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Impact of accidental hypothermia in trauma patients: A retrospective cohort study

Mozdalefa Azarkane *, Tim W.H. Rijnhout, Isa A.L. van Merwijk, Tjarda N. Tromp, Edward C.T.H. Tan

Department of Trauma Surgery, Radboud University Medical Center, Nijmegen, the Netherlands

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ABSTRACT

Background: Trauma patients with hypothermia have substantial increases in mortality and morbidity. In severely injured patients, hypothermia is common with a rate up to 50% in various geographic areas. This study aims to elucidate the incidence, predictors, and impact of hypothermia on outcomes in severely injured patients. Methods: This was a retrospective cohort study which included trauma patients with an Injury Severity Score (ISS) ≥ 16 admitted to a level 1 trauma center in the Netherlands between January 1, 2015 and December 31, 2021. Primary outcome was incidence of hypothermia on arrival at the emergency department. Factors associated with hypothermia were identified. Secondary outcomes were transfusion requirement, mortality, and intensive care unit (ICU) admission. Logistic regression analysis was used to identify associations.

Results: A total of 2032 severely injured patients were included of which 257 (12.6%) were hypothermic on hospital arrival. Predictors for hypothermia on hospital arrival included higher ISS, prehospital intubation, cervical spine immobilization, winter months, systolic blood pressure (SBP) < 90 mmHg and Glasgow Coma Scale (GCS) ≤ 8. Hypothermia was independently associated with transfusion requirement (OR, 2.68; 95% CI, 1.94 - 3.73; p < 0.001), mortality (OR, 2.12; 95% CI, 1.40 - 3.19; p < 0.001) and more often ICU admission (OR, 1.81; 95% CI, 1.10 - 2.97, p = 0.019).

Conclusions: In this study, hypothermia was present in 12.6% of severely injured patients. Hypothermia was associated with increased transfusion requirement, mortality, and ICU admission. Identified predictors for hypothermia included the severity of injury, intubation, and immobilization, as well as winter season, SBP < 90 mmHg, and GCS ≤ 8 .

Introduction

Traumatic injury remains one of the leading causes of death, accounting for 8% of all deaths worldwide [1]. Severely injured patients are continuously prone to suffer from accidental hypothermia during each phase of trauma care. On hospital arrival, the incidence of hypothermia in trauma patients is reported between 5 and 14% in various geographic regions [2–4] and increases to 50% at higher injury severity score [5.6].

Previously, it has been shown that hypothermia is more likely to emerge in trauma patients with hemorrhage, environmental exposure, infusion of non-warmed intravenous fluids, and as a side effect of anesthetic drugs [2,6,7]. Current knowledge has been evolved into a better understanding of hypothermia with identification of several factors associated with hypothermia in trauma patients. However, these

studies are sparse and limited to prehospital setting or focused on a subcategory of trauma patients such as burned patients [2,7-12].

Together with acidosis and coagulopathy, hypothermia is part of the trauma triad of death in which each component may exacerbate the other and accelerates to death [5,6,13,14]. In the last two decades multiple studies identified hypothermia as an independent risk factor for mortality in severely injured patients, with an associated mortality rate varying between 25 and 40% [3,4,8,15].

To date, several studies conducted in Australia, Canada, and Germany in a tropical and arid, cold, and partly temperate climate zone, respectively, have aimed to explore the incidence and predictors of accidental hypothermia among severely injured patients [3,7-9,16]. With this study, we aim to add to this body of knowledge on incidence and predictors of accidental hypothermia in severely injured patients on hospital arrival. The secondary aim is to investigate the relationship

^{*} Corresponding author at: Department of Trauma Surgery, Geert Grooteplein Zuid 10, 6525 GA Nijmegen, the Netherlands. E-mail address: mozdalefa.azarkane@radboudumc.nl (M. Azarkane).

between hypothermia and the outcomes regarding transfusion requirement, mortality, and intensive care unit (ICU) admission.

