Outcome After Rewarming From Accidental Hypothermia by Use of Extracorporeal Circulation

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Background. Accidental hypothermia with arrested circulation remains a condition associated with high mortality. In our institution, extracorporeal circulation (ECC) rewarming has been the cornerstone in treating such patients since 1987. We here explore characteristics and outcomes of this treatment, to identify significant merits and challenges from 3 decades of experience in ECC rewarming.

Methods. Sixty-nine patients rewarmed by ECC during the period from December 1987 to December 2015 were analyzed. One patient was excluded from the analyses because of combined traumatic cerebral injury. The analysis was focused on patient characteristics, treatment procedures, and outcomes were focused. Survivors were evaluated according to the cerebral performance categories scale. Simple statistics with nonparametric tests and χ^2 tests were used. Median value and range are reported.

Results. Median age was 30 years (minimum 1.5, maximum 76), and the cause of accidental hypothermia was cold exposure (27.9%), avalanche (5.9%), and immersion/submersion accidents (66.2%). Eighteen patients survived (26.5%). The survival rate did not improve during the years. Survivors had lower serum potassium ($p = 0.002$), higher pH ($p = 0.03$), lower core temperature ($p = 0.02$), and shorter cardiopulmonary resuscitation time ($p = 0.001$), but ranges were wide. Although suspected primary hypoxia and hypothermia were associated with lower survival, we observed a 10.5% survival of these victims. Sixteen survivors had good outcome (cerebral performance category 1 or 2), whereas 2 patients with suspected primary hypoxia survived with severe cerebral disability (cerebral performance category 3).

Conclusions. Despite extended experience with ECC rewarming, improved handling strategies, and intensive care, no overall improvement in survival was observed. Good outcome was observed even among patients with a dismal prognosis.

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Patients having severe accidental hypothermia, namely, core temperature below 28°C, represent an inhomogeneous patient group with respect to age, core temperature at submission, general health status, and the circumstances resulting in hypothermia [1, 2]. Optimal handling of unintentional hypothermia remains debated. Described strategies for rewarming are numerous, and available techniques were recently reviewed [2]. There is a general agreement that extracorporeal circulation (ECC) represents the most effective rewarming method when severe hypothermia is combined with circulatory arrest [3]. Traditionally, standard heart-lung machine equipment for open heart surgery has been utilized for rewarming from hypothermia. Recent reports also advocate the use of venoarterial extracorporeal membrane oxygenation (VA-ECMO) as the method of choice [4, 5].

Successful treatment of hypothermic patients by means of cardiopulmonary bypass was described as early as 1967 [6, 7]. Since then, a number of case reports and retrospective studies have demonstrated favorable outcomes for persons with serious and life-threatening hypothermia [8–12]. Nevertheless, this topic still attracts attention, seeking optimization of treatment procedures with the aim to improve outcome.

Policy for selecting patients for rewarming differs among institutions and may consequently affect mortality. A liberal approach to rewarming of patients most likely implies lower survival rates. Facilities for cardiopulmonary bypass rewarming are limited to specialized centers, sometimes necessitating transport of critically ill patients over long distances [13]. A challenging dilemma is related to the selection of which patients should be transported to a hospital with facilities for extracorporeal rewarming.

Precise information from the scene of accident is often unavailable at the time of hospital admission. We have, therefore, made the nationwide recommendation that all patients should be admitted to an institution with ECC facilities, with immediate rewarming unless clear

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evidence of prolonged asphyxiation exists [9]. Haukeland University Hospital is the academic medical center with regional responsibilities for offering cardiothoracic surgical services to a population of approximately 1.1 million inhabitants in the Western Region of Norway. Since 1987, ECC has been standard therapy for rewarming accidental severely hypothermic patients. We here present patient characteristics and outcomes of those rewarmed from accidental hypothermia in the period December 1987 to December 2015 with the aim to identify optimal strategies concerning rewarming and care after rewarming.

Patients and Methods

Regarding the study, official remit assessment was sent to the Regional Committee for Medical and Health Research Ethics, Western-Norway. The actual project was classified as a quality control project, and was exempted from further review. From 1987, the year of our first successful rewarming from accidental hypothermia by use of ECC [11], until the end of 2015, 69 hypothermic patients were rewarmed. Data were collected retrospectively from prehospital transport records, hospital journals, staff reports, and laboratory recordings. All patients were categorized, based on the circumstances around the accident, according to the authors' belief, as primary accidental hypothermia or as suspected primary hypoxia preceding hypothermia (submersions or avalanche victims with no air pocket).

