UMHHC Policy 03-01-025

Adult Post-Cardiac Arrest Hypothermic Targeted Temperature Management

Purpose:

The purpose of this guideline is to provide healthcare personnel with a guideline to implement and maintain hypothermic targeted temperature management (HTTM) after cardiopulmonary arrest using either external hydrogel pads or intravascular cooling catheter for patients presenting to or being cared for in the Adult Emergency Department, University Hospital, or the Cardiovascular Center.

Definition(s):

Core Temperature: Thermal component of the body is composed of the head and trunk. Under normal circumstances core body temperature is strictly regulated around a set point of 36.6+/-0.38°C. Core temperature will be monitored via the esophageal, bladder, and/or central circulation.

External Hydrogel Device: Hydrogel pads or wraps that are placed on the skin of the patient's trunk and upper legs. Temperature is controlled via a feedback loop with system with a core temperature that is attached to a central console and automatically regulates temperature according to programmed temperature targets. The feedback of the patient temperature is compared to the set target temperature and the circulating water temperature is adjusted to ensure the target temperature is maintained.

Intravascular Cooling Device: Endovascular technology that can safely and rapidly lower patient core body temperature, precisely maintain a chosen target temperature and gradually rewarm patients to normothermic levels.

Privileged Provider: Licensed Independent Practitioners (i.e., MD, DO, Dentist, Psychologist) and advanced practice professionals under physician delegation (PAs, NPs, CNMs, CRNAs).

Shivering (Rigors): Mechanism to generate heat that is involuntarily caused by contraction or twitching of the muscles. Shivering increases metabolic rate and oxygen consumption. Early shivering can be detected by palpating the mandible and feeling a "humming" vibration.

Hypothermic Targeted Temperature Management (HTTM): Continuous monitoring and regulation of core body temperature with target temperature between 33°C and 36°C for a minimum of 24 hours followed by gradual rewarming at a rate ≤ 0.25 °C/hour followed by normothermic targeted temperature management (NTTM) for an additional 48 hours. Based on the current body of evidence, our recommended target temperature is 33°C \pm 0.5°C (Bernard and HACA, 2002). However, an acceptable alternative is a target temperature of 36 \pm 0.5°C (Nielson 2013). Hypothermia used to protect the brain from post-ischemic and traumatic neurological injury. The induction of mild hypothermia decreases secondary brain injury through several possible mechanisms including reduced production of free radicals, decreased transcription of cell death genes, reduced excitotoxicity, and decreased inflammatory activation.

Normothermic Targeted Temperature Management (NTTM): Continuous monitoring and regulation of core body temperature with a target temperature of 37.0°C ± 0.5°C. The primary goal of NTTM is to prevent hyperthermia/fever, which can exacerbate brain injury caused by cardiac arrest.

Standards:

- A. The Emergency Department (ED), Intensive Care Unit (ICU) Attending Physician or Fellow, or Interventional Cardiology Attending or Fellow maintain the authority and responsibility for assessing suitable patients that meet the inclusion criteria for HTTM.
- B. Patients may be excluded at the discretion of the Attending Physician or Fellow for any reason.
- C. Treatments that may ordinarily be appropriate (including thrombolysis, coronary catheterization, heparin or aspirin) are not contraindicated by treatment with HTTM and should continue to be used as indicated.

Actions:

A. Process of Treatment Initiation

- 1. Patients successfully resuscitated from cardiac arrest may immediately be assessed for treatment with HTTM.
- 2. The nature of the arrest (evaluation of down time) and the patient's neurologic status are assessed at least 10 minutes after return of spontaneous circulation. Other usual clinical information (prior health status, quality of life, severe comorbidity, complications of CPR) is also obtained.
- 3. The decision to initiate HTTM should be made rapidly by the Attending Physician, and treatment should begin as soon as practical and feasible.

B. Identify Appropriate Patients

Treatment is always at the discretion of the ED Attending Physician, the ICU Attending Physician or Fellow, or the Interventional Cardiology Attending or Fellow.

The following criteria are modified from clinical trial eligibility criteria and other guidelines and represent non-binding guidance.

