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RESEARCH

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Indications for extracorporeal membrane oxygenation in older adult patients with accidental hypothermia and hemodynamic instability

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Abstract

Background Extracorporeal membrane oxygenation (ECMO) indications in patients with accidental hypothermia (AH) and hemodynamic instability before cardiac arrest (CA) are unclear. We aimed to identify a subgroup of these patients who would benefit from ECMO rewarming.

Methods This study was a post-hoc analysis of the ICE-CRASH study (2019–2022), a prospective, multicenter, observational study throughout Japan. Among the 499 patients (core temperature < 32 °C, age > 18 years), 175 with AH and hemodynamic instability were selected. The primary outcome was 28-day mortality. We examined the effect of ECMO on 28-day mortality after risk stratification based on age, activities of daily living (ADLs), core temperature, Glasgow coma scale (GCS) score, systolic blood pressure (SBP), arrhythmia, pH, and lactate levels. The secondary outcomes were rewarming rate, event-free days (ICU-, ventilator-, and catecholamine-free days), and complications.

Results The patients were divided into ECMO ($N = 17$) and non-ECMO ($N = 158$) groups. No significant difference was observed in the 28-day survival rates between the ECMO (13/17, 77%) and non-ECMO (120/158, 76%) groups ($p = 0.96$). The restricted cubic spline curve showed that the 28-day mortality increased with a GCS score ≤ 8; no relationship was observed between 28-day mortality and decreased SBP or core temperature. No significant difference was observed in the effectiveness of ECMO based on age (< 80 vs. ≥ 80 years), ADLs (independent vs. assistance needed/unknown), core temperature (≥ 26 vs. < 26 °C), GCS (> 8 vs. ≤ 8), SBP (≥ 60 vs. < 60 mmHg), arrhythmia (sinus rhythm vs. arrhythmia), pH (≥ 7.1 vs. < 7.1), and serum lactate level (< 3.0 vs. ≥ 3.0 mmol/L). The rewarming rate was significantly higher in the ECMO group than in the non-ECMO group (2.5 °C/h vs. 1.3 °C/h, $p < 0.001$), and ICU-, ventilator-, and catecholamine-free days were significantly higher in the non-ECMO group than in the ECMO group. Bleeding complications were significantly more common in the ECMO group than in the non-ECMO group (77% vs. 26%, $p < 0.001$).

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Conclusions We were unable to identify a subgroup of older adult patients with AH and hemodynamic instability who would benefit from ECMO. The ICE-CRASH study was registered with the University Hospital Medical Information Network Clinical Trial Registry on April 1, 2019 (UMIN-CTR ID: UMIN000036132).

Keywords Extracorporeal membrane oxygenation, Hemodynamic instability, Accidental hypothermia, Older adult patients, Systolic blood pressure

Background

Accidental hypothermia (AH) causes the failure of many organs (reduced consciousness, hemodynamic instability, and coagulopathies) with a reduced core temperature [1]. In particular, a core temperature of < 28 °C can cause ventricular fibrillation and cardiac arrest (CA), which are life-threatening and fatal. For these patients with AH, veno-arterial extracorporeal membrane oxygenation (ECMO), which can support circulation and rewarm the patient, is a viable rewarming treatment and has recently been recommended in the guidelines [1–3]. However, whether ECMO is beneficial in patients with AH and hemodynamic instability before CA remains unclear. A previous study showed that the mortality rate was two times higher in patients with severe AH who developed witnessed CA during extrication and transport (defined as "rescue collapse") than in those who did not [4]. This study demonstrated that initiating ECMO before CA may be beneficial if patients at risk of CA can be accurately identified. A recent study involving a relatively young cohort (median age 61 years) showed that patients with AH and hemodynamic instability who received ECMO had a better prognosis than those who underwent non-ECMO rewarming [5]. However, our previous Intensive Care with Extracorporeal Membrane Oxygenation Rewarming in Accidentally Severe Hypothermia (ICE-CRASH) study showed that the survival of patients with AH and hemodynamic instability did not significantly differ between the ECMO and non-ECMO groups in a population with a large number of older patients (median age 82 years) [6]. To clarify the difference between the results of these studies, we performed a post-hoc subgroup analysis of the ICE-CRASH study. We hypothesized that ECMO treatment may benefit a specific subgroup of patients with AH and hemodynamic instability before CA.