The decision to start rewarming an individual patient was made before or soon after arrival to the hospital. For all cardiac arrest patients, prehospital cardiopulmonary resuscitation (CPR) was continued during immediate transfer to the operating theater and rapid ECC rewarming was started with a gradient 5° to 10°C. Rewarming was aimed at increasing body temperature to 35° to 36°C, and avoiding nasopharyngeal temperatures above 37°C.

Central arterial and venous access for ECC was primarily performed through sternotomy in the ascending aorta and right atrium (n = 10) or through the femoral artery and vein (n = 58). Three patients were converted from femoral cannulation to central venous cannulation through sternotomy owing to insufficient venous return from the femoral vein. Standard heart-lung machine equipment for open heart surgery was used routinely. Since 2004, a limited number of patients were rewarmed primarily by use of VA-ECMO. As of 2012, VA-ECMO has been used when necessary as standard cardiorespiratory support after rewarming.

Acid-base determinants were uncorrected for actual body core temperature (alpha-stat strategy). Since 2002, cerebral neurointensive protocols involving intracranial pressure (ICP) monitoring, avoidance of hyperthermia with active cooling when necessary, and barbiturate infusion when appropriate were introduced into standard protocols. Intensive care unit (ICU) duration and total hospital stay were recorded.

Survival was defined as the patient being discharged from hospital alive with spontaneous circulation and respiration. All surviving patients were evaluated retrospectively according to the Cerebral Performance Categories (CPC) scale, and characterized as CPC 1 (good cerebral performance), CPC 2 (moderate cerebral disability), CPC 3 (severe cerebral disability), CPC 4 (coma or vegetative state), or CPC 5 (brain death).

Statistics

Data were analyzed using IBM SPSS Statistics 21 (IBM Corporation, Armonk, NY). For continuous data, values are given as median (minimum and maximum). Group differences were analyzed by Mann-Whitney *U* tests. For nominal scale data, Pearson χ^2 tests were used. A *p* value less than 0.05 was considered statistically significant.

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Results

One of the 69 patients was excluded from further analysis owing to a combination of accidental hypothermia and traumatic brain injury, confirmed by computed tomography after rewarming. Admission and outcome characteristics of the remaining 68 patients are presented in Tables 1 and 2. Hypothermia was due to sustained cold exposure in 19 patients (27.9%), avalanche in 4 patients (5.9%), and immersion or submersion in 45 patients (66.2%). Forty-one patients could be transferred from the operating theater to the ICU after rewarming. Nineteen patients were discharged from the ICU, and 18 survived (Fig 1). In 27 patients, the resuscitation attempts were stopped in the operating theater owing to irreversible cardiopulmonary failure.

Survival among female patients was higher than among male patients ($p = 0.02$). Median age of the 68 patients was 30 years (1.5 to 76), with no difference between survivors (median 32 years [1.5 to 76] and nonsurvivors (median 30 years [1.7 to 76); $p = 0.9$). Body core temperature was lower among survivors (median 22°C [19° to 27°C]) than nonsurvivors (median 25°C [17° to 34°C]; $p = 0.02$). Similarly, serum potassium level was lower (median 4.0 mmol/L [2.2 to 7.9 mmol/L] versus 6.1 [2.5 to 25 mmol/L]; $p = 0.002$) and pH higher (median 6.87 [6.36 to 7.23]; versus 6.62 [6.23 to 7.21]; $p = 0.03$).

Primary cause of death was cardiopulmonary insufficiency in 30 patients (44.1%), whereas ceased cerebral circulation and brain death were concluded for 20 victims (29.4%). Cumulative survival in the period from 1987 to 2015, as depicted in Figure 2, was slightly above one fourth (26.5%). Except for 2 patients, all had cardiac arrest before or during prehospital or inhospital rescue (Table 1). Rescue-associated cardiac arrest was followed up by CPR. Total CPR time before commencement of ECC and rewarming was shorter among survivors (95 minutes [0 to 195]) than nonsurvivors (150 minutes [45 to 298]; $p = 0.001$).

