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THE EFFECT OF ADMISSION SPONTANEOUS HYPOTHERMIA ON PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY

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Abstract

Introduction—Recent information has emerged regarding the harmful effects of spontaneous hypothermia at time of admission in trauma patients. However the volume of evidence regarding the role of spontaneous hypothermia in TBI patients is inadequate.

Methods—We performed secondary data analysis of 10 years of the Pennsylvania trauma outcome study (PTOS) database. Unadjusted comparisons of the association of admission spontaneous hypothermia with mortality were performed. In addition, full assessment of the association of hypothermia with mortality was conducted using multivariable logistic regressions reporting the odds ratios (OR) with the 95% confidence intervals (CI) and p-values.

Results—There were 11,033 patients identified from the PTOS with severe TBI. There were 4,839 deaths (43.9%). The proportion of deaths in hypothermic patients was higher than the proportion of deaths in normothermic patients (53.9% vs. 37.4% respectively; P value <0.001). In

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a multivariable logistic regression model adjusted for demographics, injury characteristics, and information at admission to the trauma centre, the odds of death among patients with hypothermia were 1.70 times the odds of death among patients with normothermia (OR 1.70, 95%CI 1.50–1.93), indicating that the probability of death was significantly higher when patients arrived hypothermic at the trauma centre.

Conclusion—The presence of spontaneous hypothermia at hospital admission is associated with a significant increase in the risk of mortality in patients with severe TBI. The benefit of maintaining normothermia in severe TBI patients, the impact of prolonged re-warming in patients with established hypothermia and the introduction of prophylactic measures to complications of hypothermia are key points that require further investigation.

Keywords

Trauma; outcome; severe head injury; hypothermia; traumatic brain injury; mortality

Introduction

Over the last fifteen years, few topics in neurosurgery have created such debate and lack of consensus as the role of hypothermia in patients with traumatic brain injury (TBI). Whilst the majority of animal studies have indicated a beneficial role for the therapeutic application of hypothermia post TBI, this has failed to translate into conclusive evidence of a protective role in clinical studies.

Recent information has emerged regarding the harmful effects of spontaneous hypothermia at time of admission in trauma patients. However the volume of evidence regarding the role of spontaneous hypothermia in TBI patients is inadequate. Additionally, there appears to be a conflict regarding the significance of the presence of hypothermia in the worsening of outcome in trauma patients, with some evidence indicating that a greater negative impact depends upon the manner and duration of patient re-warming as opposed to the presence of hypothermia itself ⁽¹⁾.

This apparent scarcity of large, quality studies investigating this topic highlighted the need for such research so as to elicit whether the development of hypothermia in these patients represents a primary factor contributing to mortality or merely an epiphenomenon of severe TBI. The objective of this study was to determine the association between admission spontaneous hypothermia and severe traumatic brain injury (TBI) mortality in a large state-wide trauma registry.

Methods

We performed secondary data analysis of 10 years of the Pennsylvania trauma outcome study (PTOS) database, a trauma registry that contains trauma patients' information from all accredited trauma centres in Pennsylvania. During 1998–2007, there were 31 trauma centres accredited by the Pennsylvania trauma systems foundation (PTSF). Patient information is submitted to the PTOS if the patient was admitted to any accredited trauma centre for treatment of trauma and with any of the following: admitted to an intensive care unit, died on or after arrival, admitted over 48 hours from the time of arrival to the emergency department, or transferred from another facility with diagnoses of trauma. Each admission in the database is assigned a unique patient identifier. Out-of-hospital deaths and injuries treated in non-accredited trauma centres in Pennsylvania are not included.

TBI patients were identified using the Barell matrix (2) to categorize injury diagnoses using international classification of disease, ninth revision, clinical modification (ICD9-CM) codes

(3). TBI severity was classified using the head-neck abbreviated injury scale (AIS) and the Glasgow coma scale (GCS) recorded at hospital admission. The AIS was derived by the computerized algorithm of the international classification of disease programs for injury categorization (ICDPIC). ICDPIC classifies ICD-9-CM codes according to severity and body region in order to allow for approximate severity scoring. ICDPIC programming algorithms and associated tables are complete open for Stata (statistical software) users (4). TBI was classified as severe if the head-neck AIS = 4 and GCS = 8.

