INDUCED HYPOTHERMIA FOR NEUROLOGIC INJURY FOLLOWING CARDIAC ARREST

GOAL:
To improve mortality and neurologic outcomes after cardiac arrest.

INITIATIVE SUMMARY AND RATIONALE:
Following cardiac arrest or episodes of prolonged severe hypotension or hypoxia, patients may show evidence of neurologic injury. This may be manifested as abnormal posturing in response to stimuli, seizure activity, unresponsiveness, or severe confusion/agitation. There continues to be an evolution of literature supporting the use of moderate hypothermia to decrease mortality and to improve neurologic outcome following arrest. The Surgical ICU is a frequent recipient of post-surgical patients who suffer cardiac arrest, whether from cardiac, post-hypoxic, or other etiologies. We thus must be prepared to initiate rapid, aggressive treatment of appropriate candidates with return of spontaneous circulation (ROSC) after cardiac arrest.

KEYS TO SUCCESS:
- Appropriate patient selection
- Immediate initial management for cardiac etiology with early disposition for cardiac patients requiring catheterization
- Prompt initiation of the hypothermia protocol
- Careful attention to physiologic changes
- Rewarming slowly by protocol

Exclusion criteria:
- Awakes spontaneously with purposeful movement
- Known pregnancy
- Initial temperature less than 93.2°F (34°C)
- New focal neurologic deficits with indications of stroke
- Other causes of coma (drug intoxication, pre-existing coma prior to arrest)
- Patients with known bleeding diathesis or ongoing bleeding
- Persistent hypotension despite volume resuscitation and vasopressor therapy.
- DNR status
**Inclusion criteria:**

- Ability to initiate protocol within **6-12 hours** of ROSC after a cardiac arrest
- Unresponsive patient not following commands after ROSC
  - r/o hypoglycemia
  - r/o intoxication/overdose
  - Brainstem reflexes (i.e. cough, gag, corneal) - pathological/posturing movements are permissible
- Estimated time from arrest to ROSC less than **60 minutes**
- Attending physician or chief of service must be notified and agree with initiation of therapy.

**STANDARD OPERATING PROCEDURE:**

**ECG:**

- **STEMI**
  - STEMI on ICE alert (call 1-1111)
  - If cath lab available, straight to cath lab
  - If any delay, initiate initial STEMI management and hypothermia protocol

- **Other**
  - Investigate alternate cause of arrest
  - Stat Cardiology consultation for evaluation if suspicion of cardiac etiology

*SEE PROTOCOL FOR WORKUP OF ETIOLOGY OF ARREST*

**SICU Induced Hypothermia Protocol**

**Initial work-up of etiology**

- Acute resuscitation including limited physical/neurologic exam, full vent support (PaCO2 40, sats> 95%), fluid administration, appropriate hemodynamic monitoring, arterial line, pressors as needed.
- Send full set of labs including at minimum CBC, CMP, ABG, lactate, ionized calcium, phosphorus, magnesium, PT, PTT, cardiac enzymes.
- Stat CXR and EKG.
- Review of Rapid Response record, code team events, current hemodynamics to classify most likely source (cardiogenic, distributive, obstructive, hypovolemic, respiratory or a combination of etiologies).
- Chart and flow sheet review (PMH, any intraoperative or postoperative issues, trends in vitals signs, recent labs results, recent medication administration).
- Cardiology consult for transthoracic or transesophageal echocardiogram and cardiac catheterization if indicated, serial cardiac enzymes.

**Once stable pressor/inotropic support AND negative coronary ischemia work-up:**
- Continue serial lab draws and hemodynamic measurements.
- CT scan of head, chest, abdomen/pelvis. Contrast at the discretion of physician if high likelihood of pulmonary embolus or abscess and if benefit outweighs risk of further kidney insult. **Renal protection must be utilized, and patient must remain on hypothermia protocol during scan.**
- Surveillance blood and urine cultures to be drawn, bronchoscopy with bronchoalveolar lavage to be performed per protocol. **If any suspicion of sepsis, initiate broad spectrum antibiotics with de-escalation pending culture results.**
- 4-extremity Doppler ultrasound may be ordered if high suspicion of pulmonary emboli and the risks of transport and/or contrast nephropathy associated with spiral CT are significant.
- EEG if seizure activity suspected or if patient remains comatose 24-48 hours after rewarming and discontinuation of sedation. The role of continuous EEG has yet to be elucidated.
- MRI imaging is appropriate if comatose > 48 hours after rewarming and discontinuation of sedation.