During the last 10 years, use of mechanical compression devices was noted in 13 patients, all but 1 of them in the nonsurviving group. Median CPR time when mechanical chest compression devices were used was 120 minutes (60 to 298). Nine patients, 8 of them in the nonsurviving group, were transported to a local hospital without cardiopulmonary bypass facilities before transfer

Table 1. Clinical Characteristics of Patients Rewarmed by Extracorporeal Circulation (n = 68)

Characteristics	n (%)	Survivors	Nonsurvivors	*p* Value
Sex				
Male	52 (76.5)	10	42	0.02
Female	16 (23.5)	8	8	
Incident				
Cold exposure	19 (27.9)	7	12	0.5
Avalanche	4 (5.9)	1	3	
Submersion/immersion	45 (66.2)	10	35	
Suspected primary asphyxia				
Yes	38 (55.9)	4	34	0.001
No	30 (44.1)	14	16	
Circulatory status				
Spontaneous circulation	2 (2.9)	2	0	0.005
Rescue cardiac arrest	15 (22.1)	7	8	
Cardiac arrest	51 (75.0)	9	42	
Mechanical compression device				
Yes	13 (19.1)	1	12	0.09
No	55 (80.9)	17	38	

to our institution with cardiac surgery service and ECC facilities.

Primary hypoxia, suspected in 38 (55.9%) of the patients, was associated with reduced survival (Table 1). Patients less than 10 years of age were all submersions with suspected primary hypoxia. Four of these patients survived, 2 of them with CPC 1, and 2 with CPC 3 (cerebral disability). Median ICU stay among survivors was 8 days (2 to 24) versus 2 days (1 to 12) for patients dying in the ICU ($p < 0.001$). All-over hospital stay was 2 days (1 to 121). One of 3 patients survived when VA-ECMO was used as the primary rewarming method, and 1 of 4 patients survived when VA-ECMO support was instituted after conventional ECC rewarming.

Since 2002, 14 patients, 10 of them survivors, had ICP monitoring as a part of the neurointensive care after primary rewarming. Barbiturate was used in 6 of these patients to treat elevated ICP. In 1 patient, craniectomy was performed successfully as an intracranial decompression procedure, with complete recovery. No serious complications were noted because of ICP monitoring. Among survivors, functional recovery was classified according to the CPC scale. In addition to the 2 reported children classified as CPC 3, the remaining survivors were classified as CPC 2 (n = 1) and CPC 1 (n = 15).

Comment

Severe hypothermia remains a condition associated with high mortality. However, several case reports and studies confirm that these patients, even when prognosis seems dismal, can survive with complete recovery. Furthermore, the long-term outcome among survivors is good [12]. In a recent review, survival rate among primary hypothermic cardiac arrest patients rewarmed by extracorporeal bypass was estimated to be approximately 50% [14]. Reported mortality rates differ according to patient characteristics. Danzl and colleagues [15] reported a survival rate of 82.9% in a multicenter hypothermia survey including patients with core temperature less than 35°C. Five of 16 patients (31.3%) survived after being rewarmed by ECC [15]. In 2001, we [9] described the course of 26 ECC rewarmed patients, with 8 survivors (30.8%), all of them included in the present report. In a study from Finland, 14 of 23 patients (60.9%) with primary hypothermia were discharged alive after ECC rewarming [16].

Table 2. Patient Characteristics and Outcome

Characteristics	All Patients	Survivors	Nonsurvivors	*p* Value
Age, years	30 (1.5–76) (68)	32 (1.5–76) (18)	30 (1.7–76) (50)	0.9
Temperature, °C	24 (17–34) (68)	22 (19–27) (18)	25 (17–34) (50)	0.02
CPR, minutes	136 (0–298) (68)	95 (0–195) (18)	150 (45–298) (50)	0.001
Serum K, mmol/L	5.5 (2.2–25) (66)	4.0 (2.2–7.9) (18)	6.1 (2.5–25) (48)	0.002
pH	6.72 (6.23–7.23) (67)	6.87 (6.36–7.23) (18)	6.62 (6.23–7.21) (49)	0.03
Base excess	−25 (−47 to −12) (66)	−21 (−34 to −12) (18)	−27 (−47 to −12) (48)	0.004

Values are median (minimum and maximum) and (n).

CPR = cardiopulmonary resuscitation; K = potassium.

