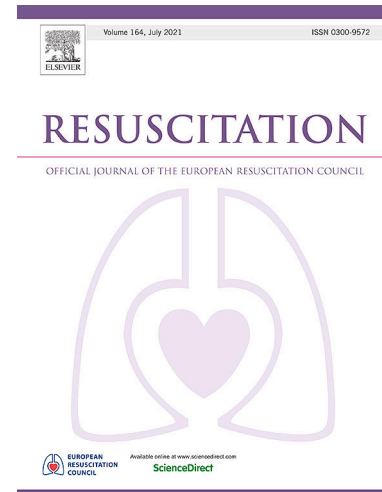


## Journal Pre-proofs



Clinical paper

Hypothermic Cardiac Arrest – retrospective cohort study from the International Hypothermia Registry

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# Hypothermic Cardiac Arrest – retrospective cohort study from the International Hypothermia Registry

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**ABSTRACT:**

**AIM:** The International Hypothermia Registry (IHR) was created to increase knowledge of accidental hypothermia, particularly to develop evidence-based guidelines and find reliable outcome predictors. The present study compares hypothermic patients with and without cardiac arrest included in the IHR.

**METHODS :** Demographic, pre-hospital and in-hospital data, method of rewarming and outcome data were collected anonymously in the IHR between 2010 and 2020.

**RESULTS :** Two hundred and one non-consecutive cases were included. The major cause of hypothermia was mountain accidents, predominantly in young men. Hypothermic cardiac arrest (HCA) occurred in 73 of 201 patients. Core temperature was significantly lower in the patients in cardiac arrest (25.0 vs. 30.0°C,  $p < 0.001$ ). One hundred and fifteen patients were rewarmed externally (93% with ROSC), 53 by extra-corporeal life support (ECLS) (40% with ROSC) and 21 with invasive internal techniques (71% with ROSC). The overall survival rate was 95% for patients with preserved circulation and 36% for those in cardiac arrest. Witnessed cardiac arrest and ROSC before rewarming were positive outcome predictors, asphyxia, coagulopathy, high potassium and lactate negative outcome predictors.

**CONCLUSIONS :** This first analysis of 201 IHR patients with moderate to severe accidental hypothermia shows an excellent 95% survival rate for patients with preserved circulation and 36% for HCA patients. Witnessed cardiac arrest, restoration of spontaneous circulation, low potassium and lactate and absence of asphyxia were positive survival predictors despite hypothermia in young, healthy adults after mountaineering accidents. However, accidental hypothermia is a heterogenous entity that should be considered in both treatment strategies and prognostication.

**INTRODUCTION:**

Accidental hypothermia (AH) is defined as involuntary drop of core temperature below 35°C.<sup>1-4</sup> Mild AH (average core temperature between 35°C and 32°C), is common, but patients do not experience major impairment in vital functions and do not need care in a specialized center. In contrast, moderate (core temperatures between 32 and 28°C) and especially severe or deep hypothermia (core temperatures below 28°C) is rare but carries a high risk for major morbidity and mortality even in previously healthy adults and children. Accidental hypothermia is therefore a "low-incidence, high-impact" condition.<sup>1,2,5</sup> Case reports of successful treatment of deep accidental hypothermia with excellent outcomes have been published, with core temperatures as low as 13.7°C in an adult and 11.8°C in a child and with resuscitation times as long as 8h40min.<sup>6-8</sup> However, data of non-survivors are rarely published and may be under-reported. Additionally, previously published case series are often single-center studies with low numbers of patients, limiting statistical power. Recently published multi-centre reports and meta-analyses have tried to overcome some of these problems.<sup>9-10</sup>

There is a lack of reliable outcome predictors for hypothermic patients. There are only a few guidelines.<sup>11-13</sup> Many questions are still unsolved such as the role of vasoactive drugs in advanced life support in hypothermia, how to choose amongst rewarming modalities, the best rate of rewarming, and the optimum target temperature.<sup>14-17</sup> Serum potassium level is currently the only widely accepted prognostic indicator in hypothermic patients with cardiac arrest. Cutoffs beyond which attempted resuscitation is likely to be futile are 8 mmol/l for hypothermic avalanche victims and 12 mmol/l for all other victims.<sup>18-19</sup> Other predictors have been identified and described (e.g. asphyxia and sex).<sup>9,10,13</sup>

