Received: 30 December 2019 | Revised: 31 March 2020 | Accepted: 1 April 2020

DOI: 10.1002/jgf2.323

ORIGINAL ARTICLE

Journal of General and Family Medicine Open Access WILEY

Hypothermia in a Japanese subtropical climate: Retrospective validation study of severity score and mortality prediction

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Abstract

Introduction: This study aimed to clarify the accuracy of an in-hospital mortality prediction score for patients with hypothermia. The score consists of five variables (age ≥70 years, mean arterial pressure <90 mm Hg, pH < 7.35, creatinine >1.5 mg/dL, and confusion). In contrast to the previously reported population in southern Israel, a desert climate, we apply the score system to a Japanese humid subtropical climate.

Methods: The study included patients with a principal diagnosis of hypothermia who were admitted to our community hospital between January 2008 and January 2019. Using the medical records from initial visits, we retrospectively calculated in-hospital mortality prediction scores along with sensitivity and specificity.

Results: We recruited 69 patients, 67 of which had analyzable data. Among them, the in-hospital mortality rate was 25.4%. Hypothermia was defined as mild (32-35°C) in 34 cases (50.7%), moderate (28-32°C) in 23 cases (34.3%), and severe (<28°C) in 10 cases (14.9%). The C-statistics of the in-hospital mortality prediction score was 0.703 (95% confidence interval, 0.55-0.84) for thirty-day survival prediction. After adjustment of the cutoff point of each item with ROC analysis and selection of the variants, the C-statistics of the in-hospital mortality prediction score rose to 0.81 (95% confidence interval, 0.69-0.92).

Conclusion: The in-hospital mortality prediction scores showed slightly less predictive value than those in the previous report. With some modification, however, the score system could still be applied efficiently in the humid Japanese subtropical climate. An appropriate management strategy could be established based on the predicted mortality risk.

KEYWORDS

clinical prediction rules, Japanese

1 | INTRODUCTION

Accidental hypothermia is defined as an unintentional drop in core temperature to 35°C or lower.[1] As the body temperature drops, consciousness, breathing, and circulation become impaired, sometimes requiring immediate VA ECMO (Extra-Corporeal Membranous Oxygenation) implementation and admission in ICU. Mortality of severely hypothermic patients remains high; the risk of death especially

increases if the core temperature drops below 32°C.[2,3] A Japanese retrospective cohort study reported that the inpatient mortality in patients with moderate-to-severe accidental hypothermia was 26%.[4] By using a prognostication system, more efficient care could be provided for patients, especially those at high risk of mortality. A simple risk score system for in-hospital mortality of hypothermic patients was developed by Elbaz in 2008.[5]

The simple risk score is based on the following five variables: age ≥70 years, mean arterial pressure <90 mm Hg, pH <7.35, creatinine level >1.5 mg/dL, and recent onset of confusion. Each variable accounts for one point except recent onset of confusion, which is associated with poor prognosis, accounted with a score of three points.

The system is derived from studies focusing on the population of southern Israel in a desert climate. However, the etiology of hypothermic death differs between geographic areas and local climates. For example, a study by Forensic Science (South Australia) and the National Forensic Database (Sweden) showed deaths from hypothermia in warmer climates occurred predominantly indoors and involved older people with multiple underlying illnesses. In Sweden, with a colder climate, deaths generally occurred outdoors.[6] Outside temperatures are similar in Hyogo Prefecture situating in the middle of Japan and southern Israel, but our local climate is more humid than it in southern Israel.

Recently, other risk assessment systems for accidental hypothermia have been developed.[7–9] The 5 "A" scoring system based on age, activities-of-daily-living status, near arrest, acidemia, and serum albumin level had good discrimination for predicting in-hospital mortality after accidental hypothermia.[7] A simple risk score system by Elbaz et al is simpler to calculate than 5 "A" scoring system. Kandori et al[8] demonstrated that the SOFA score had slightly better discrimination ability than 5 "A" scoring system. However, this study includes trauma patients, which might have interacted with the result of the SOFA score. Uemura et al[9] use measurement of FDP, PT-INR, and GCS score for the prediction of in-hospital mortality in urban patients with hypothermia. But this study is based on incomplete data.

