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Clinical paper

Characteristics and outcome of patients with hypothermic out-of-hospital cardiac arrest: Experience from a European trauma center☆

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ABSTRACT

Background: Aim of the study was to investigate patient characteristics, survival rates and neurological outcome among hypothermic patients with out-of-hospital cardiac arrest (OHCA) admitted to a trauma center.
Methods: A review of patients with OHCA and a core temperature $\leq$32 °C admitted to a trauma center between 2004 and 2016.
Results: Ninety-six patients (mean temperature 25.8 °C ± 3.9 °C) were entered in the study, 37 (39%) of them after avalanche burial. 47% showed return of spontaneous circulation (ROSC) prior to hospital admission. Survival with Glasgow-Pittsburgh Cerebral Performance Category (CPC) scale 1 or 2 was achieved in 25% of all patients and was higher in non-avalanche than in avalanche cases (35.6% vs 8.1%, $p = 0.002$). Witnessed cardiac arrest was the most powerful predictor of favourable neurological outcome (RR: 10.8; 95% Confidence Interval: 3.2–37.1; Wald: 14.3; $p < 0.001$), whereas ROSC prior to admission and body core temperature were not associated with survival with favourable neurological outcome. Cerebral CT scan pathology within 12 h of admission increased the risk for unfavourable neurological outcome 11.7 fold (RR: 11.7; 95% CI: 3.1–47.5; $p < 0.001$). Favourable neurological outcome was associated lower S 100-binding protein (0.69 ± 0.5 μg/l vs 5.8 ± 4.9 μg/l, p 0.002) and neuron-specific enolase (34.7 ± 14.2 μg/l vs 88.4 ± 42.7 μg/l, p 0.004) concentrations on intensive care unit (ICU) admission.
Conclusions: Survival with favourable neurological outcome was found in about a third of all hypothermic non-avalanche patients with OHCA admitted to a trauma center.

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Introduction

Out-of-hospital cardiac arrest (OHCA) in patients with accidental hypothermia has several unique features [1–4] and the use of extracorporeal circulation for circulatory support and rewarming (eCPR) is the standard of care for patients not responding to advanced life support (ALS) CPR [1,4,5]. Several reports describing patient characteristics and outcome of eCPR in hypothermic OHCA have been published during the last years [6–9]. However, little is known about characteristics and outcome of patients with restoration of spontaneous circulation (ROSC) prior to hospital admission. Furthermore, patients with OHCA after avalanche burial, near-drowning or severe injuries admitted to a trauma center may be particularly prone to increased mortality and poor neurological outcome [10–12].

To clarify the influence of accidental hypothermia on the outcome of OHCA in a trauma population, we studied characteristics, survival rate and neurological outcome in patients with hypothermic OHCA admitted to the emergency room (ER) of a Central European level 1 trauma center.

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Material and methods

After Institutional Review Board approval the study was conducted at the Medical University of Innsbruck, the tertiary referral hospital and level I trauma center for Western Austria. In the study region patients with OHCA are routinely served by physician-staffed emergency medical services (EMS), and ALS CPR is started already at scene in all arrested patients. According to regional EMS protocols, hypothermic patients without ROSC at scene were transported to the Medical University of Innsbruck for extracorporeal life support (ECLS). In the ER, patients without ROSC were selected for ECLS based on their history, plasma potassium concentrations and, in the case of avalanche burial, using the triage algorithm of the International Commission for Alpine Rescue (ICAR) [12]. Patients developing a stable cardiac rhythm on ECLS were not weaned, but supported for another 24–48 h to avoid cardiorespiratory failure [13]. Later during the study patients were routinely kept on mild hypothermia (34 °C–36 °C) for at least 12 h. Patients with ROSC prior to admission were not rewarmed with ECLS, but treated non-invasively using forced air rewarming. According to EMS triage protocols patients with ROSC at scene and a history of accident (alpine sports-related, near-drowning and avalanche burial) were admitted to the trauma ER, patients with ROSC at scene suffering from urban hypothermia or intoxication were admitted to the general ER and thus not included in the study. All hypothermic patients with ongoing CPR who were candidates for eCPR were admitted to the trauma ER.

Patients surviving to ICU admission underwent a whole body CT scan within 12 h of ER arrival. Low-density generalized cerebral edema with sulcal effacement and attenuation of grey matter/white matter interface on cerebral computed tomography (CT) scan was taken as indicator for ischemic brain injury.