Methods

Study design, setting and participants

This is a single center retrospective cohort study including data from trauma patients with an Injury Severity Score (ISS) ≥ 16 . Patients were included after admission to a level 1 trauma center (Radboud University Medical Center, Nijmegen) from January 1st, 2015 to December 31st, 2021. Patients with therapeutic hypothermia (e.g., after cardiopulmonary resuscitation), body temperature $\geq 38.0~^{\circ}\text{C}$ as well as patients with an unknown body temperature at the emergency department (ED) were excluded from analysis. Hypothermia was defined as body temperature $< 35.0~^{\circ}\text{C}$ in injured patients. Body temperature measurement was mainly performed with a tympanic thermometer (Genius $^{\text{TM}}$ 3, Cardinal Health). In more severe hypothermic patients, more accurate devices such as rectal or esophageal probes were used.

Data collection

Data was collected using the database of our trauma region, as part of the Dutch National Trauma Registry (DNTR). The DNTR contains prospectively collected data on all trauma patients admitted to the hospital through the ED, within 48 h after trauma. Additional data was collected from the electronic health records. All data from both resources were merged in an electronic database (Castor Electronic Data Capture).

Patient characteristics and outcome measures

Demographic variables age, gender, weight, and American Society of Anesthesiologists (ASA) score were obtained. Other variables were ISS, Abbreviated Injury Scale (AIS), type of injury, mechanism of injury, prehospital intubation, cervical spine immobilization with headblocks (indicating an uncleared cervical spine after primary survey, e.g., patients without penetrating injuries), and mode of transport. Variables on environmental conditions including trauma location and season were extracted as well.

Furthermore, in-hospital vital parameters and treatment variables were collected. Laboratory values regarding coagulation and acidosis were also collected and corrected for body temperature by the laboratory. Details on extracted variables are demonstrated in Table 1.

Primary outcome was incidence of hypothermia on arrival at the ED. Secondary outcomes were transfusion requirement, mortality and ICU admission.

Statistical analysis

All data was analyzed using SPSS (version 27.0). Categorical variables were expressed as numbers and percentages (n,%) and continuous variables as median and interquartile ranges (median, IQR) or mean and standard deviations (mean, SD). Comparisons between the hypothermia - and normothermia group for categorical variables were performed using the Pearson chi-squared test, Yates' continuity correction, and Fisher's exact test depending on the size of the groups. Comparison of continuous variables was done using independent t tests or Mann-Whitney U test. Depending on the distribution a choice was made on which test to use. To identify independent factors associated with accidental hypothermia a multivariable analysis was performed by logistic regression. Factors entered in logistic regression were variables with a p < 0.1 in univariate analysis. The association between accidental hypothermia and secondary outcomes were analyzed using logistic regression. A *p*-value < 0.05 was considered significant. The assumption of non-linearity in logistic regression was tested using the Box-Tidwell test. A p-value above 0.05 confirmed linear association between the continuous variable and dependent variable.

Results

From January 2015 until December 2021, 2585 severely injured patients were transported to the ED. Of these patients, 48 were excluded due to therapeutic hypothermia and 83 were excluded due to a body temperature $\geq 38.0\,^{\circ}$ C. Patients with an unknown body temperature at the ED were also excluded (16.3%, [n=422]), leaving 2032 patients for analysis (Fig. 1).

In total, 257 (12.6% [95% CI, 11.2 - 14.1]) patients were hypothermic on hospital arrival. The majority of patients suffered from mild hypothermia (89.9% [n=231]). Moderate and severe hypothermia were observed in 6.6% (n = 17) and 3.5% (n = 9) of cases respectively. No differences were found in demographic variables between normothermic and hypothermic patients. Hypothermic patients were more severely injured, had more often a SBP < 90 and a GCS ≤ 8 on hospital. They were more frequently intubated after sedation and administration of muscle relaxants in the prehospital setting and underwent more often cervical spine immobilization. Thermic injury, explosion injury, drowning or asphyxia was more frequent in patients with hypothermia. Hypothermic patients were more frequently transported by helicopter. During winter months, hypothermic patients were more often admitted to the emergency department. Detailed data on demographics, injury characteristics, environmental conditions, physiology, and treatment is demonstrated in Table 1..