Methods

Study design and setting

This was a post-hoc analysis of a prospective, multicenter, observational study conducted by the ICE-CRASH study group between December 2019 and March 2022. The ICE-CRASH study included patients with AH at 36 participating tertiary care centers and was registered with the University Hospital Medical Information Network Clinical Trial Registry on April 1, 2019 (UMIN-CTR ID: UMIN000036132). The ICE-CRASH study received ethical approval from Asahikawa Medical University (approval no. 18194) and was approved by the ethics committee of each participating hospital. This study was conducted in accordance with the Declaration of Helsinki, and the requirement for written informed consent was waived because of the anonymity of the data.

The ICE-CRASH study enrolled consecutive patients aged ≥ 18 years with AH, including those who developed CA [6, 7]. We defined hypothermia as a core temperature < 32 °C measured at the emergency department (ED) upon arrival. The exclusion criteria were patients aged < 18 years and those who had CA and were ineligible for resuscitation, as evaluated by the emergency physicians at each institution.

Study population

The minimum sufficient circulation for patients with AH has not been defined [3]. Consequently, based on a previous study [6], we defined patients as having AH with hemodynamic instability if they met the following criteria: (1) unmeasurable blood pressures or systolic blood pressures (SBPs) ≤ 60 mmHg, or (2) heart rates of ≤ 50 bpm upon arrival at the hospital. In this post-hoc analysis, we excluded patients who were in CA when they arrived at the hospital or developed CA after arrival.

Data collection

We collected data on age, sex, activities of daily living (ADLs), the locations where the AH occurred (indoors or outdoors), causes underlying the hypothermia, Glasgow coma scale (GCS) scores, laboratory data, core temperatures, SBP/diastolic blood pressures (DBPs), heart rates, electrocardiogram results, Sequential Organ Failure Assessment (SOFA) scores [8], rewarming times, mortality rates, Cerebral Performance Category (CPC) scores at discharge [9], event-free days (ICU-, ventilator-, renal replacement therapy [RRT]-, and catecholamine administration-free days) during the 28 days after admission, and survival at 28 days after admission. We calculated the number of event-free days within the 28-day period by subtracting the duration from the 28 days. If patients were discharged within 28 days of admission, we calculated the number of event-free days by subtracting the duration from 28 days. We assigned the patients who died with the worst possible outcome of "zero event-free days." If a patient died within 24 h of ED admission or during rewarming, we did not calculate their SOFA scores or rewarming rates. The laboratory data included pH, lactate, total bilirubin, amylase, lipase, creatine kinase, creatinine, sodium, potassium, and glucose levels. We assessed the pH using arterial blood gas analysis, and if the pH was measured via venous blood gas analysis, it was adjusted to ensure that the arterial blood gas pH was higher (by 0.03) than the venous blood gas pH, as described in a previous study [10]. The attending physician selected the method of rewarming. Rewarming methods consisted of active external (warmed blanket and bath) and active internal (warmed fluid infusion, body cavity lavage, hemodialysis, endovascular temperature management systems, and ECMO) rewarming. In addition, we collected data on the incidence of complications (bleeding, pneumonia, acute pancreatitis, and acute kidney injury [AKI]). Complications included events that occurred within 7 days of admission. We defined bleeding as any amount of bleeding that required transfusions, including red cell concentrate, fresh frozen plasma, and platelet concentrate, but not other blood products (cryoprecipitate, albumin). The radiologist diagnosed pneumonia as an obvious infiltrative shadow on chest radiography or computed tomography (CT). We defined pancreatitis as the presence of at least two of the following conditions: (1) abdominal pain, (2) a ≥ 3-fold elevation of normal pancreatic enzyme levels, and (3) pancreatic edema or peripancreatic effusion on ultrasound or CT. We defined AKI as an Acute Kidney Injury Network (AKIN) classification [11] of stage ≥ 2.

Outcome measures

The primary outcome of this study was 28-day mortality. We examined the effectiveness of ECMO treatment on 28-day mortality after risk stratification based on age (< 80 vs. ≥ 80 years), ADLs (independent vs. assistance needed or unknown), core temperatures (≥ 26 °C vs. < 26 °C), GCS scores (> 8 vs. ≤ 8), SBPs (≥ 60 vs. < 60 mmHg), arrhythmia (sinus rhythm vs. arrhythmia), pH (≥ 7.1 vs. < 7.1), and lactate levels (< 3.0 vs. ≥ 3.0 mmol/L). The secondary outcomes were rewarming rate, event-free days (ICU-, ventilator-, RRT-, and catecholamine administration-free days), and other complications (bleeding, pneumonia, acute pancreatitis, and AKI).

