〈Regular Article〉

Long-term prognostic factors for patients with accidental hypothermia

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ABSTRACT **Background**: The long-term prognosis of patients with accidental hypothermia (AH) is unclear. Therefore, the all-cause one-year mortality and long-term prognostic factors for patients with AH who were alive at discharge from the hospital were evaluated in this study.

Methods: Medical records for 390 patients with AH admitted to our hospital between January 2008 and May 2020 were retrospectively reviewed. The primary outcome was the all-cause one-year mortality rate in patients alive at discharge. At discharge, surviving patients were divided into two groups for analysis: (1) patients who were alive one year after discharge, and (2) patients who died within one year, despite being alive at discharge.

Results: One hundred and fifty-three hypothermic patients met the study criteria. The all-cause one-year mortality was 20.9% (32/153). Patients who died within a year were older ($p = 0.01$), had bradycardia ($p = 0.01$), had comorbidities including malignancy ($p = 0.02$) and dementia ($p = 0.02$), had higher Acute Physiology, and Chronic Health Evaluation-II scores ($p < 0.01$), and had increased frailty at discharge ($p < 0.01$) than patients who survived.

Conclusion: The long-term prognosis of patients with AH is poor. The deteriorating ability of patients to perform activities of daily living might be a long-term prognostic factor for AH. In addition, the one-year mortality rate remains high for patients with AH, even among those who were alive at discharge.

doi：10.11482/KMJ-E202349007 *(Accepted on May 2, 2023)*

Key words：Frail, Dementia, One-year mortality, Activities of daily living

INTRODUCTION

Accidental hypothermia (AH) is a core body temperature of ≤ 35℃. Etiologic factors for AH are as follows: increased heat loss (environmental causes / induced vasodilation / dermatologic causes / iatrogenic causes), decreased heat production (endocrinologic failure / insufficient fuel / neuromuscular physical exertion), impaired thermoregulation (peripheral failure / central nervous system failure or neurologic abnormalities), and various associated clinical states (infection / pancreatitis / carcinomatosis / uremia / vascular insufficiency / multisystem trauma / shock / cardiopulmonary disease / systemic acidosis /

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recurrent or episodic hypothermia)[1]. Prognostic factors for the in-hospital mortality of AH include age, hyperkalemia, changes in pH, frailty, and the need for assistance with activities of daily living (ADL), which were previously investigated[2, 3]. Peng *et al.*[4] reported that frail adults have a significantly higher risk of mortality from all causes. Okada *et al.*[3] also reported that frailty associated with hypothermia was a prognostic factor for the in-hospital mortality before admission. Even so, the long-term prognosis of AH is unclear. In addition, correlations between frailty before admission and at discharge and the long-term prognosis of AH are unclear. Therefore, we examined the all-cause one-year mortality in patients with AH who were alive at discharge.

MATERIALS AND METHODS

Data collection

The medical records of 390 patients admitted to Kawasaki Medical School Hospital with a diagnosis of AH between January 2008 and March 2020 were reviewed retrospectively. Patients without a recorded core body temperature and those lost to follow-up were excluded. The following parameters were collected for each patient: sex, age, cause of AH[1], frailty (before admission and at discharge for hypothermia), vital signs, laboratory data, and comprehensive past medical history. The Clinical Frailty Scale (CFS) of the Canadian Study on Health & Aging[5] were used to assess frailty before admission and at discharge. CFS scores before hospitalization and at discharge were analyzed to determine the impact of deteriorating ADL on the long-term prognosis of AH.

Patients' clinical data, including vital signs at admission (core body temperature (BT), systolic blood pressure (SBP), heart rate (HR), Glasgow Coma Scale (GCS) score, biological data (serum pH and potassium [mEq / L]), and destination post-discharge were collected. This study was approved by the Institutional Review Board of Kawasaki Medical School (No. 5277-00).

Outcome measurements

The primary outcome of this study was the all-cause one-year mortality rate in patients who were alive at discharge. The secondary outcome of this study was to determine whether the CFS score, before admission and at discharge, is a useful long-term prognostic factor for AH.

Statistical analysis

Statistical sample size calculations were not performed. Patient characteristics and in-hospital information between the two groups were evaluated using the Wilcoxon signed-rank test for numeric variables and Pearson's χ^2 test for categorical variables. In accordance with previous studies[2, 3, 6], AH, sex, age, HR, SBP, serum pH, serum potassium, frail category (no-frail, CFS 1-4; mildly frail, CFS 5; moderately frail, CFS 6; severely frail, CFS 7,8, very severely frail; CFS 9; terminally ill), past medical history (cardiovascular diseases, neurological diseases, endocrine diseases, psychiatric diseases, malignant diseases, dementia, and others (liver cirrhosis, hemodialysis, and chronic obstructive pulmonary disease)), Acute Physiology and Chronic Health Evaluation (APACHE) II score, BT category (mild, 34.9℃ - 32.1℃; moderate, 32℃ - 28.1℃; severe, 28℃ - 24.1℃; and profound, ≦ 24.0℃), impaired consciousness (mild, GCS 13 - 15; moderate, GCS 9 - 12; severe, GCS < 9), and outcomes were considered potential confounders in univariable models for mortality. Two-sided p values < 0.05 were considered statistically significant. All statistical analyses were performed with JMP®10 (SAS Institute Inc., Cary, NC, USA) and R[7].