Owing to the differences in previous studies in climates and in other factors, the prognostic value of the risk score model for use within a Japanese population is unclear. We therefore aim to clarify the accuracy of the score system for patients with hypothermia and factors associated with hypothermic death in the humid and subtropical Japanese climate.

2 | MATERIALS AND METHODS

2.1 | Study design

We conducted a retrospective study to assess the external validation of the prediction model at a teaching hospital (382 beds including eight beds of intensive care unit) in Hyogo Prefecture, Japan. This hospital is a community medical support center located in Japan and has an emergency medical care center and primary care practice. ECMO is available with a support by cardiovascular surgeon. Patients with hypothermia are treated by emergency room physician at first and admitted to the department of general internal medicine or cardiology. The study location is situated at 14 m above sea level. The local climate is humid and subtropical. January is the coldest month, with temperatures between 2 and 9°C, and August is the hottest month, with temperatures between 27 and 33°C. The average rainfall is 1073 mm per year.[10] The study was approved by the Institutional Research Ethics Committee (Approval number 31-9). Informed consent was waived. All procedures performed were in accordance with the 1964 Helsinki Declaration.

2.1.1 | Inclusion and exclusion criteria

Included in the study were patients admitted to our hospital aged ≥20 years with principal diagnosis of hypothermia between January 2008 and January 2019. Hypothermia was defined as core temperature <35°C, based on the definition by the International Classification of Diseases, Tenth Revision (ICD-10). The body temperature measurement and the diagnosis of hypothermia were made in the emergency room (ER). Rectal temperature or bladder temperature was used for temperature measurement. The cardiac arrest patients and patients died in ER were included.

Excluded from this study were patients without data on age, blood pressure, pH, creatinine level, or outcome data.

2.1.2 | Outcome measures

In this study, the primary outcome was in-hospital mortality. We retrospectively calculated in-hospital mortality prediction scores along with discriminative value for in-hospital mortality using medical records from initial hospital visits.

2.1.3 | Data collection

From patient's charts, we obtained demographic data and data on the presence of bacteremia, blood pressure, pH, creatinine level, and any incidences of mental confusion.

Severity of hypothermia was further defined as either mild (32-35°C), moderate (28-32°C), or severe (<28°C) following Swiss staging system classifications used by Durrer (2003).[11]

2.2 | Statistical analyses

We calculated C-statistics of the in-hospital mortality prediction score for in-hospital mortality using the receiver operating characteristic (ROC) curve analysis and determined the area under the receiver operating characteristic curve (AUC). To calculate the

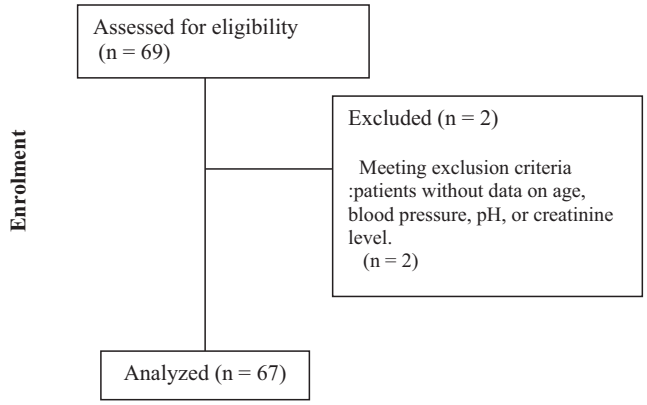

FIGURE 1 Flow of participants. Among 69 patients, 67 patients were confirmed to have hypothermia and two patients were excluded in lack of analyzable data