Patients

Patients admitted to the trauma ER between 1 January 2004 and 1 April 2016, who also received an ICD-10 (International Classification of Diseases code) of T 68 (“accidental hypothermia”) together with a documented core temperature ≤32 °C, were screened for the presence of OHCA with or without ROSC prior to admission. Those patients with OHCA were included in the study and demographic data, presence and pattern and severity of additional traumatic injuries, body core temperature on admission and reason for hypothermia were obtained. Because of the unique pathophysiology and known poor prognosis of avalanche burial, the mechanism of hypothermia was categorized as avalanche or non-avalanche. Non-avalanche cases were divided into exposure and near-drowning cases. Hypothermia was defined as moderate (32°–28 °C) and severe (<28 °C) according to international recommendations [1,2]. Prehospital data included: first documented heart rhythm at scene, history of witnessed cardiorespiratory arrest, burial time and submersion time in avalanche and near-drowning cases and time to ROSC in patients successfully resuscitated at scene. In-hospital data included: pH, base excess, plasma lactate and potassium on admission, strategy of rewarming, time to reperfusion on ECLS, neuron-specific enolase (NSE) and S 100-binding protein (S-100BP) concentrations on ICU admission and cerebral CT scan findings immediately after hospital admission.

Primary outcome measure was survival to hospital discharge with favourable neurological outcome, defined as Glasgow-Pittsburgh Cerebral Performance Category Scales 1 (good cerebral performance, leading a normal life) and 2 (moderate disability, sufficient cerebral function for independent activities of daily life). Secondary outcome measures were ROSC prior to hospital admission and survival to hospital discharge.

Statistical analysis

Statistical analysis was performed using SPSS statistical software, version 24.0 (IBM SPPS Inc.). Continuous data are presented as mean and standard deviation of mean; categorical variables were expressed as frequency and percentage. Continuous variables were tested with Student's T test or the Mann-Whitney *U* test (if assumption of a Gaussian distribution was not fulfilled). For univariate differences in categorical variables, the Pearson chi-square test was applied. Possible associations between survival with favourable neurological outcome and clinical features were assessed by means of univariate analysis. In a second step, multivariate logistic regression analysis was performed to identify independent predictors for favourable neurological outcome. Relative Risk (RR) and 95% Confidence Intervals (CIs) were determined. The selection of variables was based on univariate comparisons (entry criteria $p < 0.05$) and inclusion of clinically relevant variables. Wald statistic was used to assess the strength of the association of risk factors relative to other risk factors. A receiver operating characteristic analysis (ROC) was performed to identify cut-off values for NSE and S-100BP together with corresponding sensitivity and specificity.

Results

Between 1 January 2004 and 1 April 2016 210 (2%) of a total of 9769 trauma ER admissions received the ICD-10 code “accidental hypothermia” and had a documented core temperature ≤32 °C. Almost half (n = 101, 48%) of these 210 hypothermic patients had a history of OHCA with or without ROSC prior to hospital admission. Ongoing CPR efforts were discontinued immediately after arrival in the ER without any intervention in five patients, who were excluded from further analysis. The remaining 96 hypothermic patients with OHCA were entered in the study (66 male, 30 female, age mean ± SD 41.4 ± 21.9, body core temperature mean ± SD 25.8 °C ± 3.9 °C).

Patient outcome

Characteristics of all 96 patients are summarized in Table 1. Therapeutic interventions and patient outcome are shown in Fig. 1. Overall hospital survival was 41.7%, hospital survival with favourable neurological outcome (CPC 1 or 2) was 25%. Witnessed cardiac arrest was the most powerful predictor for survival with favourable neurologic outcome (RR: 10.8; 95% Confidence Interval: 3.2–37.1; Wald: 14.3; $p < 0.001$) whereas avalanche burial was an independent predictor of poor outcome (RR: 0.24; 95% CI: 0.07–0.90; Wald: 4.4; $p = 0.036$). ROSC prior to ER admission and body core temperature were not predictive for hospital survival with favourable neurologic outcome.

Avalanche cases

Patients resuscitated after avalanche burial had a significantly higher mortality than did patients with hypothermic OHCA due to other reasons (survival rate 8.1% versus 35.6%, $p = 0.002$). Of 37 avalanche cases 18 (48.6%) had pre-hospital ROSC, two survived long term with CPC 1. Nineteen (51.4%) patients were resuscitated with ECLS; thirteen had restoration of a perfusing rhythm on ECLS, one with witnessed OHCA after extrication survived long term with CPC 1 (Fig. 1). Avalanche victims with ROSC prior to admission had a significantly higher body core temperature and a significantly shorter duration of snow burial. ROSC prior to hospital admission was associated with a higher rate of survival to hospital discharge, but survival with favourable neurological outcome was not different from avalanche victims resuscitated with ECLS (Table 2).

