Association between frailty and mortality among patients with accidental hypothermia: a nationwide observational study in Japan

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Abstract

Background: Frailty has been associated with a risk of adverse outcomes, and mortality in patients with various conditions. However, there have been few studies on whether or not frailty is associated with mortality in patients with accidental hypothermia (AH). In this study, we aim to determine this association in patients with AH using Japan’s nationwide registry data.

Methods: The data from the Hypothermia STUDY 2018&19, which included patients of ≥18 years of age with a body temperature of ≤35 °C, were obtained from a multicenter registry for AH conducted at 120 institutions throughout Japan, collected from December 2018 to February 2019 and December 2019 to February 2020. The clinical frailty scale (CFS) score was used to determine the presence and degree of frailty. The primary outcome was the comparison of mortality between the frail and non-frail patient groups.

Results: In total, 1363 patients were included in the study, of which 920 were eligible for the analysis. The 920 patients were divided into the frail patient group (N = 221) and non-frail patient group (N = 699). After 30-days of hospitalization, 32.6% of frail patients and 20.6% of non-frail patients had died (p < 0.001). Frail patients had a significantly higher risk of 90-day mortality (Hazard ratio [HR], 1.64; 95% confidence interval [CI], 1.25–2.17; p < 0.001). Based on the Cox proportional hazards analysis using multiple imputation, after adjustment for age, potassium level, lactate level, pH value, sex, CPK level, heart rate, platelet count, location of hypothermia incidence, and rate of tracheal intubation, the HR was 1.69 (95% CI, 1.25–2.29; p < 0.001).

Conclusions: This study showed that frailty was associated with mortality in patients with AH. Preventive interventions for frailty may help to avoid death caused by AH.

Keywords: Accidental hypothermia, Frailty, Mortality, Activity of daily living, Rewarming rate

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Background

The incidence of accidental hypothermia (AH), which is defined by a body core temperature of \(< 35\,^\circ C\) [1], is low, however, severe hypothermia is associated with a high mortality rate [2, 3]. In severe hypothermia, intrinsic heat production by means of active movement and shivering, disappeared, leading to further progression in the decrease in body temperature. In Japan, which has a large elderly population, the mortality rate of all patients with AH is as high as 24.4–35% [4, 5], so effective prevention and intervention strategies are required.

Frailty is characterized by a decline in functioning across multiple physiological systems, accompanied by an increased vulnerability to stressors [6]. More recently, data have suggested that the presence of frailty places a person at increased risk of adverse outcomes, including hospitalization, and mortality [7]. Recently, frailty has also been noted in critically ill patients [8, 9]. However, to our knowledge, limited data exist regarding the relationship between AH and frailty. Clarification of the relationship between AH and frailty may provide useful insight for improving the prognosis of patients with hypothermia.

We hypothesized that frailty would be associated with a poor prognosis and mortality in patients with AH. For the purpose of verifying this hypothesis, we analyzed the Japan’s nationwide registry data on hypothermia.

Material and methods

Study design and setting

We performed a prospective, observational, multi-center registries of hypothermia: the Hypothermia STUDY 2018&2019. This study was conducted from December 2018 to February 2019 and December 2019 to February 2020, among a consortium of 120 academic and community medical centers from different geographic regions across Japan. The study has been approved by the Ethics Review Board of Teikyo University Hospital in Japan (Approval No: 17–090). The requirement for informed consent was waived due to the observational nature of the study by the Ethics Review Board of Teikyo University Hospital in Japan. In addition, the institutional review board of each hospital listed in the acknowledgements approved the study.

