

Induced Hypothermia After Cardiac Arrest in Trauma Patients: A Case Series

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Background: Induced hypothermia after cardiac arrest is an accepted neuroprotective strategy. However, its role in cardiac arrest during acute trauma care is not yet defined. To characterize recent experience with this technique at our center, we undertook a detailed chart review of acute trauma patients managed with induced hypothermia after cardiac arrest.

Patients: From Trauma Registry records, we identified all adult patients (older than 17 years) admitted to our Level I trauma center from July 1, 2008, through June 30, 2010, who experienced cardiac arrest during acute trauma care and were managed via our induced hypothermia protocol. This requires maintenance of core body temperature between 32°C and 34°C for 24 hours after arrest. Patient clinical records were then reviewed for selected factors.

Results: Six acute trauma patients (3 male and 3 female; median age, 53 years) with cardiac arrest managed per protocol were identified. All injuries were due to blunt impact, and five of six injuries were motor-vehicle-associated. Median Injury Severity Score was 27; median prearrest Glasgow Coma Scale (GCS) score was 15. One patient arrested prehospital and the other 5 in-hospital. Median duration of arrest was 8 minutes. All were comatose after arrest. One death occurred, in the patient with a prehospital cardiac arrest. Two patients were discharged to chronic care facilities with GCS11-tracheostomy; three were discharged to active rehabilitation care facilities with GCS score of 14 to 15. There were no obvious complications related to cooling.

Conclusions: Mild induced hypothermia can be beneficial in a selected group of trauma patients after cardiac arrest. Prospective trials are needed to explore the effects of targeted temperature management on coagulation in this patient group.

Key Words: Therapeutic hypothermia, Targeted temperature management, Multitrauma, Traumatic cardiac arrest.

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Although the evidence is not perfect,¹ mild hypothermia (32–34°C) is now widely accepted as neuroprotective in cardiac arrest victims who remain comatose after restoration of a functional cardiac rhythm.^{2,3} However, the potential role of the induction of intentional mild hypothermia in trauma

patients who remain comatose after resuscitation from cardiac arrest remains essentially unexplored. Indeed, for several decades now, “targeted temperature management” in trauma patients has meant avoiding hypothermia, a key factor in the coagulopathy associated with severe trauma and massive bleeding, the so-called “bloody vicious cycle.”^{4,5} Even mild hypothermia in trauma patients can be associated with coagulopathy, dysrhythmia, electrolyte disturbances, diuresis, infection, lactic acidosis, and changes in drug metabolism, all of which are potentially disastrous in seriously injured trauma patients. In addition, cardiac arrest in trauma patients and any specific postarrest interventions typically occur in the midst of a range of complicating circumstances, which must be taken into consideration in attempting therapeutic cooling of such patients. These include preexisting, event/environment-associated hypothermia, the coagulopathy of trauma independent of hypothermia-associated coagulopathy, continued active bleeding—atomic or coagulopathic—preexisting acidosis, and high risk of infection. Animal models suggest that trauma is not an absolute contraindication to the use of postarrest hypothermia;⁶ however, to date, little or no human data exploring this issue have been published.

In 2008, our Level I trauma center implemented a protocol for the induction of mild hypothermia in selected cardiac arrest patients. This specifies rapid cooling to 32° to 34°C, analgesia, and sedation, with neuromuscular blockade as appropriate (to prevent shivering), to be maintained for 24 hours, followed by slow passive rewarming at a rate no greater than 0.5 to 1°C per hour. To characterize our experience with this protocol since its inception and to glean insights into possible increased risk of bleeding with the use of hypothermia in posttrauma cardiac arrest, we undertook a detailed chart review of primary trauma patients admitted to our trauma center since the inception of this protocol who had suffered a cardiac arrest in the pre- or in-hospital setting and who were managed via the protocol.

PATIENTS AND METHODS

After securing approval for this study from the University of Maryland School of Medicine Institutional Review Board, we undertook a retrospective chart review of all trauma patients admitted to the R Adams Cowley Shock Trauma Center (STC) resuscitated from cardiac arrest but with subsequent Glasgow Coma Scale (GCS) score less than 8 and managed via the induced hypothermia protocol between July 1, 2008, and June 30, 2010. Patients included were

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older than 17 years, had sustained acute physical trauma and were admitted either directly from the scene of injury or after acute triage from an outside facility, had sustained a cardiac arrest, subsequently regained spontaneous circulation, but remained comatose, that is, with GCS score ≤ 8 , and then were managed via the induced hypothermia protocol (see Figure, Supplemental Digital Content 1, Trauma Center Guidelines for Use of Hypothermia Following Adult Cardiac Arrest, <http://links.lww.com/TA/A79>). Patients who had been managed via the hypothermia protocol were identified through the Trauma Registry; additional data were gleaned through pharmacy records and direct chart review. Data collected included age, sex, Injury Severity Score, mechanism of injury, arrest duration and location (pre- vs. in-hospital), mortality, functional outcome as assessed by GCS at 30 days after injury, and complications.

