Post Cardiac Arrest - Adult - Inpatient/Emergency Department
Consensus Care Guideline

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Plan for Review:
This guideline will be reviewed when the American Heart Association Cardiopulmonary Resuscitation and Emergency Cardiovascular Care recommendations are updated, or a minimum of every five years.

Introduction

Cardiac arrest results in 300,000 deaths per year in North America. Out-of-hospital cardiac arrest (OHCA) is a challenging condition with approximately 10.4% of patients surviving their initial hospitalization and 8.2% surviving with good functional status. In-hospital cardiac arrest (IHCA) in the US is estimated to occur in 1.2% of adult hospital admissions, with only 25.8% of patients surviving to discharge.[1]

Post cardiac arrest syndrome is sequelae of cardiac arrest with systemic manifestations. The key components include post-arrest brain injury, post-arrest myocardial dysfunction, systemic ischemia/reperfusion response, and persistent acute and chronic pathology that precipitated the event (Table 1).[2,3] There is increasing recognition that systematic post-cardiac arrest care after return of spontaneous circulation (ROSC) can improve the likelihood of survival with good quality of life. A comprehensive, structured, multidisciplinary system of care should be implemented in a consistent manner for the treatment of patients after ROSC.[1] *(AHA Class 1, LOE B-NR)*

The 2015 and 2020 AHA Post Cardiac Arrest Care Guidelines served as an outline to this document.[1,4] The clinical trials and data in regards to the care of cardiac arrest patient is not as vigorous as other cardiovascular disease processes (e.g., Acute Coronary Syndromes and Congestive Heart Failure); thus, the guideline workgroup has chosen to include some 2a and 2b level of evidence recommendations.

Scope

Intended Users: Emergency Medicine, Cardiology and Critical Care Physicians, Advanced Practice Providers, Nurses, and Pharmacists caring for patients who have suffered an OHCA or IHCA.

These recommendations are not intended for patients managed with extracorporeal membrane oxygenation (ECMO). See Extracorporeal Membrane Oxygenation (ECMO): Initiation and Management – Adult – Inpatient/Emergency Department Consensus Care Guideline.

Objective: To provide recommendations for the care of OHCA and IHCA patients which have the potential to improve long-term patient outcomes (e.g., mortality, neurological function).

Target Population: Patients ≥ 18 years of age who have suffered an OHCA or IHCA.

Interventions and Practices Considered:

- Targeted Temperature Management (TTM)
- Optimization of hemodynamics and gas exchange
- Immediate coronary reperfusion when indicated for restoration of coronary blood flow with percutaneous coronary intervention
- Glycemic control
- Neurologic diagnosis, management, and prognostication

Major Outcomes Considered:

- Sudden cardiac death
- Survival
- Morbidity
- Neurological recovery
- Quality of life

Recommendations

1. Targeted Temperature Management (TTM)

Patient Eligibility

Therapeutic hypothermia (cooled to 32°C to 36°C)[1] *(AHA Class 1, LOE B-R)* for at least 24 hours[1] *(AHA Class 2a, B-NR)* for neurologic protection is recommended in the following patient groups with sudden and unexpected cardiac arrest, that remain comatose (i.e. lack of meaningful response to verbal commands), and are without exclusion criteria:

- **Return of spontaneous circulation (ROSC)** after out-of-hospital arrest with any initial rhythm.[1] *(AHA Class 1, LOE B-R)*
- ROSC after in-hospital cardiac arrest with initial non-shockable rhythm.[1] *(AHA Class 1, LOE B-RO)* or with initial shockable rhythm.[1] *(AHA Class 1, LOE B-NR)*

Data from a recent major RCT suggests targeted normothermia confers the same benefit as targeted hypothermia in patients with OHCA, with no difference in mortality or functional outcome.[5] Surface or intravascular cooling was initiated in the normothermic group to maintain a temperature of ≤ 37.5 ºC and the hypothermic group received intravascular cooling to 33ºC. Data from a previous RCT suggested that a higher temperature **goal of 36ºC** may confer the same neurologic benefit in some circumstances.[6] Taking these data into account, the targeted goal temperature between 33°C to 37°C is a clinical decision left up to the discretion of the treating clinician on a case-by-case basis, and may be influenced by specific clinical features or the initial temperature of the patient.[4,7] *(UW Health Low quality evidence, C recommendation)*

Active or rapid rewarming should be **avoided** in comatose patients who spontaneously develop a mild degree of hypothermia (> 32°C) after resuscitation from cardiac arrest during the first 48 hours after ROSC. *(UW Health Low quality evidence, C recommendation)*

Recommended Exclusion Criteria

Targeted temperature management is not recommended for patients who meet any of the following exclusion criteria:

- > 12 hours since return of spontaneous circulation (ROSC)
- **Motor** component of Glasgow Coma Scale score ≥ 5 (i.e., patient completes purposeful movement)
- Minimal pre-morbid functional status (e.g., advanced dementia, metastatic cancer)
- Sepsis as cause of arrest
- Do Not Resuscitate (DNR) status
- Core body temperature < 30ºC

A non-enhanced CT scan of the head can provide information about structural lesions, stroke, or intracranial hemorrhage that may have contributed to cardiac arrest. This should be obtained **prior** to TTM induction.[2] *(UW Health Moderate quality evidence, S recommendation)* If intracranial process present, contact Neurosurgery for a decision of the type of cooling and goal temperature, as these patients were excluded from many of the mild hypothermia post cardiac arrest clinical trials.[6,8]

Pregnancy is a unique circumstance in post cardiac arrest care. A pregnancy test should be performed in all women of childbearing age. *(UW Health High quality evidence, S recommendation)* There are reports of TTM being used as a successful therapy in pregnant women who have

suffered a cardiac arrest.[9,10] The decision to use TTM in a pregnant patient should be made in the context of the entire clinical picture and in consultation with Obstetrics. *(UW Health Low quality evidence, C recommendation)*

Systemic Cooling

Providers should **closely monitor** patient core temperature after ROSC.[4] *(AHA Class I, LOE C)* A core body temperature should be assessed **immediately** following patient presentation. Two temperature sources should be evaluated (either tympanic, esophageal probe or a urinary probe).[2] Throughout TTM initiation, maintenance, and rewarming, temperature should be monitored continuously via esophageal, bladder, or rectal sources.[4]

Systemic cooling can occur via two mechanisms (see Appendix B for available equipment):

1. Surface cooling with cooling blankets/ hypothermic wraps
2. Intravascular cooling

Surface cooling should be initiated **immediately** following determination that a patient is a candidate for targeted temperature management (i.e., considerations of exclusion criteria and non-contrasted CT of the head has been performed). *(UW Health Moderate quality evidence, C recommendation)* There is a 20% increase in mortality for every hour of delay in TTM initiation.[11] Therefore, early communication with the accepting Critical Care service should occur, allowing for a decision on cooling method and core temperature goal.

