
 Wake Forest™
Baptist Health

Therapeutic Mild Hypothermia in the Treatment of Post-Cardiac Arrest

Sanjay K Gandhi
Wake Forest School of Medicine
Section on Cardiology



Objectives

- Review the pathophysiology of brain injury in post-cardiac arrest patients.
- Review the role of mild hypothermia following cardiac arrest and the randomized trial data supporting its use.
- Discuss which patients should be considered for mild hypothermia and review the process of treatment.

Wake Forest Baptist Health

Case 1

- August 15, 2010
- 50 y/o male with no prior cardiac hx awoke with chest pain and diaphoresis.
- EMS was called. Prior to EMS arrival, the patient passed out and was unresponsive. The wife and neighbor initiated CPR.
- EMS arrival within 10 minutes. The patient was in ventricular fibrillation.
- The patient was successfully resuscitated and transferred to the WFBMC CCU.
- Treated with mild hypothermia(24 hours), mechanical ventilation, treatment for MI, and treatment for pneumonia.
- Subsequently was extubated with full neurologic recovery; Underwent PCI of the Left Circumflex artery. EP Study showed no inducible arrhythmias
- Discharged home on August 25th, 2010. February 1, 2010 – doing well

Wake Forest Baptist Health

Case 2

- August 16, 2010
- 76 y/o female with hypertension developed new onset chest pain and weakness. She became unresponsive. The family initiated CPR and called EMS.
- On EMS arrival (? 10 minutes), she was in ventricular fibrillation. She was successfully resuscitated. She was brought to WFBMC and admitted to the CCU.
- On arrival to the CCU, she had recurrent ventricular tachycardia requiring multiple defibrillations.
- Treated with mild hypothermia, mechanical ventilation, treatment for MI, and critical care support.
- Subsequently extubated with full neurologic recovery. Underwent cardiac catheterization on August 26, 2010 which revealed severe 3 vessel coronary disease and moderately reduced left ventricular function.
- Underwent 3 vessel coronary artery bypass surgery on September 3, 2010.
- Had nonsustained ventricular tachycardia post-op; Underwent ICD placement on September 16, 2010.
- Transferred to a rehabilitation center on September 29, 2010; Discharged to home on October 19, 2010
- Required staged PCI of the Left Circumflex and Right coronary arteries in February, 2011
- Last seen for followup on March 22, 2011 – doing well.

Wake Forest Baptist Health

Case 3

- August 25, 2010
- 42 y/o male with CAD(prior PCI), hypertension, and dyslipidemia developed chest and left arm pain while doing yard work.
- His fiance drove him to the local hospital. He passed out in the parking lot.
- The Emergency Department staff were summoned. He was in pulseless ventricular tachycardia. He was resuscitated(defibrillation x 8; intubation).
- ECG showed acute inferior STEMI: given thrombolytic therapy and transferred to WFBMC CCU.
- On arrival to our CCU, he was in cardiogenic shock with recurrent ventricular fibrillation. He underwent emergency cardiac catheterization which revealed thrombosis of a previous LCx stent – underwent PCI
- Complex hospital course including cardiogenic shock, respiratory failure, and renal failure
- Treated with mild hypothermia, Impella left ventricular assist support, mechanical ventilation, and renal replacement therapy.
- Subsequently extubated with full neurologic recovery. Discharged to home with a Life Vest and plans for outpatient hemodialysis.
- Experienced full recovery of renal function. Dialysis was discontinued
- Underwent ICD placement on December 3, 2010
- Last clinic followup on January 28, 2011 – doing well.

Wake Forest Baptist Health

Out-of-Hospital Cardiac Arrests

- 350,000 to 450,000 annually in US
- Resuscitation attempted in 100,000
- 40,000 survive to make it to hospital admission
- One third of patients survive to hospital discharge

Wake Forest Baptist Health

Post-Cardiac Arrest Syndrome

- Cardiac dysfunction
- Respiratory failure
- Systemic ischemia(multi-organ failure)
- Brain injury

Wake Forest Baptist Health

Cardiac Arrest and Brain Injury

- Loss of oxygen stores
- Loss of glucose and ATP stores
- Loss of transmembrane electrochemical leads to failure in synaptic transmission, axonal conduction, and action potential firing
- Release of glutamate and consequent intracellular calcium acclumulation leading to excitotoxic brain death

Wake Forest Baptist Health

Cardiac Arrest and Brain Injury

- Restoration of circulation and reoxygenation can lead to reperfusion injury
- Alterations in the inflammatory response leads to further injury
- Hypotension, hypoxia, impaired cerebrovascular flow, and brain edema

Wake Forest Baptist Health

Targeted Temperature Management (Hypothermia): How does it work?

- Reduces brain metabolism – reduces oxygen utilization and ATP consumption
- Inhibits release of glutamate
- Reduces excitotoxic cell death
- Reduces inflammation

Wake Forest Baptist Health

Hypothermia: What's the data?

- Hypothermia After Cardiac Arrest Study Group
- Multicenter study in Europe(nine centers in 5 countries): randomized patients to treatment with mild hypothermia vs. standard treatment
- Patients, age 18-75, with witnessed cardiac arrest, v. fib or nonperfusing v. tach, an interval of no more than 60 minutes from collapse to restoration of spontaneous circulation
- Excluded for temp < 30 C, comatose prior to arrest, pregnancy, response to verbal commands, persistent hypotension, hypoxia, terminal illness, or preexisting coagulopathy

Wake Forest Baptist Health

Holzer et al, NEJM 2002:346:549-56

Hypothermia: What's the data?