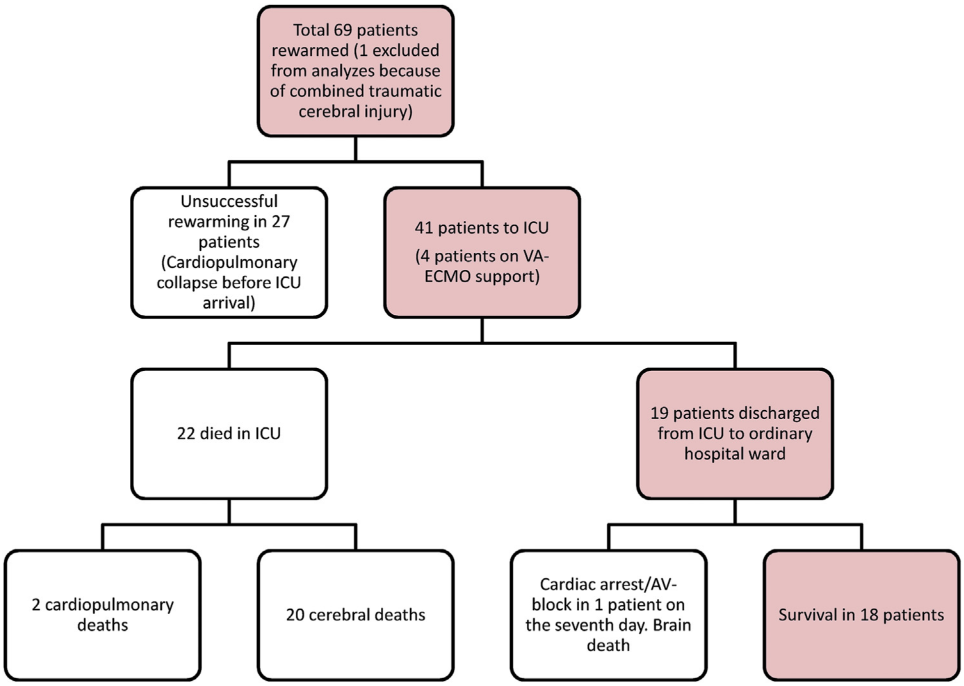

Fig 1. Schematic diagram for outcome of 69 patients rewarmed by extracorporeal circulation since 1987. (AV = atrioventricular; ICU = intensive care unit; VA-ECMO = venoarterial extracorporeal membrane oxygenation.)

In a remarkable report from Denmark, 7 hypothermic teenagers from a single accident survived after being successfully rescued and rewarmed by VA-ECMO [17].

We here report a 26.5% survival rate, strikingly similar to what was recently reported from another center in Norway, where patient characteristics and the health system are comparable to ours [10]. When excluding the patients with suspected primary hypoxia, a survival rate of 46.7% was observed after primary hypothermia in the present study.

The lower total survival rate in our study should raise some concerns. First, we think that patient selection for rewarming is of utmost importance—55.9% of our patients were classified as suspected primary hypoxia.

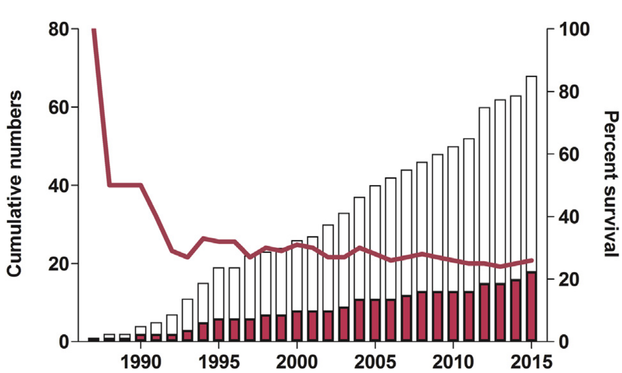

Fig 2. Cumulative survival since 1987. Red bars represent the cumulative number of surviving patients, and white bars represent the cumulative number of all patients (left y-axis). Red line shows trend in total survival in percent over the years (right y-axis).

Correct and objective reports of the accidents are hard to obtain in the emergency department. Therefore, it seems reasonable to start rewarming when in doubt. We describe 4 survivors with assumed hypoxia, all of them children, and 2 recovered completely. These cases support our liberal approach to rewarming, but also exemplify the difficulties in predicting prognosis. It can be argued that prolonged and aggressive treatment of patients with dismal prognosis is costly and unethical. The question whether to stop active treatment is, however, most often resolved within a few days.

The therapeutic value of resuscitation beyond 30 minutes in drowned children with cardiac arrest and hypothermia has recently been questioned [18]. Good neurologic recovery has, however, been described after 40 minutes and even 66 minutes of cold water submersion [19, 20]. We report 2 surviving children with CPC 1. One of them had as much as 2.5 hours of CPR, and 1 had prolonged CPR for more than 1 hour and pH as low as 6.36. Skarda and associates [21] report a 22% survival rate among hypothermic children rewarmed by means of ECC resuscitation. The same researchers observed organ donation as a potential side benefit of rewarming the patients.