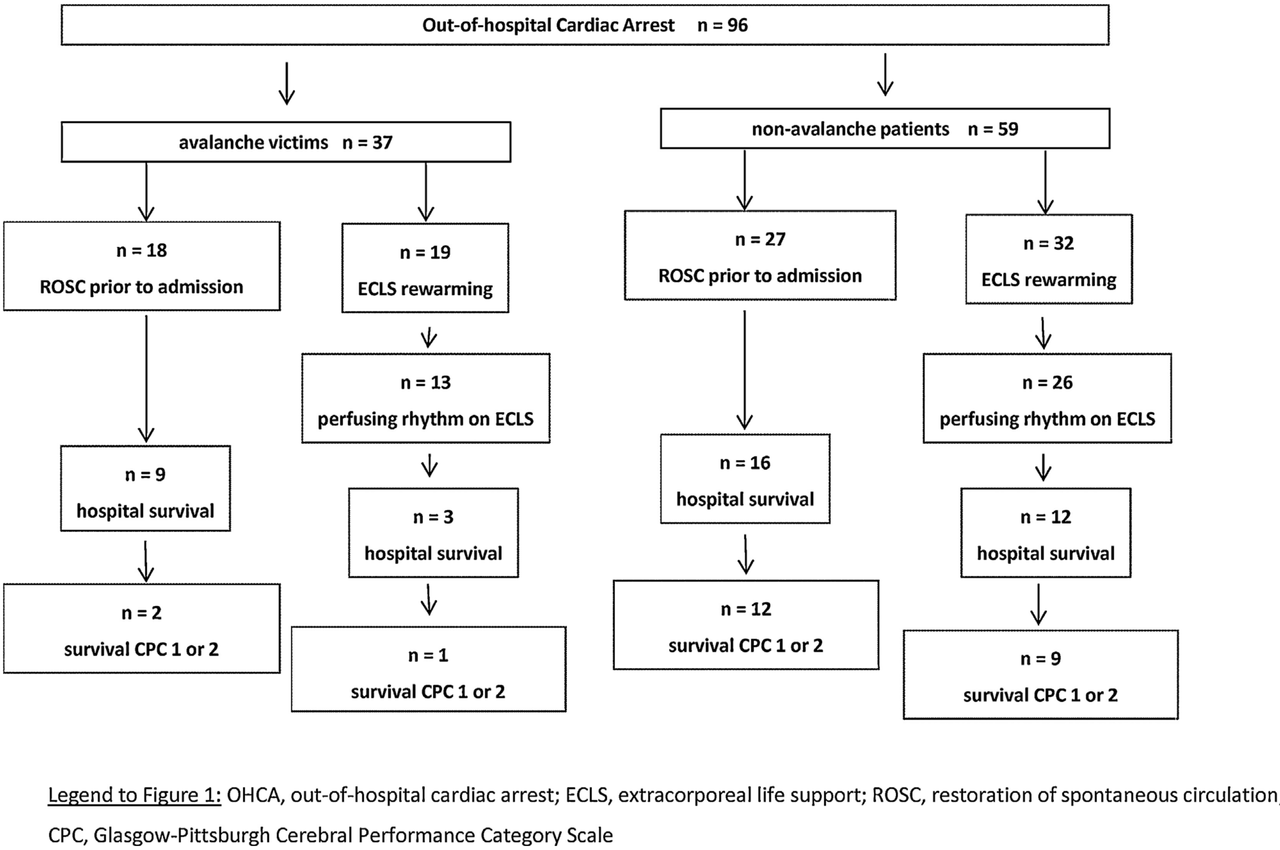

Fig. 1. Outcome in patients with hypothermic OHCA (n = 96).
OHCA, out-of-hospital cardiac arrest; ECLS, extracorporeal life support; ROSC, restoration of spontaneous circulation; CPC, Glasgow-Pittsburgh Cerebral Performance Category Scale.

Table 1
Patient characteristics (n = 96).

Male	n = 66 (69%)
Age	41.4 y ± 21.9 y
Body core temperature	25.8 °C ± 3.9 °C
Stage of hypothermia	
Moderate (28 °C–32 °C)	n = 28 (29.2%)
Profound (<28 °C)	n = 68 (70.8%)
Cause of hypothermia	
Avalanche burial	n = 37 (38.6%)
Exposure to cold	n = 25 (26.0%)
Near-drowning	n = 34 (35.4%)
Alpine sports-related accident	n = 60 (62.5%)
Concomitant injuries ISS ≥ 9	n = 33 (34.4%)
Major injuries ISS ≥ 16	n = 7 (7.3%)
Neuron-specific enolase concentration*	55.5 μg/l ± 47.1 μg/l
S100-binding protein concentration*	2.7 μg/l ± 4.0 μg/l
pH on ER admission	6.89 ± 0.30
Lactate on ER admission	13.8 mMol/l ± 5.9 mMol/l
Potassium on ER admission	5.1 mMol/l ± 2.8 mMol/l
Outcome	
ROSC prior to admission	n = 45 (46.9%)
ECLS rewarming	n = 51 (53.1%)
Hospital survival	n = 40 (41.7%)
Hospital survival with CPC 1 or 2	n = 24 (25.0%)

Legend: Data given as mean ± SD; ISS, Injury Severity Score; * obtained on ICU admission in 47 patients; ER, emergency room; ROSC, restoration of spontaneous circulation; ECLS, extracorporeal life support system; CPC, cerebral performance category.

