Summary of Practice Guideline for **Clinicians**

Practice Guideline: Reducing Brain Injury After Cardiopulmonary Resuscitation

This is a summary of the American Academy of Neurology (AAN) guideline, "Reducing brain injury after cardiopulmonary resuscitation," which was published in *Neurology*® online on May 10, 2017, and in the May 30, 2017, print issue.

Please refer to the full guideline at *AAN.com/guidelines* for more information, including definitions of the classifications of evidence and recommendations.

In patients with non-traumatic cardiac arrest, does induced mild therapeutic hypothermia (TH) or targeted temperature management improve outcome after CPR in adults who are initially comatose?

Strong Evidence	For patients who are comatose and in whom the initial cardiac rhythm is either ventricular tachycardia (VT) or ventricular fibrillation (VF) after cardiac arrest, TH (32°C–34°C for 24 hours) is highly likely to be effective in improving neurologic outcome and survival compared with normothermia and should be offered (**Level A**).
	For patients who are comatose and in whom the initial cardiac rhythm is VT/VF or pulseless electrical activity (PEA)/ asystole after cardiac arrest, prehospital cooling with 2 L 4°C IV solutions or intranasal cooling as an adjunct to in-hospital cooling should not be offered (**Level A**).
Moderate Evidence	For patients who are comatose and in whom the initial cardiac rhythm is either VT/VF or PEA/asystole after cardiac arrest, TTM (36°C for 24 hours followed by 8 hours of rewarming to 37°C and maintained below 37.5°C until 72 hours) is likely as effective as TH in improving neurologic outcome and survival and is an acceptable alternative to TH (**Level B**).
Weak Evidence	In patients who are comatose after cardiac arrest, the addition of coenzyme Q10 to TH possibly improves survival but does not improve neurologic status at 3 months and may be offered (**Level C**).
Insufficient Evidence	No recommendations are made on the following (**all Level U**): • Use of 32°C vs 34°C TH; use of TH in patients whose initial cardiac rhythm is PEA or asystole • Use of invasive cooling instead of surface cooling • Use of standardized protocols for TH • Use of epoetin alfa in addition to mild TH

Clinical Context

The success of TH in post–cardiac arrest brain injury is defined by improvement not only in survival but also in the neurologic status of survivors. This success has given rise to the possibility that other agents or combinations of agents will further enhance the neurologic outcome benefits. As an added agent to TH, coenzyme Q10 showed survival benefit but failed to show improvement in neurologic status at 3 months. Because the TH plus coenzyme Q10 study is a pilot study, more data are needed to define the role of coenzyme Q10 in patients post cardiac arrest.

In patients with nontraumatic cardiac arrest, do putative neuroprotective drugs improve outcome after CPR in adults who are initially comatose?

Moderate Evidence	In patients with cardiac arrest and return of spontaneous circulation (ROSC), the calcium channel blocker lidoflazine is likely to be ineffective in improving survival and neurologic outcome and should not be offered (**Level B**).
	In patients with cardiac arrest and ROSC, a single loading dose of thiopental is likely to be ineffective in improving survival or neurologic outcome and should not be offered (**Level B**).
	A single 10 mg loading dose of diazepam is likely to be ineffective in improving survival or awakening and should not be offered (**Level B**).
Insufficient Evidence	In patients with OHCA of presumed cardiac origin and ROSC, there is insufficient evidence to support or refute the use of the following for improving survival or neurologic outcome (**all Level U**): • Nimodipine • Selenium • A single 2 g loading dose of magnesium sulfate • Corticosteroids
	In patients with witnessed out-of-hospital cardiac arrest (OHCA), VT/VF, and ROSC, there is insufficient evidence to support or refute the routine clinical use of xenon gas in addition to TH, as it probably results in less white matter damage as measured by fractional anisotropy, but the clinical importance of this is unknown and it probably does not improve 6-month neurologic outcome as measured by the CPC. Further research into the clinical outcomes of this intervention is warranted (**Level U**).

Clinical Context

To date, no putative neuroprotective drug has been shown to be effective in improving survival or neurologic outcome in patients who are comatose after resuscitation from cardiac arrest. Despite the lack of evidence to support or refute the use of agents such as nimodipine, xenon gas, selenium, and magnesium sulfate, currently none of these agents is routinely used in clinical practice to improve neurologic outcome or survival in this patient population. Furthermore, these agents may have serious AEs in this patient population, such as hypotension with calcium channel blockers and barbiturates, infections with corticosteroids, and sedation with benzodiazepines and barbiturates.

In patients with nontraumatic cardiac arrest, do other medical interventions or combinations of interventions improve outcome after CPR in adults who are initially comatose?

Recommendation	
Insufficient Evidence	There is insufficient evidence to support or refute the use of the following in patients with OHCA and ROSC (**all Level U**): • 100% oxygen for 60 minutes immediately post resuscitation • Isovolumic high-volume HF (with or without TH)

Clinical Context

Coma is a period of prolonged unconsciousness without response to external stimuli. The studies reviewed had heterogeneous definitions of coma, which limits prognostication based on initial presentation and clinical status upon rewarming. Patients who are comatose after successful resuscitation from cardiac arrest require complex neurologic and medical care in the critical care unit. Induced mild hypothermia has emerged as an effective therapy to improve outcomes in patients with VT/VF as their initial cardiac rhythm, but its role in patients with PEA and asystole remains less certain, and the optimal therapeutic window for administering this therapy remains unclear. The 2 Class I studies provide support for induced hypothermia within 2 to 4 hours of ROSC, but the studies vary in the rate at which the target temperature range was reached. One of the studies showed that TTM followed by maintenance of normothermia seems to be equally effective in improving outcomes in patients resuscitated from cardiac arrest with shockable or nonshockable initial cardiac rhythms. It is important to note that neuroprotection was provided by adherence to TTM protocol, whether 36°C or 33°C for 24 hours. This should not be mistaken as normothermia only or no hypothermia at all. Although the 2 Class I studies used external cooling methods, other studies have used methods such as endovascular cooling with catheters, chilled IV solutions, and regional cooling (i.e., intranasal cooling). The Class I study on TTM used both external cooling and endovascular cooling with catheters. To date, no study has shown the optimal means by which to induce and maintain TH, and the rates of cooling to target temperature range need further clarification. We find no clear advantage of one method over another, but it is very important for clinicians to be aware of the existing methods and technologies so they are better informed when acquiring equipment and developing therapeutic protocols. The rewarming phase of the hypothermia therapy also varied in the studies available. Multiple brain-related complications such as seizures, status epilepticus, myoclonus, and cerebral edema have been noted in these patients. Although these conditions are believed to have a large impact on prognostication and quality of life of survivors, studies are too limited to support evidence-based treatment recommendations at this time. In the absence of adequate evidence to provide a treatment recommendation, it is best to consider prevailing local standards in the management of these complications. The guideline panel also notes that most of the studies did not specifically address the impact of withdrawal of life-sustaining therapies in their analysis (see table e-1 [in full guideline]). The impact of this practice on the outcome of the trials needs careful study. Finally, there is a great need for further studies on methods of supplementing TH protocols, such as extracorporeal membrane oxygenation (ECMO) and pharmacologic agents (e.g., xenon gas, where the most recent study had mixed results).

This practice guideline was endorsed by the Neurocritical Care Society.

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