Original Article

Derivation of a model to predict mortality in urban patients with accidental hypothermia: a retrospective observational study

Tatsuki Uemura, Akio Kimura, Wataru Matsuda, Ryo Sasaki, and Kentaro Kobayashi

Department of Emergency Medicine and Critical Care, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan

Aim: Accidental hypothermia in urban settings is associated with high mortality rates. However, the predictors of mortality remain under discussion. The purpose of this study was to evaluate prognostic factors and develop a prediction model in patients with accidental hypothermia in urban settings.

Methods: We retrospectively reviewed medical records in patients with hypothermia brought to our hospital by ambulance in a 7-year study period. Patients' records of survival discharge or in-hospital death and clinical data were collected from medical records. We analyzed factors to predict in-hospital death using multiple logistic regression analysis. Recursive partitioning analysis was used to construct a prediction model using predictors from multiple logistic regression analysis.

Results: In the study period, 192 patients were included in this study. Of them, 154 patients were discharged alive and 38 patients died. Multiple logistic regression analysis revealed that in-hospital death was related to Glasgow Coma Scale (GCS) score, prothrombin time – international normalized ratio (PT-INR) value, and fibrin degradation product (FDP). Recursive partitioning analysis revealed that patients with accidental hypothermia could be divided into four groups: very high risk (FDP $\geq$ 14 μg/mL, PT-INR $\geq$ 1.4), high risk (FDP $\geq$ 14 μg/mL, PT-INR $<$ 1.4), moderate risk (FDP $<$ 14 μg/mL, GCS $<$ 10), and low risk (FDP $<$ 14 μg/mL, GCS $\geq$ 10).

Conclusion: High FDP and PT-INR values and low GCS score on arrival at the emergency department were associated with in-hospital mortality in urban patients with hypothermia. A simple prediction model for grouping risk was developed using these predictors.

Key words: Fibrin degradation products, Glasgow Coma Scale, hypothermia, patient outcome assessment, prothrombin time

INTRODUCTION

ACCIDENTAL HYPOTHERMIA IS defined as an unintentional decrease in core body temperature below 35°C. Between 0.3 and 0.5 per 100,000 persons are estimated to die of hypothermia every year in the USA.[1] Patients with hypothermia are treated using active internal rewarming, active external and minimally invasive rewarming techniques, or a combination of these techniques. Active internal rewarming, such as by extracorporeal membrane oxygenation with a heat exchanger, might be used for severe hypothermia. Active external and minimally invasive rewarming techniques involving forced-air warming, electric heating blanket, or warm i.v. drip infusion are usually used for mild-to-moderate hypothermia.

Accidental hypothermia in urban settings differs from that in alpine settings.[2,3] In urban settings, it occurs due to trauma, sepsis, intoxication, stroke, frailty, cold environments, or a combination of these factors (secondary hypothermia). In alpine regions, it frequently occurs due to avalanche, submergence, or cold environments (primary hypothermia). Many previous studies regarding accidental hypothermia have been undertaken in alpine settings, and few studies have been carried out in urban settings. Previous studies have reported that accidental hypothermia in urban settings is associated with a high mortality rate (12%,[4] 26%,[5] 29%,[6] and 47%[7]).

Death in patients with secondary hypothermia is often associated with underlying conditions rather than with severity of hypothermia.[8] However, it is sometimes difficult to

Corresponding: Tatsuki Uemura, MD, Department of Emergency Medicine and Critical Care, Center Hospital of the National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan. E-mail: tuemura@hosp.ncgm.go.jp.
Received 5 Sep, 2019; accepted 24 Nov, 2019

Funding Information

Grant-in-Aid for Research from the National Center for Global Health and Medicine (29-2001)

identify the cause of hypothermia in the emergency department. Few studies have reported potential predictors regarding death in urban patients with hypothermia. Furthermore, to the best of our knowledge, there are only two models to predict mortality in urban patients with accidental hypothermia.[7,9] Neither model has been validated.