Statistical Methods

Given that this was intended as a case series, inferential statistical analysis was not appropriate. Simple summary statistics were used to aggregate data.

RESULTS

Twelve individuals were identified as having undergone post-arrest targeted temperature management via our protocol. Three patients had no history of traumatic injury and were excluded. Another three were admitted to the

STC in arrest after attempted suicide by hanging but had no physical trauma recorded other than skin markings from the ligature and no obvious risk for bleeding and were also excluded.

Six patients, three males and three females, met inclusion criteria for intensive review. Table 1 shows the main clinical features of the six cases. Age ranged from 25 years to 83 years (median, 53 years). One arrest occurred at the scene of injury and during transport, one in the Trauma Resuscitation Unit (TRU) on admission, and four in critical care units >24 hours after admission. Three patients were admitted to the STC directly from the scene of injury; three were taken first to an outside hospital (OSH) and subsequently transferred to the STC. Five patients were injured by motor-vehicle-associated blunt impact. Among these five patients, mean Injury Severity Score was 26 and the mode was 27. Two of these same patients had significant head injuries and were intubated at the scene of injury and admitted as GCS 3T (intubated). The other four patients were awake at admission with GCS score recorded as 15. The five in-hospital arrests were witnessed and advanced cardiac life support begun immediately; the one individual who experienced cardiac arrest prehospital is described as unconscious at the time he was found but appears to have arrested during extrication and transport to an OSH from which he was subsequently transferred to the STC. Life-support procedures were begun es-

TABLE 1. Summary of Trauma Patients With Cardiac Arrest After Major Trauma and Who Were Managed Under the Therapeutic Hypothermia Protocol, July 1, 2008, Through June 30, 2010

	Patient Number					
	1	2	3	4	5	6
Age (yr)	63	60	25	25	55	83
Sex	M	F	M	F	M	F
Injury source	MVA	MVA	MVA	MVA	MVA	Fall
Initial GCS score	3	15	3–6	15	15	15
Multitrauma	Y	Y	Y	Y	Y	N
Fracture	Y	Y	Y	Y	Y	Y
ISS	29	27	27	25	24	9
UnXd uRBC	Y	Y	Y	N	N	N
≥ 10 uRBC 1st 24 h	N	N	N	N	N	N
Admit INR	1.1	1.4	2.3	1.0	1.0	1.1
Admit PTT	27.0		41.0	31.0	29.0	
Admit platelets	256	146	103	236	254	288
Cause of arrest	Cardiac	Tension pneumothorax	Aspiration	Aspiration	Respiratory	Respiratory
Arrest rhythm	V-fib	PEA	Brady/asystole	PEA	Brady/asystole	Brady/asystole
Arrest pre- or in-hospital	Pre	In	In	In	In	In
ACLS began	Unclear	Immediately	Immediately	Immediately	Immediately	Immediately
Arrest lasted (min)	45	20	8	8	7	5
Time to cooling after injury	In TRU	7 d	14 d	In TRU	27.5 h	29 h
Cooling complications	Ventricular tachycardia	None	None	None	None	Duration of cooling unclear
Bleeding risk during/after cooling	Not apparent	INR/PTT drifted upward	Laboratory results unavailable	1st uRBC 24 h postcooling	INR 1.4 during cooling; onset unclear	Not apparent
30 d GCS score	Dead	15	11t	15	11t	14

MVA, motor-vehicle-associated; Y/N, yes or no; ISS, Injury Severity Score; UnXd uRBC, at least 1 unit of uncrossmatched group O red blood cells; uRBC, units of packed red blood cells; INR, international normalized ratio; PTT, partial thromboplastin time; V-fib, ventricular fibrillation; PEA, pulseless electrical activity; ACLS, acute cardiac life support.

entially immediately after arrest on all patients; however, duration of arrest ranged from 5 minutes to 45 minutes (median and mode, 8 minutes). All patients were GCS 3T after arrest.

Bleeding Risk

On admission, all six patients were at risk of bleeding because of the nature of their injuries, and three received at least one unit of uncross-matched group O packed red blood cells in the TRU, a clinical marker at our center for concern about potential for massive bleeding. However, only one individual had a markedly abnormal coagulation profile at admission, none went on to massive transfusion (conventionally defined as >9 units of red blood cells in the first 24 hours), and two required no blood at all. No patient experienced significant coagulopathy or bleeding complications.

Complications of Cooling

No obvious complications were observed in this patient group directly attributable to targeted temperature management. Patient 1, who had experienced cardiac arrest prehospital and undergone initial resuscitation at an OSH (during which he was rearrested several times), was started on the cooling protocol as soon as his initial TRU evaluation was completed. During initial cooling, he sustained a ventricular tachycardia rhythm. There was some concern that the cooling had been effected too rapidly and too deeply; however, it also seemed likely that he had sustained a cardiac contusion either as part of his primary injury or during initial resuscitation efforts.

