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Contemporary Approach to Neurologic Prognostication of Coma After Cardiac Arrest

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Coma after cardiac arrest (CA) is an important cause of admission to the ICU. Prognosis of post-CA coma has significantly improved over the past decade, particularly because of aggressive postresuscitation care and the use of therapeutic targeted temperature management (TTM). TTM and sedatives used to maintain controlled cooling might delay neurologic reflexes and reduce the accuracy of clinical examination. In the early ICU phase, patients' good recovery may often be indistinguishable (based on neurologic examination alone) from patients who eventually will have a poor prognosis. Prognostication of post-CA coma, therefore, has evolved toward a multimodal approach that combines neurologic examination with EEG and evoked potentials. Blood biomarkers (eg, neuron-specific enolase [NSE] and soluble 100-β protein) are useful complements for coma prognostication; however, results vary among commercial laboratory assays, and applying one single cutoff level (eg, >33 μg/L for NSE) for poor prognostication is not recommended. Neuroimaging, mainly diffusion MRI, is emerging as a promising tool for prognostication, but its precise role needs further study before it can be widely used. This multimodal approach might reduce false-positive rates of poor prognosis, thereby providing optimal prognostication of comatose CA survivors. The aim of this review is to summarize studies and the principal tools presently available for outcome prediction and to describe a practical approach to the multimodal prognostication of coma after CA, with a particular focus on neuromonitoring tools. We also propose an algorithm for the optimal use of such multimodal tools during the early ICU phase of post-CA coma.

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ABBREVIATIONS: BIS = bispectral index; CA = cardiac arrest; CPC = Cerebral Performance Category; FPR = false-positive rate; MMN = mismatch negativity; NSE = neuron-specific enolase; S-100B = soluble 100-β protein; SSEP = somatosensory evoked potential; TTM = targeted temperature management

Coma after cardiac arrest (CA) is an important cause of ICU admission for acute brain injury. Over the past decade, the number of patients who survive a coma after CA has increased significantly.[1] Two major factors have contributed to outcome improvement: postresuscitation care (ie, the number of general supportive measures, including early coronary reperfusion, fluid resuscitation, adequate cerebral and systemic perfusion pressure, controlled sedation, glycemic control, that help to

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protect a postanoxic brain against so-called secondary cerebral damage)[2] and the introduction[3,4] and clinical implementation[5,6] of targeted temperature management (TTM) with the use of induced cooling. According to the most recent studies, approximately 50% of patients experiencing coma after CA and treated with TTM survive with good long-term neurologic recovery.[7] Notwithstanding the recent controversy about the exact target temperature to adopt in this context (33°C vs 36°C),[7] TTM exerts significant neuroprotection and remains a mainstay of therapy for postanoxic coma.[8]

Despite these important advancements, at least one-half of patients will eventually have a poor prognosis. In the early phase following CA (approximately 72 h), and partly because of sedation and TTM, it is not always easy to clearly distinguish based on clinical examination alone patients with persistent coma who will have a poor prognosis from those who are transiently comatose but might subsequently awaken and eventually have a good recovery.[9] Adequate prognostication of neurologic outcome in the early phase following CA is, therefore, of great importance, particularly because it allows for targeting therapy intensity and appropriate allocation of resources.[10] Prognostication of patients with acute brain injury is a difficult task for clinicians and nurses involved in the care process as well as for family and society, who may be left with the potential burden of a long-term neurologic deficit. A major challenge is to reduce the uncertainty about outcome prediction. A new paradigm is being increasingly adopted that has switched from a standard approach primarily based on neurologic examination[11] to a more advanced multimodal approach that combines clinical examination with a series of additional tools, including EEG, evoked potentials, blood biomarkers, and neuroimaging, aimed at more precisely quantifying the severity of postanoxic brain damage and improving the accuracy of outcome prediction.

The aim of this review is to summarize the principal tools presently available for outcome prediction and to describe a practical approach to the multimodal prognostication of coma after CA, with a particular focus on neuromonitoring tools. We also propose an algorithm for the optimal use of such multimodal tools during the early ICU phase of postanoxic coma.

Available Tools for Coma Prognostication After CA

Outcome Assessment

Accuracy of coma prognostication can be defined as the false-positive rate (FPR = 1-specificity) to predict poor prognosis. The perfect prognosticator is one with 100% specificity that yields an FPR of 0 for poor prognosis. According to the Glasgow-Pittsburgh Cerebral Performance Categories (CPCs),[12] poor prognosis includes CPC 3 (severe disability, dependent in daily life activities), CPC 4 (persistent vegetative state), or CPC 5 (death). Good prognosis comprises CPC 1 (full recovery) and CPC 2 (moderate disability, allowing to return home and to be independent in daily life activities).

Neurologic Examination

Neurologic examination remains the first-line approach to initially assessing prognosis of comatose patients in general. In unconscious patients after CA, lack of motor response to painful stimulation better than extension (motor component of Glasgow coma scale ≤ 2) and absence of brain stem reflexes (including pupillary, corneal, and oculocephalic reactivity) at 72 h are classically associated with poor prognosis.[11]

Effect of Sedation and Hypothermia on Motor Response and Brain Stem Reflexes: Induced hypothermia reduces cytochrome P450-mediated clearance of the sedative and analgesic agents (eg, midazolam, fentanyl) commonly used during TTM.[13] In addition, some patients may have altered renal and hepatic function, which may further delay drug clearance. The combined effect of TTM and controlled sedation alters neurologic examination and may particularly delay reaction to painful stimuli,[14-16] thereby rendering clinical examination alone, particularly motor response (see next), less reliable and insufficiently accurate to predict prognosis in the early phase of coma after CA.

In a recent meta-analysis of 10 studies in patients treated with TTM to 33°C to 34°C after CA, Kamps et al[17] found that a motor response ≤ 2 on the Glasgow coma scale at 72 h (n = 811 patients) had an unacceptably high FPR of 21% on average (95% CI, 8%-43%). Brain stem responses had better accuracy, but absent corneal reflexes (n = 429 patients) yielded an average FPR of 2%. Bilaterally absent pupillary reactivity was available in 566 patients and had the lowest FPR to predict poor outcome. Brain stem and pupillary reflexes were performed at 48 to 72 h after CA in these studies.

Electrophysiologic Examinations

EEG: The utility of EEG in postanoxic coma is to help to improve accuracy of coma prognostication and to detect postanoxic status epilepticus.