Routine prehospital cooling of patients after ROSC with rapid infusion of cold intravenous fluids is NOT recommended.[4] *(AHA Class III, LOE A)* However, intravascular cooling may be initiated upon arrival to the Emergency Department or inpatient admission. A prototype of the catheter used at UW Health is the Zoll Quattro® catheter. This catheter is both a triple lumen central venous access for medication and fluid delivery and contains heat exchange balloons to allow for systemic body temperature modification. The Quattro® contains 4 heat exchange balloons which increases the surface area for cooling and is the longest heat exchange catheter made by Zoll at 45 cm. However, it is imperative to consider the patient's body size in selecting a cooling catheter, as smaller body sizes may not be amendable to Quattro® placement and use of a shorter catheter may be best. Once the intravascular cooling catheter has been placed appropriately in the femoral vein cooling can commence. For additional details, see Nursing Departmental Policy #1.42AP.

In the interim while placing the catheter, it is up to the discretion of the clinician as to the concomitant use of other temporary methods of cooling, such as external ice wraps or cold saline.

Prevention of Shivering

TTM is associated with shivering, which occurs in up to 40% of patients undergoing TTM.[12] Shivering may cause cerebral metabolic stress by decreasing brain tissue oxygen tension ($PbtO_2$).[13] Pharmacologic and nonpharmacologic[14] treatments are available to control shiver. Various pharmacologic protocols have been created to mitigate the effects of shivering.[15-17] A protocolized approach can effectively manage shivering and minimize the potential sedative and paralytic effects associated with some antishivering medications.[16,18] Prophylactic antishivering medications should be administered before starting temperature management.[16,18] *(UW Health Moderate quality evidence, C recommendation)* The Bedside Shivering Assessment Scale (BSAS)[19] should be performed to objectively document the degree of shivering (Table 2). *(UW Health Moderate quality evidence, C recommendation)* Pharmacologic therapy should follow a tiered protocol based on the degree of shivering (Table 3). *(UW Health Moderate quality evidence, C recommendation)*

Acetaminophen has been shown to lower hypothalmic set point.[20,21] Buspirone and meperidine can synergistically reduce the shivering threshold as well.[22-24] Magnesium peripherally vasodialates and improves comfort and cooling rates during hypothermia.[25] Analagosedation, which is often already being utilized in cardiac arrest, has the added benefit of aiding in shivering control and therefore should be optimized. Dexmedetomidine in combination with meperedine or buspirone, have been shown to reduce shivering threshold.[26,27]

Neuromuscular blockade (NMB) is an option for shivering, however, NMBs may mask appropriate sedation or seizure, lead to polyneuropathy, interfere with neurologic exam and additionally, NMBs fail to shut down central shivering mechanisms. Therefore, NMBs should be utilized after other modalities have been attempted.[16,28,29] *(UW Health Moderate quality evidence, C recommendation)* Neuromuscular blocking agents should initially be ordered as boluses, as needed to prevent shivering, with consideration given to an infusion only if shivering cannot be adequately controlled with boluses. Atracurium may be used as the first line agent for post-cardiac arrest patients due to the high incidence of renal dysfunction in this patient population. *(UW Health High quality evidence, C recommendation)* Venous thromboembolism (VTE) prophylaxis *(UW Health High quality evidence, S recommendation)* and scheduled eye lubrication *(UW Health High quality evidence, S recommendation)* are recommended for patients who receive a neuromuscular blocking agent. For complete recommendations including dosing, refer to the UW Health Continuous Infusion Neuromuscular Blocking Agents – Adult – Inpatient Guideline.

Table 2. Bedside Shivering Assessment Scale[19]

Score	Shivering	Patient Behavior
0	None	No shivering
1	Mild	Shivering localized to the neck/thorax, may be seen only as an artifact on ECG or felt by palpation
2	Moderate	Intermittent involvement of the upper extremities ± thorax
3	Severe	Generalized shivering or sustained upper/lower-extremity shivering

Table 3. Antishivering Protocol[16,18]

<table>
<tr><th>Typical BSAS Score at Initiation</th><th>Intervention</th><th>Dose</th><th>Additional Information</th></tr>
<tr><td rowspan="4">BSAS: 0

Initiate <u>before</u> starting TTM</td><td rowspan="4">Acetaminophen
and
Buspirone
and
Magnesium Sulfate
and
Skin Counterwarming</td><td>Acetaminophen 650 mg NGT q6hrs</td><td>Continue throughout TTM</td></tr>
<tr><td>Buspirone 30 mg NGT q8hr</td><td>Continue throughout TTM</td></tr>
<tr><td>Magnesium Sulfate 4 g IV infused over 4 hours followed by infusion per titration table</td><td>Obtain serum magnesium level at baseline and q 4-6hrs during TTM
Magnesium Titration Table
<table><tr><th>Serum Mg Level (mg/dL)</th><th>Intervention</th></tr><tr><td>2.0 - 2.5</td><td>Increase infusion by 0.5 g/hr</td></tr><tr><td>2.6 - 3.0</td><td>Increase infusion by 0.25 g/hr</td></tr><tr><td>3.1 - 4.0</td><td>Continue current infusion rate</td></tr><tr><td>4.1 - 4.5</td><td>Decrease infusion by 0.25 g/hr</td></tr><tr><td>> 4.5</td><td>Hold infusion and recheck serum Mg in 4 hours. When serum Mg ≤ 4 mg/dL restart infusion at 0.5 g/hr less than previous rate.</td></tr></table></td></tr>
<tr><td>Skin Counterwarming:
Bair Hugger (43°C MAX temp)</td><td>Can be used when intravascular cooling methods are utilized. Apply to hands and feet.</td></tr>
<tr><td rowspan="2">BSAS: 1</td><td rowspan="2">Opioid
or
Dexmedetomidine</td><td>Meperidine 12.5-50 mg IV q 4 hrs prn</td><td>Use with caution in elderly patients and those with impaired renal function; in these populations initial dose 12.5mg.</td></tr>
<tr><td>Fentanyl IV 25-200 mcg/hr</td><td>Transition if not already being used as primary pain control medication. May bolus and increase infusion rate.</td></tr>
<tr><td>BSAS: 2</td><td>Opioid
and
Dexmedetomidine</td><td>Dexmedetomidine IV 0.2-1.5 mcg/kg/hr</td><td>Add to baseline sedative</td></tr>
<tr><td>BSAS: 3</td><td>Propofol</td><td>Propofol IV 10-70 mcg/kg/min</td><td>Transition if not already being used as primary sedative</td></tr>
<tr><td>BSAS: 3
Use only if all other medications unable to control shivering</td><td>Neuromuscular Blocking Agent (NMBA)</td><td>Vecuronium 0.1 mg/kg IV bolus q 60 min PRN
Rocuronium 0.6 mg/kg IV bolus q 60 min PRN
Cisatracurium 0.2 mg/kg IV bolus q 60 min PRN</td><td>Neuromuscular blockade last resort after inability to control shivering despite all other medications. Check TOF (placement on face preferred) every hour and consider additional dose if > 2 out of 4 twitches. Continuous infusion of NMBA for shivering only if bolus dosing is inadequate to keep BSAS < 2.</td></tr>
</table>