We requested de-identified information on demographics (age, sex, and history of pre-existing conditions), date of the injury, ICD-9-CM codes, and information at admission to the trauma centre (date of admission, pre-hospital fluids, temperature at admission, systolic blood pressure at admission, and initial GCS). From the ICD-9-CM codes we determined the AIS, new injury severity score (NISS), the presence of penetrating and/or haemorrhagic intra cranial injury and the presence of severe extra cranial injuries defined as having any injury with AIS score of 4 through 6 in any of the body regions except head-neck (5). Our exposure of interest was admission hypothermia defined as body temperature < 35°C at admission to the trauma centre. The primary outcome was death at hospital discharge.

Description of all patients was performed using relative and absolute frequencies for qualitative variables. Continuous variables were summarised by reporting means, standard deviations (SD), medians, and 25th and 75th percentile ranges (PR). In addition, continuous variables were categorized to provide a more useful and clinical relevant interpretation. To obtain a basic idea of the association with the outcome, comparison of categorical variables was performed using Chi² tests and comparison of continuous variables was performed using nonparametric tests (Wilcoxon Mann-Whitney), given their non-normal distributions. P value <0.05 was set to indicated statistical significance.

Unadjusted comparisons of the association of admission spontaneous hypothermia with mortality were performed. In addition, full assessment of the association of hypothermia with mortality was conducted using multivariable logistic regressions reporting the odds ratios (OR) with the 95% confidence intervals (CI) and p-values. These regression models were adjusted for age, sex, pre-existing conditions, penetrating and/or haemorrhagic intra cranial injury, head-neck AIS, NISS, severe extra cranial injuries, estimated injury-to-trauma centre days, pre-hospital fluids administered, systolic blood pressure at admission, and admission GCS. Males and females respond differently after traumatic injury, with relative protection afforded to females (Sperry JL & Minei JP. Gender dimorphism following injury: making the connection from bench to bedside. *J Leukoc Biol* 2008; 83:499–506). Therefore, we examined possible interactions between hypothermia and sex, using likelihood ratio tests to assess the additional contribution of this interaction to the multivariable logistic regressions.

We were aware of missing data in temperature at admission to the trauma centre, therefore sensitivity analyses were conducted. We conservatively assigned the missing data to the hypothermia status assuming that those patients were hypothermic at admission to the trauma centre. In addition, we assigned the missing data to the normothermic status assuming that those patients were normothermic at admission to the trauma centre. Multivariable logistic regressions were repeated to evaluate the robustness of the conclusions.

The quality of the logistic regression models were assessed in terms of calibration by the Hosmer-Lemeshow goodness-of-fit (GOF) test and in terms of discrimination with the area under the receiver operation characteristic curve (AUC). The regression models demonstrated lack of fit in the entire cohort of patients. We excluded the patients with

virtually unsurvivable traumatic brain injuries, defined as TBI patients with head-neck AIS equal 6 and GCS equal 3. Subgroup analyses were performed in TBI patients with head-neck AIS scores of 4 through 5 and GCS of 4 to 8. Multivariable logistic regressions were repeated and the performance of the models was re-evaluated.

Results

There were 11,033 patients identified from the PTOS with severe TBI. The characteristics of patients with severe TBI are depicted in table 1. Median age was 35 years (PR, 20–58). Most of the patients were between 15 and 24 years of age (25.6%), males (72.1%) and at admission there were 44% of the patients with pre-existing conditions or co-morbidities. Penetrating and/or haemorrhagic intra cranial injury was evidenced in 8,399 patients (76.1%) whereas only 995 patients (9.0%) presented with severe extra cranial injuries. There were 150 patients (1.4%) with Head-neck AIS rated as virtually unsurvivable (Head-neck AIS = 6). Median NISS was 41 points (PR, 34–48) (Table 1).