Statistical analyses

We presented descriptive statistics as medians (interquartile ranges [IQRs]) or numbers (percentages). We performed a restricted cubic spline analysis to visualize how mortality varied according to changes in age, core temperature, GCS score, SBP, pH, and lactate levels. Using cut-off values determined from the cubic spline curves, we subsequently performed subgroup analyses to determine the relationship between ECMO and 28-day mortality rates by age (< 80 vs. ≥ 80 years), ADLs (independent vs. assistance needed or unknown), core temperatures (≥ 26 °C vs. < 26 °C), GCS scores (> 8 vs. ≤ 8), SBPs (≥ 60 vs. < 60 mmHg), arrhythmia (sinus rhythm vs. arrhythmia), pH (≥ 7.1 vs. < 7.1), and lactate levels (< 3.0 vs. ≥ 3.0 mmol/L). We selected targeted subgroups based on previous research [5, 12, 13] on the clinical outcomes of patients with AH. The p-values for interactions indicated whether the odds ratios for the effect of ECMO rewarming differed between subgroups. In addition, we performed a multivariate logistic regression analysis, adjusted for age, GCS score, and SBP upon arrival at the ED. We selected these covariates based on the relevant literature [12, 14]. We performed all statistical analyses using R software (version 4.1.3; R Foundation for Statistical Computing, Vienna, Austria). We defined statistical significance as two-sided p-values < 0.05 for all statistical analyses.

Results

Patient characteristics

Of the 499 patients enrolled in the ICE-CRASH study, 175 were eligible for inclusion in this post-hoc analysis, excluding those with CA ($N = 57$), stable hemodynamics ($N = 257$), unknown 28-day outcomes ($N = 6$), or missing arterial blood gas analysis results ($N = 4$) (Fig. 1). Of the patients with diagnosed hemodynamic instability, 80 (46%) had SBPs ≤ 60 mmHg or unmeasurable BPs, and 95 (54%) had HRs ≤ 50 bpm on arrival at the hospital. We divided patients into the ECMO ($N = 17$) and non-ECMO ($N = 158$) groups. Table 1 shows the patient characteristics. The median (IQR) age of the patients was 82 (69–88) years, and indoor-onset hypothermia occurred in 88% of patients. The ECMO group had lower core temperatures (26.1 °C [25.7–27.0] vs. 28.0 °C [26.7–28.9], $p = 0.005$), GCS scores (6 [3–8] vs. 9 [7–11], $p = 0.002$), SBPs (60 mmHg [54–79] vs. 100 mmHg [73–132], $p = 0.009$), and DBPs (37 mmHg [30–43] vs. 55 mmHg [43–75], $p = 0.003$), as well as higher pHs (7.36 [7.31–7.43] vs. 7.29 [7.17–7.34], $p = 0.016$), and SOFA scores (11 [9–13] vs. 7 [6–10], $p < 0.001$) than the non-ECMO group. The other variables did not differ significantly between groups.

Patient outcomes

Primary outcomes

Table 2 shows the outcomes of patients with AH and hemodynamic instability. The 28-day survival did not differ significantly between the ECMO (13/17, 77%) and non-ECMO (120/158, 76%) groups (odds ratio [OR] 0.97, 95% confidence interval [CI]: 0.30–3.16, $p = 0.96$). The results were also similar after adjustment for age, GCS score, and SBP in the logistic regression analysis (OR 0.61, 95% CI: 0.17–2.14, $p = 0.44$). The analysis limited to patients with AH and hemodynamic instability who had SBPs ≤ 60 mmHg or unmeasurable BPs was also