Patient selection and data collection

The present study included consecutive patients whose body temperature, as measured by emergency medical services (EMS) or at the emergency department (ED), was \(< 35\,^\circ C\). Patients of \(< 18\) years of age were excluded. The following data were collected: age, sex, any pre-existing conditions, activities of daily living (ADL), lifestyle, location of hypothermia incidence, mechanism underlying hypothermia (acute medical illness [stroke, ischemic cardiac disease, infectious disease, malnutrition, arrhythmia, diabetes mellitus, renal disease, hypoglycemia, cardiac failure, endocrine disease and gastrointestinal disease], trauma [submersion, distress], alcohol intoxication, other [including drugs]), Charlson comorbidity index (CCI) [10], Glasgow coma scale (GCS) [11], Sequential Organ Failure Assessment (SOFA) score [12], laboratory data, temperature, blood pressure, heart rate, respiratory rate, cardiac arrest during pre-hospital, intubation, hospital length of stay, mortality, and Cerebral Performance Category (CPC) [13] score at 30 days after admission, and complications. The temperature was recorded as the core temperature from the rectum, urinary bladder, or esophagus if available; otherwise, the peripheral temperature from the axilla or ear was noted. The severity of hypothermia was classified according to the temperature as mild (35–32\(^\circ\)C), moderate (32–28\(^\circ\)C), or severe (\(< 28\,^\circ C\)) with reference to previous studies [1] [3].

The laboratory data included the pH value, potassium level, lactate level, platelet count, CPK level, BUN level, and creatinine level measured at the ED. The pH value in principle was evaluated by an arterial blood gas analysis, and the pH value measured using the venous blood gas was adjusted as described in a previous study [14]. In the present study, the patients who did not stay in a hospital, or in whom the length of hospital stay or body temperature was unknown or \(> 35\,^\circ C\) were excluded from the present analysis.

Complications during hospitalization were recorded and classified as arrhythmia, pneumonia, pancreatitis, electrolyte abnormality, or other. Pneumonia was defined as an obvious shadow on chest radiography or computed tomography (CT). Pancreatitis was defined as cases meeting at least two of the following conditions: 1) abdominal pain, 2) elevation of pancreatic enzyme levels in the blood, and 3) edema of the pancreas or peripancreatic effusion on ultrasound/CT.

The rewarming duration to target temperature was defined as the time interval between arrival at the ED and the moment at which the target temperature was reached. The rewarming rate (\(^\circ C\) per hour) was defined as follows: (target temperature-temperature at ED) / the rewarming duration to target temperature.

Rewarming methods were divided into active external rewarming (warmed blanket, forced warm air, heating pad, and warmed bath) and active internal rewarming (warmed fluid infusion, lavage, hemodialysis, intravascular catheter, and extracorporeal membrane oxygenation [ECMO]).

Definition of frailty

The clinical frailty scale (CFS) score was used to determine the presence and degree of frailty, as described
previously [15]. The CFS score was determined using the activities of daily living and pre-existing conditions, as shown in our previous study [16]: CFS 1, very fit, defined as ADL 1 (independent) and CCI 0; CFS 2, well, defined as ADL 1 and CCI $\geq$ 1, or ADL 2 (sometimes out of the door) and CCI 0; CFS 3, well with treated comorbid disease, defined as ADL 2 and CCI 1–2; CFS 4, apparently vulnerable, defined as ADL 2 and CCI $\geq$ 3, or ADL 3 (indoors); CFS 5, mildly frail, defined as ADL 4 (almost needing assistance) and CCI $\leq$ 2; CFS 6, moderately frail, defined as ADL 4 and CCI $\geq$ 3; and CFS 7, severely frail, defined ADL 5 (needing total assistance). Patients were defined as frail if they had a CFS score of $\geq$ 5 before hospital admission.

**Outcome measures**

Patient demographics and outcomes were compared between frail and non-frail patients. The primary outcome was the comparison of mortality between the frail and non-frail patient groups. The secondary outcomes were the comparisons of the length of intensive care unit (ICU) stay, hospital stay, CPC at 30 days after admission, and complications between the frail and non-frail patient groups. A favorable outcome was defined as a CPC of 1 or 2, whereas an unfavorable outcome was defined as a CPC 3–5.