Predictors for hypothermia

Independent predictors for accidental hypothermia on arrival at the ED were higher ISS (OR, 1.03; 95% CI, 1.01 – 1.05; p < 0.001), prehospital intubation (OR, 1.83; 95% CI, 1.22 – 2.74; p = 0.004), cervical spine immobilization (OR, 2.54; 95% CI, 1.52 – 4.27; p < 0.001), winter months (OR, 2.68; 95% CI, 1.95 – 3.67; p < 0.001), SBP < 90 mmHg (OR, 4.15; 95% CI, 2.75 – 6.27; p < 0.001) and GCS \leq 8 on hospital arrival (OR, 2.82; 95% CI, 1.85 – 4.27; p < 0.001) (Table 3). Since missing data (majority cervical spine immobilization) resulted in 248 hypothermic patients (96%) and 1745 normothermic patients (98%) included in regression analysis, an additional regression analysis was performed without the variable cervical spine immobilization. Results were still very similar to the original regression analysis resulting in similar predictors for hypothermia on hospital arrival. (Supplementary file, Table 3S).

Coagulation and transfusion requirement

Patients with hypothermia were more acidotic and coagulopathic on hospital arrival, and received significantly more units of red blood cells, platelets, and plasma (Table 1). They received significantly more often blood products in the first 24 h after hospital admission (37.7% [n=97] vs 11.3% [n=201], p<0.001), and massive transfusion protocol (MTP) was significantly more often activated in the hypothermic group (22.2% [n=57] vs 3.4% [n=60], p<0.001) (Table 2). Logistic regression analysis showed that hypothermic patients were 2.7 times more likely to receive blood products compared to normothermic patients (OR, 2.68; 95% CI, 1.94 – 3.73; p<0.001). Similarly, MTP activation occurred significantly more often in hypothermic patients (OR, 4.32; 95% CI, 2.78 – 6.72; p<0.001) (Table 4). Details regarding adjustment for potential confounders were shown in Table 4S.

Mortality and ICU admission

There was significant difference in mortality rate (43.2% [n=111] vs 14.5% [n=258], p<0.001) and in ICU admission (85.2% [n=219] vs 62.1% [n=1102], p<0.001) between hypothermic and normothermic patients (Table 2). In logistic regression, hypothermia was

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Table 1Baseline characteristics in severely injured patients on hospital arrival.