RESULTS

Three hundred and ninety consecutive patients with AH were admitted to our hospital between

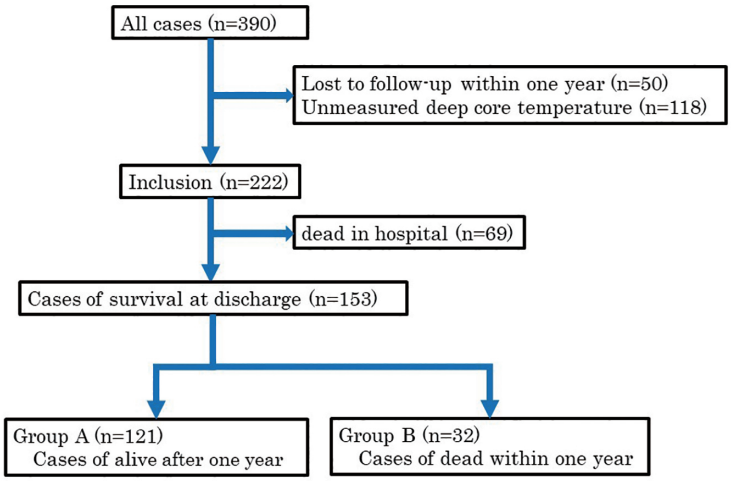

Fig. 1. Flow chart used to categorize enrolled patients

Table 1. Causes of accidental hypothermia

Clinical disorder	n = 153 (%)
Environmental causes	23 (15.0)
Induced vasodilation	12 (7.8)
Dermatologic causes	3 (2.0)
Endocrinologic failure	6 (3.9)
Insufficient fuel	21 (13.7)
neuromuscular physical exertion	6 (3.9)
Central nervous system failure or neurologic abnormalities	19 (12.4)
Sepsis	20 (13.1)
Uremia	1 (0.7)
Multisystem trauma	42 (27.5)

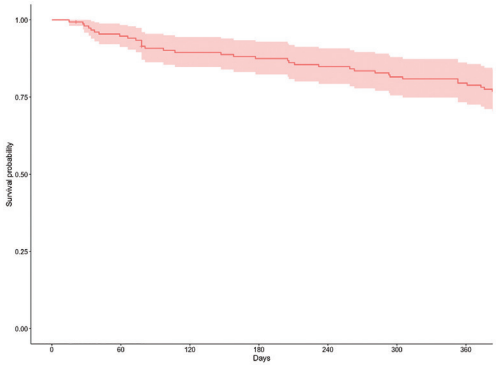

Fig. 2. Kaplan-Meier Analyses for all cases one year after discharge

January 2008 to March 2020. Fifty patients lost to follow-up within one year and 118 patients with an unmeasured core body temperature were excluded from the study. Sixty-nine of the remaining 222 patients died in-hospital and were, thus, excluded. The in-hospital mortality rate was 30.2% (69 / 222). The 153 surviving patients were enrolled in this study (Fig. 1). The core body temperature measurement site was the bladder in 150 patients and the rectum in 3 patients. Patients alive at discharge were divided into two groups: Group A, patients who were alive one year after discharge; Group B, patients who died within one year, despite being alive at discharge. The primary outcome was 20.9% (32 / 153). The causes of accidental hypothermia are shown in Table 1. Also, the results of the Kaplan-Meier analysis for one year is shown in Fig. 2.

Patient characteristics

Patient characteristics and outcomes are shown in Table 2. Also, vital signs and laboratory data on admission are shown in Table 3. Patients in Group B were older ($p = 0.01$) and had higher APACHE II scores ($p < 0.01$) compared with the characteristics of patients in Group A. Patients in Group B also had more comorbidities, including malignancy ($p = 0.02$) and dementia ($p = 0.02$), than did patients in Group A. There was a higher incidence of bradycardia ($p <$