**Data analyses**

Data are expressed as the number (%), median (interquartile range) or the mean ± standard deviation, as appropriate. Intergroup comparisons were made using the Fisher’s exact test for categorical data and Mann-Whitney U test or Student’s t-test for continuous data. Ninety-day survival was calculated using a Kaplan-Meier curve and the difference in survival between frail and non-frail patients was determined using a log-rank test. Hazard ratios (HRs) and the corresponding 95% confidence intervals (CI) of the association between frailty and 90-day survival were derived using Cox proportional hazard survival models. The following covariates were included in the multivariable model based on the relevant literature [2, 3], or the consideration of clinically significant variables: age, sex, potassium level, lactate level, pH value, CPK level, heart rate, platelet count, location of hypothermia incidence, and rate of tracheal intubation. Missing data were managed with multiple imputation by chained equations [17, 18]. The variables included in the imputation model were those from the multivariable model. Twenty-five datasets were imputed with 10 iterations each. A Cox proportional hazards analysis was applied to the 25 imputed datasets, and final estimates were obtained by averaging the 25 estimates according to Rubin’s rules. Furthermore, a complete data set was used for the sensitivity analysis. We also performed a subgroup analysis with the exclusion of cases in which a warmed blanket or ECMO were applied. All tests were two-sided, and $P$ values of $< 0.05$ were considered statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for the R software program. Multiple imputation was performed using the mice package in R (version, 4.0.3 R Foundation for Statistical Computing, Vienna, Austria).

**Results**

Of the 1363 patients with hypothermia who were included in the Hypothermia STUDY 2018&2019, 443 were excluded from the present study because of unknown temperature or temperature $\geq$ 35 °C ($N = 147$), unknown outcome ($N = 127$), unknown length of hospital stay ($N = 150$), or unknown ADL ($N = 19$). The remaining 920 patients were eligible for inclusion in the present analysis. A patient flow diagram is shown in Fig. 1. According to the CFS score, the 920 patients were divided into the frail patient group ($N = 221$) and the non-frail patient group ($N = 699$).

**Baseline characteristics of the study population**

Supplemental Fig. 1 shows the age distribution of the patients included in the present study. The present population included only a few relatively young patients, with 81% of the total patients being $\geq$65 years old, and the median patient age being 79 years old. Table 1 shows the baseline characteristics of the study population and a comparison of the clinical characteristics of frail and non-frail patients. The non-frail patient group had a larger percentage of male in comparison to the frail patient group. The frail patient group was older, had higher CCI values, and included a higher percentage of AH cases that occurred indoors in comparison to the non-frail patient group. Regarding the mechanism of hypothermia, the rate of acute medical illness in the frail patient group was higher than that in the non-frail patient group.

**Clinical and laboratory data**

Among the 920 patients, the core body temperature was measured in 585 (63.6%). The clinical and laboratory data are presented in Table 2. There were no significant differences in the severity grade of temperature, blood pressure, respiratory rate, potassium level, creatinine level, or cardiac arrest during the pre-hospital period between frail and non-frail patients. Frail patients had a lower GCS, heart rate, lactate level, platelet count, CPK level, and rate of tracheal intubation in comparison to non-frail patients. The pH values of frail patients were significantly higher in comparison to non-frail patients.
1363 patients visited ED due to hypothermia (Hypothermia study 2018&2019)

443 excluded
- 147 Body temperature >35°C or Unknown
- 127 Unknown outcome
- 150 Unknown length of stay
- 19 Unknown ADL data

920 patients admitted hospitals due to hypothermia

CFS ≥5
Frail patients
N=221

CFS <5
Non-Frail patients
N=699

Fig. 1 Flow chart of the enrolment of the study participants. Of the 1363 patients with hypothermia, 920 patients were enrolled, and 443 patients were excluded. The 920 patients were divided into the frail group (N = 221) and the non-frail group (N = 699). ED, emergency department; CFS, clinical frailty scale.