Most of the patients arrived at the trauma centre within the first day following the injury (89.6%), there were 887 patients (8.0%) that arrived during the second day after the injury and 234 patients (2.1%) arrived during the third day. In 26 patients, time or day of the injury was not available. Pre-hospital fluids were administered in 10,535 patients (95.5%), however in 5,772 patients (52.3%) the amount of pre-hospital fluids administered was unknown. Median systolic blood pressure on arrival to the trauma centre was 132 mmHg (PR, 105–154). There were 8243 patients (74.7%) that arrived with a GCS of 3. The median value of spontaneous temperature on admission to the trauma centre was 36.1 grades Celsius (PR, 35.4–36.7) and 1,663 patients (15.1%) were hypothermic on admission (Table 1).

Outcome assessment

There were 4,839 deaths (43.9%). The proportion of deaths in hypothermic patients was higher than the proportion of deaths in normothermic patients (53.9% vs. 37.4% respectively; P value <0.001). Comparisons of patients' characteristics with regards to discharge status are depicted in Table 1. Patients discharged dead were older than patients discharged alive (median of 44 [PR, 18–48] vs. 28 [PR, 23–73] years of age respectively; P value <0.001). Females died in greater proportion than males (46.6% vs. 42.8% respectively; P value <0.001) and patients with pre-existing conditions were more likely to die after a severe TBI than patients with no co-morbidities (45.3% vs. 42.7% respectively; P value = 0.006) (Table 1).

Patients with a penetrating and/or haemorrhagic intra cranial injury demonstrated lower mortality rates than patients with skull fractures with unspecified intra cranial injuries or concussions (40.7% vs. 53.9% respectively; P value <0.001). Mortality was 72.0% among patients with head-neck AIS rated as virtually unsurvivable, 68.2% among patients rated as critical, and 42.2% among patients rated as severe (P value <0.001). Mortality was higher in patients with severe extra cranial injuries than in patients with no extra cranial injuries associated (55.2% vs. 42.7% respectively, P value <0.001). The median NISS was 41 points (PR, 34–48) for patients discharge dead and alive, however mortality was 41.9% among patients with NISS between 16–25 and 77.2% among patients with NISS of 65–75 (P value <0.001) (Table 1).

The proportion of deaths was 44.3% among patients that arrived during the first day after the injury, 40.2% among patients that arrived during the second day after the injury, and 41.5% among patients that arrived during the third day after the injury; however, this difference did not reach statistical significance (P value = 0.05). Mortality rate was higher among patients without administration of pre-hospital fluids (52.4%) than among patients with pre-hospital

fluids administered (P value <0.001). Median systolic blood pressure was 121 mmHg (PR, 79–152) in dead patients and 138 mmHg (PR, 117–156) in survivors (P value <0.001). Mortality was higher among patients with admission GCS of 3 (47.9%) and lower among patients with admission GCS of 8 (19.5%) (Table 1).

Association between admission spontaneous hypothermia and mortality

In a multivariable logistic regression model adjusted for demographics, injury characteristics, and information at admission to the trauma centre, the odds of death among patients with hypothermia were 1.70 times the odds of death among patients with normothermia (OR 1.70, 95%CI 1.50–1.93), indicating that the probability of death was significantly higher when patients arrived hypothermic at the trauma centre (Table 2). The assessment of interaction between admission hypothermia and sex was not found to be statistically significant and was not included (Likelihood ratio test's p value 0.077); sex differences in mortality were not statistically significantly different after severe TBI in hypothermic patients (OR, 0.87, 95%CI 0.68–1.11) and in normothermic patients (OR, 1.11, 95%CI 0.98–1.26). The final logistic regression model demonstrated an acceptable discrimination (AUC 0.792, 95%CI 0.784–0.801), however calibration was not adequate (P value <0.001), indicating that this model may not assign appropriately the risk of death among all the severe TBI patients.