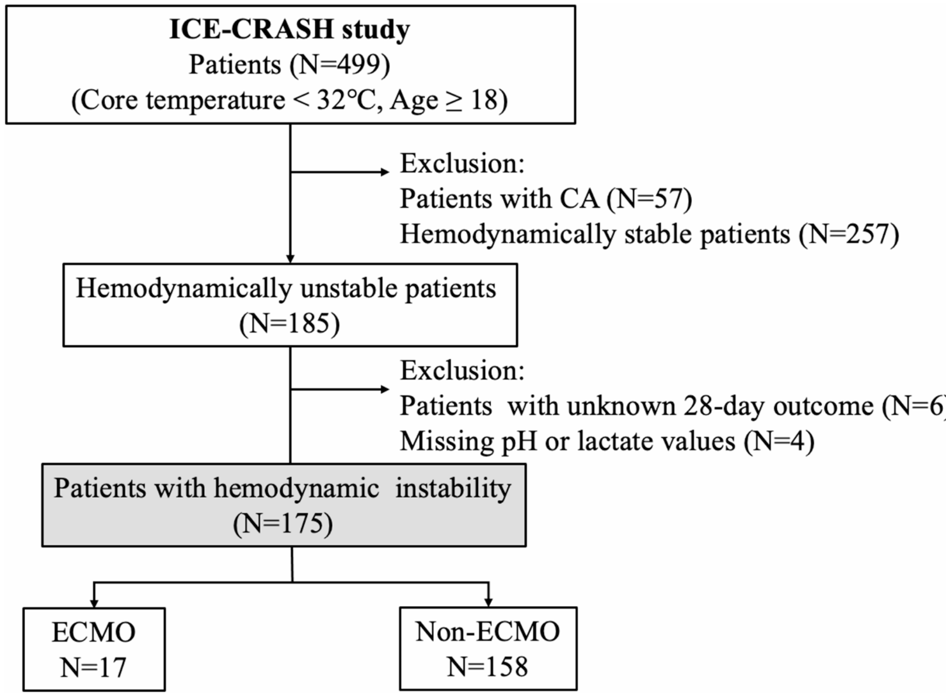

Fig. 1 Study flowchart of the 499 patients with AH included in the ICE-CRASH study, 57 with CA and 257 with stable hemodynamics whose systolic blood pressures were > 60 mmHg and heart rates were > 50 beats/min were excluded. Six patients whose 28-day outcomes were unknown and four with missing pHs or lactate values were excluded. We diagnosed a total of 175 patients with hemodynamic instability. We divided the 175 patients with hemodynamic instability into the ECMO (*N* = 17) and non-ECMO (*N* = 158) groups. AH, accidental hypothermia; CA, cardiac arrest; ECMO, extracorporeal membrane oxygenation; ICE-CRASH Intensive Care with Extracorporeal Membrane Oxygenation Rewarming in Accidentally Severe Hypothermia

consistent with the main analysis results (Supplemental Tables 1 and 2).

The restricted cubic spline curve demonstrated a non-linear relationship between 28-day mortality and age, core temperatures, GCS scores, SBPs, pHs, and lactate levels (Fig. 2). The 28-day mortality increased with GCS scores of ≤ 8. However, no relationship was observed between 28-day mortality and a decrease in SBP or core temperature.

We performed subgroup analyses using cut-off values determined from the cubic spline curves. No statistically significant interactions were observed between the effectiveness of ECMO for rewarming and each subgroup; age (< 80 vs. ≥ 80 years) ($p_{interaction}$=0.247), ADLs (independent vs. assistance needed or unknown) ($p_{interaction}$=0.216), core temperatures (≥ 26 °C vs. < 26 °C) ($p_{interaction}$=0.158), GCS scores (> 8 vs. ≤ 8) ($p_{interaction}$=0.482), SBPs (≥ 60 vs. < 60 mmHg) ($p_{interaction}$=0.663), arrhythmia (sinus rhythm vs. arrhythmia) ($p_{interaction}$=0.826), pH (≥ 7.1 vs. < 7.1) ($p_{interaction}$=0.991), and lactate levels (< 3.0 vs. ≥ 3.0 mmol/L) ($p_{interaction}$=0.379) (Fig. 3).

Secondary outcomes

The rewarming rate was significantly higher in the ECMO group than in the non-ECMO group (2.5 °C/h vs. 1.3 °C/h, $p < 0.001$), and ICU-, ventilator-, and catecholamine-free days were significantly higher in the non-ECMO group than in the ECMO group. In terms of complications, bleeding was significantly more common in the ECMO group than in the non-ECMO group (77% vs. 26%) ($p < 0.001$); however, no significant differences existed between the groups regarding other complications.

