient's behavior.

Coma is not a permanent state, and comatose patients who do not die begin to awaken within several weeks, regardless of the severity of the underlying brain injury [1]. Some patients may open their eyes and demonstrate limited movement without ever regaining consciousness or attaining higher mental functioning. The term for this condition is *persistent vegetative state,* and these patients can survive for decades without ever improving neurologically [1].

Hypoxic-Ischemic Coma

The case of Mr. Abdullah presents a patient in a comatose state as the result of a cardiac arrest, one cause of hypoxic-ischemic coma, a condition with many etiologies, all of which lead to brain tissue damage from lack of oxygen. Cardiac arrest causes the cessation of cerebral blood flow, which produces loss of consciousness within 6 seconds [3]. If oxygen is restored immediately, consciousness can return in seconds to minutes. Two minutes of anoxia can cause focal damage. If the anoxia lasts longer than 4 minutes, brain cells begin to be lost permanently [4]. When ischemic anoxia lasts longer than 10 minutes most patients do not regain consciousness [5]. The pathophysiology of hypoxic-ischemic cell death is that, as neurons are deprived of oxygen, the proteins and electrolytes necessary to maintain the membrane potentials (i.e., electrical charge inside the cell membrane relative to that of the fluid just outside the membrane) are depleted, causing the cell to depolarize and the cell body to swell. The swelling results in irreversible damage to the cell's contents, initiating cell autolysis [1].

The Levy Criteria

Twenty-five years ago, physicians had little to draw on besides their own experience to help guide the families of comatose patients in making decisions [6]. In 1985, recognizing the need of families and critical care physicians for an accurate and useful prognostic tool for patients in hypoxic-ischemic coma, David E. Levy, MD, and his colleagues at New York Hospital-Cornell Medical Center took advantage of new statistical tools and a large, existing dataset to create guidelines now called the Levy Criteria. The criteria predict a patient's long-term neurological outcome within the first few days after cardiac arrest [7].

Levy and his team analyzed 210 comatose patients after hypoxic-ischemic events, performing neurologic exams within the first day and then at intervals up to 14 days after coma onset. The patients were then followed for 1 year to record their outcomes, which ranged from continuous coma until death (from brain- or nonbrain-related conditions) to recovery of prior levels of function. Using a novel statistical analysis and algorithm, the authors created a tree that predicted best functional state within the first year based on early examination findings. Their results are summarized in table 1. Of note, the investigators found that neither patient age nor sex nor etiology of the coma had a significant impact on the patient's likelihood of recovery [7].

Therapeutic Hypothermia

After the Levy Criteria were published, physicians could deliver more accurate prognostic information to families of patients with cerebral ischemia after cardiac arrest, but until recently there was little that could be done therapeutically for these patients besides treating underlying pathologies, maintaining respiration and circulation, and providing other supportive care. In 2002, however, two studies were published, showing that patients who were made mildly hypothermic (to a temperature between 32 degrees and 34 degrees Celsius) for 12 to 24 hours following resuscitation after arrest due to ventricular fibrillation had significantly

better long-term neurologic outcomes than patients who were kept normothermic [8, 9]. The precise mechanism by which cooling benefits patients is unknown, but it is thought to relate to decreased cerebral oxygen consumption, the inhibition of excitatory neurotransmitters, and a reduction in damaging free radicals and intracellular acidosis [9].

In 2005, hypothermia after cardiac arrest was added to the American Heart Association guidelines for post-resuscitation care, but adoption of this protocol has been largely limited to major academic centers and tertiary care hospitals [10]. Reasons for this delay include the complexity of the protocol, which requires expensive cooling equipment, specialized training for physicians, nurses, and support staff, and the formation of a multidisciplinary team composed of emergency physicians, cardiologists, neurologists, and intensivists. Therapeutic hypothermia can provide real benefit to some patients and represents the first proven therapy to prevent brain damage after cardiac arrest.

For Mr. Abdullah and his family, the neurologist can best contribute by doing several careful neurological examinations over time and using his own experience and the historical outcomes literature, including the Levy Criteria, to give the patient's family the best information about his chance of meaningful recovery. Research in the field of post-anoxic interventions is ongoing and in the near future we hope to be able to offer these patients scientifically proven therapies, in addition to our best prognostic efforts.

Table 1 Guidelines to predicting long-term neurologic outcome in hypoxic-ischemic coma patients [7].

	Patients with Poorest Prognosis	**Patients with Best Prognosis**
Time after Cardiac Arrest	• Neurologic Exam Findings	• Neurologic Exam Findings
Initial Examination	• No pupillary light reflex	• Pupillary light reflexes present • Motor response: flexor or extensor • Spontaneous eye movements: roving, conjugate, or orienting
1 Day	• Motor response no better than flexor • Spontaneous eye movements neither orienting nor roving conjugate	• Motor response: withdrawal or better • Eye opening improved at least two grades from initial exam
3 Days	• Motor response no better than flexor	• Motor response: withdrawal or better • Spontaneous eye movements normal
1 Week	• Motor response not obeying commands • Initial spontaneous eye movements neither orienting nor roving conjugate • Eye opening not spontaneous	• Motor response obeying commands
2 Weeks	• Oculocephalic response not normal • Motor response not obeying commands • Eye opening not spontaneous • Eye opening not improved at least two grades from initial exam	• Oculocephalic response normal

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