Demographics	Total population ($N = 2032$)	Hypothermia ($N = 257$)	Normothermia ($N = 1775$)	p value
Age, median (IQR)	53 (28–69)	53 (26–67)	53 (28–70)	0.376
Male, n (%)	1373 (67.6%)	163 (63.4%)	1210 (68.2%)	0.129
Veight, median (IQR)	75 (64–85)	73 (63–82.3)	75 (64–85.1)	0.127
Jndocumented, n (%)	319 (15.7%)	54 (21%)	265 (14.9%)	
Comorbidity ASA (1–4), n (%)				0.359
ASA 1–2	1574 (77.5%)	205 (79.8%)	1369 (77.2%)	
ASA 3–4	456 (22.4%)	52 (20.2%)	404 (22.8%)	
Undocumented, n (%)	2 (0.1%)	0	2 (0.1%)	
njury characteristics				
SS, median (IQR)	22 (17–29)	27 (22–37) 0	21 (17–26)	<0.00
Jndocumented, n (%) AIS, n (%)	4 (0.2%)	U	4 (0.2%)	
AIS head ≥ 3	1310 (68.8%)	183 (75.9%)	1127 (67.8%)	0.016
AIS face ≥ 3	112 (7.0%)	16 (8.2%)	96 (6.9%)	0.501
AIS chest ≥ 3	742 (43.3%)	114 (50.4%)	682 (42.2%)	0.005
AIS abdomen ≥ 3	231 (15.0%)	28 (14.3%)	203 (15.1%)	0.767
AIS pelvis/extremities ≥ 3	291 (17.3%)	41 (19.6%)	250 (17.0%)	0.344
AIS external ≥ 3	37 (2.7%)	23 (12.6%)	14 (1.2%)	<0.00
Type of injury, n (%)	07 (21770)	20 (121070)	11 (11270)	0.045
Blunt injury	1979 (97.4%)	245 (95.3%)	1734 (97.7%)	3.0 10
Penetrating injury	53 (2.6%)	12 (4.7%)	41 (2.3%)	
Mechanism of injury, n (%)		Ç		
Traffic accident	1031 (50.7%)	114 (44.4%)	917 (51.7%)	0.029
Shooting/stabbing	46 (2.3%)	10 (3.9%)	36 (2.0%)	0.029
Low energy fall	408 (20.1%)	50 (19.5%)	358 (20.2%)	0.789
High energy fall	346 (17.0%)	47 (18.3%)	299 (16.8%)	0.565
Assault with blunt object	22 (1.1%)	0	22 (1.2%)	0.100
Other (explosion, thermic, drowning, asphyxia)	175 (8.6%)	36 (14.0%)	139 (7.8%)	0.001
Prehospital intubation, n (%)	597 (29.4%)	157 (61.1%)	440 (24.8%)	<0.00
Cervical spine immobilization, n (%)	1581 (79.2%)	226 (91.1%)	1355 (77.5%)	< 0.00
Indocumented, n (%)	35 (1.7%)	9 (3.5%)	24 (1.4%)	
Mode of transport, n (%)	20 (21/13)	. (6.6.4)	_ , (_, , , , ,	0.009
Ground ambulance	1758 (86.5%)	209 (81.3%)	1549 (87.3%)	
Helicopter ambulance	274 (13.5%)	48 (18.7%)	226 (12.7%)	
Environmental conditions				
Гrauma location, n (%)				0.785
Indoor	320 (15.7%)	42 (16.3%)	278 (15.7%)	
Outdoor	1710 (84.2%)	215 (83.7%)	1495 (84.3%)	
Undocumented, n (%)	2 (0.1%)	0	2 (0.1%)	
Season, n (%)				
Winter (1 December - 28 February)	447 (22.0%)	79 (37.7%)	350 (19.7%)	< 0.00
Spring (1 March - 31 May)	477 (23.5%)	71 (27.6%)	406 (22.9%)	
Summer (1 June - 31 August)	584 (28.7%)	34 (13.2%)	550 (31.0%)	
Fall (1 September - 30 November)	524 (25.8%)	55 (21.4%)	469 (26.4%)	
Arrival emergency department				
Time from injury to hospital arrival,	62 (50–76)	59 (49–78)	62 (50–76)	0.941
min, median (IQR) Undocumented, n (%)	1091 (53.7%)	132 (51.4%)	959 (54%)	
Vitals emergency department				
Respiratory rate, breaths/min, median (IQR)	16 (15–20)	16 (14–20)	16 (15–20)	0.323
Jndocumented, n (%)	23 (1.1%)	12 (4.7%)	11 (0.6%)	0.020
Saturation,%, median (IQR)	99 (97 –100)	99 (97–100)	99 (97–100)	0.134
	JJ (J) 100)	9 (3.5%)	8 (0.5%)	0.134
· · ·	17 (0.8%)			
Jndocumented, n (%)	17 (0.8%) 150 (7.4%)		83 (4.7%)	<0.00
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%)	150 (7.4%)	67 (26.1%)	83 (4.7%) 85 (73–98)	
Jndocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR)	150 (7.4%) 85 (72–98)	67 (26.1%) 82 (68–99)	85 (73–98)	< 0.0 0 0.164
Jndocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Jndocumented, n (%)	150 (7.4%)	67 (26.1%)		0.164
Jndocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Jndocumented, n (%) Glasgow Coma Scale, n (%)	150 (7.4%) 85 (72–98) 7 (0.3%)	67 (26.1%) 82 (68–99) 7 (2.6%)	85 (73–98)	0.164
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%) ≤ 8	150 (7.4%) 85 (72–98) 7 (0.3%) 684 (33.7%)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%)	85 (73–98) 0 507 (28.6%)	<0.00 0.164 <0.00
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%) ≤ 8 Undocumented, n (%)	150 (7.4%) 85 (72–98) 7 (0.3%)	67 (26.1%) 82 (68–99) 7 (2.6%)	85 (73–98) 0	0.164
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%) < 8 Undocumented, n (%) Body temperature, °C, mean (SD)	150 (7.4%) 85 (72–98) 7 (0.3%) 684 (33.7%) 2 (0.1%)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%) 1 (0.4%)	85 (73–98) 0 507 (28.6%) 1 (0.1%)	0.164 < 0.00
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%)	150 (7.4%) 85 (72–98) 7 (0.3%) 684 (33.7%) 2 (0.1%)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%) 1 (0.4%)	85 (73–98) 0 507 (28.6%) 1 (0.1%)	0.164 < 0.00
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%) < 8 Undocumented, n (%) Gody temperature, °C, mean (SD) Acidosis	150 (7.4%) 85 (72–98) 7 (0.3%) 684 (33.7%) 2 (0.1%) 36.1 (1.3)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%) 1 (0.4%) 33.7 (1.9)	85 (73–98) 0 507 (28.6%) 1 (0.1%) 36.4 (0.7)	0.164 < 0.00
Jndocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Jndocumented, n (%) Glasgow Coma Scale, n (%) ≤ 8 Jndocumented, n (%) Body temperature, °C, mean (SD) Acidosis Base excess, mmol/L, median (IQR) Jndocumented, n (%) OH, median (IQR)	150 (7.4%) 85 (72–98) 7 (0.3%) 684 (33.7%) 2 (0.1%) 36.1 (1.3) -2.7 (-4.90.9) 316 (15.5%) 7.33 (7.28–7.38)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%) 1 (0.4%) 33.7 (1.9) -5.5 (-11.12.8)	85 (73–98) 0 507 (28.6%) 1 (0.1%) 36.4 (0.7) -2.3 (-4.30.7)	0.164 <0.00 - <0.00
Undocumented, n (%) Systolic Blood Pressure < 90 mmHg, n (%) Heart rate, beats/min, median (IQR) Undocumented, n (%) Glasgow Coma Scale, n (%) \$\leq 8\$ Undocumented, n (%) Body temperature, °C, mean (SD) Acidosis Base excess, mmol/L, median (IQR)	150 (7.4%) 85 (72-98) 7 (0.3%) 684 (33.7%) 2 (0.1%) 36.1 (1.3) -2.7 (-4.90.9) 316 (15.5%)	67 (26.1%) 82 (68–99) 7 (2.6%) 177 (69.1%) 1 (0.4%) 33.7 (1.9) -5.5 (-11.12.8) 24 (9.3%)	85 (73–98) 0 507 (28.6%) 1 (0.1%) 36.4 (0.7) -2.3 (-4.30.7) 292 (16.5%)	0.164 < 0.00