2. Identify and Treat the Etiology of the Arrest

Acute coronary syndrome (ACS) is a common cause of cardiac arrest. A 12-lead electrocardiogram (ECG) should be obtained as soon as possible after ROSC to determine whether acute ST segment elevation is present.[1] *(AHA Class 1, LOE B-NR)*

Patients with ST-segment elevation myocardial infarction (STEMI)

Because it is impossible to determine the final neurological status of comatose patients in the first hours after ROSC, aggressive treatment of ST-segment elevation myocardial infarction (STEMI) should begin as in non–cardiac arrest patients, regardless of coma or induced hypothermia.[1,2] *(AHA Class 2a, LOE C-LD)*

Patients with suspected cardiac etiology

Emergent coronary angiography should be strongly considered for all OHCA patients with suspected cardiac etiology of arrest and ST elevation on ECG.[1] *(AHA Class 1, LOE B-NR)* The decision to proceed with coronary angiography should be made with discussion with the interventional cardiologist, and after weighing the potential risks and benefits of the procedure. Because of the high incidence of acute coronary ischemia, consideration of emergent coronary angiography may be reasonable in select patients (e.g., electrically or hemodynamically unstable) even in the absence of STEMI.[1] *(AHA Class 2a, LOE B-NR)* Patients with ventricular fibrillation (VF) or ventricular tachycardia (VT) arrest and shockable rhythm on presentation should be strongly considered due to the benefits demonstrated in the Parisian Registry.[30] *(UW Health Moderate quality evidence, C recommendation)* TTM can be safely combined with primary percutaneous coronary intervention (PCI) after cardiac arrest caused by acute myocardial infarction (AMI).[31]

Continuous telemetric monitoring should take place to detect and treat arrhythmias.[1] *(UW Health High quality evidence, S recommendation)* Post cardiac arrest myocardial dysfunction is sequelae of OHCA and a transthoracic echocardiogram should be obtained within 24 hours of presentation; in order ensure there is no reversible etiology behind the cardiac arrest and to guide ongoing management.[32] *(UW Health Moderate quality evidence, C recommendation)*

In post cardiac arrest patients with arrest due to confirmed pulmonary embolism, thrombolysis, surgical embolectomy, and mechanical embolectomy are reasonable emergency treatment options.[1] *(AHA Class 2a, LOE C-LD)* In patients with arrest presumed due to pulmonary embolus**,** fibrinolytics may be considered.[1] *(AHA Class 2b, LOE C-LD)*

3. Optimize Mechanical Ventilation to Minimize Lung Injury

Pulmonary dysfunction after cardiac arrest is common. Etiologies include hydrostatic pulmonary edema from left ventricular dysfunction; noncardiogenic edema from inflammatory, infective, or physical injuries; severe pulmonary atelectasis; or aspiration occurring during cardiac arrest or resuscitation.

During postresuscitation care, both hyperoxemia and hypoxemia have been associated with worse outcomes.[33] Hyperoxemia may increase oxidative stress and organ damage after reperfusion and hypoxemia may increase ischemic injury to the brain and other organs. It is important to optimize mechanical ventilation in the post arrest setting to minimize further pulmonary compromise. The well-established ventilation management strategies for patients at risk for acute lung injury and adult respiratory distress syndrome (ARDS)[34] are also appropriate strategies in the post cardiac arrest population.

Aggressive ventilator management should be performed to avoid both hypoxia and hyperoxia, using the following strategies:

1. Hypoxemia should be avoided in all patients who remain comatose after ROSC.[1] *(AHA 1, LOE B-NR)* It is reasonable to use the highest available oxygen concentration until the arterial oxyhemoglobin saturation or the partial pressure of arterial oxygen can be measured.[1]
2. Avoid hyperoxemia by titrating the FiO2 to target an oxygen saturation of 92-98% once reliable measure of peripheral blood oxygen saturation is available.[1] *(AHA Class 2b, LOE B-R)*
3. Maintain the $PaCO_2$ within a normal physiological range (generally 35-45 mmHg).[1] *(AHA Class 2b, LOE B-R)*

   Note: Hypothermia can affect the accuracy of the PaO_2 measurement because the process of measuring PaO_2 involves pre-heating specimens to 37°C. At this time, the UW Health Laboratory does not adjust for the patient's body temperature at the time the sample was obtained; therefore, the PaO_2 may be artificially elevated.
4. A chest radiograph should be obtained to ensure proper endotracheal tube placement. *(UW Health High quality evidence, S recommendation)*
5. It is reasonable to consider the titrated use of sedation and analgesia in critically ill patients who require mechanical ventilation or shivering suppression during induced hypothermia after cardiac arrest. *(UW Health Moderate quality evidence, C recommendation)*

   Note: Hypothermia can reduce the clearance of sedatives and analgesics; initiate treatment with bolus dosing of these agents as needed rather than continuous infusions to facilitate assessment after normothermia. Continuous infusions are recommended for patients receiving neuromuscular blocking agents (see UW Health Continuous Infusion Neuromuscular Blocking Agents – Adult – Inpatient Guideline).

