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Hypothermia and Rapid Rewarming Is Associated With Worse Outcome Following Traumatic Brain Injury

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Abstract

Purpose—The purpose of the present study was to determine (1) the prevalence and degree of hypothermia in patients on emergency department admission and (2) the effect of hypothermia and rate of rewarming on patient outcomes.

Methods—Secondary data analysis was conducted on patients admitted to a level I trauma center following severe traumatic brain injury (n = 147). Patients were grouped according to temperature on admission according to hypothermia status and rate of rewarming (rapid or slow). Regression analyses were performed.

Findings—Hypothermic patients were more likely to have lower postresuscitation Glasgow Coma Scale scores and a higher initial injury severity score. Hypothermia on admission was correlated with longer intensive care unit stays, a lower Glasgow Coma Scale score at discharge, higher mortality rate, and lower Glasgow outcome score–extended scores up to 6 months postinjury ($P < .05$). When controlling for other factors, rewarming rates more than 0.25°C/h were associated with lower Glasgow Coma Scale scores at discharge, longer intensive care unit length of stay, and higher mortality rate than patients rewarmed more slowly although these did not reach statistical significance.

Conclusion—Hypothermia on admission is correlated with worse outcomes in brain-injured patients. Patients with traumatic brain injury who are rapidly rewarmed may be more likely to have worse outcomes. Trauma protocols may need to be reexamined to include controlled rewarming at rates 0.25°C/h or less.

Keywords

Complications; Function; Head injury; Length of stay; Mortality

Patients often experience accidental hypothermia ($T < 35$°C) following a traumatic injury and current trauma resuscitation standards integrate strong measures for its prevention and treatment.[1] Admission hypothermia is associated with increased mortality following major trauma.[2–4] Generally hypothermic patients are actively rewarmed as part of the trauma protocol[5]; however, when the patient has a traumatic brain injury (TBI), this active rewarming may be detrimental.[6] The rate of rewarming following therapeutic hypothermia in both experimental and clinical TBI has been shown to be an important factor in its

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success or failure.[7–11] No study to date has evaluated rewarming, its side effects, or outcomes, and currently there is no standard of care for patient management in this area.[12]

PURPOSE

Hypothermia severity is classified as being mild (32°C–35°C), moderate (28°C–32°C), or severe (<28°C).[13] Signs and symptoms of mild hypothermia include shivering, tachycardia, tachypnea, and vasoconstriction. While shivering is absent in patients with moderate hypothermia, they may experience arrhythmias, bradycardia, and altered level of consciousness. Accidental hypothermia thus has detrimental effects on many body systems that are important to survival postinjury.

Following traumatic injury, admission hypothermia is associated with increased mortality.[2–4,14] Risk factors for hypothermia in major trauma patients include age, time spent in the field, injury severity, hypovolemia, and blood alcohol level.[15,16] Hypothermia and associated shivering have been associated with increased oxygen consumption,[1,17] increased blood loss,[18] and coagulopathies,[19] which may worsen outcome following trauma. In severe TBI patients, hypothermia within the first 24 hours of admission has been independently associated with risk of in-hospital mortality.[14] Furthermore, the National Acute Brain Injury Study-Hypothermia trial, TBI patients with admission hypothermia assigned to the normothermia arm had significantly worse outcomes than those persons who were normothermic on admission.[20]

Currently available literature identified the need for the present study since the rate of rewarming following therapeutic hypothermia in experimental TBI has been shown to be an important factor in its success or failure.[7–11] Fast rewarming has been associated with worsened neuronal and axonal damage[7,8] in experimental studies of TBI. In addition, rapid rewarming has been associated with a decrease in jugular venous hemoglobin saturation and increased oxygen consumption in models of cardiopulmonary bypass[21] which has clear implications for TBI.

Generally hypothermic patients are actively rewarmed as part of established protocols. These rates vary significantly from 0.20°C to 2.95°C/h.[12,22] However, when the patient has a TBI, this more rapid and active rewarming may be detrimental. Rates of rewarming in the therapeutic hypothermia trials published to date in TBI range widely from 1°C/d[23,24] to 1°C/h,[25,26] with the majority of investigators using a rate of 0.25°C/h.[12,20,27] In published clinical practice guidelines for management of severe TBI,[28] there was no difference in mortality rates among different rewarming protocols. In contrast, in a meta-analysis conducted examining other outcomes, McIntyre and colleagues[9] found a higher risk of poor neurological outcome when rewarming occurred within 24 hours of ending therapeutic hypothermia. The guideline developers did not examine outcomes other than mortality, so a full comparison to the meta-analysis is not possible.