The lower potassium levels together with higher pH among survivors versus nonsurvivors in our study are in accordance with earlier publications [9, 16, 22]. The prognostic value of these variables has been questioned. Successful rewarming was described for a child with a potassium value as high as 11.8 mmol/L [8], and an upper limit of 12 mmol/L for attempting rewarming has been suggested [23]. Only 5 of the nonsurvivors in our study had values of 12 mmol/L or higher. The same challenge is observed if trying to use pH as a prognostic factor, as only 2 patients had values lower than 6.36, which is the lowest value among our intact survivors.

Hypothermia protects the brain by slowing down the process of irreversible tissue damage. Case reports have emphasized the importance of continuous CPR, even when there is long transport time to rewarming facilities [24, 25]. Even so, time plays into the matter, and we found significantly shorter CPR time among survivors compared with nonsurvivors. Therefore, rescuers and emergency doctors should bring the hypothermic patient to the nearest hospital offering cardiothoracic surgical expertise without delay. At least 9 of the patients in our study were initially brought to a local hospital without ECC facilities. In some cases, that could be explained by a very short distance to the nearest hospital, or by an initial unrecognized diagnosis of severe hypothermia. "Circum-rescue collapse" was described already at the time of the Titanic disaster [26], and intact cardiovascular circulation may have obscured a correct diagnosis of hypothermia during initial handling. We argue that severely hypothermic patients, even with intact circulation, should be transported directly to a center with cardiopulmonary bypass facilities.

The challenges in performing CPR over long distances and times have led to the development of mechanical devices for performing chest compressions automatically. Use of such devices has been advocated for accidental hypothermia [27]. Interestingly, only 1 of the patients with device-performed chest compressions survived. In 1 of the nonsurviving patients, autopsy showed severe intrathoracic injuries. Recently, more rib fractures were reported with use of a mechanical chest compression device compared with manual compressions [28]. We speculate whether vigorous and nonsensible mechanical compressions could predispose to injuries and bleeding in the hypothermic patient characterized by tissue stiffness. Such possible iatrogenic incidents complicate heparinization therapy and use of ECC. This fact is underscored in the Bernese hypothermia algorithm, where severe trauma is an argument against extracorporeal rewarming [29].

Because VA-ECMO allows lower levels of anticoagulation than conventional heart-lung machine, it can be used for prolonged support and has been considered as the preferable rewarming method [14]. Rewarming on VA-ECMO was associated with improved total survival when two historic groups were compared [5], and no patients with restoration of spontaneous circulation after rewarming died of pulmonary edema in the VA-ECMO group. The referred report includes many (75%) asphyxia-associated cases, and describes a very low survival rate of 8.8% (3/34) for the conventional extracorporeal group, increasing to 36.0% (9 of 25) after introduction of VA-ECMO. In experimental studies, cardiac dysfunction after rewarming has been described [30]; and in a case report, pulmonary occlusion pressure as high as 30 to 35 mm Hg after rewarming was reported [11]. Therefore, VA-ECMO may offer a significant advantage during the vulnerable period after rewarming, associated with serious cardiopulmonary instability. Furthermore, use of portable and percutaneous cardiopulmonary bypass systems has been reported as feasible and with excellent results [4]. Hypothermia is associated with extensive microvascular fluid extravasation [31]. During rewarming, massive fluid shifts takes place, with possible intravascular fluid overloading. Use of a conventional heart-lung machine offers good possibilities for fluid unloading, and has remained as our standard rewarming method. We have introduced VA-ECMO as cardiopulmonary support after rewarming during recent years, when deemed necessary.

In spite of more systematic neurointensive protocols after the rewarming period, survival has not improved during the last decade. Although single successful cases are described, where ICP monitoring has had a direct impact on the treatment, there are too few data to draw conclusions about the general usefulness of this strategy. Furthermore, increased use of VA-ECMO after the rewarming period complicates this approach, as concurrent need of heparinization therapy may predispose patients to bleeding complications during ICP monitoring. Conversely, cardiopulmonary instability with pulmonary edema is common after rewarming, and as a result, some of our patients may have had a combination of hypoxia, hypercarbia, and high intrathoracic airway pressures during this critical period. When considering the neuroprotective approach, these are all negative conditions. Therefore, increased use of VA-ECMO support could represent a more feasible solution, where optimizing oxygen and carbon dioxide tension is possible without generating high intrathoracic pressures.

This study has several limitations as the material includes patients from 3 decades, during which time ECC equipment, treatment options, and monitoring have changed. Despite these weaknesses, we find the unchanged outcome surprising, as therapeutic interventions from our viewpoint have improved during the years. A confounder in this setting may be increased focus and a more liberal approach to rewarming, even for victims with a dismal prognosis. However, our data support such a liberal approach.

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