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Table 1 (continued)

	Total population ($N = 2032$)	Hypothermia ($N = 257$)	Normothermia ($N = 1775$)	p value
Demographics				•
Undocumented, n (%)	316 (15.5%)	21 (8.2%)	295 (16.6%)	
Coagulation				
INR, sec, median (IQR)	1.1 (1.0–1.2)	1.2 (1.1–1.3)	1.1 (1.0–1.2)	< 0.001
Undocumented, n (%)	485 (23.9%)	46 (17.9%)	439 (24.7%)	
APTT, sec, median (IQR)	29 (27-32)	31 (28–37)	28 (26-31)	< 0.001
Undocumented, n (%)	514 (25.3%)	49 (19.1%)	465 (26.2%)	
PT, sec, median (IQR)	15 (14–17)	17 (15–19)	15 (14–17)	< 0.001
Undocumented, n (%)	509 (25%)	42 (16.3%)	467 (26.3%)	
Fibrinogen, g/L, median (IQR)	2.57 (2.05-3.15)	2.11 (1.55-2.82)	2.62 (2.11-3.20)	< 0.001
Undocumented, n (%)	559 (27.5%)	47 (18.3%)	512 (28.8%)	
Calcium, mmol/L, median (IQR)	1.16 (1.13–1.20)	1.15 (1.12-1.20)	1.17 (1.13-1.20)	0.064
Undocumented, n (%)	325 (16%)	21 (8.2%)	304 (17.1%)	
Treatment				
Emergency intervention, n (%)	375 (18.5%)	86 (33.5%)	289 (16.3%)	< 0.001
Red blood cells ≤24 h, median (IQR)	2 (2-4)	3 (2–5)	2 (2–3)	< 0.001
Platelets ≤24 h, median (IQR)	1 (1–2)	2 (1–2)	1 (1–2)	< 0.001
Plasma ≤24 h, median (IQR)	2 (2-4)	3 (2–5)	2 (2-4)	< 0.001
Rewarming methods applied, n (%)				
- Passive rewarming	19 (0.9%)	15 (5.8%)	4 (0.2%)	$< 0.001^{a}$
- Active external rewarming	49 (2.4%)	31 (12.1%)	18 (1.0%)	< 0.001 ^b
- Active internal rewarming	28 (1.4%)	21 (8.2%)	7 (0.4%)	< 0.001 ^a
- Extracorporeal rewarming	1 (0.0%)	1 (0.4%)	0 (0.0%)	-
- Undocumented	1969 (96.9%)	218 (84.8%)	1775 (98.6%)	< 0.001