Identifying the risk of mortality in urban patients with accidental hypothermia on admission could lead to proper use of medical resources such as intensive care unit (ICU) beds. In addition, accidental hypothermia can often be a problem in the aftermath of disasters, such as severe earthquakes[10] and extreme weather events. It is important for patient triage to understand the risks of patients with accidental hypothermia. Therefore, we undertook a single-center retrospective observational study to evaluate prognostic factors and develop a prediction model for grouping risk of in-hospital death.

METHODS

Study design

WE CARRIED OUT this retrospective, single-center observational study at the Center Hospital of the National Center for Global Health and Medicine, a 781-bed tertiary care teaching medical hospital located in Tokyo (Japan) with approximately 11,000 annual emergency department visits by ambulance.

Study cohort and treatments

Using database and medical records, we identified eligible patients. Patients who were brought by ambulance to our hospital between April 2008 and March 2015 were eligible for this study if they met the inclusion criteria of core body temperature <35°C on arrival, and admission to our hospital or death at the emergency department. The exclusion criteria were age <16 years, cardiac arrest on arrival at the hospital, transfer to another hospital from the emergency department, and a do not attempt resuscitation order on arrival.

We measured core body temperature using a rectal or urinary bladder catheter with a temperature sensor. If patients whose core body temperature was <34°C on arrival, all patients were rewarmed using active external and minimally invasive rewarming techniques in addition to removing all wet clothing. None of the patients was rewarmed with extracorporeal circulation. To avoid temperature overshooting, rewarming was stopped when core body temperature reached 34°C. Patients who had an underlying disease or injury were treated as necessary in addition to temperature management. All patients were followed up until hospital discharge or death.

Assessments

The following physiological data were collected from medical records that were obtained immediately on arrival at the emergency department: core body temperature, respiratory rate, pulse rate, blood pressure, and Glasgow Coma Scale (GCS) score. The following laboratory data were also collected from medical records that were obtained in the emergency department prior to the rewarming procedure: complete blood count, total bilirubin, blood urea nitrogen (BUN), creatinine, sodium, potassium, C-reactive protein (CRP), prothrombin time – international normalized ratio (PT-INR), fibrin degradation product (FDP), and blood gas analysis. The level of FDP was measured by the latex agglutination method using a commercial immunoassay kit (LIAS AUTO P-FDP; Sysmex, Kobe, Japan) with CS-5100 analyzer (Sysmex). The clinical and demographic characteristics, including the patients' age, sex, found indoors/outdoors, and possible causes of hypothermia, were collected from medical records. The disseminated intravascular coagulation (DIC) score of the Japanese Association of Acute Medicine (JAAM)[11] and the Acute Physiology and Chronic Health Evaluation (APACHE II) score were determined within the first 24 h of admission. We created the electronic database and all of the above data were stored.

Statistical analyses

Previous studies have shown that accidental hypothermia in urban settings is associated with a mortality rate of 12%[4] to 47%.[7] A Japanese study revealed the mortality rate in patients with accidental hypothermia as 29%.[6] Therefore, we expected a mortality rate between 19% and 39% to have a ±10% margin. We considered a model based on precision of 90% sensitivity for mortality with a 95% confidence interval of ±10%. The required number of patients with in-hospital death was calculated to be 35. We calculated the required number of patients with accidental hypothermia as between 90 and 184. We designed a 7-year period for this study because the average annual number of patients with accidental hypothermia who came to our institution was approximately 30, although different from year to year.

We divided all eligible patients into two groups: survivors and non-survivors. Clinical and demographic characteristics of patients between the two groups were presented, with continuous variables as medians with interquartile ranges and categorical variables as numbers. Univariable analysis was carried out using the Mann–Whitney *U*-test for

continuous variables and Pearson's χ^2-test for categorical variables. A P-value < 0.05 was considered statistically significant. Missing data were not imputed and handled with pairwise deletion.