There were 1,939 patients (17.6%) with missing data in temperature at admission to the trauma centre (Table 1). In sensitivity analyses, missing values were coded arbitrarily as hypothermia or normothermia. When missing values were coded as hypothermia, the multivariable logistic regression model indicated that hypothermia was statistically significantly associated with higher mortality rates than normothermia (OR 1.57, 95%CI 1.43–1.74) (Table 2). This model demonstrated excellent discrimination (AUC 0.807, 95%CI 0.800–0.815), however calibration was not adequate (P value <0.001). When missing values were coded as normothermic, the multivariable logistic regression model indicated that hypothermia remained as a significant predictor of mortality in severe TBI (OR 1.58, 95%CI 1.40–1.79) (Table 2). This model demonstrated excellent discrimination (AUC 0.806, 95%CI 0.799–0.814), however calibration remained not adequate (P value <0.001).

Subgroup analysis

There were 2,773 severe TBI patients with head-neck AIS of 4 through 5 and GCS of 4 through 8. Admission spontaneous hypothermia was present in 289 patients (10.4%) and admission spontaneous normothermia was present in 2,106 patients (76.0%).

Overall mortality rate was 31.8% (883 patients). There were 128 deaths in hypothermic patients and 608 deaths in normothermic patients (44.3% vs. 28.9%, respectively; P value <0.001). In the multivariable logistic regression model adjusted for demographics, injury characteristics, and information at admission to the trauma centre, the odds of death among patients with hypothermia were 2.15 times the odds of death among patients with normothermia (OR 2.15, 95%CI 1.57–2.95). This indicates that in this subgroup of patients, the probability of death was significantly higher when they arrived hypothermic at the trauma centre (Table 3). This logistic regression model demonstrated acceptable discrimination (AUC 0.760, 95%CI 0.751–0.769) and adequate calibration (P value = 0.078).

There were 378 patients (13.6%) with missing data in temperature at admission to the trauma centre; 147 of them (38.9%) died. In sensitivity analyses, the multivariable logistic regression models indicated that hypothermia remained statistically significantly associated

with higher mortality rates than normothermia (Table 3). When missing values were coded as hypothermia, the multivariable logistic regression model demonstrated acceptable discrimination (AUC 0.784, 95% CI 0.776–0.791); however, calibration remained not adequate (P value = 0.024). When missing values were coded as normothermia, the multivariable logistic regression model demonstrated acceptable discrimination (AUC 0.782, 95% CI 0.774–0.790) and adequate calibration (P value = 0.180).

Discussion

The established acceptance of the negative impact of spontaneous hypothermia in general trauma patients is reflected by its incorporation within the lethal triad (along with acidosis and coagulopathy) often seen in the severely injured patient ^(1,6,7,8). Whilst there has been much research and debate regarding the effects of therapeutic hypothermia on the outcome of patients with severe TBI there has been, to date, a distinct absence of large-scale studies focused upon the prognostic impact of spontaneous hypothermia.

Several recent large studies and a meta-analysis have shown that the application of therapeutic hypothermia in the management of the severe TBI patient was not associated with any benefit in mortality or neurological outcome. ^(9, 10, 11, 12) This is somewhat perplexing given the significant weight of evidence showing a benefit for hypothermia in severe TBI animal and pathophysiological models ^(13,14) as well as the significant reduction in ICP (a mainstay in the successful treatment of TBI), witnessed with the use of hypothermia in several human studies ^(15,16,17).

Whilst therapeutic and spontaneous hypothermia share the same homeostatic end-point, the pathophysiological mechanisms and conditions through which they occur are distinctly separate and thus the prognostic outcomes in studies focusing on therapeutic hypothermia cannot be accurately assumed to apply in spontaneous hypothermia cases. Thus, prior to the undertaking of this study, there was an apparent need for a large-scale study into the prognostic impact of spontaneous admission hypothermia in the severe TBI population.

Our study revealed that admission spontaneous hypothermia (<35 degrees Celsius) was associated with a significant increase in mortality when compared to normothermic patients. After the exclusion of patient with virtually unsurvivable traumatic brain injuries, the multivariable regression analyses indicated even higher associations between admission spontaneous hypothermia and mortality. Our findings that spontaneous admission hypothermia is associated with a significant increase in mortality compared to the normothermic patient is supported by the results of a recent smaller study by Konstantinidis et al. ⁽¹⁸⁾ which revealed that the presence of spontaneous hypothermia was associated with a odds ratio of mortality of almost three times that of the normothermia severe TBI group.