The International Hypothermia Registry (IHR) <https://hypothermia-registry.org> was created in Geneva in 2010 to collect data from a large numbers of accidental hypothermia cases. By

collecting 'real world patient data' from the main hypothermia centers worldwide, the IHR is intended to improve the evidence available to answer open questions regarding triage, pre-hospital and in-hospital treatment as well as outcome predictors. The aim of this study was to analyze demographics, pre-hospital and hospital data as well as rewarming methods and outcome of patients in hypothermic cardiac arrest (HCA), compared to patients with preserved circulation.

## **METHODS:**

### Structure and Access to the International Hypothermia Registry:

The majority of moderate or severe accidental hypothermia victims (non-consecutive and worldwide) regardless of etiology and outcome, are eligible for the IHR which is anonymized and registered in Switzerland. It has ethical approval from the University Hospital of Geneva (08-04OR 2008) and is hosted on its highly secured server. The data management is in accordance with the Swiss Federal Act on Research Involving Human Beings. A total of 51 centers worldwide have access to the IHR, of which only 11 centers have entered cases (see list of centers in Acknowledgements and Supplemental Table 1).

Data from a total of 239 accidental hypothermia victims were entered into the IHR between 2010 and 2020. Thirty-eight patients were excluded from further analysis due to essential missing values (e.g. temperature). . Therefore 201 hypothermia victims were included in the study (Supplemental Table 2). Prospective and retrospective collected data in the IHR is composed of three main sections:

1. Pre-hospital data (accident and medical features);
2. Hospital data (pre-rewarming, rewarming techniques and post rewarming ICU and hospital outcome);

### 3. Follow-up (complications and quality of life).

#### Analysis and Statistics

All data were analyzed as number of cases and percentages (%), median and inter-quartile range (IQR) or mean values and standard deviations (SD) for continuous variables as appropriate. We used Wilcoxon rank sum test when we present median and IQR and t-test when we present mean(SD). The level of statistical significance (uni-variate analysis) was set at  $p < 0.05$  (bi-lateral).

#### **RESULTS:**

The median age of all patients was 38 (27 - 54) years; 74% of patients were male. One hundred and forty one accidents occurred during recreational activities in mountainous terrain, of which 54 were related to falls into crevasses, 50 to other incidents with outdoor exposure and 32 to avalanche burial. Forty-five events occurred after cold exposure in urban or rural environment, and the remaining 15 cases were associated with immersion or submersion in cold water (Table 1).

Seventy-three (36%) of the 201 patients had suffered cardiac arrest (Table 2). Thirty-two (44%) patients were already in cardiac arrest when the rescue team arrived, and 41 of 51 available data (80%) sustained witnessed cardiac arrest during initial pre- or in-hospital management before rewarming. Data on the underlying rhythm of cardiac arrest on-site were available in 47 patients. The ECG showed asystole in 24 (51%) patients, ventricular fibrillation in 17 (36%) and PEA in 6 (13%). ROSC (return of spontaneous circulation) after pre- or in-hospital resuscitation occurred in 13 patients (19%) before rewarming. The majority of patients remained in cardiac arrest. Defibrillation was attempted in 18 cases, with a median core temperature of 25°C. Defibrillation led to ROSC in five of the 18 cases. On admission approximately half of the patients in cardiac

arrest had a shockable rhythm. Most of the patients in cardiac arrest were intubated on-site (85%). CPR included the application of a mechanical chest compression device in 39%. Thirty-eight of 73 HCA victims (52%) were transferred by helicopter to a center with the possibility of ECLS rewarming.