Variables that were considered statistically significant in the univariable analyses and were considered clinically meaningful were evaluated using stepwise methods. Multiple logistic regression was undertaken to determine independent factors for hospital death in patients with hypothermia. Receiver operating characteristic (ROC) curves were constructed to predict in-hospital death, and the curves were compared according to the method described by DeLong *et al*.[12]

Using the above factors, we constructed a prediction model for grouping risk in patients with accidental hypothermia by recursive partitioning analysis.[13] Patients who were not measured with the above factors were excluded from constructing a model. The constructed model was evaluated with ROC curves and the corrected Akaike information criterion. All statistical analyses were undertaken using JMP 13.1 (SAS Institute, Cary, NC, USA).

RESULTS

FIGURE 1 shows the flowchart for patient selection. Of 201 candidates with a core body temperature <35°C, 192 patients were included in this study. In total, 154 patients were discharged alive and 38 patients died, and we analyzed data from both groups.

Clinical and demographic characteristics of the two groups are summarized in Table 1. Compared with survivors, non-survivors had significantly higher total bilirubin, creatinine, CRP, PT-INR, and FDP values, and significantly lower GCS score, platelet count, and sodium levels. Non-survivors had significantly higher JAAM DIC and APACHE II scores compared with survivors.

Probable causes of accidental hypothermia in survivors and non-survivors are summarized in Table 2. Intoxication, infection, and frailty were frequent causes of accidental hypothermia. The cause remained unknown in 26 patients. The most common cause of accidental hypothermia was intoxication in survivors (n = 25) and infection in non-survivors (n = 9).

The stepwise method selected GCS, PT-INR, and FDP from the variables that were considered statistically significant in the univariable analyses and were considered clinically meaningful. Lower GCS score, higher PT-INR value, and elevated FDP were found to be independent predictors for in-hospital death in patients with hypothermia (Table 3).

For the three independent predictors, the ROC curves for prediction of in-hospital death and the results of area under the ROC curve (AUC) analysis are shown in Figure 2. The AUC was 0.643 for GCS, 0.727 for PT-INR, and 0.805 for FDP, with FDP showing a significantly higher AUC than GCS score.

Using data from 192 patients, we created a prediction model for in-hospital death in patients with accidental hypothermia. We undertook recursive partitioning analysis using FDP, PT-INR and GCS (Fig. 3). Patients with FDP ≥14 μg/mL had a high risk of in-hospital death and could be divided into a very high-risk group and a high-risk group using a PT-INR cut-off value of 1.4. Patients with FDP

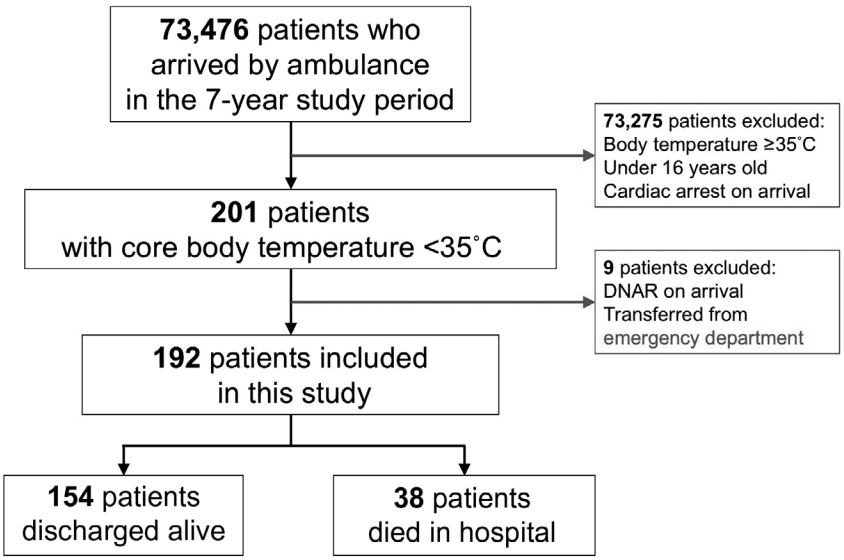


Fig. 1. Patient flow through the study. DNAR, do not attempt resuscitation.