Non-avalanche cases

Hospital survival with CPC 1 or 2 was 35.6%, including nine patients after ECLS-assisted resuscitation and 12 patients with ROSC prior to ER admission. Hospital survival with favourable neurological outcome did not differ between patients with and without ROSC prior to ER admission (Table 3). Patients with ROSC prior to admission had a significantly higher core temperature (28.3 °C ± 2.2 °C vs. 24.1 °C ± 2.2 °C; p = 0.001) and submersion time was significantly shorter in near-drowning cases (21 ± 11 min versus 36 ± 14 min; p = 0.001). Witnessed cardiac arrest was not a predictor of out-of-hospital ROSC (Table 3). Table 4 shows clinical parameters evaluated for their ability to predict favourable neurological outcome in non-avalanche victims. Patients with CPC 1 or 2 were significantly more likely to experience witnessed cardiac arrest (61.9% versus 21.9%; p = 0.003). Patients with favourable neurological outcome also had a significantly shorter time to ROSC or reperfusion on extracorporeal circulation (43 min ± 14 min vs. 71 min ± 12 min; p = 0.03).

Evaluation of early CT scan and initial NSE and S-100BP concentrations to predict outcome

Cerebral CT scan within 12 h of hospital admission was performed in 84 patients experiencing ROSC prior to hospital admission or developing a stable perfusing cardiac rhythm on ECLS. Among survivors with favourable neurological outcome, 20 (83.3%) patients had normal cerebral CT scans and four (16.7%) patients had brain oedema indicated by sulcal effacement and/or attenuation of grey matter/white matter interface (two of the three survivors with favourable outcome after avalanche burial and two of the 21 non-avalanche cases with favourable neurological outcome). Cerebral CT scan pathology increased the risk for unfavourable neurological outcome 11.7 fold (RR: 11.7; 95% CI: 3.1–47.5; p < 0.001) with

Table 2
Characteristics and outcome of avalanche victims with and without ROSC prior to hospital admission (n = 37).

	ECLS (n = 19)	ROSC at scene (n = 18)	p value
Male	n = 16 (84.2%)	n = 15 (83.3%)	n.s.
Age	39.1 y ± 13.2 y	38.9 y ± 12.4 y	n.s.
Body core temperature	24.5 °C ± 3.2 °C	27.8 °C ± 3.5 °C	0.004
Stage of hypothermia			
Moderate (28 °C–32 °C)	n = 4 (21.1%)	n = 8 (44.4%)	n.s.
Profound (<28 °C)	n = 15 (78.9%)	n = 10 (55.6%)	
Duration of burial	50.6 min ± 33.2 min	27.3 min ± 16.2 min	0.01
Time to ROSC/reperfusion on ECLS	62.5 min ± 23 min	35.3 min ± 20.8 min	0.001
First rhythm at scene			
shockable rhythm	n = 3 (15.8%)	n = 1 (5.6%)	n.s.
Witnessed cardiac arrest	n = 2 (10.5%)	none	n.s.
Hospital survival	n = 3 (15.8%)	n = 9 (50%)	0.03
Survival CPC 1 or 2	n = 1 (5.3%)	n = 2 (11.1%)	n.s.

Legend: Data given as mean ± SD; ROSC, restoration of spontaneous circulation; ECLS, extracorporeal life support system; CPC, cerebral performance category.

a corresponding sensitivity of 70% (56.8–81.1%) and a specificity of 83% (62.6–95.3) and a positive predictive value of 91%.

NSE and S-100BP concentrations were available in 47 patients admitted to the ICU after ROSC prior to admission or after ECLS rewarming. Survivors with favourable neurological outcome had lower NSE (34.7 ± 14.2 vs. 88.4 ± 42.7 μg/l, p = 0.004) and S-100BP levels (0.69 ± 0.5 vs. 5.8 ± 4.9 μg/l, p = 0.002) than did patients with unfavourable outcome (death or survival with CPC 3–5). Using ROC analysis NSE levels higher than 34.5 μg/l were associated with non-favourable neurological outcome (RR: 2.7, 95% CI: 1.11–6.75, p = 0.01) with a corresponding sensitivity of 65% (95% CI: 0.38–0.85), a specificity of 73% (95% CI: 0.54–0.87) and a positive predictive value of 58%. S-100BP levels higher than 0.65 μg/l (RR: 3.5; 95% CI: 1.5–7.1; p < 0.001) were predictive for non-favourable outcome with a corresponding sensitivity of 71% (95% CI: 0.44–0.89), a specificity of 85% (95% CI: 0.62–0.96) and a positive predictive value of 80%.