**HYPOTHERMIA PROTOCOL:**

A. **Temperature monitoring**
1. Place an esophageal temperature probe or rectal temperature probe if unable to place esophageal.
2. When a Foley catheter is inserted, use a temperature-sensing catheter if available.
3. If a Pulmonary Artery (PA) catheter is in place, also record temperature via the PA port.
4. Avoid axillary, tympanic, and oral temperature measurement.

B. **Methods of cooling**
1. **External cooling with ice packs**
   1. Place ice packs (groin, axilla, side of neck, head) ensuring protection of skin by wrapping ice packs in towels or gown.
   2. Assess ice pack location and skin site frequently.
2. **Cooling with IV saline**
• Infuse room temperature normal saline IV 30 mL/kg (maximum of 2L) or chilled (4 degrees C) over 30 minutes. May acquire chilled NS from Pharmacy. **Chilled NS to be given by peripheral IV only.**

• Do not give normal saline infusion if starting temperature less than 35 degrees C.

3. **External Cooling with Arctic Sun pads**
   1. Application of Arctic Sun device per protocol and training.
   2. In general, **target temperature should be 32-34°C for 24 hours from the time of the initial cardiac arrest.**

C. **Decision on which cooling method to use**
   1. On arrival to SICU, initiate cooling with ice packs (B.1) and saline (B.2) while preparing for Arctic Sun use. **Place temperature probe (A).**
   2. For direct transfer to cath lab:
      1. Continue ice packs and saline, if initiated
      2. Place temperature probe
      3. Apply Arctic Sun device
   3. For direct transfer to CVICU:
      1. Apply Arctic Sun device
      2. Place temperature probe
      3. Consider ice packs and saline if not hypothermic on arrival

D. **Prevent shivering**
   1. **Sedation**
      • Place a BIS monitor if available.
      • **Propofol 10-50 mcg/kg/min, start at 20mcg/kg/min** (Remember Propofol metabolism decreased 30% during hypothermia)
      • **Fentanyl 100 mcg IV x1, then infuse drip at 100 mcg/hr,** titrate to BIS 40-60. Fentanyl 100 mcg IV q5 min PRN.

Alternatives to Propofol:
   • Midazolam 2 mg IV q5 minutes until unresponsive to painful stimulation and for BIS 40-60.
   • Midazolam 2 mg IV bolus q5 min PRN.
   • Dexmedetomidine 0.3-1.5 mcg/kg/min.

*Propofol, benzodiazepines, meperidine, Dexmedetomidine all shown to decrease shivering threshold*
2. **Skin counter-warming** to face, palms, and feet. Air warming blanket may be used to upper extremities. (For each 4 degree C skin increase, will decrease shivering threshold by 1 degree)

3. **Acetaminophen 650mg PR/PO Q6h prn** unless contraindicated (i.e. hepatic dysfunction or recent low rectal anastomosis)

4. **Magnesium 4gm/100ml sterile water IV x1 at 25 ml/hr**
   followed immediately by magnesium 2gm/50ml sterile water IV x1 at 25 ml/hr (total dose Mag 6 gm)
   *6 hr after target temp, draw magnesium level. Magnesium is <3mg/dl, give magnesium 4 gm/100ml IV x1 at 25 ml/hr.

5. **Buspirone 15 mg Q12h PO/NGT x 48h**
   *CONTRAINDICATIONS:*
   - MAO inhibitor within past 2 wks
   - concomitant verapamil or diltiazem

5. **Meperidine 25 mg IV Q2 hour prn for shivering**
   Meperidine (Demerol) 12.5 mg IV Q2 hours prn shivering (if CrCl less than 30 ml/min)

   *Buspirone and meperidine synergistic to prevent shivering*

6. **Neuromuscular blockade**
   - **Cisatracurium (Nimbex) 0.2 mg/kg bolus. Repeat Cisatracurium 0.03 mg/kg in 40 minutes if needed.**
     Infusion at 1-5 mcg/kg/min, titrate to Train of Four 2:4 or to suppress shivering. Particularly appropriate if significant hepatic or renal dysfunction.
   
   - **Alternative:** Vecuronium 0.1 mg/kg IV bolus. Repeat vecuronium 0.1 mg/kg IV bolus in one hour (may be earlier if patient demonstrating evidence of inadequate paralytic effect).

E. **Cardiovascular/Hemodynamic considerations**

1. Sinus bradycardia is the anticipated rhythm; unnecessary to treat unless clinical sequelae are present. If treatment is necessary, consider increasing target temperature or temporary pacing.

2. ECG may show Osbourne waves and/or QT-prolongation; these do not require specific treatment.

3. Ventricular fibrillation caused by hypothermia is rare at 32-34°C.

4. Mean arterial pressure target is 80-90 mmHg to maintain adequate cerebral perfusion pressure; vasopressors may be used as appropriate to hemodynamic monitoring.