Table 1. Clinical and demographic characteristics of 192 patients with accidental hypothermia

Factor	Survivors (*n* = 154)	Non-survivors (*n* = 38)	*P*-value	Missing (%)
Age, years	71 (60, 82)	77 (63, 86)	0.08	0
Sex, male/female	93/61	25/13	0.54	0
Found indoors/outdoors	103/51	31/7	0.08	0
Vital signs on arrival at the hospital				
Core body temperature (°C)	30.8 (29.0, 32.8)	30.6 (29.0, 32.4)	0.58	0
Respiratory rate (/min)	18 (15, 20)	18 (15, 21)	0.56	0
Pulse rate (/min)	71 (59, 87)	70 (51, 94)	0.66	0
Mean arterial pressure (mmHg)	82 (66, 96)	80 (60, 93)	0.35	0
Glasgow Coma Scale	11 (9, 14)	10 (8, 11)	0.006	0
Laboratory data on arrival				
Total bilirubin (mg/mL)	0.6 (0.4, 1.0)	1.2 (0.7, 2.0)	<0.0001	3 (1.6)
BUN (mg/dL)	36.3 (20.4, 60.2)	54.5 (42.0, 75.2)	0.008	0
Creatinine (mg/dL)	0.95 (0.61, 1.74)	1.72 (0.99, 2.36)	0.003	0
Sodium (mEq/L)	139 (135, 143)	135 (131, 141)	0.04	0
Potassium (mEq/L)	4.1 (3.5, 4.7)	4.4 (3.5, 5.1)	0.25	0
CRP (mg/dL)	1.2 (0.2, 6.5)	4.3 (0.8, 11.4)	0.01	0
WBC (/μL)	9,900 (6,600, 14,500)	10,200 (5,400, 12,400)	0.19	0
Hemoglobin (g/dL)	12.6 (10.5, 14.3)	12.6 (11.3, 14.0)	0.68	0
Platelets (10^4/μL)	19.7 (14.3, 25.3)	14.5 (8.5, 20.0)	0.0005	0
PT-INR	1.14 (1.02, 1.28)	1.40 (1.15, 1.65)	<0.0001	2 (1.0)
FDP (μg/mL)	4.9 (2.0, 8.8)	18.2 (9.6, 49.6)	<0.0001	14 (7.3)
pH	7.27 (7.19, 7.35)	7.24 (7.11, 7.35)	0.44	6 (3.1)
HCO_3 (mmHg)	22.4 (14.6, 27.8)	17.3 (9.6, 25.8)	0.06	10 (5.2)
Lactate (mmol/L)	2.9 (1.6, 7.0)	3.3 (2.3, 9.3)	0.15	43 (22.4)
Severity score				
JAAM DIC score	1 (0, 2)	3 (2, 5)	<0.0001	
APACHE II score	19 (15, 23)	24 (21, 29)	<0.0001	

Data are presented as medians (25th, 75th percentiles) or number.
APACHE, Acute Physiology and Chronic Health Evaluation; BUN, blood urea nitrogen; CRP, C-reactive protein; DIC, disseminated intravascular coagulation; FDP, fibrin degradation product; JAAM, Japanese Association of Acute Medicine; PT-INR, prothrombin time – international normalized ratio; WBC, white blood cells.

<14 μg/mL could be divided into a low-risk group and moderate-risk group using a GCS cut-off score of 10.