Table 2. Patient characteristics and outcomes

	Total (n=153)	Group A ※ (n=121)	Group B ※ (n=32)	p value
Sex				
Male, n (%)	82 (53.6)	69 (57.0)	13 (40.6)	0.09
Age (y) (median (IQR))	77 (64.5 - 85.5)	72 (60 - 79)	81 (71 - 87)	0.01
Frail category (before admission)				0.07
1 - 4	99 (64.7)	84 (69.4)	15 (46.9)	
5	27 (17.6)	17 (14.0)	10 (31.3)	
6	16 (10.5)	13 (10.7)	3 (9.4)	
7, 8	10 (6.5)	6 (5.0)	4 (40.0)	
9	1 (0.6)	1 (0.8)	0 (0)	
Systolic blood pressure (mmHg) (median (IQR))	120 (95.5 - 145)	120 (96 - 146.5)	121 (93.75 - 130.75)	0.45
Heart rate (beat per minute) (median (IQR))	79 (59.5 - 97)	82 (61 - 98.5)	70.5 (50.25 - 86.5)	0.01
Serum pH (± SD)	7.26 ± 0.13	7.27 ± 0.12	7.25 ± 0.14	0.478
Serum K (mEq/L) (± SD)	4.11 ± 1.21	4.02 ± 0.86	4.42 ± 2.04	0.675
Past medical history				
Cardiovascular, n (%)	68 (44.4)	51 (42.1)	17 (53.1)	0.27
Neurological, n (%)	31 (20.2)	22 (18.2)	9 (28.1)	0.22
Endocrine, n (%)	39 (25.5)	31 (25.6)	8 (25.0)	0.94
Psychiatric, n (%)	38 (24.8)	32 (26.4)	6 (18.8)	0.35
Malignant, n (%)	22 (14.8)	13 (10.7)	9 (28.1)	0.02
Dementia, n (%)	33 (21.6)	21 (17.4)	12 (37.5)	0.02
Other, n (%)	15 (9.8)	12 (9.9)	3 (9.3)	0.92
APACHE-II score (median (IQR))	21 (16 - 27.5)	20 (15 - 25)	27 (19.25 - 31.75)	< 0.01

IQR, *interquartile range*, SOFA *sequential organ failure assessment*, APACHE *Acute Physiology, and Chronic Health Evaluation*
※ Group A: Patients who were alive one year after discharge. Group B: Patients who died within one year, despite being alive at discharge.

0.01) in patients in Group B at discharge than that in Group A. There was no significant difference in the BT between the two groups.

Frailty

There were no differences in frailty scores before admission between the two groups. In contrast, a comparative analysis of frailty at discharge showed that a higher number of patients in Group B had deteriorating ADLs than did those in Group A. The one-year mortality rates in CFS before admission and at discharge are shown in Table 4. The one-year mortality rate for patients who progressed to a CFS of 7 or 8 at discharge was 28.6 - 60.0%.

Causes of death

The causes of death within one year among patients with AH who were alive at discharge at our hospital (32 cases) included respiratory infections (7 cases, 21.9%), multiple organ failure (4 cases, 12.5%), malignancy (3 cases, 9.4%), intracranial disease (3 cases, 9.4%), suicide (1 case, 3.1%), cervical spinal cord injuries (1 case, 3.1%), and unspecified (13 cases, 40.6%).

DISCUSSION

This is the first study to analyze the one-year outcome of patients who were alive at discharge after AH.

A nationwide survey in Japan revealed that the in-hospital mortality rate for hypothermia ranged from 26.3%[3] to 29%[8]. Similarly, the in-hospital mortality rate identified in this study was 30.2%. The one-year mortality rate for AH in this study was high at 45.5% (101 / 222). Notably, the one-year mortality rate among patients alive at discharge was high at 20.9% (32 / 153).

The high one-year mortality rate after AH may

Table 3. Vital signs and laboratory data on admission.

	Total patients (n = 153)	Group A ※ (n = 121)	Group B ※ (n = 32)	p value
Core temperature (℃)				0.12
32.1 - 34.9, n (%)	84 (54.9)	71 (58.7)	13 (40.6)	
28.1 - 32.0	49 (32.0)	34 (28.1)	15 (46.9)	
24.1 - 28.0	20 (13.1)	6 (5.0)	4 (12.5)	
≦ 24.0	0 (0)	0 (0)	0 (0)	
Impaired consciousness category Glasgow coma scale				0.26
13 - 15, n (%)	53 (34.6)	45 (37.2)	8 (25.0)	
9 - 12	42 (27.5)	34 (28.1)	8 (25.0)	
< 9	58 (37.9)	42 (34.7)	16 (50.0)	
Frail category (at discharge)				< 0.01
1 - 4, n (%)	32 (20.9)	29 (24.0)	3 (9.4)	
5	24 (15.7)	21 (17.4)	3 (9.4)	
6	37 (24.2)	35 (28.9)	2 (6.3)	
7, 8	59 (38.6)	35 (28.9)	24 (75.0)	
9	1 (0.6)	1 (0.8)	0 (0)	
Outcome				0.06
home discharge, n (%)	42 (27.5)	38 (31.4)	4 (12.5)	
hospital transfer	110 (71.9)	82 (67.7)	28 (87.5)	
facility	1 (6.5)	1 (0.8)	0 (0)	

※ Group A: Patients who were alive one year after discharge. Group B: Patients who died within one year, despite being alive at discharge.