Outcome

The one patient who experienced cardiac arrest preadmission was declared dead 52 hours after admission, having had no discernable neurologic recovery and after his family requested withdrawal of care. Two patients were discharged to long-term care centers 46 days and 72 days after admission with GCS 11T (1 had been admitted with GCS score of 3 and both required tracheostomy). The three female patients were discharged at 13 days, 17 days, and 42 days postadmission to acute rehabilitation centers with GCS scores of 14, 15, and 15, respectively.

DISCUSSION

This small case series nonetheless includes both sexes and a wide range of ages and clinical courses. All patients were admitted with injuries that suggested significant risk for bleeding, arguably the principal concern regarding the use of targeted temperature management in post-cardiac-arrest trauma patients, but none seemed to experience excess bleeding associated with induced hypothermia after cardiac arrest.

Entirely consistent with outcomes in cardiac arrest victims in the nontrauma setting, time to successful, sustained, restoration of spontaneous pulse was the single most important risk factor for mortality. The experiences of patients 2 and 4 are perhaps the most interesting. Patient 2 experienced cardiac arrest after a central line insertion and tension pneumothorax, underwent immediate cooling per protocol, and had excellent recovery, suggesting that the

efficacy of cooling may extrapolate to other circumstances of arrest, not just out-of-hospital ventricular fibrillation arrest as described in the literature. Patient 4 was the only individual in whom cooling was begun in the TRU despite her multi-trauma. Her course was complicated by multiple clonic jerks, and both her magnetic resonance imaging and the clinical consensus of the critical care team supported a diagnosis of anoxic brain injury. Despite this, her eventual recovery was excellent.

Even relatively brief (minutes) periods of cerebral anoxia are associated with significant cellular pathology including excitatory changes, inflammation, and regulatory shifts related to glutamate release, calcium shifts, mitochondrial damage, and oxidative stress.⁷⁻⁹ Not surprisingly, the most metabolically active, supratentorial, portions of the brain are typically the worst affected by these changes,⁹ which become radiologically visible quite rapidly as decreased density and loss of gray-white differentiation in the supratentorial brain due to edema and the relatively increased density of the cerebellum, the so-called dense cerebellum sign.¹⁰ Mild hypothermia has been shown to decrease cerebral and cellular metabolism by 7% with every degree celsius reduction in core temperature, to reduce intracellular acidosis, and to reduce inflammation and cytokine release.¹¹ The potential efficacy of therapeutic induction of mild hypothermia in the clinical circumstances described above is therefore logical, particularly in relatively younger patients.

Future Research

Any number of pathophysiological and clinical issues remain to be explored regarding the neuroprotective potential of therapeutic hypothermia and therapeutic hypothermia after cardiac arrest. This is particularly true for the trauma care setting¹² and involves several potentially significant variant presentations: cardiac arrest because of direct trauma to the heart—so-called traumatic cardiac arrest—cardiac arrest occurring over the course of acute care for multitrauma, and either of these two situations in patients at excess risk of massive bleeding. The case series presented here is hampered by being small, retrospective, dependent on general hospital records rather than dedicated, study-protocol documentation, and limited to cardiac arrest occurring only in the context of blunt injury, mainly motor-vehicle-associated. In addition, the 30-day GCS was the only metric of long-term outcome available to us. However, before larger prospective clinical studies are undertaken, small and large animal models must be developed that can support exploration and calibration of the issues specific to the use of therapeutic hypothermia as a neuroprotective strategy after cardiac arrest in trauma patients. The degree and timing of any alterations in the coagulation profile must be elucidated over the course of various post-cardiac-arrest therapeutic hypothermia protocols in both nontrauma and trauma physiologic systems.

In both bench research and clinical studies, documentation of the effects of hypothermia on platelet function will be crucial, particularly in light of the work emerging now suggesting that early platelet repletion during trauma resuscitation is associated with improved survival and improved neurologic outcome.^{13,14} Platelets are the most cold-sensitive

element of the coagulation cascade,^{15,16} but conventional laboratory assessments of platelet function, as against platelet count, are cumbersome, time-consuming, and of little direct clinical utility. Various measures of clot strength or thromboelastography may offer a clinically useful point-of-care alternative to conventional platelet function testing.^{17,18} The inclusion of thromboelastography, with a focus on the platelet-sensitive portions of the tracing, may prove to be of particular interest in laboratory and clinical research on the effects of therapeutic hypothermia protocols on coagulation.

Summary and Conclusions

Our very preliminary review of six cases of the use of therapeutic hypothermia after cardiac arrest in the acute trauma care setting suggests that this clinical strategy may be useful. However, much research remains to be done regarding the use of hypothermia as a neuroprotective strategy after cardiac arrest in trauma patients, most particularly regarding its effects on coagulation and platelet function.

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