TABLE 1 Study subject characteristics

		Mean [SD] or n (%)
		All patients, n = 67
Female gender		27 (40.3)
Age, y		75.1 [16.2]
Place	Indoor	60 (89.6)
	Outdoor	7 (10.4)
Blood culture taken		50 (74.6)
Bacteremia		12 (17.9)
Body temperature		31.4 [31.7]
Degree of hypothermia	Mild	34 (50.7)
	Moderate	23 (34.3)
	Severe	10 (14.9)
Background	CIHD	10 (14.9)
Illness	CHF	6 (9)
	Diabetes	16 (23.9)
	Stroke	13 (19.4)
	PVD	3 (4.5)
	Dementia	14 (20.9)
	CKD	7 (10.4)
	Hypothyroidism	5 (7.5)
	Malignancy	7 (10.4)
	Psychiatric disease	6 (9)
	Alcohol abuse	11 (16.4)
Mean blood pressure, mm Hg		90.3 [26.2]
Ph		7.31 [0.13]
Creatinine, mg/dL		1.54 [1.42]
Confusion		54 [80.6]
30-d mortality		17 (25.4)

Abbreviations: CIHD, chronic ischemic heart disease; CHF, congestive heart failure; PVD, peripheral vascular disease.

TABLE 2 Characteristics of survivors and decedents

		Mean [SD] or n (%)	
		Survivors n = 50	Decedents n = 17
Female gender		19 (38.0)	8 (47.1)
Age, y		73.5 [17.6]	79.9 [10.1]
Place	Indoor	44 (88.0)	16 (94.1)
	Outdoor	6 (12)	1 (5.9)
Body temperature		31.6 [2.9]	30.8 [2.8]
Degree of hypothermia	Mild	28 (56)	6 (35.3)
	Moderate	15 (30)	8 (47.1)
	Severe	7 (14)	3 (17.6)
Background	CIHD	7 (14)	3 (17.6)
Illness	CHF	5 (10)	1(5.9)
	Diabetes	11 (22)	5 (29.4)
	Stroke	8 (16)	5 (29.4)
	PVD	2 (4)	1 (5.9)
	Dementia	12 (24)	2 (11.8)
	CKD	5 (10)	2 (11.8)
	Hypothyroidism	4 (8)	1 (5.9)
	Malignancy	3 (6)	4 (23.5)
	Psychiatric disease	6 (12)	0(0)
	Alcohol abuse	10 (20)	1 (5.9)
Mean blood pressure, mm Hg		91.4 [23.9]	86.6 [32.7]
Ph		7.34 [0.09]	7.25 [0.20]
Creatinine, mg/dL		1.44 [1.43]	1.85 [1.37]
Confusion		38 (76.0)	16 (94.1)

Abbreviations: CIHD, chronic ischemic heart disease; CHF, congestive heart failure; PVD, peripheral vascular disease.

optimum cutoff points of each item in the prediction model with ROC analysis, AUC analysis was performed to predict 30-day mortality with a stepwise logistic regression adjustment for the clinical parameters. In stepwise regression, we adopted backward algorithm with Akaike's information criteria. All statistical analyses were performed using JMP Pro 11.2.1 software (SAS Institute Inc).

3 | RESULTS

Among 69 patients (male: 42, female: 27), 67 (mean age: 76.1 [16.2] years) had analyzable data (Figure 1). Seventeen patients (25.4%) died within 30 days. The major medical conditions associated with hypothermia were as follows: sepsis (14 patients, 20.9%); endocrine-related (six patients, 9.0%); drug/alcohol-related (eight patients, 11.9%); stroke (one patient, 1.5%); and others, including end-stage cancer and starvation (32 patients, 47.8%). Among the patients, seven (10.4%) were found outdoors (one on outdoor stairs, one in a pond, one by a river side, one in a street, and three in the sea) and

60 (89.6%) were found indoors (one in a nursing home, one in hospital, two in toilets, three in bathrooms, four in jail, and forty-nine in living rooms). Hypothermia was classified as mild in 34 patients (50.7%), moderate in 23 patients (34.3%), and severe in 10 patients (14.9%). Table 1 shows patient background diseases, demographics, and living conditions. The prevalence of background diseases was not associated with 30-day mortality. As was to be expected, winter months (December to February) had the most cases of hypothermia (41 cases, 61.2%), but four (6%) of the patients were admitted during summer (June to August). Thirty-day mortality did not differ between seasons. Fifty patients were examined for blood culture, and bacteremia was found in 12 patients. Arterial pH was lower in patients who died than in patients who survived (7.25 vs 7.34) (Table 2).