Discussion

Overall survival with favourable neurological outcome was 25% and increased to 35.6% in the non-avalanche population. This survival rate is similar to survival rates published in recent case series reporting the outcome of hypothermic OHCA after eCPR [6–9]. Considering the large number of patients undergoing prolonged external chest compression in an often difficult rescue scenario and those sustaining concomitant hypoxia, our results underline the protective effects of hypothermia also in trauma patients and support recommendations to continue resuscitation in the case of hypothermia even in extremities [1–3,5]. Brown and co-workers estimated the survival rate of OHCA patients to be around 50% for primary hypothermic cardiac arrest [1], and a few case series yielded such high survival rates [14]. In our study population more than half of all patients with hypothermic OHCA sustained concomitant asphyxia or had unwitnessed cardiac arrest, an experience also reported by others [6–8]. Our data once again underline the particularly poor prognosis of hypothermic cardiac arrest after avalanche burial [10,12]. Obviously, the majority of avalanche victims die from asphyxia or trauma before cooling under the snow masses [10].

ECLS rewarming was used only in patients remaining in cardiac arrest and undergoing external chest compression on emergency room admission. Patients with ROSC prior to hospital admission were all rewarmed without ECLS, and none of these patients rearrested during initial in-hospital management. Non-invasive rewarming is an accepted therapeutic approach for non-arrested hypothermic patients [3] and the feasibility of this approach also in patients with a history of OHCA with ROSC prior to admission has been described [15,16]. ECLS has been recommended in selected high-risk patients without cardiac arrest [1]. However, convincing data demonstrating the superiority of ECLS rewarming in non-arrested patients are still missing, and therefore ECLS is rarely used in these patients in most European centres [6,7].

Hypothermic cardiac arrest often cannot be reversed with ALS CPR interventions prior to rewarming [1–3]. Consequently, CPR guidelines limit ALS CPR to three defibrillation attempts and recommend immediate transfer of the hypothermic patient to hospital for rewarming [3]. ROSC with ALS CPR has been described [15], but the actual incidence of ROSC after ALS CPR in hypothermic OHCA has not been studied yet. In our data almost half of all patients with hypothermic OHCA showed ROSC prior to hospital admission. Factors associated with ROSC were a higher core temperature and a shorter submersion time in near-drowning cases, whereas witnessed cardiac arrest, underlying rhythm and cause of hypothermia were not correlated with ROSC. We observed occasional cases of hypothermic sudden cardiac death responding to pre-hospital defibrillation. However, in the majority of cases ROSC was associated with reversal of hypoxia and administration of epinephrine. Obviously, low coronary perfusion pressure during prolonged CPR [3] can be reversed in some patients with hypothermic OHCA, resulting in ROSC despite low body core temperature. Taken together, our data indicate that in some hypothermic patients prolonged ALS CPR at scene may be justified.

Witnessed cardiac arrest was a predictor of survival in hypothermic OHCA in most studies [1,3,5,17] and it was also a predictor of favourable outcome in our study. In contrast to previous data [17], a shockable rhythm was not a significant predictor of favourable outcome in this study. Reversible OHCA in our study population was not only due to hypothermia-induced ventricular fibrillation, a phenomenon that has already been described in a previous report including victims of urban hypothermia [18]. Survival has been reported after prolonged CPR efforts lasting several hours [2,19] and in some reports duration of CPR was not a predictor of survival [6,9]. Duration of CPR was significantly correlated with outcome in our study and similar experience has been reported by others [7]. The difficult rescue circumstances regularly found in our alpine trauma-related study population made continuous, high-quality CPR difficult, and duration of CPR may have consequently become a determinant of outcome despite hypothermia. ROSC prior to hospital admission was not associated with improved neurological outcome, despite the significantly shorter duration of CPR in these patients. However, patients with prehospital ROSC also had a sig-

Table 3
Characteristics and outcome of non-avalanche patients with and without ROSC prior to hospital admission (n = 59).

	ECLS (n = 32)	ROSC at scene (n = 27)	p value
Male	n = 21 (66%)	n = 16 (59%)	n.s.
Age	42.2 y ± 21.6 y	44.5 y ± 30.8 y	n.s.
Body core temperature	24.1 °C ± 2.2 °C	28.3 °C ± 2.2 °C	0.001
Stage of hypothermia			
Moderate (28 °C–32 °C)	n = 5 (15.6%)	n = 15 (55.6%)	
Profound (<28 °C)	n = 27 (84.4%)	n = 12 (44.4%)	0.001
Cause of hypothermia			
Drowning	n = 18 (56.3%)	n = 16 (59.3%)	
Exposure to cold	n = 14 (43.7%)	n = 11 (40.7%)	n.s
Submersion time (drowning)	36 min ± 14 min	21 ± 11 min	0.001
Time to ROSC/reperfusion on ECLS	94 min ± 38 min	27 min ± 20 min	0.001
First rhythm at scene			
shockable rhythm	n = 13 (40.6%)	n = 16 (59.3%)	n.s.
Witnessed cardiac arrest	n = 12 (37.5%)	n = 8 (29.6%)	n.s.
Hospital survival	n = 12 (37.5%)	n = 16 (59.3%)	n.s.
Survival CPC 1 or 2	n = 9 (28.1%)	n = 12 (44.4%)	n.s.