Causes of death in patients with hypothermia and values of FDP, PT-INR, and GCS score are summarized in Table 4. Patients who died of trauma, malignancy, intestinal necrosis, gastrointestinal perforation, stroke, and infection tended to have high levels of FDP. Patients who died of stroke tended to have almost normal levels of PT-INR and low GCS scores.

DISCUSSION

WE UNDERTOOK THIS retrospective study to evaluate prognostic factors and develop a prediction model in patients with accidental hypothermia in urban settings. A total 192 patients were included, and we found that FDP and PT-INR values and GCS score were prognostic factors. We also constructed a prediction model using these factors.

The incidence of accidental hypothermia in urban settings is unclear. Accidental hypothermia was suggested to be a rare cause of admission to hospital in a French study.[14] In Japan, there have been few studies of accidental hypothermia and the incidence remains unclear. During the 7-year period of this study, a diagnosis of accidental hypothermia was given to 0.27% of all patients brought to our hospital by ambulance. The in-hospital mortality rate was 20% in the present study, which is slightly lower than 26%[5] or 29%[6] reported in a previous multicenter study in Japan.

In previous studies that have investigated predictors for mortality in urban patients with hypothermia, poor outcome was associated with shock, need for vasoactive drugs,[14] high BUN value, low platelet count,[2] indoor occurrence,[2,15] age

Table 2. Probable causes of accidental hypothermia in survivors and non-survivors

Factor	Survivors (n = 154)	Non-survivors (n = 38)
No. (%)		
Intoxication	25 (16)	1 (3)
Infection	24 (16)	9 (24)
Frailty	23 (15)	6 (16)
Endocrine and metabolic disorders	16 (10)	1 (3)
Trauma	12 (8)	4 (11)
Dementia	10 (6)	0 (0)
Stroke	4 (3)	5 (13)
Others	17 (11)	9 (24)
Unknown	23 (15)	3 (8)

Percentages may not equal 100 because of rounding.

Table 3. Multiple logistic regression analysis for predicting in-hospital death in patients with hypothermia

	Coefficient	*P*-value	Odds ratio	95% CI
GCS	−0.142	0.020	0.868	0.769, 0.978
PT-INR	1.438	0.001	4.213	1.890, 10.706
FDP	0.010	0.031	1.010	1.002, 1.019

CI, confidence interval; FDP, fibrin degradation product; GCS, Glasgow Coma Scale; PT-INR, prothrombin time – international normalized ratio.

75 years old or older, need for assistance with activities of daily living (ADL), hemodynamic instability, and hyperkalemia.[5] Danzl *et al*.[9] advocated a hypothermia outcome score consisting of five parameters: BUN value, systolic blood pressure, with or without prehospital cardiopulmonary resuscitation, need for tracheal intubation, and nasogastric tube placement. Elbaz *et al*.[7] also suggested five parameters as risk factors for in-hospital death in patients with hypothermia in an urban setting in a desert climate: age ≥70 years, mean arterial pressure <90 mmHg, pH < 7.35, creatinine > 1.5 mg/dL, and confusion.

We did not investigate the need for vasoactive drugs, tracheal intubation, and nasogastric tube placement in this study. We thought they were not suitable as predictors because these factors were generally treatment itself. We also did not investigate the need for assistance with ADL. At the emergency department, we often could not understand whether patients need assistance with ADL or not because of their disturbance of consciousness due to hypothermia.