Table 1 Baseline characteristics

|                          | All patients | Missing | Frail | Non-Frail | p-value |
|--------------------------|--------------|---------|-------|-----------|---------|
|                          | n = 920      | n, (%)  | n = 221 | n = 699   |         |
| Age, years               | 79 (68–87)   | 0       | 85 (78–90) | 77 (66–86) | < 0.001 |
| Male                     | 513 (55.8%)  | 0       | 105 (47.5%) | 408 (58.4%) | < 0.001 |
| Charlson comorbidity index | 1 (0–2) 1.2 ± 1.6 | 0       | 1 (0–2) 1.5 ± 1.7 | 1 (0–2) 1.1 ± 1.5 | < 0.001 |
| Severity                 |              |         |       |           |         |
| SOFA total               | 6 (3–8)      | 71 (7.7) | 6 (4–8) | 5 (3–8) | 0.286   |
| Clinical Frailty Scale score | 2 (1–4) | 0       | 5 (5–7) | 2 (1–3) | < 0.001 |
| Lifestyle                | 10 (1.1)     |         |       |           | < 0.001 |
| Living alone             | 298 (32.4%)  |         | 39 (17.8%) | 259 (37.5%) |         |
| Not living alone         | 549 (59.7%)  |         | 144 (65.8%) | 405 (58.6%) |         |
| Homelessness             | 3 (0.3%)     |         | 0 (0.0%) | 3 (0.4%) |         |
| Nursing home             | 48 (5.2%)    |         | 34 (15.5%) | 14 (2.0%) |         |
| Unknown                  | 12 (1.3%)    |         | 2 (0.9%) | 10 (1.4%) |         |
| Location of hypothermia incidence | 24 (2.6) |         |       |           | < 0.001 |
| Outdoor                  | 218 (23.7%)  |         | 14 (6.5%) | 204 (30%) |         |
| Indoor                   | 678 (73.7%)  |         | 203 (93.5%) | 475 (70%) |         |
| Hypothermia caused mechanism | 57 (6.2) |         |       |           | < 0.001 |
| Acute medical illness    | 465 (50.5%)  |         | 123 (60.6%) | 342 (51.8%) |         |
| Trauma, Submersion, and distress | 126 (13.7%) |         | 17 (8.4%) | 109 (16.5%) |         |
| Alcohol intoxication     | 41 (4.5%)    |         | 3 (1.5%) | 38 (5.8%) |         |
| Others (Unknown, drug)   | 231 (25.1%)  |         | 60 (29.6%) | 171 (25.9%) |         |

SOFA Sequential Organ Failure Assessment; The data are expressed as the number (%), median (interquartile range) or mean ± standard deviation.

*The values were presented as the median and 25th–75th percentile because the Charlon comorbidity index showed a skewed distribution. However, these values were the same in the frail and non-frail groups despite the Mann-Whitney U test showing significance, so the mean and standard deviation are shown as well.
Primary outcome

As shown in Table 3, the overall 30-day mortality rate was 23.5% (N = 216). After 30 days of hospitalization, 32.6% of frail patients and 20.6% of non-frail patients had died (p < 0.001). A survival time analysis revealed that there was significant difference between frail and non-frail patients (log-rank test p < 0.001) (Fig. 2). The results of the Cox proportional hazards analysis are summarized in Table 4. In the unadjusted analysis, frail patients had a significantly higher risk of 90-day mortality (Hazard ratio [HR], 1.64; 95% confidence interval [CI], 1.25–2.17; p < 0.001). Based on the Cox proportional