1. Inclusion Considerations

- a. Return of spontaneous circulation after a witnessed cardiac arrest with any presenting rhythm.
- b. Return of spontaneous circulation after **unwitnessed** cardiac arrest with a shockable (VF/VT) or organized (PEA) presenting rhythm.
- c. Impaired CNS function (i.e., lack of meaningful response to verbal commands after ROSC), which is thought to be due to hypoxic ischemic encephalopathy and not due to other conditions (such as medication or intoxication).
- d. Patients of any age greater than 17 years transferring to an adult ICU
- e. Life expectancy greater than 6 months/no terminal illness
- f. No known patient goals of care that would preclude further resuscitation/targeted temperature management (TTM)
- g. Discretion of Attending Physician

2. Exclusion Considerations

a. Age less than 18 years (refer to PICU guidelines for patients < 18 years of age)

- b. Life expectancy less than 6 months/terminal illness/clinical condition that precludes aggressive resuscitation
- c. Coma due to other causes (CNS depressing drugs, stroke, or trauma)
- d. Surface cooling only: inability to cover greater than 40% body surface area with external hydrogel pads
- e. Use of TTM in conjunction with extracorporeal membrane oxygenation (ECMO) should be done in consultation with the ECMO team
- f. Discretion of Attending Physician

3. Considerations for trauma patients

- a. No prospective randomized trials have been conducted on hypothermic targeted temperature management after trauma
- b. Very few post traumatic contraindications to this therapy except for significant active bleeding that cannot be controlled; if identified and controlled, targeted temperature management can be considered.
- c. Rib fractures are not a contraindication to cooling as many times this occurs in medical patients receiving cardiopulmonary resuscitation.
- d. If bleeding complications are a concern, HTTM with a target temperature of $36 \pm 1^{\circ}$ C can be considered.³

4. Considerations for pregnant patients

- a. No prospective randomized trials have been conducted on hypothermic targeted temperature management in pregnant patients
- b. Recommend decision on HTTM in consultation with OB/GYN.

C. Orders for Initiation and Treatment Course

- 1. Patient care orders will be placed into the electronic health record (EHR) by the ED team, ICU team, or Interventional Cardiology team. For ED patients, the ED/EC3 Post-Cardiac Arrest Orderset (ID 1600080004) should be used. For all non-ED patients, the MCM ICU Hypothermia TTM Orderset (ID 3600240642) should be used. Orders will include:
 - a. A date and time of HTTM initiation
 - b. Vital sign frequency and privileged provider notification parameters.
 - c. Initiation of HTTM is intended to be a bundle of three simultaneous elements:
 - i. Neuromuscular blockade and sedation as needed;
 - ii. Bolus of chilled 4°C 0.9% saline where applicable
 - iii. Initiation of cooling device
 - d. Refer to Appendix A for process to obtain intravascular and external hydrogel consoles and supplies
 - e. Target Temperature is preset at 33°C on the cooling console (unless alternative target of 36°C is chosen in which case the desired target temperature would need to be manually programmed) and the rate of cooling is set to "maximum" when the device is placed, and is maintained at these settings for 24 hours after placement.
 - f. Shivering Evaluation and Management refer to Section D under ICU Maintenance
 - g. Re-warming at a rate of 0.25°C/hour will be initiated at 24 hours from reaching target temperature.

h. Paralytic, if used, should be discontinued during re-warming phase.

D. ICU Maintenance

1. Cooling

- a. The target patient temperature range will be 33.0° ± 0.5° C (unless alternative of 36°C is chosen). The target temperature will be maintained for 24 hours from time target temperature was achieved.
- b. Temperature will be monitored continuously from two core sites, and recorded and documented from both every 30 minutes.
- c. Esophageal temperature probes (placed by a privileged provider) are the preferred site for monitoring patient core temperature, and should be the site connected to the cooling console. A second site, either a temperature sensing urinary catheter or a central circulation temperature, is used as a redundant check and should be connected directly to the patient's bedside monitor. Prolonged discrepancies of greater than 1°C are possible but should be investigated.
- d. The ventilator circuit should not be heated.
- e. All patients should have their sedation doses reviewed when they reach target temperature. Smaller doses may be needed.