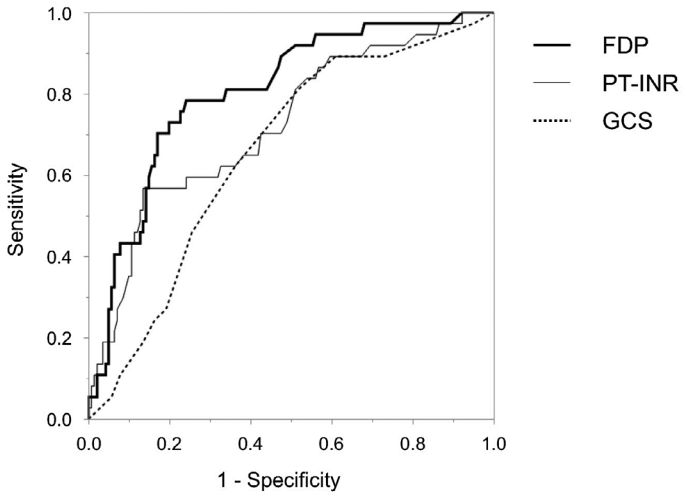
We found the results of the univariable analysis also identified high BUN value, low platelet count, and elevated creatinine as possible predictors for identifying high risk in patients with accidental hypothermia. Indoor occurrence, age, mean arterial pressure, hyperkalemia, and pH were not significantly related to in-hospital mortality in this study. We thought these differences in results might reflect differences of background in patients with hypothermia. Patients in this study were older and fewer were found outdoors compared with a previous study.

In this study, patients with hypothermia due to stroke, infection, frailty, or trauma tended to have high risk of in-hospital mortality (Table 2). Patients with hypothermia in urban areas such as Tokyo tend to have a heterogeneous background. However, it is often difficult to determine the cause of hypothermia in the emergency department, and therefore objective indicators and a model for predicting mortality are needed.

We selected six factors as candidates for constructing a prediction model from results of the univariable analysis and considered clinically meaningful: GCS score, BUN, creatinine, CRP, PT-INR, and FDP. We considered the differences between the two groups in terms of the levels of total bilirubin and sodium or platelet count were not clinically meaningful. From the six factors, stepwise and multiple logistic regression analyses showed that GCS score, PT-INR, and FDP can be predictors of in-hospital mortality in patients with urban accidental hypothermia (Table 3). As mentioned earlier, confusion has been identified as a risk factor for in-hospital death.[7] Because the diagnosis of confusion can be ambiguous, we opted to use the more objective GCS to determine consciousness and confusion.

We constructed a prediction model for grouping risk in patients with accidental hypothermia using GCS, PT-INR, and FDP (Fig. 3). Elbaz *et al*.'s proposed prediction model for in-hospital death in hypothermic patients uses five parameters and had an ROC AUC of 0.81. Our simpler prediction model uses only three objective parameters – FDP, PT-INR, and GCS – and had a slightly higher ROC AUC of 0.84. The corrected Akaike information criterion for this model was 483. We think our prediction model is simple and effective for grouping risk in urban patients with accidental hypothermia in the emergency department.

To the best of our knowledge, this is the first study to identify FDP as a predictor of in-hospital mortality in patients with accidental hypothermia. Fibrin degradation product, in particular, was a strong predictor (Fig. 2). The FDP level is a known prognostic biomarker associated with poor outcome in patients in the ICU.[16] In general, levels of



	AUC	95% CI
GCS	0.643	0.545-0.730
PT-INR	0.727	0.624-0.810
FDP	0.805	0.715-0.871

	p value
GCS - PT-INR	0.38
PT-INR - FDP	0.12
FDP - GCS	0.03

Fig. 2. Receiver operating characteristic (ROC) curves for in-hospital death in patients with accidental hypothermia based on Glasgow Coma Scale (GCS), prothrombin time – international normalized ratio (PT-INR), and fibrin degradation product (FDP). Analysis of areas under the ROC curve (AUC) to predict hospital death in patients with accidental hypothermia and comparison of ROC curves.