### Table 2 Clinical and laboratory data of the patients with hypothermia

|                      | All patients n = 920 | Missing n, (%) | Frail n = 221 | Non-Frail n = 699 | p-value |
|----------------------|----------------------|----------------|---------------|------------------|---------|
| Temperature          | 30.6 (28.2–33.1)     | 0              | 30.6 (28.6–33.0) | 30.6 (28.1–33.2) | 0.810   |
| Mild (35–32 °C)      | 348 (37.8%)          | 81 (36.7%)     | 267 (38.2%)   | 20.6%            |         |
| Moderate (32–28 °C)  | 360 (39.1%)          | 99 (44.8%)     | 261 (37.3%)   |                  |         |
| Severe (< 28 °C)     | 212 (23.0%)          | 41 (18.6%)     | 171 (24.5%)   |                  |         |
| GCS                  | 10 (7–14)            | 50 (5.4)       | 10 (7–13)     | 11 (7–14)        | < 0.001 |
| Systolic BP (mmHg)   | 117 (90–146)         | 82 (8.9)       | 115 (90–143)  | 117 (91–147)     | 0.705   |
| Diastolic BP (mmHg)  | 68 (51–86)           | 96 (10.4)      | 67 (51–82)    | 69 (51–88)       | 0.454   |
| Heart rate           | 72 (53–90)           | 30 (3.3)       | 62 (48–82)    | 73 (56–92)       | < 0.001 |
| Respiratory rate     | 18 (15–22)           | 89 (9.7)       | 18 (15–21)    | 18 (15–23)       | 0.423   |
| pH                   | 7.30 (7.19–7.37)     | 61 (6.6)       | 7.32 (7.23–7.39) | 7.29 (7.18–7.37) | < 0.001 |
| Potassium (mEq/L)    | 4.2 (3.7–4.9)        | 7 (0.8)        | 4.3 (3.7–4.9) | 4.2 (3.7–4.9)    | 0.674   |
| Lactate (mmol/L)     | 3.5 (1.8–7.6)        | 121 (13.2)     | 2.3 (1.1–6.8) | 3.8 (2.0–8.2)    | < 0.001 |
| Pht (× 10^9/μL)      | 18.1 (12.6–24.3)     | 13 (1.4)       | 16.1 (10.9–22.3) | 18.7 (13.3–24.7) | < 0.001 |
| CPK (U/L)            | 347 (138–1239)       | 72 (7.8)       | 249 (104–617) | 393 (150–1494)   | < 0.001 |
| BUN (mg/dL)          | 31.7 (19.3–55.0)     | 13 (1.4)       | 35.1 (22.0–57.0) | 30.4 (18.5–54.2) | 0.020   |
| Creatinine (mg/dL)   | 1.1 (0.7–1.8)        | 14 (1.5)       | 1.1 (0.7–1.9) | 1.1 (0.7–1.8)    | 0.736   |
| CPA                  | 62 (6.7%)            | 2 (0.2)        | 12 (5.5%)     | 50 (7.2%)        | 0.443   |
| Intubation           | 157 (17.1%)          | 60 (6.5)       | 23 (11.4%)    | 134 (20.3%)      | < 0.001 |
| ICU                  |                       |                |               |                  |         |
| GCS                  |                       |                |               |                  |         |
| CPA                  |                       |                |               |                  |         |
| The data are expressed as the number (%), median (interquartile range)

### Table 3 Mortality, hospital length of stay, neurological score, and complications

|                      | All patients n = 920 | Frail n = 221 | Non-Frail n = 699 | p-value |
|----------------------|----------------------|---------------|------------------|---------|
| 30-day mortality     | 216 (23.5%)          | 72 (32.6%)    | 144 (20.6%)      | < 0.001 |
| Length of stay at ICU| 3 (2–6)              | 3 (2–5)       | 4 (2–7)          | 0.090   |
| Length of stay at hospital | 13 (4–27) | 11 (3–23)     | 13 (4–29)        | 0.081   |
| CPC at 30 days       |                      |               |                  | < 0.001 |
| good (1–2)           | 302                  | 27 (20.0%)    | 275 (57.2%)      |         |
| poor (3–5)           | 314                  | 108 (80.0%)   | 206 (42.8%)      |         |
| Complication         |                      |               |                  |         |
| Anrhythmia           | 22                   | 6 (2.7%)      | 16 (2.3%)        | 0.800   |
| Pneumonia            | 5                    | 2 (0.9%)      | 3 (0.4%)         | 0.599   |
| Pancreatitis         | 1                    | 1 (0.5%)      | 0 (0%)           | 0.240   |
| Electrolyte abnormalities | 3                 | 0 (0%)        | 3 (0.4%)         | 1.000   |
| Coagulopathy         | 5                    | 2 (0.9%)      | 3 (0.4%)         | 0.599   |
| Other                | 10                   | 6 (2.7%)      | 4 (0.6%)         | 0.016   |
| ICU                  |                       |                |                  |         |
| CPC                  |                       |                |                  |         |
| The data are expressed as the number (%), median (interquartile range)
hazards analysis using multiple imputation, after adjustment for age, potassium level, lactate level, pH value, sex, CPK level, heart rate, platelet count, location of hypothermia incidence, and rate of tracheal intubation, frail patients still had a significantly higher risk of 90-day mortality (Hazard ratio [HR], 1.69; 95% confidence interval [CI], 1.25–2.29; \( p < 0.001 \)). A sensitivity analysis performed using the complete dataset of cases excluding cases with missing values (\( N = 679 \)) confirmed the robustness of the results.