4. Reduce the Risk of Multi-Organ Injury & Support Organ Function

During the cooling process the patient should have a systemic evaluation to ensure that each system is maximally supported.

Hemodynamic Support

Hemodynamic instability is common after cardiac arrest.[2,35] Death due to multi-organ failure is associated with a persistently low cardiac index during the first 24 hours after resuscitation. Early goal directed hemodynamic optimization is hypothesized to decrease the systemic inflammatory syndrome and reduce the post cardiac arrest brain injury.[36,37]

Bleeding Risk

TTM induces coagulative abnormalities which can make the patient more prone to bleeding.[38] Therefore, any concern for bleeding should be investigated thoroughly. If no active bleeding is detected, consider starting venous thromboembolism (VTE) prophylaxis as patients are at an increased risk for deep venous thrombosis or pulmonary embolism given immobility. *(UW Health Moderate level of evidence, C recommendation)* For detailed recommendations, refer to the UW Health Venous Thromboembolism Prophylaxis Guideline.

Mean Arterial Pressure Goals

Following cardiac arrest, cerebral auto regulation is significantly modified, and in some cases absent. These changes mean that cerebral perfusion pressure becomes even more dependent

upon mean arterial pressure (MAP).[8,31,33,39-44] A systolic blood pressure of ≥ 90 mmHg and a MAP of ≥ 65 mmHg should be maintained to avoid hypotension.[1] *(AHA Class 2a, LOE B)*

Continuous arterial blood pressure monitoring should be undertaken with placement of an intra-arterial catheter to constantly follow these values. Use of central venous oxygen saturation to guide therapy is reasonable and clinicians can consider further treatment when central venous oxygenation levels are < 70%.

Hypotension Treatment

Fluid administration in the absence of contraindications is typically the first line treatment of hypotension.[38] *(UW Health High quality evidence, S recommendation)*

Vasodilation may occur from loss of sympathetic tone and from metabolic acidosis. In addition, the ischemia/reperfusion of cardiac arrest and electric defibrillation both can cause transient myocardial stunning and dysfunction that can last many hours, but may improve with use of vasoactive drugs.[38] If hypotension is persistent, pharmacotherapeutic agents can be employed. Vasoactive (e.g., norepinephrine), inotropic (e.g., dobutamine), and inodilator (e.g., milrinone) agents should be titrated as needed to optimize blood pressure, cardiac output, and systemic perfusion. *(UW Health High quality evidence, C recommendation)*

There is no evidence supporting one pharmacotherapeutic agent over another. For detailed recommendations on vasoactive medications, refer to the UW Health Vasoactive Continuous Infusions in Adult Patients - Adult - Inpatient Guideline.

Blood Glucose Control

The benefit of any specific target glucose range is uncertain in adults with ROSC after cardiac arrest.[1] *(AHA Class 2b, LOE B-R)* Strategies to target moderate glycemic control (140-180 mg/dL) may be considered.[1] *(UW Health Low quality evidence, C recommendation)* Attempts to control glucose concentration within a lower range (80 to 110 mg/dL [4.4 to 6.1 mmol/L]) should NOT be implemented after cardiac arrest due to the increased risk of hypoglycemia. *(UW Health Low quality evidence, C recommendation)*

Targeted arterial glucose levels of 140-180 mg/dL or current insulin infusion algorithm goal of 110-150 mg/dL in intensive care unit patients are recommended per UW Health Wisconsin Insulin Infusion Practice Protocol and are supported by an American Association of Clinical Endocrinologists/American Diabetes Association (AACE/ADA) consensus statement on inpatient glycemic control.[45] These ranges are consistent with the American Heart Association (AHA) guideline recommendations to target moderate glycemic control in adult patients with ROSC after cardiac arrest.[1,2] *(UW Health Moderate quality evidence, C recommendation)*

Hyperglycemia is common[2,38] and serial whole blood glucose samples should be obtained through a Basic Metabolic Panel (BMP) at least every 6 hours in addition to POC glucose testing every hour throughout cooling and rewarming. *(UW Health Moderate quality evidence, C recommendation)*

Metabolic Considerations

Following presentation to the hospital (likely via the Emergency Department), the following labs should be assessed: CBC with differential, magnesium, phosphate, liver function tests (ALT, AST, albumin), troponin, prothrombin time/INR, PTT, lactate, electrolytes, BUN, calcium, and creatinine. *(UW Health Moderate quality evidence, C recommendation)*

Hypothermia induces many metabolic effects, which need to be carefully monitored throughout the cooling period. These patients are critically ill with changing volume status. Hypothermia induces an intracellular shift and diuresis[46,47] which will result in low potassium, magnesium, and phosphate levels which could be a trigger for cardiac arrhythmias or respiratory complications. Therefore, serial electrolyte, calcium, magnesium, BUN, creatinine, and phosphate labs should be measured at least every 6 hours. Potassium should be replaced to maintain serum levels within a normal range, magnesium to ≥ 2.0 mg/dL, and phosphate to ≥ 2.5 mg/dL. It is important to note that rewarming reverses the potassium flux and increases serum levels,[47] so repletion should be held 4 hours before rewarming begins.[46] Serial lactate labs[47] will allow the clinician to ensure adequate tissue oxygenation and are helpful in modifying vasoactive medications.

Central Nervous System Support

Brain injury is a common cause of morbidity and mortality in post–cardiac arrest patients. Brain injury is the cause of death in 68% of patients after out-of-hospital cardiac arrest and in 23% after in-hospital cardiac arrest.[48] The pathophysiology of post–cardiac arrest brain injury involves a complex cascade of molecular events that are triggered by ischemia and reperfusion and then executed over hours to days after ROSC. Events and conditions in the post–cardiac arrest period have the potential to exacerbate or attenuate these injury pathways and impact ultimate outcomes.[38]

An electroencephalogram (EEG) should be performed, with prompt interpretation as soon as possible, and should be monitored frequently or continuously in comatose patients after ROSC.[4] *(AHA Class I, LOE C-LD)* Continuous EEG monitoring will allow for early detection and treatment of seizures which may be masked due to the use of neuromuscular blockades, and pose a risk of further neurologic injury if not treated. The Neurology resident on call should be notified of the patient to initiate the continuous EEG process.