Thus questions remain regarding the effect of admission hypothermia and rate of rewarming on outcomes following TBI. The purpose of this study was therefore to determine (1) the prevalence and degree of hypothermia in a sample of TBI patients on admission to the emergency department (ED) and (2) the effect of (*a*) hypothermia and (*b*) rate of rewarming on patient outcomes, controlling for severity of injury, gender, age, and number of complications.

METHODS

Secondary data analysis of available hospital records from the parent study (R01NR4901) was conducted on patients admitted to a level I trauma center following severe TBI from

January 2000 to January 2002. The study was approved by the institutional review board under the parent study. Subjects were included in the study if they had a temperature recorded while they were in the ED (n = 147).

Demographic data

age at the time of injury, gender, transport method (air vs ground), and time in the field.

Severity of initial injury

This was captured using the Glasgow Coma Scale score Post-Resuscitation (GCS-PR) and injury severity score (ISS).

GCS-PR

the GCS score reported following initial resuscitation in the ED.

ISS

the sum of squares of the most severe injury in each of the 3 most severely injured body regions (ranges from 1 [*least severe*] to 75 [*most severe*]).[29]

Number of complications during hospitalization

This was the total number of complications that occurred for an individual subject. Complications extracted included hypocapnia, hypercapnia, hypoxemia, hypotension, increased intracranial pressure, seizure, acute respiratory distress syndrome, sepsis, pneumonia, urinary tract infection, and multiorgan dysfunction syndrome.

Time and temperature data

This included time and initial temperature on arrival to the ED. All subsequent temperatures with timing of measurement were extracted until temperature reached 36.5°C or more.

Hypothermia

Defined as an admission temperature of $T < 35°C$.[19,30]

Rate of rewarming

Calculated by determining time to 36.5°C or more.

Rapid rewarming

Defined as a rate more than 0.25°C/h.[6,12]

Patient outcomes

Outcomes examined in this study included intensive care unit (ICU) length of stay (LOS), hospital LOS, Glasgow Coma Scale score at hospital discharge and mortality at discharge and 6 months postinjury. Functional status was further evaluated using the 8-point Glasgow Outcome Score–Extended (1 = dead, 8 = upper good recovery) at discharge and 6 months postinjury.

DATA ANALYSIS

Patients were first grouped on the basis of admission temperature in ED as either hypothermic or normothermic, and descriptive statistics were performed. Second, the hypothermic patients were further categorized into slow rewarming or rapid rewarming and descriptive statistics were again performed. Pearson correlations, analysis of covariance, and multinomial logistic regression were performed for both hypothermia and rate of rewarming as the predictor variable with patient outcome as the dependent variable. Covariates controlled for in the analyses included age, gender, severity of initial injury (GCS-PR and ISS), and number of complications during hospitalization. Data are expressed as mean ± standard error of the mean. A *P* value less than .05 was considered statistically significant.

FINDINGS

Hypothermia was common in this sample, present in 40% of subjects. The mean temperature on arrival to the ED of normothermic subjects (n = 88) was 36.3°C ± 0.1°C. The mean temperature of hypothermic subjects (n = 59) was 34.2°C ± 0.1°C. There was no seasonal variation or difference in time spent in the field noted.

With the exception of a single subject who had moderate hypothermia, all remaining subjects experiencing hypothermia (58 of 59) experienced a mild degree of hypothermia on admission. There were no differences in age or gender among the group of subjects who were hypothermic on admission versus those who were normothermic (Table 1). However, those experiencing hypothermia had more severe injury as indicated by the GCS-PR and the ISS (Table 1). Furthermore, the hypothermic subjects experienced, on average, one more complication during their hospitalization than normothermic subjects (Table 1). This difference was also statistically significant. Other than the rate of rewarming, there were no differences in any demographic or injury factor between rapidly or slowly rewarmed hypothermic subjects (Table 2).

Hypothermia on admission was correlated with longer lengths of stay, worse neurological outcome at discharge, and higher mortality rates up to 6 months postinjury (Table 3). Mortality rates at discharge for patients who were warmed at rates 0.25°C/h or less were lower (16.7% vs 23.4%) than those who were rapidly rewarmed (>0.25°C/h). Controlling for other factors, the ICU LOS was longer (13.6 days vs 10.1 days) and the GCS at discharge was lower (12.8 vs 10.4) in patients who were rapidly rewarmed compared to slow rewarming in regression analyses, but these did not reach statistical significance.