2. Shivering

- a. Shivering is a challenging side effect of therapeutic hypothermia and should be avoided. Shivering causes adverse effects on physiological parameters, including increased oxygen utilization and decreased rate of cooling or inability to achieve target temperature.
- b. Shivering should be assessed objectively every hour and may include observation of piloerection (e.g. goosebumps), tactile confirmation of a vibration in the mandible and neck region, visualization of tremors, and measurements with electrical signals of muscle activity (e.g. electromyography). A validated and reliable tool should be used to measure shivering (e.g. Bedside Shivering Assessment Scale [BSAS], Appendix B).
- c. During initiation of cooling, shivering is best controlled by neuromuscular paralysis by either continuous or intermittent dosing.
- d. During maintenance, after target temperature has been achieved, paralytics may be removed and replaced with other anti-shivering treatments as needed. Paralytics should always be discontinued by the end of the 24 hour maintenance period unless needed for another indication.
- e. During maintenance and rewarming, treatments for mitigating shivering, in order of preference, include:
 - 1) Skin counter-warming (e.g. Bair hugger) or warm blankets;
 - 2) Increase dosages of analgesic and sedative infusions
 - 3) Meperidine

All patients should have their sedation doses reviewed when they reach target temperature. Smaller doses may be needed.

3. Care of the patient with intravascular cooling device

- a. Refer to Mosby's Skills Warming and Cooling Devices: External and Intravascular
- b. The sheath introducer through which the device is placed is dressed and cared for per central line dressing policy
 (http://www.med.umich.edu/i/policies/ice/ICM_IV/cvc2.htm).
 Dressing should be changed if it becomes soiled, wet or loose.
- c. An infusion of 0.9% NS at minimal rate of 10cc/hour must be maintained until the sheath is discontinued.
- d. Neurovascular Checks: pulses, cap refill, color change, edema, asymmetry, thigh and calf compartment pliability, etc. should be checked every 2 hours in the lower extremities while using intravascular device
- e. The endovascular cooling catheter can be disconnected from the console for patient transports, if needed. See device specific operating instructions.
- f. Documentation
 - 1. Patient temperature (from 2 sources) every 30 minutes.
 - 2. Heart rate, respiratory rate, and blood pressure hourly and as clinically indicated.
 - 3. Bedside Shivering Assessment Scale should be recorded hourly
- 4. Care of the patient with external hydrogel device
 - a. Refer to Mosby's Skills Warming and Cooling Devices: External and Intravascular
 - b. If target temperature is not reached within 4 hours of initiating cooling with the external hydrogel pads, there may be prolonged exposure of the skin to low water temperatures which may increase the risk for skin injury. Identify and correct the impediment to cooling or increase the minimum water temperature setting.
 - c. Examine the skin under the external hydrogel pads often, especially those at higher risk of skin injury (diabetics, peripheral vascular disease patients, those with poor nutritional status, steroid use, or high dose vasopressor therapy). Recommend skin inspections in all patients every 4 hours.
 - d. Do not bathe under the pads.
 - e. Do clean or replace soiled pads.
 - f. Do not allow urine, antibacterial solutions or other agents to pool underneath the external hydrogel pads. Urine and antibacterial agents can absorb into the pad hydrogel and cause chemical injury and loss of pad adhesion. Replace pads immediately if these fluids come into contact with the hydrogel.
 - g. The external hydrogel pads can be disconnected from the console for patient transports, if needed. See device specific operating instructions.
 - h. Documentation
 - 1. Patient temperature (from 2 sources) and water temperature every 30 minutes.
 - 2. Heart rate, respiratory rate, and blood pressure hourly and as clinically indicated.
 - 3. Bedside Shivering Assessment Scale should be recorded hourly.

4. Skin assessment under pads every 4 hours.

5. Rewarming

- a. 24 hours after target temperature is reached, rewarming will begin.
- b. Assess for need of analgesics, sedation, paralytics and external skin warming device. Medication dose adjustments may be needed as patient is rewarming.
- c. Rewarming should target a temperature of 36.5°C, achieving this over 24 hours, with a rate of rewarming around 0.25°C per hour (preprogrammed into the device).
- d. Some patients will require additional blood volume expansion during rewarming and inotropic requirements should be closely watched. Use Pulmonary Artery Catheter, Esophageal Doppler Monitoring, or flowbased hemodynamic monitor via arterial catheter, if necessary.