Our understanding as to why admission spontaneous hypothermia is associated with a higher risk of mortality in severe TBI is relatively unclear at present. One explanation may be that the poorer outcome may be attributed to the occurrence of detrimental complications that are associated with the presence of hypothermia.

Hypothermia-related coagulopathy has been demonstrated in both animal and human studies ^(19,20) and has been shown to reduce platelet function as well as slow enzymatic activity resulting in a decrease in the coagulation cascade ^(21,22). Hypothermia-related coagulopathy has been shown to increase blood loss and subsequently increases the need for transfusion during elective surgery ⁽²³⁾. However, at present, uncertainty regarding the depth of hypothermia required to induce coagulopathy ⁽²⁴⁾ and whether its presence actually increases the risk of intracranial hemorrhage complications in the post TBI patient ⁽²⁵⁾ still remain.

Cardiac arrhythmias have been shown to be more common in patients with hypothermia^(26, 27) with one study demonstrating a three-fold increase in the incidence of ventricular tachycardia as well as morbid cardiac events⁽²⁷⁾. Whilst the increased risk of arrhythmias appears significant in TBI patients with mild hypothermia, this risk appears to be heightened with more profound levels of hypothermia (<30°C)⁽²⁸⁾.

Hypothermia has been demonstrated to result in the inhibition of proinflammatory reactions, resulting in the potential suppression of the individuals' immune system thus increasing their susceptibility to infections. Additionally, the expression of heat shock protein 60 by leukocytes, which is believed to play an important role in innate immune system function, has been shown to be reduced in the presence of hypothermia⁽²⁹⁾. The increased susceptibility of the hypothermic patient to infection has been demonstrated by several studies that revealed higher incidences of infection compared to normothermic individuals^(19, 30).

Cerebral blood flow (CBF) has been shown to reduce in hypothermic animal models of TBI⁽³¹⁾. This may result in reduced perfusion and oxygenation of the already vulnerable perilesional penumbra occurring as a result of the initial traumatic event. This may increase the ischemic insult to these potentially salvageable areas of brain tissue and may exacerbate the TBI-related damage. However, interestingly hypothermia has also been shown to reduce cerebral metabolism and subsequent oxygen demand by as much as 50% in animal models⁽³¹⁾.

Evidence has emerged indicating that rapid rewarming following hypothermia may play an equal or even greater role, than hypothermia itself, in the poor outcome of these individuals following TBI⁽³²⁾. Expeditious rewarming is associated with haemodynamic instability requiring vasoactive drugs and also rebound rises in ICP that may be difficult to control^(12,33,34). Therefore it has been suggested that to limit the occurrence of secondary damage in the hypothermic severe TBI patient, the rewarming process should be accomplished gradually over a more prolonged period of 12–24 hours or even more⁽³³⁾.

Increased injury severity has been shown to be an independent risk factor for the development of spontaneous hypothermia in both the general trauma and severe TBI patient, indicating a failure of the thermostatic mechanisms and greater body heat loss in the more critically injured individual^(18, 35, 36). Thus, rather than representing an incidental contributor to poorer outcomes in patients with TBI, spontaneous hypothermia may in fact be an independent epiphenomenon of more severe injury, with its presence signifying a harbinger for increased mortality in the severe TBI population.

Limitations

Out of hospital deaths and severe TBI treated in non-trauma centres or other inpatient or outpatient settings are not included in PTOS. Information regarding the mechanisms and duration of patient re-warming during hospitalisation was not possible to obtain from the database, thus the effects of this factor upon prognosis could not be determined. Further limitations were that the respective incidences of recognized complications of hypothermia were not analysed and also the seasonal effect upon the incidence of spontaneous hypothermia and outcome was not determined. Finally, the results of this study cannot be generalized to mild and moderate TBI.