The C-statistics of the in-hospital mortality prediction score was 0.70 (95% confidence interval, 0.55-0.84) for thirty-day survival prediction (Figure 2). According to our initial results, we calculated optimum cutoff points with ROC analysis. After the adjustment of the cutoff point of each item (the optimal cutoff points were as follows: age = 79 years; mean arterial pressure = 81 mm Hg; pH = 7.39; and creatinine level = 1.5 mg/dL) and selection of the variants using stepwise logistic regression for the clinical parameters (including mean arterial pressure <81 mm Hg, creatinine level >1.5 mg/dL, and female gender as independent variables), the C-statistics of the in-hospital mortality prediction score rose to 0.81 (95% confidence interval, 0.69-0.92) (Table 3, Figure 3).

4 | DISCUSSION

4.1 | Summary of main findings

We examined in-hospital mortality prediction scores among patients with hypothermia in a humid Japanese subtropical climate for the first time, to the best of our knowledge. Our study showed suboptimal C-statistics of the in-hospital mortality prediction score compared with the original study by Elbaz (2008),[5] which was based in a desert climate (0.70 vs 0.81) (Figure 2). After adjustment of the cutoff point of each item with ROC analysis and selection of the variants, the C-statistics of the score rose up to 0.81 with only three variables: low mean blood pressure, high serum creatinine level, and female gender. In a Japanese community hospital setting, a simpler prediction model based on only these parameters might therefore be sufficient to define high-risk populations for hypothermic death.

4.2 | Differences between studies and the present study's strengths

The mortality rate in our population was lower than that in the original (25.4% vs 47.3%), although the average age and the proportion of patients with moderate and severe hypothermia in our population were higher than those in the original (76.1 [16.2] years vs 62.3 [22.6] years and 49% vs 21%, respectively).[5]