Discussion

This study showed that it was not possible to identify subgroups of patients who would benefit from ECMO induction before CA in older adult patients with AH. Guidelines for AH management have recommended the transport of patients with AH (SBPs < 90mmHg, hemodynamic instability, and core temperatures < 32 °C in older patients and patients with comorbidities or core temperatures < 30 °C in younger, healthy patients) to hospitals with ECMO [3]. An SBP < 90mmHg is a reasonable prehospital estimate of hemodynamic instability, but whether it is an indicator of hemodynamic instability in-hospital is unknown [3]. Therefore, the criteria for using ECMO in patients with AH and hemodynamic instability remains unclear. Previous studies have suggested that the criteria for the application of ECMO were an SBP ≤ 90 mmHg [15] or ≤ 60 mmHg [5] or severe arrhythmia. Surprisingly, the restricted cubic spline analysis in the

Table 1 Baseline characteristics of patients with AH and hemodynamic instability ($n = 175$)

Variable	Overall	ECMO	Non-ECMO	*p*-value
	n **= 175**	***n*** **= 17**	***n*** **= 158**	
Age, years	82 (69–88)	79 (64–84)	83 (70–88)	0.164
Male	95 (54%)	12 (71%)	83 (53%)	0.203
ADL				0.674
Independent	91 (52%)	11 (65%)	80 (51%)	
Mild/moderate assistance needed	60 (34%)	4 (24%)	56 (35%)	
Maximal assistance needed	18 (10%)	2 (12%)	16 (10%)	
Unknown	6 (3%)	0 (0%)	6 (4%)	
Location where accidental hypothermia occurred				0.128
Outdoor	21 (12%)	4 (24%)	17 (11%)	
Indoor	154 (88%)	13 (76%)	141 (89%)	
Cause of accidental hypothermia				0.647
Intoxication (Alcohol, drugs, carbon monoxide)	9 (5%)	0 (0%)	9 (6%)	
Cerebrovascular disease	7 (4%)	0 (0%)	7 (4%)	
Endocrine disease (Hypoglycemia)	27 (15%)	2 (12%)	25 (16%)	
Infection	50 (29%)	5 (29%)	45 (29%)	
Cardiovascular disease	5 (3%)	1 (6%)	4 (3%)	
Trauma	10 (6%)	0 (0%)	10 (6%)	
Others	31 (18%)	5 (29%)	26 (17%)	
Unknown	36 (21%)	4 (24%)	32 (20%)	
Core temperature on arrival at ED (°C)	27.9 (26.4–28.8)	26.1 (25.7–27.0)	28.0 (26.7–28.9)	0.005
GCS score	9 (6–11)	6 (3–8)	9 (7–11)	0.002
Systolic BP (mmHg)	97 (69–126)	60 (54–79)	100 (73–132)	0.009
Diastolic BP (mmHg)	53 (40–72)	37 (30–43)	55 (43–75)	0.003
Heart rate	47 (40–59)	43 (36–50)	47 (40–59)	0.756
Systolic BP ≤ 60 (mmHg) or unmeasurable BP	80 (46%)	11 (65%)	69 (44%)	0.126
ECG on arrival at ED				0.780
Sinus rhythm	93 (53%)	9 (53%)	84 (53%)	
Atrial fibrillation	38 (22%)	3 (18%)	35 (22%)	
A-V block	12 (7%)	1 (6%)	11 (7%)	
Junctional rhythm	25 (14%)	3 (18%)	22 (14%)	
Ventricular rhythm	3 (2%)	0 (0%)	3 (2%)	
Other	4 (2%)	1 (6%)	3 (2%)	
Initial blood gas analysis on arrival at ED				
pH	7.29 (7.17–7.35)	7.36 (7.31–7.43)	7.29 (7.17–7.34)	0.016
Potassium (mEq/L)	4.3 (3.6–5.1)	4.1 (3.6–4.4)	4.3 (3.6–5.2)	0.360
Lactate (mmol/L)	2.4 (1.1–5.1)	2.9 (1.1–4.1)	2.4 (1.1–5.1)	0.709
Total SOFA score* on the day of arrival at ED	8 (6–10)	11 (9–13)	7 (6–10)	< 0.001

ADL, activities of daily living; ED, emergency department; GCS, Glasgow Coma Scale; BP, blood pressure; SOFA, Sequential Organ Failure Assessment

The data are expressed as the numbers (%) or medians (interquartile ranges)

* If a patient died within 24 h of admission to the ED or during rewarming, the SOFA score was not calculated

present study showed no relationship between SBP and mortality. In other words, hemodynamic instability may not necessarily mean hemodynamic instability in patients with hypothermia. SBPs < 90mmHg or ≤ 60mmHg may still provide the minimum oxygen requirement during severe AH. This suggests that the decision to use ECMO based on SBPs as an indicator may not be appropriate. A possible explanation for this is the metabolic suppression, extremely low oxygen consumption, and neuroprotective effects of hypothermia. Experimental animal studies have shown that cerebral oxygen consumption decreases by 6–7% for every 1 °C drop in core temperature [16]. Recent studies showed that intermittent chest compressions are acceptable during cardiopulmonary resuscitation for hypothermic CA [17], owing to the neuroprotective effects associated with hypothermia [18]. Previous studies have focused on lactate levels and pHs instead of SBPs as indicators of organ hypoperfusion [13]. However, the results of the present study also showed no relationship between lactate levels or pHs and death. Alternative indicators of left ventricular function, such as ejection fraction (EF), may be useful in defining