### Rewarming Methods

Four patients were declared dead without rewarming because their clinical status was not compatible with survival according to the emergency physician. One hundred and fifteen of 201 patients (57%) were rewarmed non-invasively by external rewarming, fifty three patients (26%) were treated with ECLS. The remaining 21 patients (10%) were rewarmed using various techniques of active internal rewarming (Table 3). ECLS resulted in the fastest rate of rewarming (3.1°C/h), which was significantly higher than alternative invasive internal (1.3°C/h) or external (2.0°C/h) methods of rewarming (p=0.003). The group warmed by ECLS had the greatest proportion of patients in cardiac arrest (81%) and the lowest median core temperature (25.4°C). Successful rewarming with survival to ICU admission was observed in 93% of patients with active external rewarming, 71% with active internal rewarming and in 40% with ECLS rewarming. Forty-three of 69 patients (62%) with a history of cardiac arrest for whom data were available were rewarmed using ECLS. The remaining were either declared dead without rewarming (n = 4, 6%) or rewarmed using alternative internal techniques (n = 21, 32%). The main reasons for not using ECLS in arrested hypothermic patients were that ROSC had been achieved before hospital admission (n=13) or that the patient had mild hypothermia (core temperature  $\geq 32^{\circ}\text{C}$ ). Other reasons for not using ECLS were: elderly victim (n=1) and transient non-invasive rewarming until the decision to terminate resuscitation efforts (n=4). . All patients were in a life-threatening condition with a core temperature  $< 28^{\circ}\text{C}$ , deep coma and significant hemodynamic compromise.

### Outcome

One hundred and twenty-one of the 128 patients not in cardiac arrest (95%) survived to hospital discharge, compared to 26 of 73 patients in cardiac arrest (36%;  $p < 0.001$ ) (Table 4 & Figure 1). The median time spent in the ICU and the median length of hospital stay was 2 and 10.5 days for patients not in cardiac arrest and 4 and 17.5 days for HCA patients, respectively. The most common post-rewarming complication was respiratory failure. This was significantly higher in the patients in cardiac arrest (73% vs. 36%;  $p = 0.002$ ). The incidence of cardiovascular collapse, neurologic dysfunction and Glasgow Outcome Score (GOS) did not differ significantly between the patients with preserved circulation and those in cardiac arrest. Arrested hypothermia victims had a lower median core temperature ( $25[23-27]^{\circ}\text{C}$  vs  $30[28-33]^{\circ}\text{C}$ ;  $p < 0.001$ ), a lower Glasgow Coma Scale (GCS) ( $3[3-3]$  vs.  $7[3-15]$ ;  $p < 0.001$ ) and more often sustained asphyxia (24 vs 3;  $p < 0.001$ ) (Table 2 & Figure 1). Fifty one percent of patients not in cardiac arrest had major trauma, requiring hospitalization, compared to 34% in the HCA group ( $p < 0.03$ ). Relevant clinical and laboratory variables for patients in cardiac arrest and patients not in cardiac arrest are shown in Table 2. HCA patients had significantly lower pH ( $6.9 \pm 0.3$  vs.  $7.2 \pm 0.2$ ;  $p < 0.001$ ) and higher lactate values ( $14 \pm 6$  vs.  $8 \pm 12$ ;  $p < 0.01$ ) at hospital admission. Potassium was  $3.9 \pm 1$  mmol/l in the non-arrested, compared to  $5.3 \pm 3$  mmol/l in the patients in cardiac arrest ( $p < 0.001$ ). Coagulopathy (ACT  $> 150$  sec and/or Quick  $< 70\%$ ) was more common in patients in cardiac arrest (81 vs. 41%,  $p < 0.001$ ).