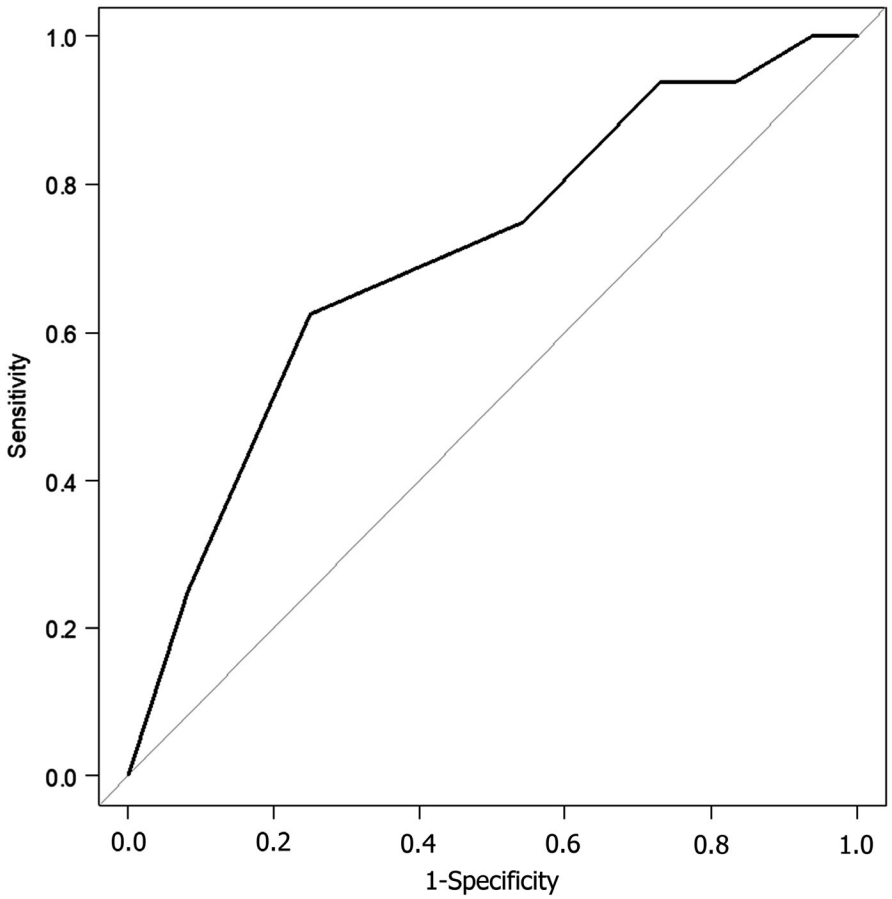

FIGURE 2 Receiver operating characteristic curve of the in-hospital mortality prediction score for thirty-day survival prediction. The C-statistics of the in-hospital mortality prediction score was 0.70 (95% confidence interval, 0.55-0.84) for thirty-day survival prediction

According to the epidemiological studies on the accidental hypothermia in Japan, the mortality from hypothermia occurred predominantly indoors,[12–14] which was consistent with a result of the study by Elbaz et al.[5] The median age of the study participants was older in Japanese registry study compared with the study by Elbaz et al (79% vs 62.3%).[5,14] Aged person is more likely to fatal hypothermia than younger ones.[14] Reports support an association between hypothermia and mortality in several conditions, such as sepsis and hip fracture.[15,16] Along with advanced age, such multimorbidity would be an explanation for hypothermic death. Average age and severity of hypothermia based on the Swiss staging system in the present study were not significant predictors of mortality. Accessibility of medical facilities and management of underlying treatable medical conditions might therefore explain differences in mortality rate between countries. There were fewer patients found outdoors in our study than in the original (10.4% vs 27.8%). However, the mortality in our patients did not differ depending on the location of where patients were found, which was inconsistent with a previous report by Bright (2014).[6] This indicates hypothermic death in warmer climates occurs with greater prevalence indoors. This could be explained by the insufficient power to detect statistical differences in mortality rates among subgroups of patients according to location.

Another aspect we must consider is the mechanism of hypothermia between studies. Sepsis, endocrine-related, and drug/alcohol-related hypothermia were common in our study and the original study by Elbaz (20.9% vs 38.5%, 9.0% vs 11.2%, and 11.9% vs 8.9%, respectively). No trauma patients were found in the present study; on the contrary, approximately one-fifth of the patients in the original study had trauma. This difference in the medical condition associated with hypothermia may confer the mortality and clinical parameters included in the prediction model.

The present study has several strengths. This is the first study to examine the external validity of simple risk score system for in-hospital mortality of hypothermic patients in the other geographical location outside southern Israel. Second, we found simpler prediction model based on only these parameters with high discrimination value after adjustment of the cutoff point of each item in the score.

TABLE 3 Multiple logistic regression analysis of factors associated with 30-d mortality

Factor	OR	95%CI	*P*-value
Mean blood pressure	3.57	0.63-20.4	.15
Creatinine, mg/dL	25.2	3.56-178	.001*
Gender, female = 0, male = 1	0.23	0.05-1.08	.06

Note: Dependent variable: 30-d mortality.
Independent variables: mean blood pressure, creatinine, and gender.
**P*-value < .05.