Table 2 Outcomes of patients with AH and hemodynamic instability ($n = 175$)

Variable	Overall	ECMO	Non-ECMO	*p*-value
	***n* = 175**	***n* = 17**	***n* = 158**	
28-day survival	133 (76%)	13 (77%)	120 (76%)	1.000
Favorable neurological outcome (CPC 1 or 2) at discharge	106 (61%)	12 (71%)	94 (60%)	0.442
Rewarming rate (°C/h)	1.4 (0.9–2.1)	2.5 (1.9–3.4)	1.3 (0.9–1.9)	< 0.001
Event-free days				
ICU-free days	23 (0–25)	20 (0–22)	23 (0–26)	0.036
Ventilator-free days	28 (0–28)	24 (0–25)	28 (2–28)	0.002
RRT-free days	28 (7–28)	28 (15–28)	28 (4–28)	0.760
Catecholamine-free days	26 (8–28)	24 (15–26)	26 (5–28)	0.032
Complications				
Bleeding	54 (31%)	13 (77%)	41 (26%)	< 0.001
Pneumonia	52 (30%)	5 (29%)	47 (30%)	1.000
Pancreatitis	8 (5%)	2 (12%)	6 (4%)	0.176
Renal injury	47 (27%)	3 (18%)	44 (28%)	0.565
Others	28 (16%)	2 (12%)	26 (17%)	1.000

CPC, Cerebral Performance Category; RRT, renal replacement therapy

The data are expressed as the numbers (%) or medians (interquartile ranges)

hemodynamic instability. However, the data of the present study did not include EF values; therefore, we were unable to evaluate this.

GCS scores of < 8 points showed an increased mortality on the spline curve. Recently, the revised Swiss criteria identified the assessment of impaired consciousness as an important indicator of the risk of CA [19], and the results of the present study are consistent with these diagnostic criteria. Although subgroup analysis for GCS scores (> 8 vs. ≤ 8) showed no statistically significant association with the effectiveness of ECMO, selecting subgroups based on GCS scores with age and core temperature may allow us to identify patients with AH and hemodynamic instability who would benefit from ECMO. However, the small sample size in this study did not allow such an analysis.

The results of this study differed from previous studies in other countries [5, 20]. This is mainly due to the fact that the present study focused on patients with AH who were characterized by advanced age, indoor onset, and comorbidities, whereas other countries have focused on patients with AH who were characterized by younger age, outdoor onset, and exposure to extremely low temperatures [5]. In the present study, most deaths in the ECMO group occurred in patients who had completed rewarming and were weaned off of ECMO. The causes of death were an underlying disease that caused AH or subsequent organ failure rather than the ECMO rewarming itself. In addition, bleeding complications were also more common in the ECMO group than the non-ECMO group in the present study, probably due to age-related vascular fragility and hypothermia-associated coagulopathies [21]. The Extracorporeal Life Support Organization (ELSO) registry analysis showed that the incidence of ECMO-related complications also increases significantly with advancing age [22]. This suggests that ECMO is highly invasive for older adult patients with AH and hemodynamic instability. Recently, minimally invasive rewarming (e.g., an endovascular catheter) has been used. We are currently performing a randomized study to evaluate the efficacy of intensive care with endovascular catheter rewarming for accidental severe hypothermia (ICE-CRASH II study) (https://jrct.niph.go.jp/en-latest-detail/jRCT1012240051). The results of this study may indicate that an endovascular catheter could be an effective alternative to ECMO for rewarming therapy in older adult patients with AH.

Limitations

The number of patients with AH and hemodynamic instability who were treated using ECMO was relatively small in this study. In addition, this study was a post-hoc analysis and was not designed to evaluate whether ECMO is useful in patients with AH and hemodynamic instability. Therefore, interpretation of the results may be limited.

As mentioned above, the cohort of patients with AH in this study was very different from the patients with AH in studies from other countries. For this reason, it is difficult to generalize the results of this study to patients with AH in other countries. Further large-scale studies are required to clarify the effectiveness and safety of ECMO rewarming in patients with AH and hemodynamic instability.