Legend: Data given as mean ± SD; ROSC, restoration of spontaneous circulation; ECLS, extracorporeal life support system; CPC, cerebral performance category.

Table 4
Factors associated with favourable neurological outcome (CPC 1 or 2) in non-avalanche patients surviving to ICU admission (n = 53)*.

	non-favourable outcome death or CPC 3–5 n = 32	favourable outcome CPC 1–2 n = 21	p value n
Male gender	n = 21 (66%)	n = 16 (76%)	n.s.
Age	46.5 y ± 26.6 y	37.3 y ± 24.4 y	n.s.
Cause of hypothermia			
Drowning	n = 17 (53.1%)	n = 11 (52.4%)	
Exposure to cold	n = 15 (46.9%)	n = 10 (47.6%)	n.s.
ROSC prior to admission	n = 15 (46.9%)	n = 12 (57.1%)	n.s.
Body core temperature	25.9 °C ± 4.9 °C	26.3 °C ± 3.2 °C	n.s.
Witnessed cardiac arrest	n = 7 (21.9%)	n = 13 (61.9%)	0.003
Initial shockable rhythm	n = 18 (56.3%)	n = 12 (57.1%)	n.s
Submersion time+	39 min ± 26 min	29 min ± 30 min	n.s.
Time to ROSC/reperfusion on ECLS	71 min ± 12 min	43 min ± 14 min	0.03
Cerebral CT scan pathology	n = 19 (59.4%)	n = 2 (9.5%)	<0.001
Neuron specific enolase*	88.4 μg/l ± 42.7 μg/l	34.7 μg/l ± 14.2 μg/l	0.004
S 100 binding protein*	5.8 μg/l ± 4.9 μg/l	0.69 μg/l ± 0.5 μg/l	0.002

Legend: * 6 non-avalanche patients in whom cardiac function could not be restored after ECLS rewarming were excluded, data given as mean ± SD; CPC, cerebral performance category ICU, intensive care unit; ROSC, restoration of spontaneous circulation; + only near-drowning patients; ECLS, extracorporeal life support system; * obtained on ICU admission in 47 patients.

nificantly higher body core temperature. Higher core temperature may not only be associated with less protection from ischemic brain injury, but can also indicate that factors apart from hypothermia decisively contributed to cardiorespiratory arrest.

Submersion time is a predictor of mortality in many studies of near-drowning accidents [20,21]. In our data submersion time was not a parameter significantly correlated with outcome, perhaps due to the fact that many near-drowning victims sustained ice water submersion, resulting in very rapid cooling. This made submersion time a less important factor for outcome. In contrast to previous reports [7,11,12,21], we also did not find a significant difference in survival in exposure-related OHCA as compared to OHCA after near-drowning. High survival rates after near-drowning accidents have been previously reported for children or after ice water near-drowning [22,23]. In contrast to many previous reports [7,11,12], our study also included patients with ROSC prior to hospital admission. Furthermore, unwitnessed cardiac arrest or a difficult rescue scenario was regularly found in exposure-related cases, perhaps resulting in an unusually high mortality in these patients in our study population.

Early cerebral CT scan has been evaluated as a prognostic tool in survivors of cardiac arrest [24–28]. Similar to our results in hypothermic patients, these studies demonstrated a significant correlation between cerebral CT scan pathology and unfavourable outcome [25–28]. We found a rather high rate of false-positive prediction of unfavourable neurological outcome, in particular in avalanche cases, as four patients with initial CT scans suggestive for hypoxia survived to hospital discharge with CPC 1 or 2. False-positive prediction of poor outcome is a problem encountered in CT scan prognostication in many studies, markedly limiting the value of CT scans for decision-making in individual patients [24,25,28]. Hypercapnia and thoracic compression in avalanche victims [29] or increased tissue oedema formation during ECLS [30] might have caused mild brain oedema, mimicking cerebral hypoxia, thereby further limiting the prognostic value of cerebral CT scan in our study population. Early detection of cerebral oedema might not only be of prognostic significance, but could also raise the question of specific interventions like intracranial pressure monitoring. Intracranial pressure monitoring has never gained widespread acceptance in survivors of cardiac arrest [31]. Intracranial pressure monitoring combined with neuroprotective treatment strategies were used by Svendsen and co-workers after hypothermic cardiac arrest. The number of patients reported, however, was too small to permit definite conclusions to be drawn [7].

S-100BP and NSE determination are recommended parts of the multimodal approach for prognostication in comatose survivors of cardiac arrest [24,31]. Our data demonstrate that S-100BP and NSE may also be useful modalities for prognostication of neurological outcome in the scenario of hypothermic cardiac arrest, although theoretically haemolysis associated with ECLS and muscle and fat tissue breakdown due to freezing injuries might reduce diagnostic accuracy [24,31]. In our study population NSE and S-100BP levels predicting unfavourable outcome were comparable to those found in survivors of normothermic cardiac arrest [24].