#### Survivors vs. Non-survivors after Hypothermic Cardiac Arrest

Factors associated with improved survival were witnessed cardiac arrest (71% vs. 30%;  $p < 0.005$ ), and ROSC before rewarming (35% vs. 7%;  $p < 0.007$ ), lower potassium ( $3.5 \pm 0.9$  vs.  $6.5 \pm 2.5$  mmol/L,  $p = 0.001$ ), and lower lactate levels ( $11 \pm 5$  vs.  $16 \pm 5$  mmol/L,  $p = 0.003$ ), at hospital admission. (Table 5) Patients with asphyxia had a trend to higher mortality (49% vs. 23%,  $p <$



0.059). In the non-survivors, the median age was 8 years younger (37 [13-61] vs. 45 [16-78] years,  $p=0.02$ ). Hypothermia was more common in mountain accidents than with other causes (79% vs. 42%,  $p=0.005$ ). There was no difference in underlying cardiac rhythm, core temperature or pH value at hospital admission between survivors and non-survivors.

## **DISCUSSION:**

The present study is the first analysis of data from the International Hypothermia Registry (IHR).. During the last ten years, 11 centres mainly in European mountainous regions entered data into the IHR. Consequently, a large number of patients in the Registry were involved in recreational accidents in the mountains. The patients were rather young with a median age of 38 years. The majority were male. The study population represents a unique subgroup of hypothermic patients and may not be representative for hypothermic patients encountered in rural or urban regions, in whom comorbid conditions, intoxication and older age are often associated with hypothermia.<sup>15,20-22</sup> Our data emphasize that patients with accidental hypothermia represent a heterogeneous group. Clinical presentations and prognoses may vary substantially depending on the underlying mechanism of cooling, age, and comorbidities.

Accidental hypothermia impairs organ function. Cardiovascular collapse, respiratory failure and renal failure are common in patients rewarmed from severe accidental hypothermia. Cardiovascular, renal and lung failure were regularly seen in patients who sustained cardiac arrest. The low 5.5% mortality in patients with preserved circulation is remarkable. This contrasts with previous publications that have reported mortality rates (26-38%) in hypothermic patients not in cardiac arrest.<sup>21,23</sup> Age, pre-existing conditions and urban hypothermia are consistently reported to be predictors for poor outcomes in hypothermic patients.<sup>21,23</sup> The large percentage of young and healthy hypothermia victims is the most likely explanation for the low mortality

observed in our registry (selection bias). The low mortality in patients not in cardiac arrest in our study is particularly remarkable considering the 51% rate of major trauma. Hypothermia associated with severe trauma is also common in victims exposed only to mild cold conditions. Traumatic hypothermia is part of the lethal triad of trauma (acidosis, coagulopathy, hypothermia).<sup>24</sup> A core temperature below 32°C in multi-system trauma is associated with a poor prognosis and a high mortality rate.<sup>25</sup> Our data suggest that hypothermia in trauma victims exposed to severe external cold does not necessarily increase mortality, even when core temperature falls below 32°C. Hypothermia was associated with significant coagulopathy in approximately 41% of the hypothermic patients not in cardiac arrest. Although not reflected in the high mortality rate in our data, coagulopathy associated with hypothermia is an important factor that should always be addressed when treating a hypothermic patient with major trauma.<sup>24</sup>

The most feared complication of accidental hypothermia is sudden circulatory arrest during initial pre-hospital or in-hospital treatment, often referred to as 'rescue collapse'. Cardiac arrest was witnessed during pre-hospital or initial in-hospital treatment in 80% of our HCA patients. Our Registry data suggests that rescue collapse is a very common problem complicating rescue and initial treatment of severely hypothermic patients. The underlying mechanism for rescue collapse is not completely understood and likely multifactorial.<sup>26-28</sup> Few general preventive measures, such as avoiding postural changes, are available to reduce the incidence of 'rescue collapse' in hypothermic patients.<sup>26,28</sup> Rescue collapse has been reported to occur in about one third of difficult rescues and in about one third of patients with a core temperature below 24°C.<sup>30</sup>

Overall survival rate in patients in cardiac arrest was 36%. Reported survival of patients in hypothermic cardiac arrest varies over a wide range, mainly depending on the circumstances of cooling, and coexisting conditions.<sup>1,9,31-35</sup> Asphyxia during drowning or avalanche burial is the major reason for poor outcome in hypothermia victims in cardiac arrest and was present 40% of