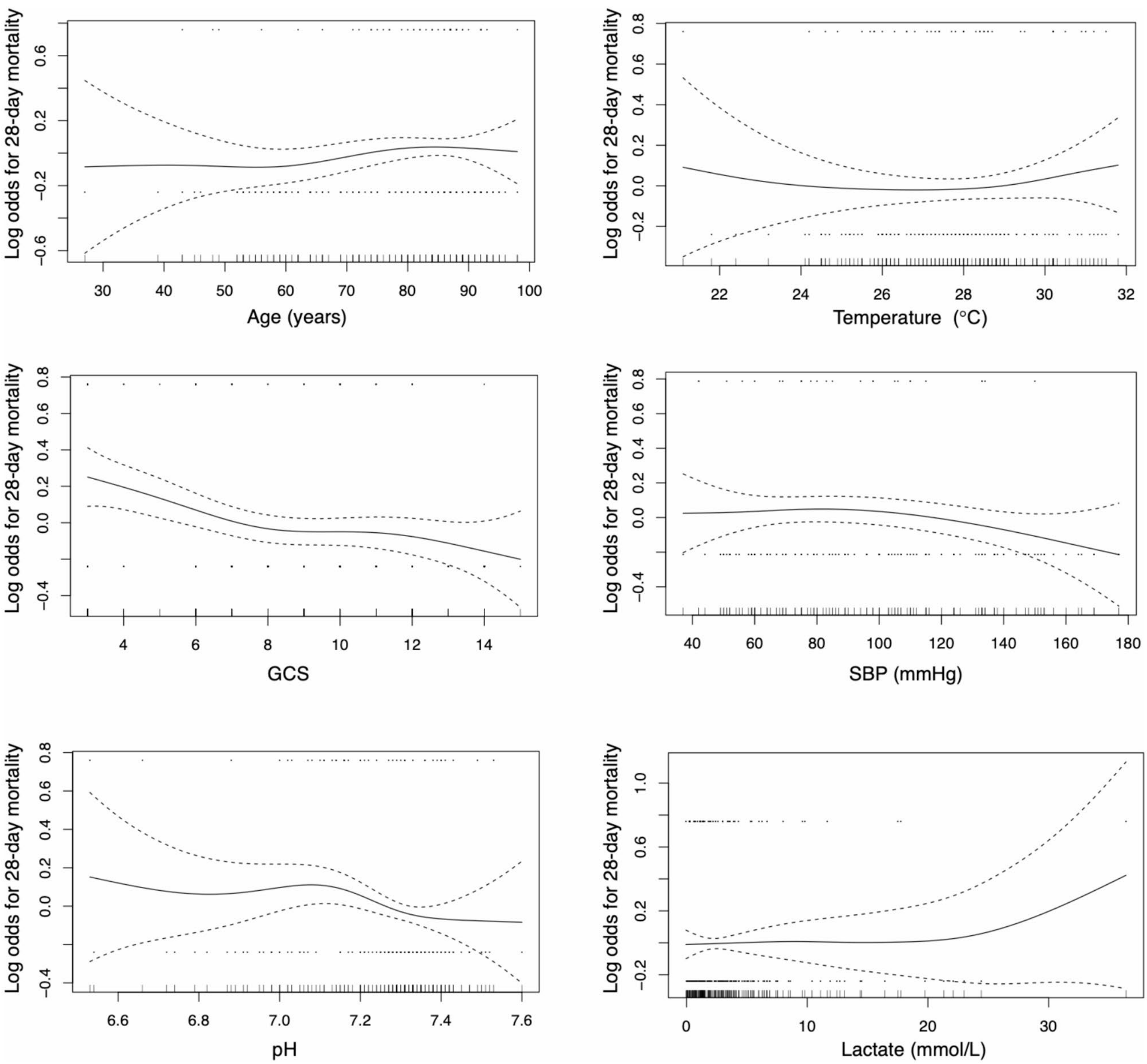

Fig. 2 Restricted cubic spline curve for 28-day mortality. Restricted cubic spline curves showing the relationships between 28-day mortality and age, core temperatures, GCS scores, SBPs, pHs, and lactate levels. The 28-day mortality log odds increased with a GCS score of ≤ 8. However, the SBP curves remained horizontal even when the blood pressure decreased, and the core temperature curves remained almost flat as the core temperature decreased. GCS, Glasgow Coma Scale; SBP, systolic blood pressure