Study limitations

Hypothermia was diagnosed and classified using body core temperature measurements on hospital admission. Reliable data concerning core temperature at scene were not available for many patients as most pre-hospital measurements were performed with epitympanic devices. The low reliability of epitympanic measurement in the prehospital environment was recently underlined [32]. We thus were not able to obtain a reproducible time course of core temperature from scene to ER admission in many patients. However, it is very likely that in some patients significant cooling occurred while undergoing CPR at scene or during transfer to hospital. The phenomenon of cooling during CPR in a cold environment has been described for avalanche victims [33]. Secondary cooling during CPR in a cold environment must be considered when assessing possible protective effects associated with hypothermia, and it is important to identify patients in whom core temperature on admission is markedly lower than core temperature when cardiac arrest occurred.

Results of this study may not reflect characteristics of hypothermic OHCA in urban regions, as more than half of our patient sustained hypothermia during alpine sports-related activities and cases of urban hypothermia or intoxication were included only when ECLS was needed.

Conclusions

ROSC prior to hospital admission was achieved in about half of all patients with hypothermic OHCA. Prehospital ROSC was found in patients with a higher body core temperature and was not associated with improved survival with favourable neurological outcome. Favourable neurological outcome was found in more than a third of all non-avalanche patients with hypothermic OHCA admitted to a trauma center.

Conflict of interest statement

None of the authors has any financial or personal relationship that could have inappropriately influenced the work.