Clinical manifestations of post–cardiac arrest brain injury include coma, seizures, myoclonus, various degrees of neurocognitive dysfunction (ranging from memory deficits to persistent vegetative state), and brain death.[3] The same anticonvulsant regimens for the treatment of seizures (including myoclonic status epilepticus) used for status epilepticus caused by other etiologies may be considered after cardiac arrest.[4] *(AHA Class IIb, LOE C-LD)*

5. Rewarm Slowly

If the patient tolerates TTM to goal temperature for 24 hours, rewarming should subsequently ensue. It is important that rewarming occurs slowly. While the optimal re-warming rate is not known, literature suggests rates between 0.2 to 0.5º C/hour.[49] Rewarming should occur at 0.25º C per hour.[46] *(UW Health Moderate quality evidence, C recommendation)*

Pyrexia Risk

It may be reasonable to actively prevent fever in comatose patients after TTM.[1] *(AHA Class 2b, LOE C-LD)* Rebound hyperthermia is a recognized complication of OHCA. There is as an association of poor neurological outcome in patients with fever after ROSC who have not been treated with TTM; however this finding is not consistently reported in patients treated with TTM.[1] Current guidelines recommend intervening to prevent pyrexia; however, there is a lack of randomized controlled data on methods of treatment (anti-pyretics or cooling techniques). **Post rewarming core body temperature should be maintained at 37º C with surface cooling devices for the next 48 hours.** To facilitate this, anti-pyretic pharmacotherapy with acetaminophen may be used in the absence of hepatic dysfunction. Carefully consider the contribution of nosocomial infectious processes during this time period.

6. Prognostication of Neurological Outcome

In patients who remain comatose after cardiac arrest, decisions to withdraw life sustaining treatment should not be based on one variable alone but based on the integration of clinical scenario (e.g., comorbidities) and several clinical and diagnostic tests. **Neuroprognostication should involve a multimodal approach and not be based on any single finding**[1] *(AHA Class 1, LOE B-NR)* and should be delayed until adequate time has passed to ensure avoidance of confounding by medication effect or a transiently poor examination in the early postinjury period.[1] *(AHA Class 1, LOE B-NR)* The accuracy of clinical examinations may be confounded in post-cardiac arrest patients, due to slower metabolism of sedatives and neuromuscular blockers and residual sedation or paralysis.[1] Neuroprognostication should be delayed until serum pentobarbital levels measure < 0.5 mcg/mL and for at least 72 hours after discontinuing sedatives and neuromuscular blockers. *(UW Health Moderate quality evidence, C recommendation)*

It is reasonable to perform multimodal neuroprognostication at a minimum of 72 hours after the return to normothermia, though individual prognostic tests may be obtained earlier than this.[1] *(AHA Class 2a, LOE B-NR)* A retrospective analysis of the Parisian Region OHCA Registry demonstrated that 29% of comatose survivors of cardiac arrest who recovered consciousness after TTM awoke more than 48 hours after discontinuation of sedation.[50] Delayed awakening is more likely to occur in patients with renal insufficiency on admission, post-resuscitation shock, and older age (> 59 years).[50]

Teams caring for patients who remain comatose after ROSC should have regular and transparent multidisciplinary discussions with surrogates regarding neuroprognostication uncertainties and anticipated time course.[1] *(AHA Class 1, LEO C-EO)*

Neurological Assessments

Clinical Examination

The neurological examination is the most widely studied parameter to predict outcome in comatose post–cardiac arrest patients. Neurological examination for this purpose can be reliably undertaken only in the absence of confounding factors (hypotension, seizures, sedatives, or neuromuscular blockers).[38] On the basis of existing studies, no clinical neurological signs reliably predict poor outcome < 24 hours after cardiac arrest.[28,38,51]

Among adult patients who remain comatose after ROSC, the absence of pupillary light reflex ≥ 72 hours after cardiac arrest is a reasonable exam finding with which to predict poor neurologic outcome.[1] *(AHA Class 2b, LOE B-NR)* The bilateral absence of corneal reflexes ≥ 72 hours after cardiac arrest is also supportive of the prognosis of poor neurological outcome.[1] *(AHA Class 2b, LOE B-NR)*

The absence of vestibulo-ocular reflexes at ≥ 24 hours (FPR 0%, 95% CI 0% to 14%) or Glasgow Coma Scale (GCS) score < 5 at ≥ 72 hours (FPR 0%, 95% CI 0% to 6%) are less reliable for predicting poor outcome or were studied only in limited numbers of patients. Given their unacceptable FPR, the findings of either absent motor movements or extensor posturing should NOT be used alone for predicting a poor neurologic outcome.[2,4,38] *(AHA Class III, LOE B-NR)* Other clinical signs, including the presence of myoclonus, are not recommended for predicting poor outcome.[4] *(AHA Class III, LOE B-NR)* In combination with other diagnostic tests at ≥ 72 hours after cardiac arrest, the presence of status myoclonus during the first 72hours after cardiac arrest is a reasonable finding to help predict poor neurologic outcomes.[1] *(AHA Class 2b, LOE B-NR)* If status myoclonus is present, an EEG is recommended to determine if there is underlying ictal activity.[1] *(AHA Class 2b, LOE B-NR)*

EEG Findings
In comatose patients it may be reasonable to consider persistent burst suppression on EEG after in the absence of sedatives at ≥ 72 hours after cardiac arrest to predict a poor outcome.[1] *(AHA Class 2b, LOE B-NR)* Persistent status epilepticus ≥ 72 hours after cardiac arrest may be reasonable to predict poor outcome.[1] *(AHA Class 2b, LOE B-NR)* In patients who remain comatose after cardiac arrest the usefulness of rhythmic period discharges and of seizures for neuroprognostication is uncertain.[1]*(AHA Class 2b, LOE B-NR)* Results obtained from patients who recently received, or who are receiving a barbiturate, propofol, or sedative at the time of the EEG, should be interpreted with caution. These agents may impact EEG results and therefore may not be an accurate indicator of prognosis. The effects of drug induced alteration of EEG findings are variable and can depend on both medication and patient characteristics, such as medication elimination half-life and organ dysfunction.