Conclusion

The presence of spontaneous hypothermia at hospital admission is associated with a significant increase in the risk of mortality in patients with severe TBI. The benefits of

maintaining normothermia in severe TBI patients, the impacts of prolonged re-warming in patients with established hypothermia, and the introduction of prophylactic measures to counter the potential complications of hypothermia are key points that require further investigation.

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Table 1

Characteristics of patients with severe traumatic brain injury by discharge status

Variables	Total N=11,033		Discharge status				P value
	n	(%)	Alive		Death		
Exposure of interest							
Admission spontaneous hypothermia							
No (Temperature >35° Celsius)	7,431	(67.4)	4,650	(62.6)	2,781	(37.4)	<0.001
Yes (Temperature ≤ 35 ° Celsius)	1,663	(15.1)	767	(46.1)	896	(53.9)	
Missing	1,939	(17.6)	777	(40.1)	1,162	(59.9)	
Covariates							
Age (years)							
Mean [SD]	40.1	[24.5]	34.4	[21.5]	47.3	[26.1]	<0.001
Median [PR]	35	[20–58]	28	[18–48]	44	[23–73]	
0–4	441	(4.0)	295	(66.9)	146	(33.1)	<0.001
5–9	307	(2.8)	223	(72.6)	84	(27.4)	
10–14	449	(4.1)	335	(74.6)	114	(25.4)	
15–19	1,420	(12.9)	954	(67.2)	466	(32.8)	
20–24	1,400	(12.7)	883	(63.1)	517	(36.9)	
25–29	792	(7.2)	477	(60.2)	315	(39.8)	
30–34	623	(5.6)	366	(58.7)	257	(41.3)	
35–39	650	(5.9)	415	(63.8)	235	(36.2)	
40–44	722	(6.5)	433	(60.0)	289	(40.0)	
45–49	639	(5.8)	402	(62.9)	237	(37.1)	
50–54	504	(4.6)	299	(59.3)	205	(40.7)	
55–59	405	(3.7)	221	(54.6)	184	(45.4)	
60–64	368	(3.3)	166	(45.1)	202	(54.9)	
65–69	326	(3.0)	140	(42.9)	186	(57.1)	
70–74	406	(3.7)	142	(35.0)	264	(65.0)	
75–79	560	(5.1)	184	(32.9)	376	(67.1)	
80–84	522	(4.7)	140	(26.8)	382	(73.2)	

Variables	Total N=11,033		Discharge status				P value
	n	(%)	Alive		Death		
85+	486	(4.4)	118	(24.3)	368	(75.7)	
Missing	13	(0.1)	1	(7.7)	12	(92.3)	
Sex							
Female	3,073	(27.9)	1,640	(53.4)	1,433	(46.6)	<0.001
Male	7,956	(72.1)	4,553	(57.2)	3,403	(42.8)	
Missing	4	(0.0)	1	(25.0)	3	(75.0)	
Pre-existing conditions							
No	6,167	(55.9)	3,533	(57.3)	2,634	(42.7)	0.006
Yes	4,866	(44.1)	2,661	(54.7)	2,205	(45.3)	
Penetrating intra-cranial injury							
No	2,634	(23.9)	1,213	(46.1)	1,421	(53.9)	<0.001
Yes	8,399	(76.1)	4,981	(59.3)	3,418	(40.7)	
Head-neck abbreviated injury scale							
4 (Severe)	10,348	(93.8)	5,982	(57.8)	4,366	(42.2)	<0.001
5 (Critical)	535	(4.8)	170	(31.8)	365	(68.2)	
6 (Unsurvivable)	150	(1.4)	42	(28.0)	108	(72.0)	
New injury severity score (NISS)							
Mean [SD]	39.2	[11.3]	37.8	[10.2]	41.0	[12.4]	<0.001
Median [PR]	41	[34–48]	41	[34–48]	41	[34–48]	
16–25	1,258	(11.4)	731	(58.1)	527	(41.9)	<0.001
26–35	3,503	(31.8)	2,232	(63.7)	1,271	(36.3)	
36–45	2,411	(21.9)	1,456	(60.4)	955	(39.6)	
46–55	3,251	(29.5)	1,582	(48.7)	1,669	(51.3)	
56–65	298	(2.7)	122	(40.9)	176	(59.1)	
66–75	312	(2.8)	71	(22.8)	241	(77.2)	
Severe extra-cranial injuries							
No	10,038	(91.0)	5,748	(57.3)	4,290	(42.7)	<0.001
Yes	995	(9.0)	446	(44.8)	549	(55.2)	
Time between injury and admission (days)							