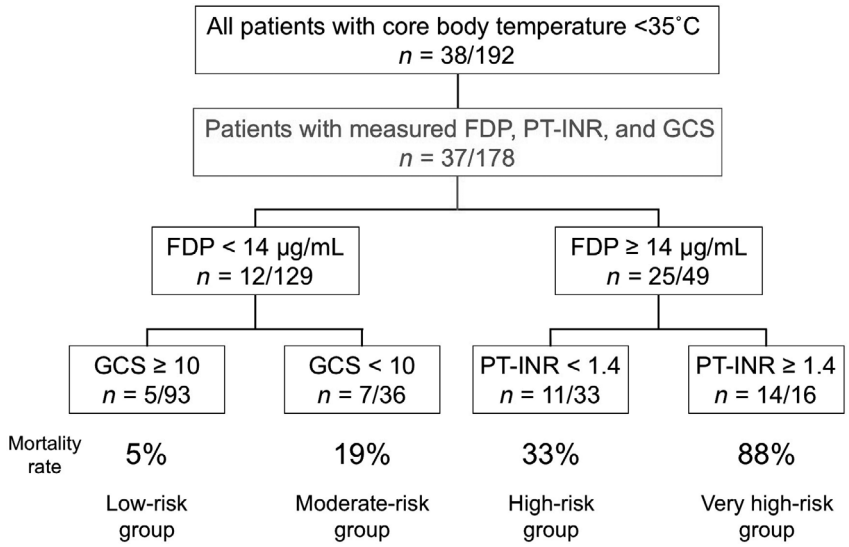


Fig. 3. Prediction model constructed by recursive partitioning analysis grouping high risk in patients with accidental hypothermia. Data are presented as *n* = (patients with hospital death) / (all patients). FDP, fibrin degradation product; GCS, Glasgow Coma Scale; PT-INR, prothrombin time – international normalized ratio.

Table 4. Causes of death in patients with hypothermia and median values of fibrin degradation product (FDP), prothrombin time – international normalized ratio (PT-INR), and Glasgow Coma Scale (GCS) score

Causes	No. (%)	FDP (μg/mL)	PT-INR	GCS
Infection	10 (26)	26.2	1.57	10.5
Multiple organ failure	7 (18)	17.6	1.49	10
Stroke	5 (13)	32.1	1.05	4
Trauma	3 (8)	772.6	1.38	7
ARDS	2 (5)	15.2	1.68	10
Gastrointestinal perforation	2 (5)	39.4	1.32	11.5
Intestinal necrosis	2 (5)	44.0	1.30	8.5
Malignancy	2 (5)	54.7	1.40	12
Others	5 (13)	18.2	1.53	10

Percentages may not equal 100 because of rounding.
ARDS, Acute respiratory distress syndrome.

FDP in patients with infection, trauma, and malignancy are considered to be high. In fact, patients who died of the above causes had high levels of FDP (Table 4). A previous study in patients with stroke also shows that FDP values are high and values of prothrombin time are almost normal.[17] This result appears to be consistent with the result of this study. Given that hypothermia was shown to inhibit fibrinogen synthesis but have no effect on fibrinogen degradation,[18] high FDP values in patients with hypothermia might be suggestive of the presence and severity of underlying disease. Although the number of patients in this study was small, we thought that the levels of FDP and PT-INR and GCS score in patients with hypothermia reflected causes of death. Measurement of FDP, PT-INR, and GCS score might be useful for prognostic prediction of patients with hypothermia in urban settings.

Our study had several limitations. First, this was a single-center retrospective observational study, and our model might be statistically overfitting the data. Therefore, external multicenter validation studies are needed. Second, there were some missing data, including 14 records for FDP and 2 for PT-INR, so a larger data sample is needed to confirm our findings. Finally, we did not investigate direct relationships between predictors and cause of death in patients with hypothermia, because patients with accidental hypothermia in urban settings tend to have a heterogeneous background. The relationship between predictors and death in patients with hypothermia might be understood by comparing patient groups with homogeneous backgrounds.

CONCLUSIONS

HIGH FDP AND PT-INR values and low GCS score on arrival at the emergency department were associated with in-hospital mortality in urban patients with hypothermia. We developed a simple prediction model that might be divided into four groups in order of risk using these three predictors.

