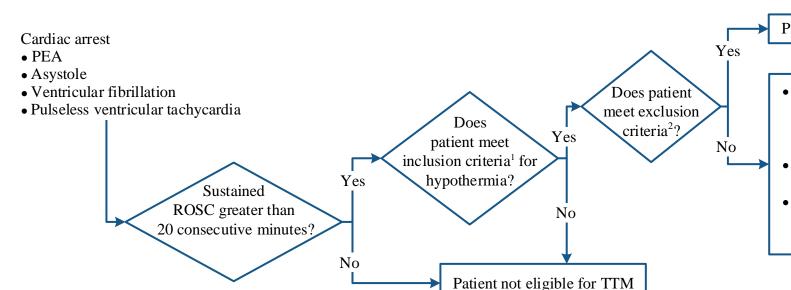


Page 1 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

Note: TTM should not delay imaging studies, renal replacement therapy or re-perfusion therapy

PATIENT PRESENTATION



PEA = pulseless electrical activity ROSC = return of spontaneous circulation

¹Inclusion criteria:

- Down time < 60 minutes (< 15 minutes for asystole)
- Intubated requiring mechanical ventilation
- No meaningful response to verbal stimuli (Glascow Coma Scale < 9, see Appendix A)
- ≤ 12 hours from ROSC

²Exclusion criteria:

- Major traumatic injury or isolated head injury
- Major operative procedure within 72 hours
- Pregnancy • Uncontrolled arrhythmias
- Age < 18 years
- Uncontrolled bleeding • Hypothermia – temperature < 30°C
- Hypoxemia oxygen saturation < 88% on 100% FiO2 for > 30 minutes • Mean arterial pressure (MAP) < 70 mmHg despite aggressive fluid resuscitation and vasopressor support
- Poor prognosis as discussed with primary team

³ If temperature < 36°C, no cooling required. If temperature > 36°C within 24 hours, ICU team to initiate TTM order set.

COOLING Patient not eligible for TTM See Page 2 for re-warming phase • Initiate Post Cardiac Arrest TTM order set³ with target Yes Development temperature of 36°C • See Page 3 for complications⁴? TTM protocol No • Initiate shivering management (see Page 4) Yes Continue TTM Continue shivering management (see Page 4) No Target temperature maintained for 24 hours?

> Department of Clinical Effectiveness V4 Approved by the Executive Committee of the Medical Staff on 06/16/2020

⁴See Appendix B for Complications

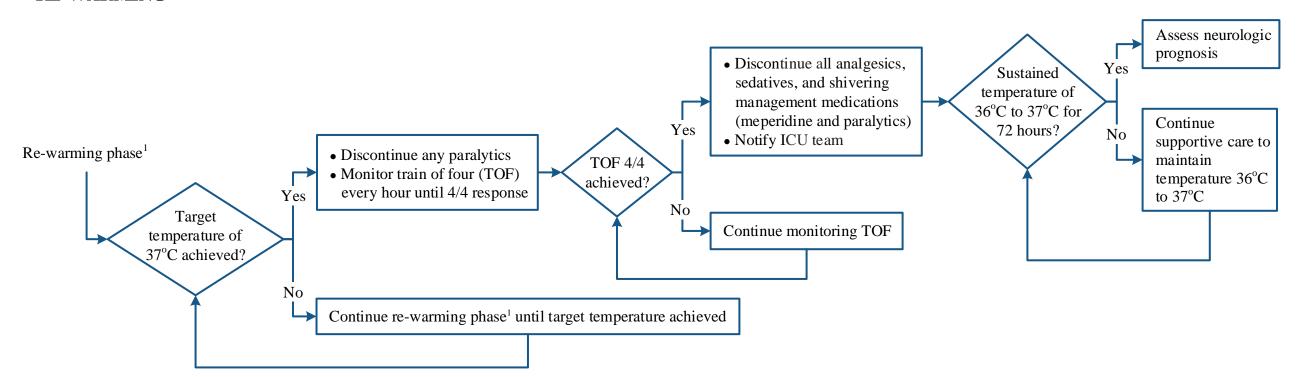


Page 2 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

RE-WARMING

NORMOTHERMIA¹



¹ See Page 3 for TTM Protocol



Page 3 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

TTM Protocol (TTM should not delay imaging studies, continuous renal replacement, or re-perfusion therapy)