Evoked Potentials
SSEPs are less affected by sedatives or temperature manipulation than the EEG or clinical examination. In patients who are comatose after resuscitation from cardiac arrest regardless of treatment with TTM, it is reasonable to consider bilateral absence of the N20 SSEP wave > 24 hours after cardiac arrest a predictor of poor outcome.[1] *(AHA Class 2a, LOE B-NR)*

Imaging Tests
In patients who are comatose after resuscitation, it may be reasonable to use the presence of a marked reduction of the gray-white ratio (GWR) on brain CT to predict poor outcome.[1] *(AHA Class 2b, LOE B-NR)* It may be reasonable to consider extensive restriction of diffusion on brain MRI at 2-7 days after cardiac arrest in combination with other established predictors to predict a poor neurologic outcome.[1] *(AHA Class 2b, LOE B-NR)* It may be reasonable to consider extensive areas of reduced apparent diffusion coefficient (ADC) on brain MRI at 2-7 days after cardiac arrest to predict poor outcome.[1] *(AHA Class 2b, LOE B-NR)*

Blood Markers
When performed with other prognostic tests, it may be reasonable to consider high serum values of neuron-specific enolase (NSE) within 72 hours after cardiac arrest to support the prognosis of poor neurological outcome.[1] *(AHA Class 2b, LOE B-NR)* The neuroprognostic usefulness of other serum biomarkers including S100 calcium-binding protein (S100B), Tau, neurofilament light chain, and glial fibrillary acidic protein is uncertain.[1] *(AHA Class 2b, LOE C-LD*)

7. Organ Donation

Despite maximal support and adequate observation, some patients will be brain-dead after cardiac arrest. Studies suggest that there is no difference in functional outcomes of organs transplanted from patients who are brain-dead as a consequence of cardiac arrest when compared with donors who are brain-dead due to other causes. Adult patients who progress to brain death after resuscitation from cardiac arrest should be evaluated for organ donation.[2,4] *(AHA Class IIb, LOE B-NR)* For specific procedures (including contact information for the UW Organ and Tissue Donation team) refer to Policy 1.2.14.

Patients who do not have ROSC after resuscitation efforts or who would otherwise have termination of efforts may be considered candidates for kidney or liver donation in settings where programs exist.[4] *(AHA Class IIb, LOE B-NR)*

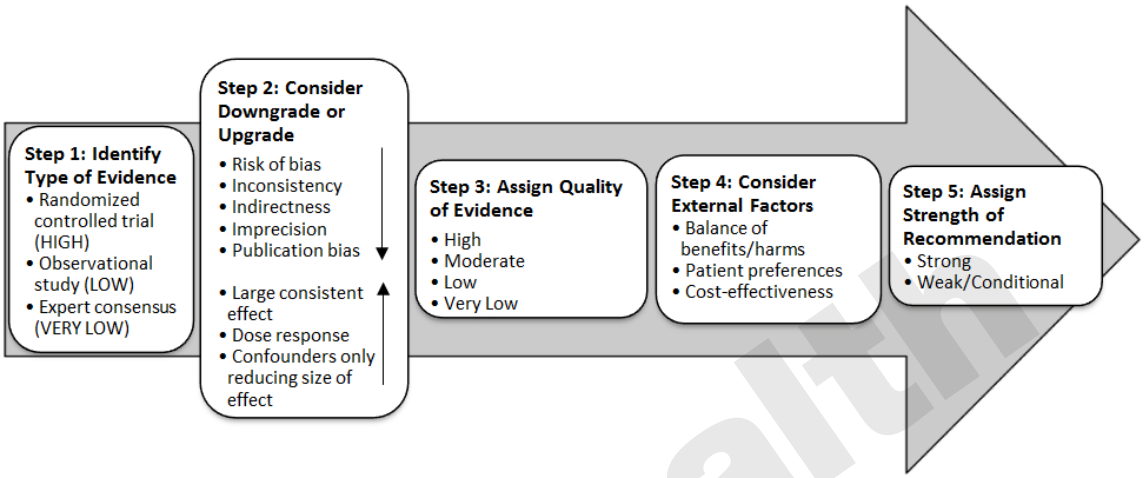
Table 1. Post-Cardiac Arrest Syndrome: Pathophysiology, Clinical Manifestations, and Potential Treatments

Syndrome	Pathophysiology	Clinical Manifestation	Potential Treatments
Post–cardiac arrest brain injury	• Impaired cerebrovascular autoregulation • Cerebral edema (limited) • Postischemic neurodegeneration	• Coma •Seizures • Myoclonus • Cognitive dysfunction • Persistent vegetative state • Secondary parkinsonism • Cortical stroke • Brain death	• Therapeutic hypothermia • Early hemodynamic optimization • Airway protection and mechanical ventilation • Seizure control • Controlled reoxygenation (SaO_2 94%–96%) • Supportive care
Post–cardiac arrest myocardial dysfunction	• Global hypokinesis (myocardial stunning) • ACS	• Reduced cardiac output • Hypotension • Dysrhythmias • Cardiovascular collapse	• Early revascularization of AMI • Early hemodynamic optimization • Intravenous fluid • Inotropes • IABP • LVAD • ECMO
Systemic ischemia/reperfusion response	• Systemic inflammatory response syndrome • Impaired vasoregulation • Increased coagulation • Adrenal suppression • Impaired tissue oxygen delivery and utilization • Impaired resistance to infection	• Ongoing tissue hypoxia/ischemia • Hypotension • Cardiovascular collapse • Pyrexia (fever) • Hyperglycemia • Multi-organ failure • Infection	• Early hemodynamic optimization • IV fluid • Vasopressors • High-volume hemofiltration • Temperature control • Glucose control • Antibiotics for documented infection
Persistent precipitating pathology	• Cardiovascular disease (AMI/ACS, cardiomyopathy) • Pulmonary disease (COPD, asthma) • CNS disease (CVA) • Thromboembolic disease (PE) • Toxicological (overdose, poisoning) • Infection (sepsis, pneumonia) • Hypovolemia (hemorrhage, dehydration)	• Specific to cause but complicated by concomitant PCAS	• Disease-specific interventions guided by patient condition and concomitant PCAS

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; IV, intravenous; LVAD, left ventricular assist device; PCAS, post–cardiac arrest syndrome; and PE, pulmonary embolism.