Registry patients.<sup>10,14</sup> Major trauma was present in about one third of patients but did not contribute substantially to mortality. This supports suggestions from previous case reports that major trauma is not a reason to withhold ECLS rewarming in arrested hypothermia victims.<sup>36-37</sup> Witnessed cardiac arrest, return of spontaneous circulation despite hypothermia and exposure to cold in young and previously healthy hypothermia victims were factors favoring survival in registry patients, while age, sex, core temperature, cardiac rhythm and duration of CPR did not affect outcome.<sup>14,38,39</sup> Data regarding prognostic markers in hypothermic cardiac arrest vary substantially in recently published work on this topic. As in our study, rhythm was not correlated with survival in other publications<sup>9,40</sup> but was a significant predictor in others.<sup>10</sup> One study found that core temperature was not a predictor of survival, whilst lower core temperatures were associated with increased survival in two other studies.<sup>10,40</sup> In contrast to our study other studies have found survival decreased with increasing duration of CPR.<sup>10,35,40</sup> Accidental hypothermia is a heterogeneous diagnosis making it difficult to predict outcomes. There is no single treatment strategy. Available prognostic scores and markers should be used cautiously when assessing prognosis in an individual patient as these scores often do not sufficiently consider all relevant circumstances.

Only three of the 128 patients with preserved circulation had asphyxia whereas almost 40% of patients in circulatory arrest had been asphyxiated. (Table 2). This suggests that asphyxia is not only a common condition in arrested hypothermia victims, but also an important cause of cardiac arrest and mortality. Asphyxia must always be considered when starting CPR in a hypothermic patient with unwitnessed cardiac arrest or persistent asystole. The concept “nobody is dead until warm and dead” should be applied very cautiously whenever asphyxia is present. In contrast to most previous publications, asphyxia showed only a borderline association with mortality in hypothermic cardiac arrest in our study.<sup>14,35</sup> However, cardiac arrest occurring during mountaineering accidents is an important risk factor of increased mortality, most likely because

of the difficulty of performing CPR in mountain rescue. The large number of victims of mountain accidents in the IHR, with its high mortality rate biases the actual significance of asphyxia for mortality.

Glasgow Outcome Scores were not significantly different between patients in cardiac arrest and patients not in cardiac arrest. Neurological outcomes were favourable in both groups. These findings support previous work suggesting that prolonged CPR and ECLS rewarming are justified in hypothermic cardiac arrest as they often result in a high rate of good neurological outcomes.<sup>1,32,41</sup>

In the registry, the majority of patients not in cardiac arrest were safely rewarmed using active external rewarming. External forced air rewarming is the cornerstone of management in such patients with a survival rate of 93% in our study. Three fourths of patients not in cardiac arrest had a median GCS of 10 and a core temperature above 26°C, indicating that they were not profoundly hypothermic and had stable vital signs. This is in accordance with current recommendations for assessing hypothermia patients.<sup>4,42,43</sup>

Invasive rewarming techniques were used mainly in patients with a history of cardiac arrest with restoration of spontaneous circulation. Use of these techniques in this subgroup seems reasonable as it yields a survival rate of 71%. Only 8 patients not in cardiac arrest received invasive internal rewarming as compared to 106 patients rewarmed externally.

In view of the invasiveness of internal rewarming, the low rewarming rate of 1.3°C/hour, compared to the good results obtained with external rewarming, use of internal rewarming methods should be reconsidered.<sup>44,46</sup> Many clinicians have also observed lower rewarming rates with invasive internal methods compared to data from experimental studies.<sup>17</sup>

Almost all the patients with cardiac arrest on hospital admission were rewarmed with ECLS, whilst those with pre-rewarming ROSC were not rewarmed with ECLS in accordance with the guidelines.<sup>13, 42, 43</sup> In hypothermic patients without ROSC prior to hospital arrival, ECLS provides prolonged support of failing organ function after rewarming, improving outcome.<sup>31,41</sup>