References

[1]. Brown D, Brugger H, Boyd J, Paal P. Accidental hypothermia. N Engl J Med 2012;367:1930–8.
[2]. Paal P, Gordon L, Strapazzon G, Brodmann-Maeder M, Putzer G, Walpoth B, et al. Accidental hypothermia –an update. Scand J Trauma Resusc Emerg Med 2016;24:111–31.
[3]. Truhlar A, Deakin CD, Soar J, Khalifa GE, Alfonzo A, Bierens JJ, et al. European resuscitation council guidelines for resuscitation 2015: section 4. Cardiac arrest in special circumstances. Resuscitation 2015;95:148–201.
[4]. Dunne B, Christou E, Duff O, Merry C. Extracorporeal-assisted rewarming in the management of accidental deep hypothermic cardiac arrest: a systematic review of the literature. Heart Lung Circ 2014;23:1029–35.
[5]. Walpoth B, Walpoth-Aslan B, Mattle H, Radanov B, Schroth G, Schaeffler L, et al. Outcome of survivors of accidental deep hypothermia and circulatory arrest treated with extracorporeal blood warming. N Engl J Med 1997;337:1500–5.
[6]. Debaty G, Moustapha I, Bouzat P, Maignan N, Blancher M, Rallo A, et al. Outcome after severe accidental hypothermia in the French Alps: a 10-year review. Resuscitation 2015;93:118–23.
[7]. Svendsen OS, Grong K, Andersen KS, Husby P. Outcome after rewarming from accidental hypothermia by use of extracorporeal circulation. Ann Thorac Surg 2017;103:920–5, http://dx.doi.org/10.1016/j.athoracsur.2016.06.093.
[8]. Hilmo J, Naesheim T, Gilbert M. Nobody is dead until warm and dead: prolonged resuscitation is warranted in arrested hypothermic victims also in remote areas −a retrospective study from northern Norway. Resuscitation 2014;85:1204–11.
[9]. Sawamato K, Bird SB, Katayama Y, Maekawa K, Uemura S, Tanno K, et al. Outcome from severe accidental hypothermia with cardiac arrest resuscitated with extracorporeal cardiopulmonary resuscitation. Am J Emerg Med 2014;32:320–4.
[10]. Mair P, Brugger H, Mair B, Moroder L, Ruttmann E. Is extracorporeal rewarming indicated in avalanche victims with unwitnessed hypothermic cardiorespiratory arrest. High Alt Med Biol 2014;15:500–3.
[11]. Champigneulle B, Bellenfant-Zegdi F, Follin A, Lebard C, Guinvarch A, Thomas F, et al. Extracorporeal life support (ECLS) for refractory cardiac arrest after drowning: an 11-year experience. Resuscitation 2015;88:126–31.
[12]. Brugger H, Durrer B, Elsensohn F, Paal P, Strapazzon G, Winterberger E, et al. Resuscitation of avalanche victims: evidence-based guidelines of the international commission for mountain emergency medicine (ICAR MEDCOM): intended for physicians and other advanced life support personnel. Resuscitation 2013;84:539–46.
[13]. Ruttmann E, Weissenbacher A, Ulmer H, Mueller L, Hoefer D, Kilo J, et al. Prolonged extracorporeal membrane oxygenation-assisted support provides improved survival in hypothermic patients with cardiocirculatory arrest. J Thorac Cardiovasc Surg 2007;134:594–600.
[14]. Khorsandi M, Dougherty S, Young N, Kerslake D, Giordano V, Lendrum R, et al. Extracorporeal life support for refractory cardiac arrest from accidental hypothermia: a 10 year experience in Edinburgh. J Emerg Med 2017;52:160–8.
[15]. Koller R, Schnider TW, Neidhart P. Deep accidental hypothermia and cardiac arrest −rewarming with forced air. Acta Anaesthesiol Scand 1997;41:1359–64.
[16]. Kornberger E, Schwarz B, Lindner KH, Mair P. Forced air surface rewarming in patients with severe accidental hypothermia. Resuscitation 1999;41:105–11.
[17]. Vretenar DF, Urschel JD, Parrot JC, Unruh HW. Cardiopulmonary bypass resuscitation for accidental hypothermia. Ann Thorac Surg 1994;58:895–8.
[18]. Schober A, Sterz F, Handler C, Kuerkciyan I, Laggner A, Roeggla M. Cardiac arrest due to accidental hypothermia −a 20 year review of a rare condition in an urban area. Resuscitation 2014;85:749–56.
[19]. Lexow K. Severe accidental hypothermia: survival after 6 h 30 min of cardiopulmonary resuscitation. Arctic Med Res 1991;50(Suppl. 6):112–4.
[20]. Quan L, Bierens JJ, Lis R, Rowhani-Rahbar A, Morley P, Perkins GD. Predicting outcome of drowning at scene: a systematic review and meta-analyses. Resuscitation 2016;104:63–75.
[21]. Kieboom JK, Verkade HJ, Burgerhof JG, Bierens JJ, Rheenen PF, Kneybert MC, et al. Outcome after resuscitation beyond 30 minutes in drowned children with cardiac arrest and hypothermia: Dutch nationwide retrospective cohort study. BMJ 2015;350:h418.
[22]. Skarda D, Barnhart D, Scaife E, Molitor M, Meyers R, Rollins M. Extracorporeal cardiopulmonary resuscitation (EC-CPR) for hypothermic arrest in children: is meaningful survival a reasonable expectation. J Pediatr Surg 2012;47:2239–43.
[23]. Wanscher M, Agersnap L, Ravn J, Yndgaard S, Nielsen JF, Danielsen ER, et al. Outcome of accidental hypothermia with or without circulatory arrest: experience from the Danish Praesto Fjord boating accident. Resuscitation 2012;83:1078–84.
[24]. Sandroni C, Cariou A, Cavallaro F, Cronberg T, Friberg H, Hoedemaekers C, et al. Prognostication in comatose survivors of cardiac arrest: an advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Resuscitation 2014;85:1779–89.
[25]. Langkjaer S, Hassager C, Kjaergaard J, Salam I, Thomsen JH, Lippert FK, et al. Prognostic value of reduced discrimination and oedema on cerebral computed tomography in a daily clinical cohort of out-of-hospital cardiac arrest patients. Resuscitation 2015;92:141–7.
[26]. Inamasu J, Miyatake S, Suzuki M, Nakatsukasa M, Tomioka H, Honda M, et al. Early CT signs in out-of-hospital cardiac arrest survivors: temporal profile and prognostic significance. Resuscitation 2010;81:534–8.
[27]. Inamasu J, Miyatake S, Nakatsukasa M, Koh H, Yagami T. Loss of gray-white matter discrimination as an early CT sign of brain ischemia/hypoxia in victims of asphyxia cardiac arrest. Emerg Radiol 2011;18:295–8.
[28]. Kim SH, Choi SP, Park KN, Youn CS, Oh SH, Choi SM. Early brain computed tomography findings are associated with outcome in patients treated with therapeutic hypothermia after out-of-hospital cardiac arrest. Scand J Trauma Resusc Emerg Med 2013;21:57–65.
[29]. Grissom CK, Radwin MI, Harmston CH, Hirshberg EL, Crowley TJ. Respiration during snow burial using an artificial air pocket. JAMA 2000;283:2266–71.
[30]. Harris DN, Oatrigde A, Dob D, Smith PL, Taylor KM, Bydder GM. Cerebral swelling after normothermic cardiopulmonary bypass. Anesthesiology 1998;88:340–5.
[31]. Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert V, Deakin CD, et al. European resuscitation Council and European Society of intensive care medicine 2015 guidelines for post-resuscitation care. Intensive Care Med 2015;41:2039–56.
[32]. Strapazzon G, Procter E, Putzer G, Avanzini G, Dal Capello T, Ueberacher N, et al. Influence of low ambient temperature on epitympanic temperature measurement: a prospective, randomized clinical study. Scand J Trauma Resusc Emerg Med 2015;23:90–6.
[33]. Moroder L, Mair B, Brugger H, Voelckel W, Mair P. Outcome of avalanche victims with out-of-hospital cardiac arrest. Resuscitation 2015;89:114–8.