6. Post-HTTM

- a. NTTM with a target temperature of $37.0 \pm 0.5^{\circ}$ C should be maintained for a minimum of 72 hours after ROSC or 48 hours after rewarming. This will typically require continued management with the intravascular or surface cooling device used for HTTM. Subsequent intensive therapies will depend on the results of a sedative-free clinical assessment of CNS function but no further hypothermia will be given.
- b. Neurological consultation should be obtained in all patients in whom consistent assessment of neurological prognosis is desired or in patients who remain comatose after rewarming. See APPENDIX C.
- c. DNAR orders and any consideration of withdrawal of life support based on anticipated functional outcome should generally be deferred until a reliable neurological prognosis can be determined which is 72 hours after rewarming.
- d. Intravascular devices are removed and disposed of per UMHHC guidelines for central venous catheters.
 - a. The sheath and device line must be removed together by a physician or a person trained to remove the lines.
 - b. Removal of cooling device and catheter should occur post treatment or after 48 hours if not in use.

References

- American Association of Critical Care Nurses. (2011). AACN Procedure Manual for Critical Care (6th Ed.). Elsevier, St. Louis, MO.
- American Heart Association (2005) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Part 7.5 Post-resuscitation Support, Circulation 112; IV-84-IV-88.
- American Heart Association (2010) Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Part 9: Post–Cardiac Arrest Care. Circulation 2010.Bernard, SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K, (2002). Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. New England Journal of Medicine 2 (21); 346 (8): 557-63.
- Badjatia, N., et al. (2008). Metabolic impact of shivering during therapeutic temperature modulation. *Stroke 39*, 3242-3247.
- Doufas AG, et al. (2003). Dexmedetomidine and meperidine additively reduce the shivering threshold in humans. Stroke 34: 1218-1223.
- Dragancea I, Horn J, Kuiper M, et al. Neurological prognostication after cardiac arrest and targeted temperature management 33°C versus 36°C: Results from a randomized controlled clinical trial. *Resuscitation*. Aug 2015: 93: 164-170.
- Hypothermia after Cardiac Arrest Study Group (2002). Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med. Feb 21:346:549-56.
- Mokhtarani M, Mahgoub AN, Morioka N, Doufas AG, Sessler DI. (2001). Busprione and meperidine synergistically reduce the shivering threshold. Anesth Analg. 93: 1233-1239.
- Mosby's Skills. Warming and Cooling Devices: External and Intravascular. Accessed online from http://mns.elsevierperformancemanager.com/SkillsConnect/Default.aspx?Token=MNS739 &SkillID=105.
- Nielson, N., et al (2013). Targeted temperature management at 33 degrees Celsius versus 36 degrees Celsius after cardiac arrest. *New England Journal of Medicine* 369 (23), 2197-2206.
- Nolan JP, Morley PT, Vanden Hoek TL, hickey RW, Kloeck WGJ, Billi J, et al. (2003). Therapeutic Hypothermia after cardiac arrest: An advisory statement by the advanced life support task force of the International Liaison Committee on Resuscitation. Circulation Dec. 112:IV-84-IV-88.
- Olson DM, et al. Interrater Reliability of the Bedside Shivering Assessment Scale. Am J Crit Care 2013
- Presciutti, M., Bader, M., & Hepburn, M. (2012). Shivering management during therapeutic temperature modulation: Nurses' perspective. *Critical Care Nurse 32* (1), 33-41
- Safar PJ, Klochanek PM. (2002). Therapeutic hypothermia after cardiac arrest. N Engl J Med February 21: 346 (8): 612-3.
- Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: An advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. *Intensive Care Medicine* 40 (12), 1816-1831.
- Streat, Stephen (2002). Posted protocol on behalf of the Intensivists of the Auckland District Health Board in New Zealand. May 17.