## **CONCLUSIONS :**

This first analysis of 201 IHR patients with moderate to severe accidental hypothermia shows an excellent 95% survival rate for patients with preserved circulation. The survival rate for patients with pre-rewarming cardiac arrest was 36%. The majority were young men involved in mountain accidents. Witnessed cardiac arrest and ROSC before rewarming were predictors of good outcome, whereas asphyxia, coagulopathy, high potassium levels and lactate levels were predictors of poor outcomes. There are major differences between IHR 'real world' data compared to data from previous studies. This suggests that accidental hypothermia is a heterogenous diagnosis, which should be considered in both treatment strategies and prognostication. Including patients from centres treating mainly patients with urban hypothermia, or victims of cold water immersion or submersion, might increase the available scientific evidence necessary for development of effective widely accepted treatment guidelines.

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**Conflicts of Interest – None**

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## CRediT Author Statement

Beat H. Walpoth: Conceptualization, Methodology, Investigation, Original Draft Preparation, Reviewing & Editing. Monika Brodmann Maeder: Investigation, Original Draft Preparation, Reviewing & Editing. Delphine S. Courvoisier: Methodology, Software, Validation. Marie Meyer: Conceptualization, Investigation, Methodology. Evelien Cools: Investigation, Methodology, Validation. Tomasz Darocha: Investigation, Reviewing. Marc Blancher: Investigation. Frédéric Champly: Investigation. Lorenzo Mantovani: Investigation. Christian Lovis: Methodology, Software. Peter Mair: Original Draft Preparation, Reviewing & Editing.



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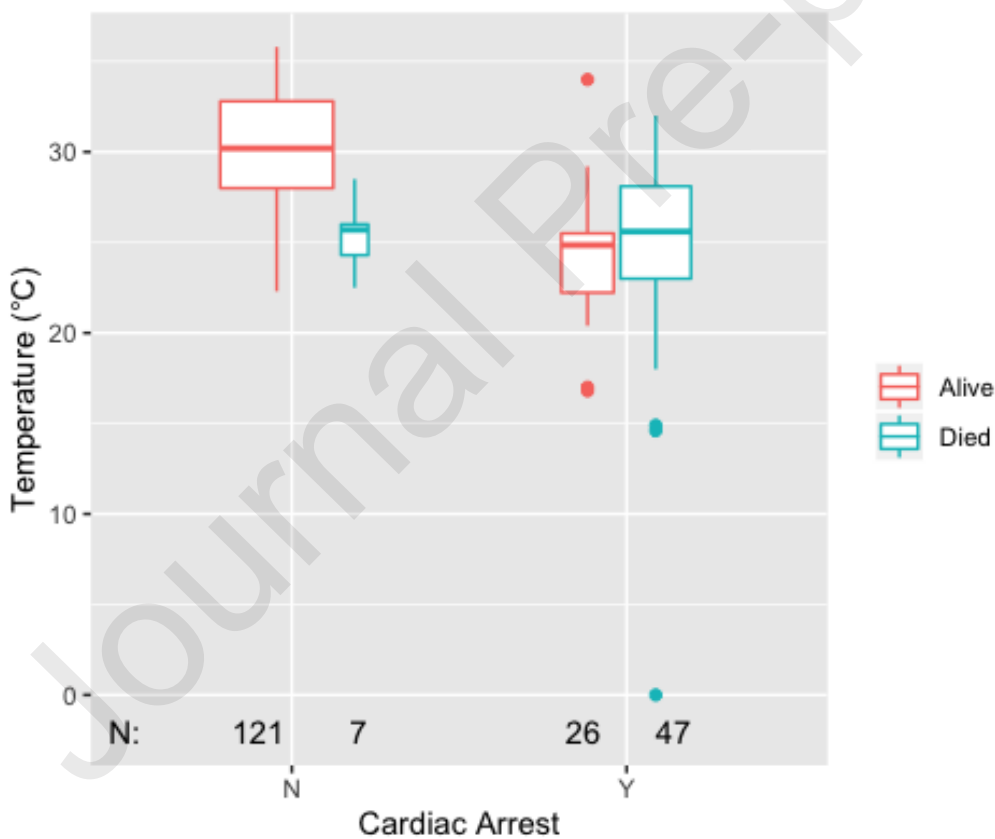
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**LEGENDS TO FIGURES**

Figure 1

Temperature according to cardiac arrest (N=no; Y=yes) and outcome at ICU discharge. The box plots are sized for the number of patients and discriminates between those alive and dead according to the temperature.