Secondary outcomes
Among the 920 total patients, the median length of ICU stay was 3 days, and the median length of hospital stay was 13 days. There was no significant difference in the length of stay at the ICU or hospital between frail and non-frail patients (Table 3). However, in the neurological assessment, frail patients showed a higher rate of patients with a worsened neurological score (CPC 3–5) at 30 days after admission in comparison to non-frail patients, while non-frail patients showed a significantly higher rate of patients with a favorable neurological outcome (CPC 1–2) in comparison to frail patients. There was no significant difference in the incidence of complications between the frail and non-frail patient groups.

Rewarming method and rewarming rate
The rewarming method and rewarming rate are presented in Table 5. The rates of warmed blanket (\( P < 0.001 \)) and ECMO (\( P = 0.039 \)) use in the frail patient group were lower in comparison to the non-frail patient group. However, the other rewarming methods did not differ between the two groups to a statistically significant extent. The rewarming rate in frail patients was significantly slower than that in non-frail patients (\( p < 0.001 \)).

Subgroup analyses
In the subgroup analysis with the exclusion of cases in which a warmed blanket or ECMO were applied, the rewarming rate in frail patients was still lower than that in non-frail patients (Supplemental Table 1).
The rewarming rate in frail patients was slower than that in non-frail patients. Although the rates at which ECMO or a warmed blanket were used in the frail patient group were lower in comparison to the non-frail patient group, the results were also similar in the subgroup analysis that excluded cases in which ECMO or a warmed blanket were used. The reasons for the difference in the rewarming rate may be as follows. It is hypothesized that intrinsic heat production by the patient, such as shivering thermogenesis, does not occur sufficiently in frail patients with AH, resulting in delayed rewarming. In the present study, the finding that the CPK level was lower in the frail patient group may support this mechanism. A previous study showed that a decreased rewarming rate in patients with AH is associated with a high risk of underlying infection [30] and mortality [31]. In recent years, many studies have shown that the prognosis of septic patients with hypothermia is poor [32–34]. For this reason, it has been pointed out that homeostatic dysfunction, such as immune dysfunction, is related to the poor prognosis of these patients [35, 36]. Although there was no significant difference in the occurrence of infectious complications between the frail and non-frail patient groups in the present study, a similar mechanism may be responsible for the relationship between frailty and a poor prognosis in patients with AH. On the other hand, the results of this study could not clarify whether or not the rapid rewarming using invasive internal rewarming methods will reduce mortality and improve the prognosis of frail patients with AH. Thus, further studies are needed to address this problem.

In our previous study, we found that frail patients with AH showed prolonged hospitalization [16]. However, in this study, there was no significant difference in the length of hospital stay between the frail and non-frail patient groups. The reasons are as follows: the previous study excluded patients who died within 30 days, whereas the present study included these patients. The rate of early mortality within 30 days was higher in the frail group than in the non-frail group. As a result, the length of hospital stay in the frail group was shorter than that in the non-frail group, although the difference was not statistically significant.

A previous study showed that, among ICU patients requiring mechanical ventilation, the presence of frailty increased the likelihood of short-term mortality, and that these findings might play a role in informed shared decision-making with patients and families prior to the provision of mechanical ventilation [37]. In this study, the rate of tracheal intubation was lower among frail patients than among non-frail patients. This may be because these patients and their
families did not wish to receive invasive treatment with intubation and ventilation.