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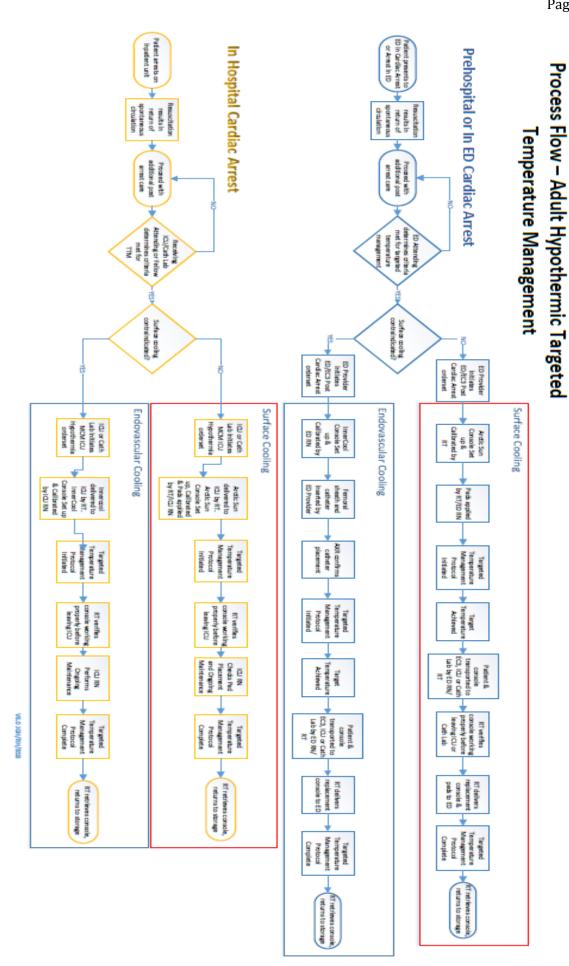
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APPENDIX BBedside Shivering Assessment Scale

Score	Definition
0	None: no shivering noted on palpation of the masseter, neck, or chest wall
1	Mild: shivering localized to the neck and/or thorax only
2	Moderate: shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Severe: shivering involves gross movements of the trunk and upper and lower extremities

APPENDIX C

Neuroprognostication in comatose survivors of cardiac arrest treated with Hypothermic Therapeutic Temperature Management

Background:

Neuroprognostication following cardiac arrest has focused on the accurate prediction of poor outcome (defined as death, persistent vegetative state or severe disability). In 2006, the Quality Standards Subcommittee of the American Academy of Neurology (AAN) proposed evidence-based step-wise algorithm for the prediction of poor outcome following cardiac arrest. These guidelines identified three clinical predictors with a false positive rate (FPR) close to zero for the identification of patients likely to have a poor outcome (Strong evidence, Level A)- absent pupillary reflexes, absent corneal reflexes and absent or extensor motor response 72 hours following cardiac arrest.1 The 2006 guidelines also identified the presence of myoclonic status epilepticus within the first day following circulatory arrest, absence of bilateral N20 responses on Somatosensory Evoked Potential (SSEP) testing and a serum Neuron Specific Enolase (NSE) level >33mcg/L as having "good" (Level B) evidence as predictors of poor outcome. The majority of studies that formed the basis for the 2006 guidelines were, however, conducted prior to the widespread use of Hypothermic Therapeutic Temperature Management (HTTM) for the management of comatose survivors of cardiac arrest. Since the use of TTM, as well as the sedatives and paralytics frequently used with HTTM protocols, may have a profound impact on the clinical examination as well as, potentially, other predictors following cardiac arrest, i several subsequent studies, including a sub study of the TTM clinical trial, iii have re-examined the accuracy of these predictors. iv In 2014, the European Resuscitation Council and the European Society of Intensive Care medicine issued an advisory statement on prognostication in comatose survivors of cardiac arrest, following a review that included both studies of patients treated with HTTM as well as studies from the pre-HTTM era.v

The purpose of this Appendix is to review the role of commonly utilized clinical, electrophysiological, laboratory and imaging predictors of outcome **following the use of HTTM** in comatose survivors of cardiac arrest and, specifically, to identify predictors with evidence of high accuracy (FPR<3%, upper limit of 95% CI <10%) for the identification of patients likely to have a poor outcome.