Continuous variables presented as median and interquartile ranges (median, IQR) or mean and standard deviations (mean, SD) | Categorical variables presented as numbers and percentages (n,%) | ISS=Injury Severity Score; AIS=Abbreviated Injury Scale © 2005, update 2008; ASA=American Society of Anaesthesiology score | Bold p-values are significant values. ^aFisher's exact test. ^bYates' continuity correction. Missing values are reported as undocumented.

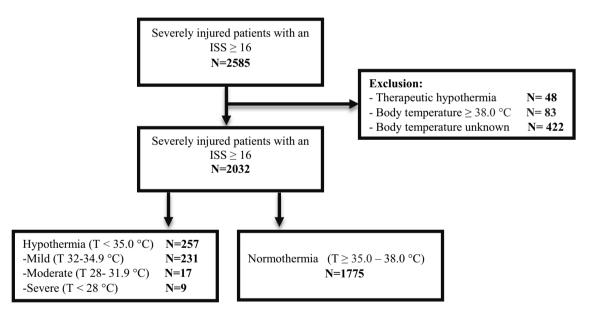


Fig. 1. Flowchart of the study population of severely injured patients on arrival at Radboud University Medical Center Nijmegen from January 1st, 2015 until December 31st, 2021.

associated with a twofold increase in mortality compared with normothermia (OR, 2.12; 95% CI, 1.40 – 3.19; p < 0.001). Further, hypothermic patients were 1.8 times more likely to be admitted to the ICU than normothermic patients (OR, 1.81; 95% CI, 1.10 – 2.97; p = 0.019) (Table 5). Likewise, details regarding adjustment for potential confounders were shown in Table 5S.

Discussion

This retrospective study investigated the incidence, predictors, and impact of accidental hypothermia in severely injured patients. The

incidence of hypothermia on hospital arrival was 12.6%. Our secondary findings were threefold; severely injured patients with hypothermia required more often blood products, showed a higher mortality rate and were more likely to be admitted to the ICU. Six predictors of hypothermia on hospital arrival were identified including: higher ISS, prehospital intubation, cervical spine immobilization, winter months, SBP $<90~\rm mmHg$, and GCS ≤ 8 .

Although variable rates as high as 50% have been reported in various geographic regions [5,17-19], this study reported a relatively low rate of 12.6%. Similar rates of hypothermia were found in countries with relatively short transport times to the treating hospital [2,7]. Another

 Table 2

 Comparison of outcomes between study groups.

	Total population $(N = 2032)$	Hypothermic $(N = 257)$	Normothermic $(N = 1775)$	p value
Outcome				
ICU admission, n (%)	1321 (65.0%)	219 (85.2%)	1102 (62.1%)	< 0.001
No ICU admission, n (%)	711 (35%)	38 (14.8%)	673 (37.9%)	
Mortality				
-Overall mortality, n (%)	369 (18.2%)	111 (43.2%)	258 (14.5%)	< 0.001
-30 d mortality, n (%)	369 (18.2%)	111 (43.2%)	258 (14.5%)	< 0.001
MTP activation, n (%)	117 (5.8%)	57 (22.2%)	60 (3.4%)	< 0.001
No MTP activation, n (%)	1915 (94.2%)	200 (77.8%)	1715 (96.6%)	
Received blood products ≤24 h, n (%)	298 (14.7%)	97 (37.7%)	201 (11.3%)	< 0.001
No blood products ≤24 h, n (%)	1734 (85.3%)	160 (62.3%)	1574 (88.7%)	
=				

Categorical variables presented as numbers and percentages (n,%) | ICU=Intensive Care Unit; MTP=Massive Transfusion Protocol | Bold p-values are significant values. No missing values.