Regarding complications, previous studies have reported that the incidence of complications is higher in frail patients [7]. However, in this study, the incidence of complications in the frail and non-frail patient groups did not differ to a statistically significant extent. The complications defined in this study (arrhythmia, pneumonia, pancreatitis, electrolyte abnormality and coagulopathy) occurred infrequently, which may have contributed to the lack of a significant difference.

The present study was associated with some limitations. First, we used the CFS score, which was calculated based on ADL and the CCI to determine frailty, while the standard tools for the diagnosis of frailty are the frailty index [38] or frailty phenotype [39]. Therefore, it remains to be verified whether the diagnosis of frailty in this study was accurate. In this regard, a comparative study regarding the accuracy of the CFS score is currently in progress [40]. Second, there were numerous missing data in relation to the rewarming rate. However, the volume of data including in this nationwide study was sufficient; thus, the results are considered robust. Third, we could not determine the rewarming rate according to individual rewarming methods, because several rewarming methods were used in combination. Finally, this study was based on the findings of registry data on hypothermia, and it did not include any data that was related to frail research, such as ADL after a long-term follow-up. Therefore, further studies will be needed to investigate the long-term ADL of frail patients with AH.

Conclusions
This study found that, after adjustment for multiple factors, mortality in frail patients with AH was higher than that in non-frail patients with AH. According to the neurological outcome after 30 days, the percentage of patients with a poor prognosis in the frail patient group was higher than that in the non-frail patient group. It is important to recognize that frail patients with AH are at risk for more severe hypothermia.

Abbreviations
AH: Accidental hypothermia; CFS: Clinical frailty scale; HR: Hazard ratio; CI: Confidence interval; EMS: Emergency medical services; ED: Emergency department; ADL: Activities of daily living; CCI: Charlson comorbidity index; GCS: Glasgow coma scale; SOFA: Sequential Organ Failure Assessment; CPC: Cerebral Performance Category; ECMO: Extracorporeal membrane oxygenation; ICU: Intensive care unit; CT: Computed tomography

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12877-021-02459-5.

Acknowledgements

Additional file 1: Supplemental Fig. 1. The age distribution of patients with accidental hypothermia. Of the 920 patients, 746 (81%) were ≥65 years old.

Additional file 2: Supplemental Table 1. The rewarming rate in the sub-analysis after excluding cases in which ECMO or a warmed blanket was used.
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National Hospital Organization Nagoya Medical Center.
National Hospital Organization Osaka National Hospital.
Nagoya City General Hospital.
Nihon University Hospital.
Nihon University Ibaraki Hospital.
Nihonkai General Hospital.
Niigata University Medical & Dental Hospital.
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Tokushima Prefectural Myoshi Hospital.
Tokuyama Central Hospital.
Tokyo Metropolitan Tama Medical Center.
Tosei General Hospital.
Toyama University Hospital.
Tsuyama Chuo Hospital.
Uji Tokushukai Medical Center.
University of Tokyo Hospital.
University of Yamanashi Hospital.
Wakayama Red Cross Medical Center.
Yamagata Prefectural Central Hospital.
Yamagata University Hospital.
Yamanashi University Hospital.
Yokkaichi Municipal Hospital.
Yokohama Minami Kyosai Hospital.

Authors’ contributions
ST and JK contributed to the conception and design of this analysis. ST wrote the manuscript. TH, SY, YK, KH, and JS supervised the work. YS provided statistical advice on the study design and the analyzed data. TM, MY, JJ, YO, YO, HK, TK, NF, KS, HY, and AY contributed to the interpretation of the results. All authors read and approved the final manuscript.

Funding
None.

Availability of data and materials
The datasets and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study has been confirmed that all the experiments were performed in accordance with relevant guidelines and regulations. The study has been approved by the Ethics Review Board of Teikyo University Hospital in Japan (Approval No: 17–090). The requirement for informed consent was waived due to the observational nature of the study by the Ethics Review Board of Teikyo University Hospital in Japan. In addition, the institutional review board of each hospital listed in the acknowledgements approved the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests in association with the present study.

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Received: 16 April 2021 Accepted: 10 September 2021
Published online: 25 September 2021

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