The Role of Clinical Predictors:

The bilateral absence of pupillary light reflexes 72 hours following Return of Spontaneous Circulation (ROSC) appears to have a FPR of 0-2 (95% CI 0-8%) for prediction of poor outcome, but has low sensitivity (~18%).³⁻⁵ Bilateral absence of a corneal reflex has a slightly higher FPR of around 4% (95% CI 1-7%), possibly because the corneal reflex is more likely to be impaired by medications, and relatively low sensitivity (~34%).³⁻⁵ Absent or extensor motor response (GCS M score <3) 72 hours following ROSC appears to have an unacceptably high FPR (~27%, 95% CI 12-48%) following use of HTTM, although some reduction in the FPR to 10-15% may be seen after 5 days.³⁻⁵ While the presence of myoclonic status epilepticus demonstrated a near-zero FPR in studies not including patients treated with HTTM, several case reports have described excellent neurological recovery in patients with early, severe, generalized myoclonic status epilepticus

treated with HTTM, with one meta-analysis suggesting an FPR of at least 5% (95% CI 2-11%).⁴ Myoclonic status epilepticus must be differentiated from the presence of myoclonic jerks following cardiac arrest, which have an FPR>10% in predicting poor outcome.⁵

The Role of Laboratory and Clinical Electrophysiological Studies:

While a serum NSE level >33mcg/L was identified as an accurate predictor of poor outcome (predominantly in patients not treated with HTTM) in the 2006 AAN guidelines, an appropriate threshold serum value with FPR close to zero has not been identified in patients treated with HTTM. The available evidence suggests, however, that most patients treated with HTTM with an NSE level >60 mcg/L 48-72 hours following ROSC will have a poor outcome.⁵ The bilateral absence of N20 waves on SSEP is typically less prone to confounding from HTTM and medication use than other predictors and may be the best validated diagnostic tool for the prediction of poor outcome with an FPR close to zero both during HTTM (95% CI 0-5%) and following rewarming, beyond 72 hours (95% CI 0-2%).³⁻⁵ Isolated case reports of patients treated with HTTM with good recovery despite the bilateral absence of N20 waves do, however, exist.³⁻⁵ Potential pitfalls of SSEP include errors from artifact and the impact of the self-fulfilling prophecy. The presence of poor grey-white differentiation and diffuse sulcal effacement on a non-contrast head CT, as well the presence of a pattern of widespread restricted diffusion on Magnetic Resonance Imaging with Diffusion Weighted Imaging (MRI-DWI) at 2-5 days following ROSC has been demonstrated in several studies to predict poor outcome, however, the relatively small sample size in these studies limits the ability to reliably estimate an FPR.5

The role of Electroencephalography (EEG) in neuroprognostication: Several EEG patterns predict poor outcome following cardiac arrest.⁵

- 1. Absence of EEG reactivity to external stimuli 48-72 hours following ROSC (FPR 0-2%, 95% CI 0-7%).⁵
- 2. Electrographic status epilepticus (FPR 6%, 95% CI 2-20%).vi
- 3. Burst suppression present ≥72 hours following ROSC, defined as >50% of the record with voltage <10mcV with alternating bursts.^{vii}
- 4. Low-voltage (≤20mcV) record. This finding appears to have the least specificity, with FPR up to 17%.

While the EEG may facilitate neuroprognostication, studies of EEG for neuroprognostication have had several limitations, including small sample size, lack of standardization of criteria for EEG reactivity and electrographic status epilepticus and operator dependence. The presence of low voltage alone, in particular, may be unreliable, particularly in the setting of HTTM and medication use.

<u>Self-fulfilling prophecies</u>: It is important to recognize that all studies of predictors of outcome following cardiac arrest, including those with near-zero FPR, are prone to confounding by the self-fulfilling prophecy. Caution must therefore be taken to not make definitive prognoses on the basis of a single predictor, including those such as SSEPs with a seemingly near-zero FPR in published studies.