Disclaimer
Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Figure 1. GRADE Methodology adapted by UW Health



Rating Scheme for the Strength of the Evidence/Recommendations:

GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

Conflicts of Interest

A conflict of interest declaration must be signed/submitted by guideline workgroup and/or committee members to ensure balance, independence, objectivity, and scientific rigor in activities pertaining to the guideline development process. Guideline members must complete a conflict of interest statement annually or as new interest(s) arises. Potential, current and

planned future, conflicts of interest will be identified and managed in accordance with institutional policies and procedures. This may include, but is not limited to, conflict disclosure, abstaining from voting, dismissal during comment and voting period, or recusal from requesting and/or participation in the decision-making process.

Collateral Tools & Resources

Companion Documents

1. Post –Cardiac Arrest Therapeutic Targeted Temperature Management (TTM) Care Algorithm
2. Post Cardiac Arrest Syndrome: Pathophysiology, Clinical Manifestations, and Potential Treatments
3. Continuous Infusion Neuromuscular Blocking Agents (NMBAs) – Adult – Inpatient Guideline
4. Assessment and Treatment of Pain, Agitation, and Delirium in the Mechanically Ventilated Intensive Care Unit Patient Guideline
5. Venous Thromboembolism Prophylaxis – Adult – Inpatient/Ambulatory Guideline
6. Vasoactive Continuous Infusions in Adult Patients – Adult – Inpatient Guideline

Metrics

1. Evaluation of overall patient survival rate
2. Retrospective assessment of whether goal core temperature was achieved within 6 hours following initiation of TTM
3. Number of patients targeted core temperatures of 33°C vs. 36°C
4. Average length of inpatient hospitalization
5. Percent of patients receiving TTM and post arrest care with significant neurologic recovery
6. What % of patients remained at goal temperature for duration of therapy?
7. What % of patients achieved fever prophylaxis? What were temps 24-48 hours post TTM?
8. Method of cooling (IV vs. surface)?

Order Sets & Smart Sets

1. IP – Targeted Temperature Management – Adult – Intensive Care – Admission [701]
2. IP – Comprehensive Donation After Cardiac Death (DCD) – Adult – Intensive Care – Supplemental [3627]

Patient Resources

1. Health Facts For You #6583 What to Expect after Cardiac Arrest
2. Health Facts For You #5784- Organ Donation
3. Health Information- Cardiac Arrest

Policies

1. Nursing Departmental Policy #1.42AP, Intravascular Cooling Catheter System – Thermogard XP (Adult & Pediatric)
1. UW Health Clinical Policy #2.1.2, Admission and Discharge of Patients to and from the Cardiac Intensive Care Unit UW Health Clinical Policy #1.2.14, Organ and Tissue Donation

Protocols

Wisconsin Insulin Infusion (HIGH DOSE) - Adult- Practice Protocol (ICU ONLY)

Reporting Workbench Reports

Targeted Temperature Management (TTM) Patients [190376]

Appendix A. Evidence Grading Schemes

Figure 2. 2015 AHA Grading Scheme

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — Benefit = Risk
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCTs
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

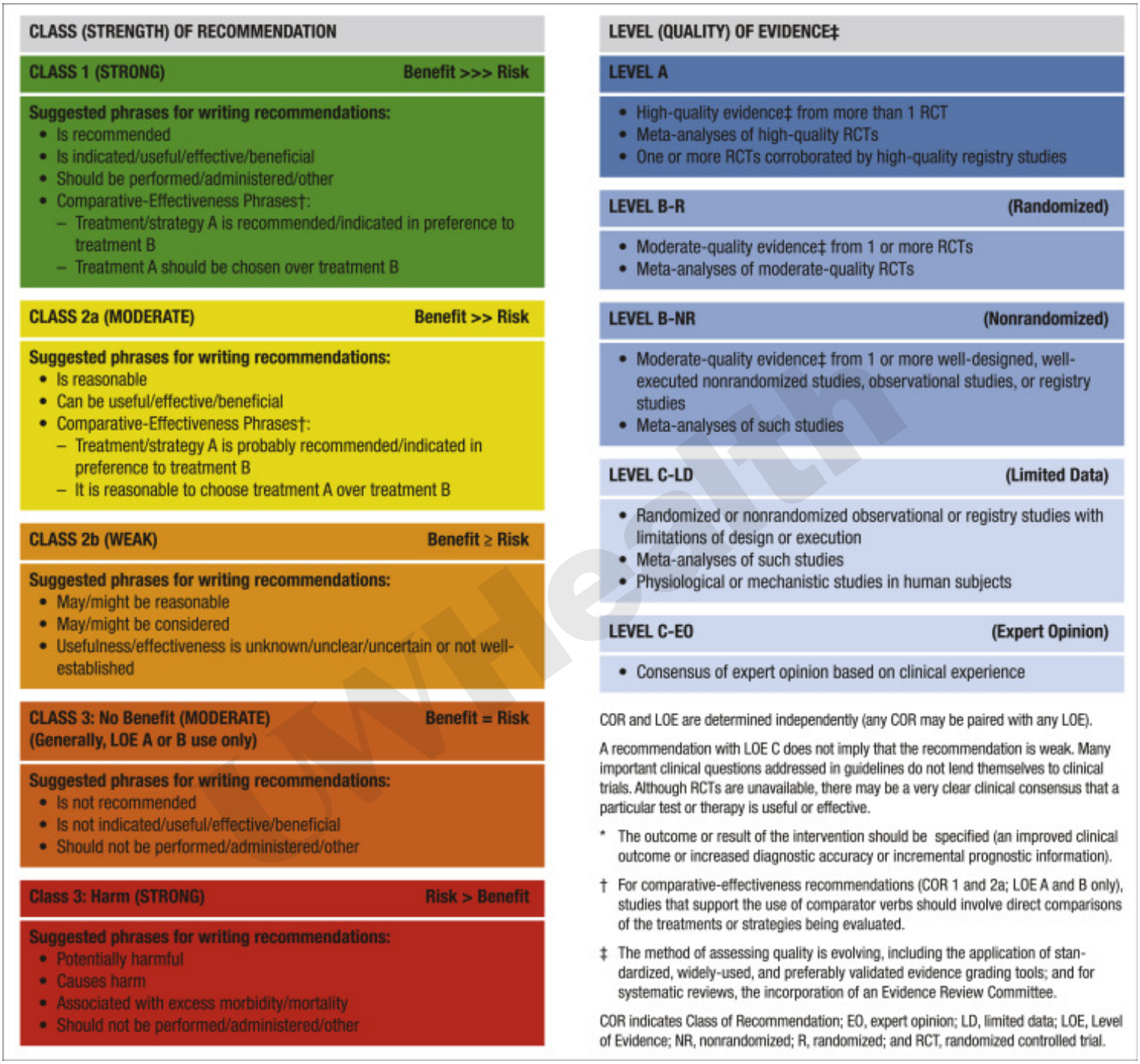
* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Figure 3. 2020 AHA Grading Scheme