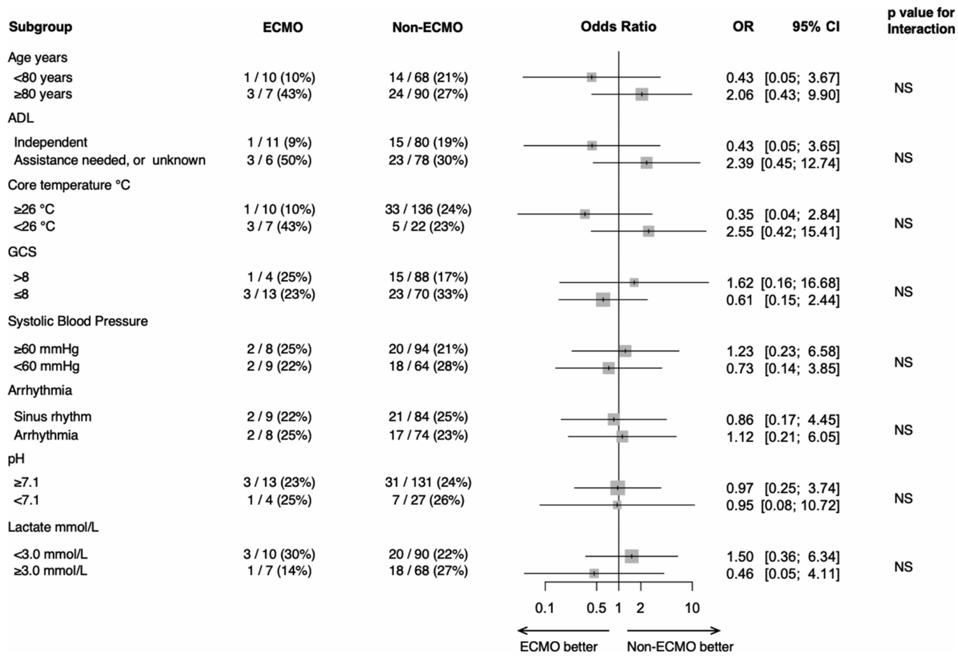

Fig. 3 Subgroup analysis of the association between ECMO and 28-day mortality. We determined the threshold values for age (< 80 vs. ≥ 80 years), core temperature (≥ 26 vs. < 26 °C), GCS score (> 8 vs. ≤ 8), SBP (≥ 60 vs. < 60 mmHg), pH (≥ 7.1 vs. < 7.1), and lactate levels (< 3.0 vs. ≥ 3.0 mmol/L) using cut-off values determined from the restricted cubic spline curves. No statistically significant interactions exists between the effectiveness of ECMO for rewarming and each subgroup. CI, confidence interval; GCS, Glasgow Coma Scale; SBP, systolic blood pressure

Conclusion

We were unable to identify a subgroup of patients with AH and hemodynamic instability who would benefit from ECMO among patients who were mainly older adults. It may not be appropriate to select SBPs as the indicator for ECMO use in these patients.

Abbreviation

AH	Accidental hypothermia
CA	Cardiac arrest
ECMO	Extracorporeal membrane oxygenation
ED	Emergency department
SBP	Systolic blood pressure
ADL	Activity of daily living
GCS	Glasgow coma scale
DBP	Diastolic blood pressure
SOFA	Sequential organ failure assessment
CPC	Cerebral performance category
RRT	Replacement therapy
CT	Computed tomography
AKIN	Acute kidney injury network
OR	Odds ratio
CI	Confidence interval
ELSO	Extracorporeal life support organization

Supplementary Information

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Supplementary Material 1

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Author contributions

ST designed the study. ST and MH performed data analysis and interpretation. ST, MH, and RY performed writing and critical revision. All authors read and approved the final manuscript.

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Data availability

The data of this study are available from the ICE-CRASH study group; however, restrictions apply to the availability of these data, which were used under license for the current study and are not publicly available. Nevertheless, data are available from the authors upon reasonable request and with the permission of the ICE-CRASH study group.

Declarations

Ethics approval and consent to participate

The ICE-CRASH study (on which this post-hoc analysis is based) received ethical approval from Asahikawa Medical University (approval no. 18194) and was approved by the ethics committee of each participating hospital. This study was conducted in accordance with the Declaration of Helsinki. The requirement for written informed consent was waived because of the anonymity of the data.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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