Guidelines for Neuroprognostication following Therapeutic Hypothermia:

1. Neuroprognostication is distinct from an assessment for brain death.

- 2. Neurocritical Care consultation, obtained through the on-call Neurology consult resident, is available to assist with neuroprognostication at UMHS.
- 3. Accurate neuroprognostication is ideally performed ≥72 hours following ROSC, following completion of rewarming and at least 12 hours following cessation of all sedative and paralytic medications. Individual circumstances may justify prognostication of outcome at an earlier time point, based on a global assessment of the patient's medical condition and comorbidities.
- 4. Major confounders must be excluded before an assessment for neuroprognostication is performed. These include sedation and neuromuscular blockade, persistent hypothermia, severe hypotension, hypoglycemia and other profound metabolic derangements.
- 5. Patients who regain a motor response of flexion or better following rewarming have a reasonable possibility of good neurological recovery and are unlikely to benefit from further attempts at neuroprognostication while in the intensive care unit. In general, any sign of definitive neurological improvement over the course of evaluation should prompt careful consideration that this might indicate potentially better prognosis, and may preclude the need for further prognostic testing. The neurocritical care consult is available to assist with this assessment, following rewarming.
- 6. Multimodal prognostication is recommended. Decisions to limit care based on neurologic prognosis should not be made based on the results of a single prognostication parameter.
- 7. Continuous EEG, initiated as soon as possible following ROSC, should be **strongly** considered in all comatose survivors of cardiac arrest treated with HTTM, to monitor for potentially treatable electrographic status epilepticus and to assist with neuroprognostication.
- 8. When assessing an EEG for prognosis, a specific verbal request should be made to the EEG fellow on call prior to the study, as that assessment requires special procedure and evaluation. Specifically, increasing levels of stimulation are required, including endotracheal suctioning, and all sedation must be absent for at least 12 hours. The report should specifically address that it is for prognosis.
- 9. Somatosensory Evoked Potential testing ≥72 hours following ROSC should be **strongly** considered in all comatose survivors of cardiac arrest treated with HTTM to assist with neuroprognostication, since clinical predictors have poor sensitivity and/ or an unacceptably high FPR/ 95% CI. If the patient has any reassuring clinical signs that indicate potential recovery (e.g. a reactive EEG or motor response of flexion or better), the SSEP testing may be unnecessary.
- 10. Brain imaging with noncontrast CT or MRI with DWI should be considered >72 hours from ROSC, particularly when strong predictors of poor outcome (absent pupillary/ corneal reflexes and bilateral absence of N20 on SSEP) are absent.
- 11. Neuroprognostication should begin with an assessment for the presence of strong predictors of poor outcome (FPR<3% with upper limit of 95% CI <10%). These include the absence of pupillary and corneal reflexes, which are ideally assessed together, and the absence of bilateral N20 waves on SSEP.
 - An isolated absence of either the pupillary or corneal reflex should raise concern for confounders, such as medication effect (corneal reflex) or a very sluggish pupillary reflex.
 - Multiple providers should ideally confirm the absence of pupillary/ corneal reflexes.
- 12. A poor outcome, defined as death, persistent vegetative state or severe disability, is **VERY LIKELY** (>95% probability, based on the available data) when pupillary and corneal reflexes are absent AND there is bilateral absence of N20 waves on SSEP.
 - When only one of these predictors of poor outcome (absent pupillary and corneal reflexes OR bilateral absence of N20 on SSEP) are present, a poor outcome remains quite likely, however, other predictors of poor outcome must be taken into

consideration.

- 13. When pupillary or corneal reflexes are present AND at least one N20 wave present on SSEP, the presence of **two or more** of the following 24 hours following the initial assessment (i.e, >96 hours) makes a poor outcome **LIKELY** (>80-90% probability), however, the presence of uncertainty must be acknowledged during prognostication.
 - 1) Myoclonic status epilepticus <48 hours from ROSC.
 - 2) Presence of one of the following patterns on EEG- absence of reactivity to external stimuli, electrographic status epilepticus or burst suppression ≥72 hours following ROSC.
 - 3) Presence of diffuse loss of grey-white differentiation and sulcal effacement on head CT <u>OR</u> presence of a diffuse restricted-diffusion pattern on MRI-DWI.
 - 4) Serum NSE level >60 mcg/L at 48-72 hours following ROSC.
- 14. When none of the above criteria are present, the neurological outcome is considered indeterminate.