Table 4. One-year mortality based on CFS score before admission and at discharge

		CFS at discharge					mortality
		1 - 4	5	6	7, 8	9	
CFS before admission	1 - 4	3/32 (9.4%)	3/23 (13.0%)	1/16 (6.3%)	8/28 (28.6%)	–	15/99 (15.2%)
	5	–	–	1/12 (8.3%)	9/15 (60.0%)	–	10/27 (37.0%)
	6	–	–	0/8 (0%)	3/8 (37.5%)	–	3/16 (18.8%)
	7, 8	–	0/1 (0%)	0/1 (0%)	4/8 (50.0%)	–	4/10 (40.0%)
	9	–	–	–	–	0/1 (0%)	0/1 (0%)
mortality		3/32 (9.4%)	3/24 (12.5%)	2/37 (5.4%)	24/59 (40.7%)	0/1 (0%)	32/153 (20.9%)

CFS, *clinical frail scale*

be due to natural disease occurrence in older adults and those with poor ADL. The Japanese Ministry of Health, Labour, and Welfare (JMHLW) published one-year mortality rates by age group. The 2019 JMHLW reports showed that the one-year mortality rates ranged from a low of 1.9% (range: 70 - 74 years), 3.3% (range: 75 - 79 years), and 5.9% (range: 80 - 84 years) to a high of 29.7% (range: 95 - 99 years). The median age of the patients in this study was 77 (64.5 - 85.5) years. Although direct comparisons are difficult, these data suggested a high mortality rate after AH.

Based on the findings of previous studies[3, 4], we hypothesized that the degree of frailty before admission and at discharge might be a useful long-term prognostic factor to determine AH survival at discharge. Correlations between the mortality rate and deteriorating ADLs after AH were also

investigated. There was no significant difference in CFS before admission ($p = 0.07$) in the one-year mortality rate. However, there was a notable difference in CFS at discharge ($p < 0.01$). The one-year mortality rate increased as the patient's ability to perform ADL deteriorated at discharge (Table 4). The one-year mortality rate was 40.7% in the group with CFS 7 or 8 at discharge. In addition, the one-year mortality rate for patients who had progressed to a CFS 7 or 8 at discharge ranged from 28.6% to 60.0%, an unusually high rate. The one-year mortality rate among the frail categories before admission was 15.2 - 40.0%. These results suggest that a deteriorating ability to perform ADLs after AH is a prognostic factor that correlates with decreasing prognoses.

Prognostic factors for in-hospital mortality in hypothermic patients, including patients aged 75 and older, hyperkalemia, and acidosis, have been previously reported[2, 3]. Based on the findings mentioned above, we aimed to determine the significance of these factors as long-term prognostic factors in patients who are alive at discharge. Significant differences were identified based on age alone. As shown in Table 2, patients in Group B had higher APACHE II scores than did patients in Group A. Therefore, APACHE II scores might be a prognostic factor for the long-term prognosis of patients with AH. However, as mentioned above, the APACHE II scores are severity scores in the acute phase. Therefore, it would be judicious to use them as prognostic factors after discharge.

Fukuda *et al.*[9] also reported that impaired consciousness correlates with severe hypothermia and in-hospital mortality in patients with AH in Japan. In this study, no significant differences in impaired consciousnesses were identified between Groups A and B. The study also showed that explanatory factors differed between the short- and long-term prognoses of patients with hypothermia. Okada *et al.*[3] showed that in-hospital deaths of patients with AH are associated with dementia. Similarly, this study found an increased incidence of dementia among patients in Group B than that in Group A ($p = 0.02$).

Patients with AH who are aged 75 and over, have dementia, and have ADL deterioration after admission may have a poorer long-term prognosis after discharge. Preventing ADL deterioration during hospitalization may improve the long-term prognosis of patients with AH.

This study had some limitations. First, it was a single-hospital retrospective cohort study. Second, a multivariate analysis was not performed since the mortality rate was low, and the number of variables was limited. A prospective multi-institutional study of the long-term prognosis of AH is needed to combat these limitations.

CONCLUSION

The long-term prognoses of patients with AH are poor. ADL deterioration after AH may be a long-term prognostic factor for AH. The one-year mortality rate might remain high, even among patients alive at discharge.

ACKNOWLEDGMENTS

Not applicable.

FUNDING

This study received no commercial interests or financial and / or commercial support.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

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