DISCUSSION AND CONCLUSIONS

In this study, the severity of initial injury as indicated by a higher ISS and lower GCS-PR is associated with the development of hypothermia in this sample of brain-injured patients. This confirms findings from previous studies in all-cause trauma patients.[2,3] Blood alcohol levels were not available on subjects within the parent study; therefore, we were unable to determine any association with admission hypothermia. We did not see any gender differences in the hypothermic and normothermic groups. This is in contrast to findings in surgical patients that found females to be at higher risk[31] likely because of lower lean body mass.

The presence of hypothermia on admission was correlated with worse outcomes including ICU LOS, functional outcomes (GCS and Glasgow Outcome Score-Extended), and death in our sample of brain-injured patients. This finding is similar to that from the National Trauma Data Bank, which also found longer ICU LOS and higher mortality rates in hypothermic trauma patients compared with normothermic.[3]

When accompanied by rapid rewarming, hypothermic subjects in the present report had worsened short-term neurological outcomes and higher mortality rates postinjury.

However, after controlling for other factors such as injury severity, age, and gender among rapid and slow rewarming groups, these differences in outcome were not statistically significant. This is perhaps due to underpowering within the rapid rewarming group (n =12), which is a limitation of retrospective studies using a fixed sample. Further study with larger sample sizes is recommended to clarify this relationship. Although the current study included only cases from 2000 to 2002, other changes in care delivery over the 3-year period could have affected patient outcomes.

Rapid rewarming may be associated with afterdrop, which results when warm blood shunts to the periphery and cold blood to the core due to vasodilation. Monitoring both skin and core temperature is recommended to avoid this phenomenon. Of additional note, the method of monitoring core temperature (eg, bladder, rectal) may be associated with delayed response to change and is an important consideration in monitoring site choice.[32]

The use of therapeutic hypothermia has been shown in other forms of brain injury, specifically hypoxic postcardiac arrest and neonatal hypoxic encephalopathy, to be beneficial in reducing mortality and improving outcome[33–37]; however, clinical trials to date in TBI have been negative.[20] In the present study, we examined hypothermia on admission, rather than therapeutic hypothermia; thus, a full consideration and discussion of therapeutic hypothermia is beyond the scope of this article (for further information on the topic, see McIntyre et al,[9] Polderman,[12] Bratton et al,[28] and Zeitzer[38]).

Given the present findings associating rapid rewarming of hypothermic brain-injured patients with poorer outcomes, trauma protocols may need to be reexamined to include controlled rewarming at rates 0.25°C/h or less in TBI patients presenting with mild or moderate hypothermia. In TBI patients, passive rewarming may not be possible as thermoregulatory mechanisms may be altered. For that reason and to reduce variability, the best method of rewarming the TBI patient is controlled. However, it is unclear which device (eg, air or water blanket, intravascular catheter) provides the best control in this population and this is worthy of further prospective study.

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Table 1

Baseline Characteristics by Temperature on Admission to Emergency Department[a]

	Hypothermic (n = 59)	Normothermic (n = 88)
Age (y)	34.9 ± 2.3	37.5 ± 2.0
% Male	78	76
Postresuscitation Glasgow Coma Scale score	6.3 ± 0.4	7.8 ± 0.3[b]
Injury severity score	31.8 ± 1.1	27.5 ± 1.0[b]
Number of complications during hospitalization	2.3 ± 0.2	1.3 ± 0.2[b]

[a]Data are presented as mean ± standard error of the mean unless noted.

[b]$P < .01$.

Table 2

Baseline Characteristics of Hypothermic Patients Grouped by Rate of Rewarming

	Slow Rewarm (n = 12)	Rapid Rewarm (n = 47)
Temperature on arrival (°C)	34.5 ± 0.1	34.1 ± 0.1
Rate of rewarming (°C/h)	0.22 ± 0.01	0.65 ± 0.04[a]
Postresuscitation Glasgow Coma Scale score	5.5 ± 0.6	6.5 ± 0.4
Injury severity score	31.6 ± 2.5	31.9 ± 1.3
Number of complications	2.1 ± 0.5	2.2 ± 0.3

[a] $P < .0005$.

Table 3

Correlation of Outcomes With Emergency Department Hypothermia

	R	P
Glasgow Coma Scale score at discharge	−0.200	.015[a]
Glasgow Outcome Scale–Extended at discharge	−0.163	.049[a]
Intensive care unit length of stay	0.226	.006[b]
Mortality at discharge	0.181	.028[a]
Mortality at 6 months	0.202	.018[a]

[a] $P < .05$.

[b] $P < .01$.