 $\begin{tabular}{ll} \textbf{Table 3} \\ \textbf{Factors independently associated with accidental hypothermia in multivariable} \, . \end{tabular}$

Variable	OR	95% CI	p value
ISS	1.03	1.01 - 1.05	< 0.001
AIS head ≥ 3	0.79	0.54 - 1.16	0.225
AIS chest ≥ 3	1.02	0.72 - 1.46	0.900
Traffic accident	0.59	0.43 - 0.81	< 0.001
Type of injury			
- Blunt (reference)			
- Penetrating	2.00	0.88 - 4.50	0.096
Prehospital intubation	1.83	1.22 - 2.74	0.004
Cervical spine immobilization	2.54	1.52 - 4.27	< 0.001
Mode of transport			
- Ground ambulance (reference)			
- Helicopter ambulance	0.84	0.57 - 1.25	0.386
Winter	2.68	1.95 - 3.67	< 0.001
Hypotension	4.15	2.75 - 6.27	< 0.001
GCS ≤ 8	2.82	1.85 – 4.27	<0.001

ISS, Injury Severity Score; AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale | OR, Odds Ratio; CI, Confidence Interval | Bold variables are independent predictors for hypothermia.

Categorized variables included: AIS head ≥ 3 (≥ 3 vs < 3), AIS chest ≥ 3 (≥ 3 vs < 3), Traffic accident (yes vs no), Type of injury (blunt vs penetrating), Prehospital intubation (yes vs no), Cervical spine immobilization (yes vs no), Mode of transport (ground ambulance vs helicopter), Winter (yes vs no), Hypotension (< 90 vs ≥ 90), GCS ≤ 8 (≤ 8 vs > 8). | N = 248 hypothermic patients. 1 missing from GCS, and 8 missing from cervical spine immobilization.

contributor to the relatively low incidence, may be the difference in awareness of hypothermia as our EMS system consists of highly trained registered nurses. Documentation of body temperature still failed in 16.3% of cases, whereas body temperature measurement is part of the initial assessment of a trauma patient. This observation is not unique with several studies reporting missing documentation in up to 68% of cases [7,20,21], which suggests that hypothermia is still an overlooked and possibly undertreated entity in trauma care. In addition, with a rate of even 12.6% in our temperate climate zone and reported rates of 13% in warm climate zones [3,8], hypothermia is a global occurrence in trauma care which warrants widespread awareness.

Table 4 Adjusted outcomes for severely injured patients with hypothermia.

	OR (95% CI)	<i>p</i> -value
Received blood products	2.68 (1.94 – 3.73)	< 0.001
MTP-activation	4.32 (2.78 – 6.72)	< 0.001

Adjusted for injury severity, hypotension and type of injury.

Categorized variables included hypothermia, hypotension, type of injury, received blood products and MTP activation. MTP activation n=117; received blood products n=298.

See Table 4S for details.

Table 5 Adjusted outcomes for severely injured patients with hypothermia.

	OR (95% CI)	<i>p</i> -value
Mortality	2.12 (1.40 – 3.19)	< 0.001
ICU-admission	1.81 (1.10 – 2.97)	0.019

Adjusted for age, injury severity, type of injury, comorbidities, hypotension, heart rate

 $\mbox{GCS} \leq 8,$ saturation , respiratory rate, blood products transfusion, emergency intervention.

Categorized variables included type of injury, comorbidities, hypotension, GCS \leq 8, blood products transfusion, emergency intervention. Mortality n=346; ICU-admission n=1307.

See Table 5S for details.