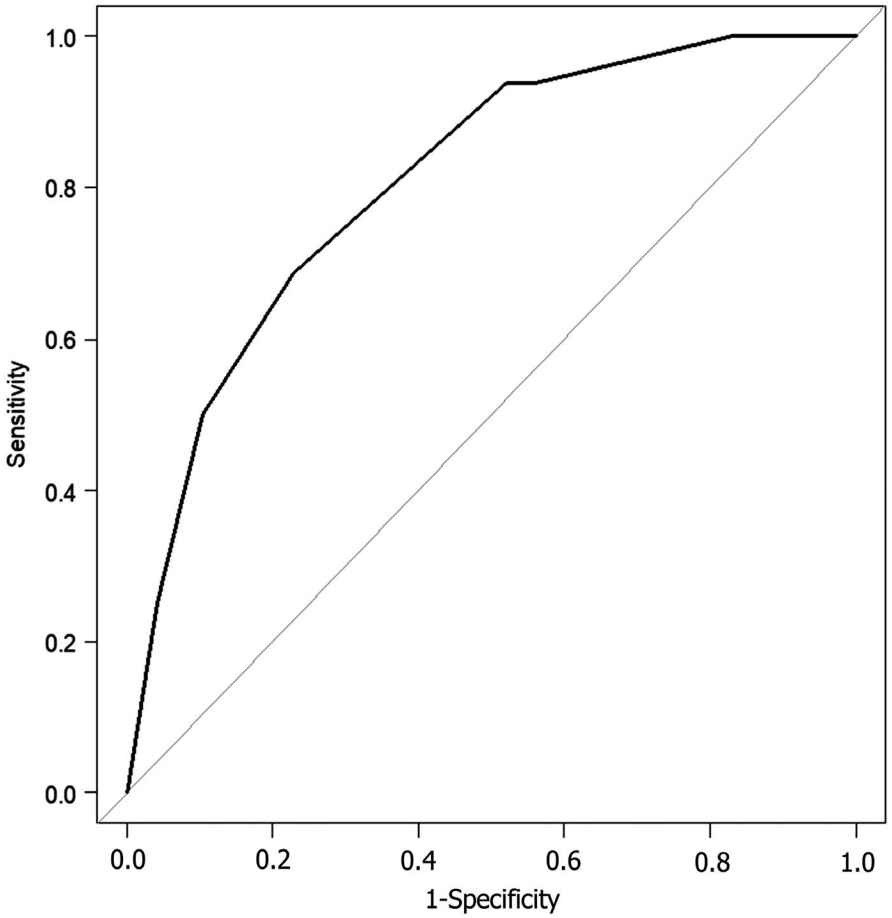

FIGURE 3 Receiver operating characteristic curve of the adjusted in-hospital mortality prediction score. After adjustment of the cutoff point of each item with ROC analysis and selection of the variants, the C-statistics of the in-hospital mortality prediction score rose up to 0.81 (95% confidence interval, 0.69-0.92)

This adjusted simpler scoring system potentially leads to faster decision-making and disposition in real practices. Third, higher age of our study patients is concordant with aging population in Japan. Our simpler model could be applicable for the general population, especially for nontraumatic patients.

4.3 | Clinical implications

The present study may have pragmatic implications for the clinical care of patients with hypothermia. For hypothermic female patients with low blood pressure and high creatinine level, invasive treatment and admission in ICU are necessary. Further studies are needed to investigate whether these dispositions based on the prediction model could reduce mortality and cost regarding the management of patients or not.

5 | LIMITATIONS

Our study has several limitations. First, data were collected from a single institution only. Nonetheless, the Japanese community hospital study location may be comparable to similar community settings. A second limitation is that we retrospectively calculated in-hospital mortality prediction scores. Prospective validation of outcomes in a multicenter setting is needed.

It might be possible to establish an appropriate management strategy based on the predicted mortality risk. In patients with high in-hospital mortality score, customized precautious management is needed.

6 | CONCLUSIONS

Our in-hospital mortality prediction scores showed slightly less predictive value than those in the previous report. With modifications, however, the scoring system could still be efficiently applied in the humid Japanese subtropical climate. An appropriate management strategy based on the predicted mortality risk might be possible.

ACKNOWLEDGEMENTS

We thank Benjamin Phillis of Akashi Medical Center for proofreading and editing the manuscript.

CONFLICT OF INTERESTS

The authors have no potential conflicts of interest to declare. The study design was registered as a University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) Clinical Trial (UMIN trial ID: UMIN 000 036 025) on February 14, 2019 (UMIN-CTR URL: http://www.umin.ac.jp/ctr/index.htm).

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How to cite this article: Ishimaru N, Kinami S, Shimokawa T, Seto H, Kanzawa Y. Hypothermia in a Japanese subtropical climate: Retrospective validation study of severity score and mortality prediction. *J Gen Fam Med*. 2020;21:134–139. https://doi.org/10.1002/jgf2.323