Variables	Total N=11,033		Discharge status				P value
	n	(%)	Alive		Death		
	n	(%)	n	(%)	n	(%)	
First day	9,886	(89.6)	5,507	(55.7)	4,379	(44.3)	0.050
Second day	887	(8.0)	530	(59.8)	357	(40.2)	
Third day	234	(2.1)	137	(58.5)	97	(41.5)	
Missing	26	(0.2)	20	(76.9)	6	(23.1)	
Pre-hospital fluids							
None infused	498	(4.5)	237	(47.6)	261	(52.4)	<0.001
<500ml	1,953	(17.7)	1,175	(60.2)	778	(39.8)	
500ml–2000ml	2,500	(22.7)	1,526	(61.0)	974	(39.0)	
>2000ml	310	(2.8)	181	(58.4)	129	(41.6)	
IV fluids unknown	5,772	(52.3)	3,075	(53.3)	2,697	(46.7)	
Systolic blood pressure (mmHg)							
Mean [SD]	125.3	[49.6]	136.9	[33.4]	110.4	[61.6]	<0.001
Median [PR]	132	[105–154]	138	[117–156]	121	[79–152]	
<49	853	(7.7)	48	(5.6)	805	(94.4)	<0.001
50–69	290	(2.6)	84	(29.0)	206	(71.0)	
70–109	1,830	(16.6)	896	(49.0)	934	(51.0)	
110–129	2,029	(18.4)	1,354	(66.7)	675	(33.3)	
130–159	3,466	(31.4)	2,349	(67.8)	1,117	(32.2)	
>159	2,310	(20.9)	1,347	(58.3)	963	(41.7)	
Missing	255	(2.3)	116	(45.5)	139	(54.5)	
Glasgow coma scale							
3	8,243	(74.7)	4,296	(52.1)	3,947	(47.9)	<0.001
4	411	(3.7)	201	(48.9)	210	(51.1)	
5	435	(3.9)	264	(60.7)	171	(39.3)	
6	737	(6.7)	502	(68.1)	235	(31.9)	
7	721	(6.5)	540	(74.9)	181	(25.1)	
8	486	(4.4)	391	(80.5)	95	(19.5)	

standard deviation ; PR, 25th and 75th percentile range

Table 2

Association of admission spontaneous hypothermia with in-hospital mortality in patients with severe traumatic brain injury (N=11,033)

	Unadjusted comparison			Adjusted logistic regression		
	OR	95%CI	P	OR	95%CI	P
Admission spontaneous hypothermia (35° Celsius)	1.95	1.75–2.17	<0.001	1.70	1.50–1.93	<0.001
Sensitivity analyses						
Missing data = Hypothermia	2.22	2.05–2.41	<0.001	1.57	1.43–1.74	<0.001
Missing data = Normothermia	1.60	1.44–1.78	<0.001	1.58	1.40–1.79	<0.001

OR, odds ratio; CI, confidence interval

Subgroup analysis – Association of admission spontaneous hypothermia with in-hospital mortality in patients with virtually survivable (Head-neck AIS 4–5 and Glasgow coma scale 4–8) severe traumatic brain injury (N=2,773)

	Unadjusted comparison			Adjusted logistic regression		
	OR	95%CI	P	OR	95%CI	P
Admission spontaneous hypothermia (35° Celsius)	1.95	1.52–2.51	<0.001	2.15	1.57–2.95	<0.001
Sensitivity analyses						
Missing data = Hypothermia	1.72	1.44–2.07	<0.001	1.77	1.41–2.23	<0.001
Missing data = Normothermia	1.82	1.42–2.33	<0.001	1.98	1.46–2.69	<0.001

OR, odds ratio; CI, confidence interval