CLASS (STRENGTH) OF RECOMMENDATION

CLASS 1 (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS 2a (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS 2b (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well-established

CLASS 3: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

Class 3: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
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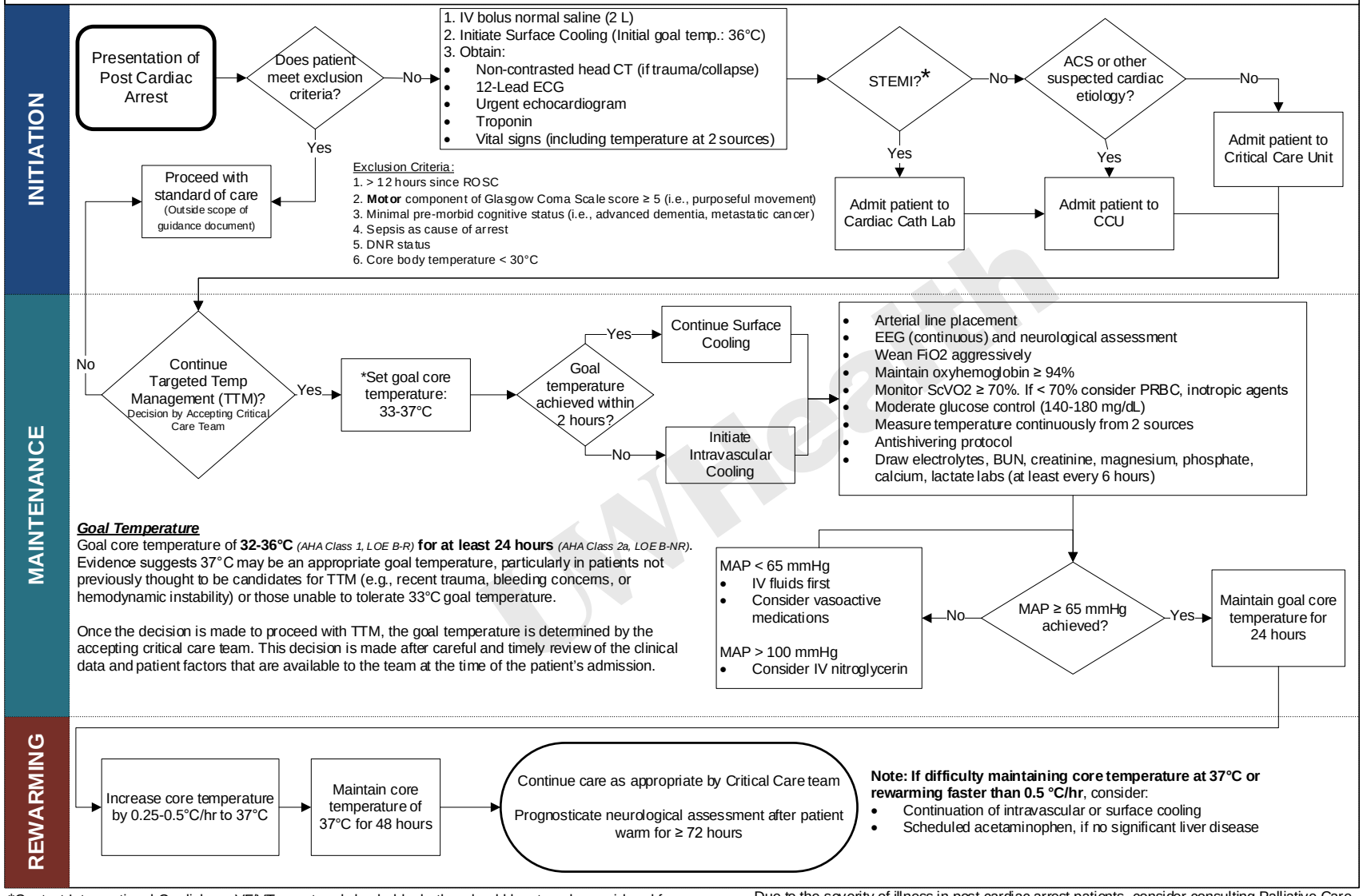
COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Appendix B. TTM Cooling Products

UW Health Targeted Temperature Management (TTM) Cooling Products			
Note: No single cooling method has proven to be optimal[38,49] and no formal comparative cost analyses have been completed.			
Method	**Equipment Type & Name**		**Obtain From:**
Intravascular Cooling	Thermogard machine by Zoll (formerly Coolgard)		TLC, F4M5, F8/4 Sign equipment out from home unit
	Intravascular Catheter	Quattro (4 balloon heat exchange catheter)- 9.3 Fr, 45 cm	Central Services "Catheter femoral (Coolgard) trpl lumen" Item # 1004968 Note: Some units may stock this item on unit
	Tubing		Central Services "Kit start-up Coolgard machine" Item# 1004957 Note: Some units may stock this item on unit
Surface Temperature Regulation*	Hyper/Hypothermia machines by Gaymar (bought by Stryker)		Central Services "Hyper/hypothermia machine"
	Cooling Wraps		Central Services "Vest hyper/hypothermia large 46"- 54" chest" Item# 1004749 "Vest hyper/hypothermia sm/med 32"- 46" chest" Item# 1005340 "Wrap leg hyper/hypothermia" Item# 1005342 Note: Some units may stock this item on unit
	Cooling Blanket		Central Services "Blanket hyper/hypothermia 25" x 64"" Item# 1004749 Note: Some units may stock this item on unit

Appendix C. Post Cardiac Arrest Algorithm

Post Cardiac Arrest Algorithm- Adult – Emergency Dept/Inpatient



*Contact Interventional Cardiology. VF/VT arrest and shockable rhythm should be strongly considered for emergent coronary angiography.

Due to the severity of illness in post cardiac arrest patients, consider consulting Palliative Care.
If patient is pregnant, consult Obstertrics.

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