ALGORITHM FOR NEUROPROGNOSTICATION IN COMATOSE SURVIVORS OF CARDIAC ARREST TREATED WITH THERAPEUTIC TEMPERATURE MANAGEMENT

FROM: 2014 GUIDELINES OF THE EUROPEAN RESUSCITATION COUNCIL AND THE EUROPEAN **SOCIETY OF INTENSIVE CARE MEDICINE**

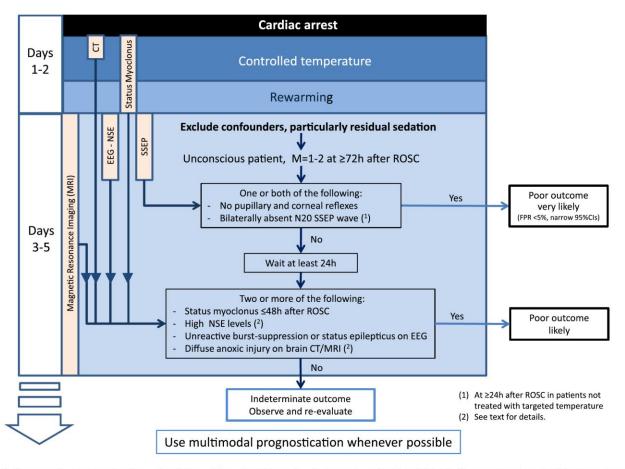


Fig. 1 Suggested prognostication algorithm. The algorithm is is present, wait at least 24 h before reassessing. At this stage, two or entered ≥72 h after ROSC if, after the exclusion of confounders indicates a poor outcome is very likely. If neither of the features consider continue to observe and re-evaluate

more of the following indicate that a poor outcome is likely: status (particularly residual sedation), the patient remains unconscious myoclonus ≤48 h; high neuron-specific enolase values; unreactive with a Glasgow Motor Score of 1 or 2. The absence of pupillary and corneal reflexes, and/or bilaterally absent N20 SSEP wave, injury on brain CT and/or MRI. If none of these criteria are met

Sandroni C, Cariou A, Cavallaro F, Cronberg T, Friberg H, Hoedemaekers C, Horn J, Nolan JP, Rossetti AO, Soar J. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Intensive Care Med. 2014 Dec; 40(12):1816-31.

REFERENCES

- i. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006 Jul 25;67(2):203-10. Review.
- ii. Samaniego EA, Mlynash M, Caulfield AF, Eyngorn I, Wijman CA.Neurocrit Care. Sedation confounds outcome prediction in cardiac arrest survivors treated with hypothermia. 2011 Aug;15(1):113-9.
- iii. Dragancea I, Horn J, Kuiper M, Friberg H, Ullén S, Wetterslev J, Cranshaw J, Hassager C, Nielsen N, Cronberg T; TTM trial investigators. Neurological prognostication after cardiac arrest and targeted temperature management 33°C versus 36°C: Results from a randomised controlled clinical trial. Resuscitation. 2015 Aug;93:164-70. doi: 10.1016/j.resuscitation.2015.04.013.
- iv. Golan E, Barrett K, Alali AS, Duggal A, Jichici D, Pinto R, Morrison L, Scales DC. Predicting neurologic outcome after targeted temperature management for cardiac arrest: systematic review and meta-analysis. Crit Care Med. 2014 Aug;42(8):1919-30.
- v. Sandroni C, Cariou A, Cavallaro F, Cronberg T, Friberg H, Hoedemaekers C, Horn J, Nolan JP, Rossetti AO, Soar J. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Intensive Care Med. 2014 Dec;40(12):1816-31.
- vi. Legriel S, Hilly-Ginoux J, Resche-Rigon M, Merceron S, Pinoteau J, Henry-Lagarrigue M, Bruneel F, Nguyen A, Guezennec P, Troché G, Richard O, Pico F, Bédos JP. Prognostic value of electrographic postanoxic status epilepticus in comatose cardiac-arrest survivors in the therapeutic hypothermia era. Resuscitation. 2013 Mar;84(3):343-50.
- vii. Hirsch LJ, LaRoche SM, Gaspard N, Gerard E, Svoronos A, Herman ST, Mani R, Arif H, Jette N, Minazad Y, Kerrigan JF, Vespa P, Hantus S, Claassen J, Young GB, So E, Kaplan PW, Nuwer MR, Fountain NB, Drislane FW. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. J Clin Neurophysiol. 2013 Feb;30(1):1-27.