Supportive Care	Cooling Phase ⁴	Maintenance Phase	Re-Warming Phase	Normothermia Phase
Consultation:	 ◆ Cool to 36°C (goal to target 	Basic metabolic panel,	Begin re-warming 24 hours after	• Once temperature is 37°C:
o Neuro-oncology	temperature < 4 hours)	magnesium, phosphorous,	target temperature achieved –	 Discontinue any paralytics
∘ Cardiology	 Record time of initiation of TTM 	ionized calcium, CBC with	0.20°C/hour for a target	 Monitor TOF every hour until
Baseline labs and imaging	and time of achieving 36°C	differential, PT/PTT every	temperature of 37°C	4/4 response
Nursing assessment:	 Keep room as cool as possible 	6 hours	Maintain target temperature of	• Once TOF is 4/4:
 Pupil checks every 1 hour 	 Magnesium sulfate 32 mEq IV for 		36°C to 37°C	 Discontinue all sedatives,
∘ BPS¹ per TTM order set	one dose over 1 hour		• Call ICU team for temperature > 37°C	shivering management
∘ BSAS² per TTM order set	Respiratory therapy:		Warm room to normal temperature	medications, and analgesics
∘ RASS³ per TTM order set	 No spontaneous breathing trials 		Respiratory therapy:	Notify ICU team
 Skin assessment every hour 	• Shivering management (see Page 4)		 No spontaneous breathing trials 	
• Placement of:	 Notify ICU team for development 			
 Nasogastric <u>or</u> 	of complications (see Appendix B)			
o Orogastric tube				
 Placement of cooling blanket 				
• Placement of foley temperature probe				
○ If foley temperature probe				
contraindicated, physician to place				
esophageal temperature probe				
Daily 30 minute EEG				
 May convert to continuous EEG if 				
seizures identified				

¹See Appendix C Behavioral Pain Score (BPS)

² See Appendix D Bedside Shivering Assessment Scale (BSAS)

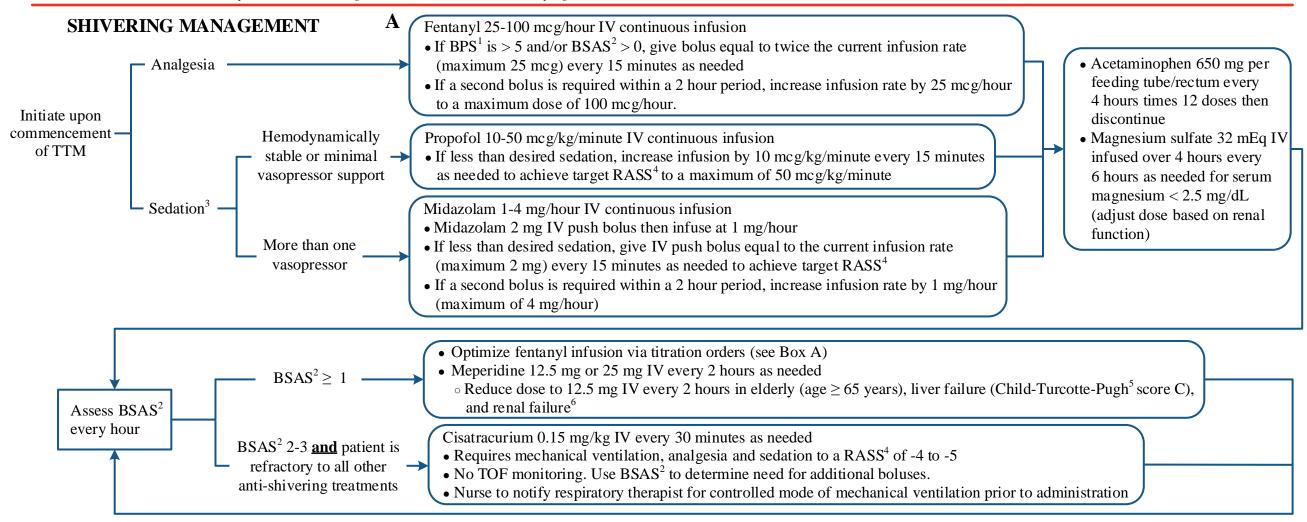
³ See Appendix E Richmond Agitation-Sedation Scale (RASS)

⁴ If temperature < 36°C, no cooling required. If temperature > 36°C within 24 hours, ICU team to initiate TTM order set.



Page 4 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.