- Hypothermia After Cardiac Arrest Study Group
- Randomized to standard therapy vs. mild hypothermia
- All patients sedated and paralyzed
- Hypothermia group randomized to cooling with external device: goal temp of 32-34 C within 4 hours(then add ice packs if necessary)
- Cool for 24 hour; Passive rewarming over 8 hours
- 3551 patients screened; 275 patients enrolled
- Neurologic assessment at 6 months in survivors (evaluated blinded to treatment)

Wake Forest Baptist Health

Holzer et al, NEJM 2002:346:549-56

Hypothermia: What's the data?

TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

Outcome*	HYPOTHERMIA	NORMOTHERMIA
	(N=43)	(N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

Good Outcome (normal or with minimal/moderate disability)

Hypothermia: 49%

Normothermia: 26%

P=0.046

After adjustment for age and time from collapse to return of spontaneous circulation: odds ratio 5.25(1.47-18.76 odds ratio); P=0.011

Wake Forest Baptist Health

Bernard et al, NEJM 2002;346:557-63

Mild Hypothermia for Post-Cardiac Arrest

- Critical care support
- Mechanical ventilation
- Hemodynamic support
- Treat MI
- Close electrolyte management
- Sedation +/- paralysis
- Prevent shivering

Wake Forest Baptist Health

Mild Hypothermia for Post-Cardiac Arrest

- Initiate cooling as soon as possible
- Probable window of benefit: within 8-10 hours post-arrest
- Multiple options for mode of cooling available
- Maintain mild hypothermia for up to 24 hours
- Slow rewarming: 0.3-0.5 C/hour to achieve normal temperature of 36.5-37.5

Wake Forest Baptist Health

Mild Hypothermia for Post-Cardiac Arrest: Potential Pitfalls

- Hypokalemia, hypomagnesemia, hypophosphatemia, or hyperglycemia
- Severe thrombocytopenia
- Coagulopathy
- Pancreatitis
- Seizures: ? EEG monitoring
- Arrhythmias
- Pneumonia

Wake Forest Baptist Health

Table 1. Indications and Contraindications for Targeted Temperature Management in Comatose Patients after Cardiac Arrest.

Patients for whom therapeutic hypothermia should be considered

Adult patients successfully resuscitated from a witnessed out-of-hospital cardiac arrest of presumed cardiac cause (patients after in-hospital cardiac arrest may also benefit)²⁸

Patients who are comatose (i.e., patients with a score on the Glasgow Coma Scale of less than 8 or patients who do not obey any verbal command at any time after restoration of spontaneous circulation and before initiation of cooling)

Patients with an initial rhythm of ventricular fibrillation or nonperfusing ventricular tachycardia (patients presenting with other initial rhythms such as asystole or pulseless electrical activity may also benefit)²⁸

Patients whose condition is hemodynamically stable (retrospective data suggest that patients in cardiogenic shock may also safely undergo hypothermia treatment)^{29,30}

Holzer. NEJM 2010;363:1256-64

Hypothermia: Exclusions

Patients for whom therapeutic hypothermia should not be considered

Patients with tympanic-membrane temperature below 30°C on admission

Patients who were comatose before the cardiac arrest

Pregnant patients

Patients who are terminally ill or for whom intensive care does not seem to be appropriate

Patients with inherited blood coagulation disorders

Wake Forest Baptist Health

Holzer. NEJM 2010;363:1256-64

2010 AHA Guidelines for Post-Cardiac Care

- Comatose adult patients with return of spontaneous circulation(ROSC) after out-of hospital VF cardiac arrest should be cooled to 32-34 C(89.6-93.2 F) for 12-24 hours(Class I indication)

- Consider mild hypothermia for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electrical activity or asystole(Class IIb)

Peberdy M, et al. Circulation. 2010;122[suppl 3]:S768-S786

Conclusions

- Neurologic injury is a significant determinant of outcome in comatose survivors of cardiac arrest.
- Therapeutic hypothermia improves clinical outcomes in patients surviving ventricular fibrillation or pulseless ventricular tachycardia.
- Therapeutic hypothermia should be considered in any patient surviving cardiac arrest; Therapy should be initiated as soon as possible.
- There is no current consensus regarding patients presenting initially with asystole or pulseless electrical activity.

Wake Forest Baptist Health

Question 1

When treating a post-cardiac arrest patient with mild hypothermia, the goal core temperature should be:

- A. 28-30 degrees Celcius
- B. 30-32 degrees Celcius
- C. 32-34 degrees Celcius
- D. 34-36 degrees Celcius

Wake Forest Baptist Health

Question 2

- Randomized trial data has shown that therapeutic mild hypothermia improves clinical outcomes in out-of-hospital cardiac arrest survivors who initially presented with:
 - A. Asystole
 - B. Ventricular fibrillation
 - C. Pulseless electrical activity
 - D. Atrial fibrillation

Wake Forest Baptist Health

Question 3

- Potential complications of therapeutic hypothermia include all of the following except:
- A. Hyperkalemia
 - B. Hypomagnesemia
 - C. Shivering
 - D. Hyperglycemia
 - E. Pancreatitis

Wake Forest Baptist Health