ACKNOWLEDGEMENT

THIS WORK WAS supported in part by a Grant-in-Aid for Research from the National Center for Global Health and Medicine (29-2001).

DISCLOSURE

Approval of the research protocol: This study was approved by National Center for Global Health and Medicine research ethics committee (NCGM-G-001401-00).
Informed consent: N/A.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None.

REFERENCES

1 Meiman J, Anderson H, Tomasallo C. Hypothermia-related deaths–Wisconsin, 2014, and United States, 2003–2013. MMWR Morb. Mortal. Wkly Rep. 2015; 64: 141–3.
2 Roeggla M, Holzer M, Roeggla G, Frossard M, Wagner A, Laggner AN. Prognosis of accidental hypothermia in the urban setting. J. Intensive Care Med. 2001; 16: 142–9.
3 Bierens JJ, Uitslager R, Swenne-van Ingen MM, van Stiphout WA, Knape JT. Accidental hypothermia: incidence, risk factors and clinical course of patients admitted to hospital. Eur. J. Emerg. Med. 1995; 2: 38–46.

4 Miller JW, Danzl DF, Thomas DM. Urban accidental hypothermia: 135 cases. Ann. Emerg. Med. 1980; 9: 456–61.
5 Okada Y, Matsuyama T, Morita S *et al*. Prognostic factors for patients with accidental hypothermia: A multi-institutional retrospective cohort study. Am. J. Emerg. Med. 2019; 37: 565–70.
6 Heatstroke Surveillance Committee of Japanese Association for Acute Medicine. The clinical characteristics of hypothermic patients in the winter of Japan – the final report of Hypothermia STUDY 2011. J. Jpn. Assoc. Acute Med. 2013; 24: 377–89.
7 Elbaz G, Etzion O, Delgado J, Porath A, Talmor D, Novack V. Hypothermia in a desert climate: severity score and mortality prediction. Am. J. Emerg. Med. 2008; 26: 683–8.
8 Brown DJ, Brugger H, Boyd J, Paal P. Accidental hypothermia. N. Engl. J. Med. 2012; 367: 1930–8.
9 Danzl DF, Hedges JR, Pozos RS. Hypothermia outcome score: development and implications. Crit. Care Med. 1989; 17: 227–31.
10 Furukawa H, Kudo D, Nakagawa A *et al*. Hypothermia in victims of the great East Japan earthquake: a survey in Miyagi prefecture. Disaster Med. Public Health Prep. 2014; 8: 379–89.
11 Gando S, Iba T, Eguchi Y *et al*. A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: comparing current criteria. Crit. Care Med. 2006; 34: 625–31.
12 DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988; 44: 837–45.
13 Kass GV. An exploratory technique for investigating large quantities of categorical data. Appl. Stat. 1980; 29: 119–27.
14 Vassal T, Benoit-Gonin B, Carrat F, Guidet B, Maury E, Offenstadt G. Severe accidental hypothermia treated in an ICU: prognosis and outcome. Chest 2001; 120: 1998–2003.
15 Mégarbane B, Axler O, Chary I, Pompier R, Brivet FG. Hypothermia with indoor occurrence is associated with a worse outcome. Intensive Care Med. 2000; 26: 1843–9.
16 Fei A, Lin Q, Liu J, Wang F, Wang H, Pan S. The relationship between coagulation abnormality and mortality in ICU patients: a prospective, observational study. Sci Rep. 2015; 5: 9391.
17 Matsuda T, Ogawara M, Seki T, Murakami M. Changes of coagulability of blood and fibrinolysis before and after onset of acute myocardial infarction and stroke -studies in 73 autopsied cases. Blood Vessel 1979; 10: 371–8.
18 Martini WZ. Coagulopathy by hypothermia and acidosis: mechanisms of thrombin generation and fibrinogen availability. J. Trauma 2009; 67: 202–9. discussion 8–9.