In contrast to the impact of hypothermia on transfusion requirement in severely injured patients, the effect of hypothermia on coagulopathy is well established [22]. Several pathways are described in which hypothermia can impair hemostasis including reduced platelet function, reduced coagulation factor function, and increased fibrinolysis [22,23]. It has been demonstrated that at temperatures between 37 and 33 $^{\circ}\text{C}$ hemostatic defects primarily result from impairments in platelet adhesion/aggregation. When temperature drops below 33 °C, reduced platelet function and coagulation enzyme activity both contribute to coagulopathy [23]. In trauma patients, Ireland et al. reported significant differences in coagulopathy parameters between hypothermic and normothermic patients, and no difference in transfusion requirement [3]. In contrast, Mommsen et al. and Winkelmann et al. reported a significant increase in transfusion requirement in severely injured hypothermic patients compared to normothermic patients [5,24]. With a mean ISS of 31.2 and 35.6 respectively, both study populations consisted of hypothermic patients with more severe injuries compared to our study population. One could argue that their findings indicate that hypothermia could be a marker for injury severity which results in transfusion requirement. In our study, patients with hypothermia required more often blood products after correcting for confounders such as injury severity. The multifactorial and interconnected causes of traumatic coagulopathy including hypothermia, contribute all to the need of transfusion after trauma. Therefore, measures for hypothermia prevention and treatment are crucial in order to optimize coagulation in trauma patients.

Multiple studies aimed to investigate the effect of hypothermia on mortality in severely injured patients [3-5,8,15]. Most studies reported a significant association, even after adjustment for injury severity and other confounders [3,4,8,15]. A recent systematic review and meta-analysis studies found a strong association with mortality in trauma patients [25]. Our data support these findings, as hypothermia is in this study with an OR of 2.12 (95% CI 1.40-3.19) significantly associated with mortality and falls into the OR range of 1.54 and 4.05

reported in previous studies [3,4,8,15]. The same applies for the association with ICU admission, which is described in our study to occur nearly two times more likely in hypothermic trauma patients [5,8,15]. This finding suggests an additional effect of accidental hypothermia on physiological derangements in severely injured patients.

Regarding the identified predictors for hypothermia, our results are in line with previous studies on severely injured patients including one prospective study [3,7,9]. In addition to these studies, patients with cervical spine immobilization appeared in our study to be associated with an increased risk of hypothermia. This can be explained by the fact that continued immobilization of the patient could result in a decreased heat production, and that thermoregulation may be impaired due to caused injury to the cervical spine [26]. Additionally, cervical spine immobilization could hamper body temperature measurement through the conventional tympanic site which may result in a delayed recognition of decrease in body temperature.

Limitations

Besides the common drawbacks of retrospective and single center studies, several other limitations need to be acknowledged. In relation to the identified association between hypothermia and adverse outcomes. it should be first emphasized that our results are not causative. Further, several limitations regarding body temperature measurement need to be mentioned. First, the limited temperature detection range of tympanic thermometers could result in an underdiagnosis of hypothermia. Second, although the conventional temperature measurement site at the emergency department was tympanic, the route of temperature measurement was frequently undocumented, might in some cases differ between patients and might therefore result in a varied accuracy of body temperature [27]. Third, although demographics and injury severity of the excluded patients without documented temperature (16.3%) were comparable with the included cohort, bias of our results cannot be excluded. Further, not all possible confounders for hypothermia were controlled for due to inability to collect this data in retrospect (e.g., any rewarming method applied, prehospital infusion of (non-warmed) fluids, wet clothes removal). Finally, no adjustments for coagulation or acidosis parameters have been done for outcomes regarding transfusion requirement due to incomplete data.

Recommendation

Body temperature assessments should be performed through the entire chain of trauma care. Based on these results we suggest applying passive and active rewarming strategies on all severely injured, immobilized, and intubated patients, since these patients are susceptible to develop hypothermia. This can be realized through small interventions such as removal of wet clothing, avoidance of cold surfaces, warming the environment, using warming blankets (preferable a hypothermia wrap, consisting of insulation and a vapor barrier), and avoiding administration of cold fluids [28,29]. On hospital arrival, rewarming can be continued depending on the depth of hypothermia, and more invasive rewarming strategies can be considered such as peritoneal, bladder and thoracic lavage, or extracorporeal rewarming [29]. Although hypothermic patients received various rewarming strategies, our data are not appropriate to draw strong recommendations on effectiveness of different rewarming strategies. Therefore, future studies are warranted to investigate the effectiveness of different rewarming strategies.

Conclusion

In conclusion, our results suggest that accidental hypothermia is a common occurrence in severely injured patients, which is significantly associated with increased transfusion requirement, mortality, and ICU admission. The increasing evidence for adverse outcomes of hypothermia underscores the importance of hypothermia prevention and

treatment.

Declaration of Competing Interest

There are no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2023.110973.

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