See Appendix C Behavioral Pain Score (BPS)

²See Appendix D Bedside Shivering Assessment Scale (BSAS)

³ Sedation

[•] Propofol recommended as agent of choice due to more predictable clearance

[•] Use midazolam only if patient requires use of more than one vasopressor with at least one infusing at a maximum rate

[•] Midazolam clearance decreases by 11% for every degree drop in temperature less than 36.5°C

⁴ See Appendix E Richmond Agitation-Sedation Scale (RASS)

⁵ See Appendix F Child-Turcotte-Pugh (CTP) Scale

⁶ Serum creatinine > 1.5 mg/dL, serum creatinine change > 0.5 mg/dL from baseline, creatinine clearance < 50 mL/minute, and/or urine output < 500 mL in previous 24 hours



Page 5 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

APPENDIX A: Glasgow Coma Scale (GCS)¹

Item	Description	Score
	Spontaneous	4
Eye Opening Response	To verbal stimuli, command, speech	3
J. I. B. M.	To pain only (not applied to face)	2
	No response	1
	Oriented	5
W 1 1D	Confused conversation, but able to answer questions	4
Verbal Response	Inappropriate words	3
	Incomprehensible speech	2
	No response	1
	Obeys commands for movement	6
	Purposeful movement to painful stimulus	5
Motor Response	Withdraws in response to pain	4
TF.	Flexion in response to pain	3
	Extension in response to pain	2
	No response	1

¹GCS is obtained by adding the total score for each parameter

[•] Score < 9 = coma (no eye opening, no ability to follow commands, no word verbalizations)

Page 6 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

APPENDIX B: Complications

- MAP < 70 mmHg despite aggressive fluid resuscitation and vasopressor support
- Uncontrolled arrhythmias
- Hypoxemia oxygen saturation < 88% on 100% FiO2 for > 30 minutes
- Uncontrolled bleeding

APPENDIX C: Behavioral Pain Score (BPS)¹

Item	Description	Score
	Relaxed	1
Facial Expression	Partially tightened (e.g. brow lowering)	2
1 worm 2.1p.0001011	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
	No movement	1
TT T' 1	Partially bent	2
Upper Limbs	Fully bent with finger flexion	3
	Permanently retracted	4
	Tolerating movement	1
Compliance with Ventilation	Coughing but tolerating ventilator most of time	2
r	Fighting ventilator	3
	Unable to control ventilator	4

¹BPS is obtained by adding the total score for each parameter

[•] Target: BPS ≤ 5

[•] Score $\leq 3 = \text{no pain}$

[•] Score of 12 = maximum pain

[•] Document BPS per TTM order set



Page 7 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

APPENDIX D: Bedside Shivering Assessment Scale (BSAS)¹

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 the neck and thorax)

3 Severe: Shivering involves gross movements of the trunk and

upper and lower extremities

• Target: BSAS = 0

• Document BSAS every 1 hour during TTM

APPENDIX E: Richmond Agitation-Sedation Scale (RASS)²

4 Combative:	Overtly combative, violent, danger	-1 Drowsy:	Awakens to voice with eye contact for more
	to staff		than 10 seconds
3 Very agitated:	Pulls/removes tube(s) or catheter(s);	-2 Light Sedation:	Awakens to voice with eye contact for less
	aggressive		than 10 seconds
2 Agitated:	Frequent non-purposeful movement,	-3 Moderate Sedation:	Any movement (no eye contact to voice)
	fights ventilator	-4 Deep Sedation:	No response to voice, or any movement to
1 Restless:	Anxious but movements not	•	physical stimulation
	aggressive or vigorous	-5 Unarousable:	No response to voice or physical stimulation
0 Alert and calm			F-5

² RASS:

• Target: RASS -4 to -5

• Document RASS per TTM order set

¹ BSAS:



Page 8 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

APPENDIX F: Child-Turcotte-Pugh (CTP) Scoring System¹

Chemical and Biochemical Parameters	Scores (Points) for Increasing Abnormality		
	1	2	3
Hepatic encephalopathy	None	Grade 1 or 2, or suppressed with medication	Grade 3 or 4, or refractory to medication
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Serum albumin	> 3.5 g/dL	2.8 – 3.5 g/dL	< 2.8 g/dL
Total bilirubin For primary biliary cirrhosis	< 2 mg/dL < 4 mg/dL	2-3 mg/dL $4-10 mg/dL$	> 3 md/dL > 10 mg/dL
Prothrombin time prolonged or international normalized ratio	< 4 seconds < 1.7	4 – 6 seconds 1.7 – 2.3	> 6 seconds > 2.3

¹CTP score is obtained by adding the score for each parameter CTP class:

Class A = 5 to 6 points

Class B = 7 to 9 points

Class C = 10 to 15 points



Page 9 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS

- Badjatia, M., Strongilis, D., Gordon, A., Prescutti, A., Fernandez, A., Fernandez, A., . . . Mayer, A. (2008). Metabolic impact of shivering during therapeutic temperature modulation: The bedside shivering assessment scale. Stroke, 39(12), 3242-3247. https://doi.org/10.1161/STROKEAHA.108.523654
- Broessner, G., Fischer, M., Schubert, G., Metzler, B., & Schmutzhard, E. (2012). Update on therapeutic temperature management [Abstract]. Critical Care, 16(2), A1. http://ccforum.com/supplements/16/S2
- Crepeau, Z., Rabinstein, A., Fugate, E., Mandrekar, F., Wijdicks, D., White, W., & Britton, W. (2013). Continuous EEG in therapeutic hypothermia after cardiac arrest: Prognostic and clinical value. Neurology, 80(4), 339–344. https://doi.org/10.1212/WNL.0b013e31827f089d
- Hypothermia after Cardiac Arrest Study Group. (2002). Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. New England Journal of Medicine, 346(8), 549–556. https://doi.org/10.1056/NEJMoa012689
- McKean, S. (2009). Induced moderate hypothermia after cardiac arrest. AACN Advanced Critical Care, 20(4), 343-355. https://doi:10.4037/15597768-2009-4008
- Nielsen, N., Wetterslev, J., Cronberg, T., Erlinge, D., Gasche, Y., Hassager, C., ... Friberg, H. (2013). Target temperature management at 33°C versus 36°C after cardiac arrest. The New England Journal of Medicine, 369(23), 2197-2206. https://doi.org/10.1056/NEJMoa1310519
- Payen, J., Bru, O., Bosson, J., Lagrasta, A., Novel, E., Deschaux, I., . . . Jacquot, C. (2001). Assessing pain in critically ill sedated patients by using a behavioral pain scale. Critical Care Medicine, 29(12), 2258–2263. https://doi.org/10.1097/00003246-200112000-00004
- Polderman, H. (2009). Mechanisms of action, physiological effects, and complications of hypothermia. Critical Care Medicine, 37(7 Suppl), S186-S202. https://doi.org/10.1097/CCM.0b013e3181aa5241
- Pugh, R., Murray-Lyon, I., Dawson, J., Pietroni, M., & Williams, R. (1973). Transection of the oesophagus for bleeding oesophageal varices. *British Journal of Surgery*, 60(8), 646–649. https://doi.org/10.1002/bjs.1800600817
- Scirica, M. (2013). Therapeutic hypothermia after cardiac arrest. Circulation, 127(2), 244–250. https://doi.org/10.1161/CIRCULATIONAHA.111.076851
- Šunjić, M., Webb, C., Šunjić, L., Palà Creus, L., & Folse, L. (2015). Pharmacokinetic and other considerations for drug therapy during targeted temperature management. Critical Care Medicine, 43(10), 2228–2238. https://doi.org/10.1097/CCM.000000000001223
- U.S. Food & Drug Administration. (2003). Pharmacokinetics in patients with impaired hepatic function: Study design, data analysis, and impact on dosing and labeling. Retrieved from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pharmacokinetics-patients-impaired-hepatic-function-study-design-data-analysis-and-impact-dosing-and
- Weant, K., Martin, J., Humphries, R., & Cook, A. (2010). Pharmacologic options for reducing the shivering response to therapeutic hypothermia. *Pharmacotherapy: The Journal of Human* Pharmacology and Drug Therapy, 30(8), 830–841. https://doi.org/10.1592/phco.30.8.830



Page 10 of 10

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the TTM experts at the University of Texas MD Anderson Canær Center for the patient population. These experts included:

Reagan Collins, PharmD, BCCCP (Pharmacy Clinical Programs)^T Wendy Garcia, BS Rhea Herrington, MSN, RN-BC, CCRN-K (Nursing) Neetha Jawe, MSN, RN, CCRN, CNL (Nursing) Lorraine Layton, MSN, RN, CVCRN (Nursing) Tiffany Mundie, MSN, APRN, ACNP-BC, CCRN (Critical Care & Respiratory Care) Amy Pai, PharmD, BCPS Egbert Pravinkumar, MD, FRCP (Critical Care & Respiratory Care)[†] Anne Tucker, PharmD, BCNSP (Pharmacy Clinical Programs) Mary Lou Warren, DNP, APRN, CNS-CC

[†]Core Development Team

^{*}Clinical Effectiveness Development Team