5. For hypertension, consider nitroglycerin or nicardipine infusion.
6. Consider central access, arterial line placement, and PA catheter placement for management. (May have increased arrhythmias with CVL or PA catheterization)
7. Consider TransEsophageal Echocardiography (TEE) or Imacor guidance of volume and vasopressor/inotropic management.
8. Avoid hypovolemia as hypothermia can induce diuresis.

F. Metabolic considerations
1. Oxygen consumption decreases by ~8% per °C fall in temperature
   - Renal metabolism affected most up to 32°C
2. Anticipate hypokalemia during hypothermia; not necessary to treat unless level is below 2.8 mEq/L or arrhythmias are present. Intracellular shifts will reverse with rewarming and must anticipate possible hyperkalemia.
3. Hyperglycemia is common during hypothermia due to decreased insulin release; liver glycogen stores may also be reduced.
   1. Blood glucose monitoring to be done via arterial line. Vasoconstriction may cause finger-stick accuchecks to be inaccurate.
   2. Recommend target glucose of 110-160 while hypothermic.
4. Target magnesium level is 2 mEq/L or greater; if level is below target, give magnesium sulfate 4 grams IV and check levels q8 hours until normothermic. Hypomagnesemia may increase shivering.
5. Hypophosphatemia due to increased renal excretion
   - May increase infection risk, reduce ability to wean from mechanical ventilation

G. Acid-Base Disturbances
1. Hypothermia shifts the oxyhemoglobin dissociation curve to the left, resulting in oxygen saturation at a lower oxygen partial pressure; this results in less tissue oxygen extraction
2. CO₂ production is decreased, leading to an initial respiratory alkalosis during cooling - may cause cerebral vasoconstriction and decreased cerebral perfusion pressure
3. Lactic acidosis can occur during mild hypothermia, due to increased fat metabolism.
4. Knowledge about the normal partial pressures of gases at varying temperatures is limited
   1. In hypothermia, PO₂ and PCO₂ are overestimated, pH is underestimated
   2. To correct, subtract 5mm Hg PO₂ and 2mm Hg PCO₂ and add 0.012 pH units for each °C below 37°
   3. General consensus is not to correct ABG for temperature (alpha stat method)
4. Thus, to avoid respiratory alkalosis, target PCO2 should be 45-50 and pH 7.35

H. Neurological considerations
1. Electroencephalography (EEG) – consider use due to increased risk of seizure during hypothermia.
2. **BIS and TOF monitors** are recommended to target sedation.
3. **Draw serum Neuron-Specific Enolase (NSE) at 24 and 48 hours after arrest.** (less specific for neurologic prognostication in patients with recent spinal surgery, traumatic brain injury, or hemorrhagic shock)

I. Other considerations
1. Hypothermia impairs leukocyte function, resulting in increased risk of infection.
2. Hypothermia impairs platelet function, resulting in increased risk of bleeding; recent surgery is a *relative* contraindication to therapeutic hypothermia.
3. Anticipate ileus during hypothermia – assess and document bowel sounds every 2-4 hours – consider nasogastric tube placement and intravenous nutrition (TPN and Lipids) as needed.
4. Keep NPO except for medications per feeding tube during hypothermia and rewarming process.
5. Avoid medications labeled “do not refrigerate,” including mannitol, which may precipitate if cooled

J. Rewarming Phase
1. **Rewarm slowly, increasing temperature 0.25°C per hour**, beginning 24 hours after hypothermia initiated.
2. Leave Arctic Sun pads on for a minimum of 12 hours after normothermia is achieved. If temperature is labile, continue to use Arctic Sun to maintain normothermia.
3. **Anticipate hypotension** during rewarming phase secondary to vasodilatation.
4. **Anticipate a rise in potassium levels**, a drop in glucose levels, and a decrease in arterial pressure during rewarming.
5. Neuromuscular blockade may be discontinued when patient temperature reaches 36 ºC.

K. Patient/Family Education
1. Educate patient/family at the level of their understanding of the following:
   a. Indications and rationale for induced hypothermia
   b. Indications and rationale for sedation and paralytics
c. Effects of induced hypothermia on body systems and measures implemented to support or protect body
   system

d. Length of time patient will be cooled

e. Risks associated with rewarming and steps taken to support patient during rewarming

2. Consult the Palliative Care Service, regardless of the expected outcome

References:


5. Marjaana Tiainen, MD; Risto O. Roine, MD, PhD; Ville Pettitä, MD, PhD Olli Takkunen, MD, PhD. Serum Neuron-Specific Enolase and S-100B Protein in Cardiac Arrest Patients Treated With Hypothermia. Stroke. 2003;34:2881-288.