Figure 1



**TABLE 1:****DEMOGRAPHICS AND REASONS FOR HYPOTHERMIA IN PATIENTS WITH AND WITHOUT CARDIAC ARREST**

|                                     | <b>NO CARDIAC ARREST<br/>(total n = 128)</b> |                             | <b>CARDIAC ARREST<br/>(total n = 73)</b> |                             | <b>P</b> |
|-------------------------------------|--|-----------------------------|--|-----------------------------|----------|
|                                     | <i>data available</i>                        |                             | <i>data available</i>                    |                             |          |
| <b>Sex male</b>                     | <i>n = 128</i>                               | <b>91 (71%)</b>             | <i>n = 73</i>                            | <b>58 (80%)</b>             | 0.24     |
| <b>Age years (median [IQR])</b>     |  | <b>38.3</b><br>[26.2, 54.5] |  | <b>38.5</b><br>[27.8, 54.0] | 0.72     |
| <b>Accident type</b>                | <i>n = 128</i>                               |                             | <i>n = 73</i>                            |                             | 0.01     |
| Alpine                              |  | <b>93 (73%)</b>             |  | <b>48 (66%)</b>             |          |
| Urban/Rural                         |  | <b>31 (24%)</b>             |  | <b>14 (19%)</b>             |          |
| Water                               |  | <b>4 (3%)</b>               |  | <b>11 (15%)</b>             |          |
| <b>Aetiology of alpine accident</b> | <i>n = 90</i>                                |                             | <i>n = 46</i>                            |                             | <0.001   |
| Avalanche                           |  | <b>10 (11%)</b>             |  | <b>22 (48%)</b>             |          |
| Crevasse                            |  | <b>42 (47%)</b>             |  | <b>12 (26%)</b>             |          |
| Outdoor exposure                    |  | <b>38 (42%)</b>             |  | <b>12 (26%)</b>             |          |

TABLE 2

**CLINICAL AND LABORATORY FINDINGS IN PATIENTS WITH AND WITHOUT CARDIAC ARREST**

|   | NO CARDIAC ARREST<br>(total n = 128) |                                | CARDIAC ARREST<br>(total n = 73) |                                | P      |
|---|--------------------------------------|--------------------------------|----------------------------------|--------------------------------|--------|
|   | <i>data available</i>                |                                | <i>data available</i>            |                                |        |
| <b>Shivering</b>  | <i>n = 37</i>                        | <b>n = 13 (35%)</b>            | -                                | -                              |        |
| <b>Witnessed Cardiac Arrest</b>                         | -                                    | -                              | <i>n = 51</i>                    | <b>n = 41 (80 %)</b>           | -      |
| <b>Pre-warming ROSC</b>                                 | -                                    | -                              | <i>n = 68</i>                    | <b>n = 13 (19 %)</b>           | -      |
| <b>Successful Defibrillation</b>                        | -                                    | -                              | <i>n = 18</i>                    | <b>n = 5 (28%)</b>             |        |
| <b>Glasgow Coma Scale</b><br>(median [IQR])             | <b>n = 128</b>                       | <b>7 [3, 15]</b>               | <b>n = 73</b>                    | <b>3 [3, 3]</b>                | <0.001 |
| <b>Temperature hospital admission</b><br>(median [IQR]) | <b>n = 128</b>                       | <b>30.0°C [27.7;<br/>32.6]</b> | <b>n = 73</b>                    | <b>25.0°C [22.5;<br/>27.4]</b> | <0.001 |
| <b>Asphyxia</b>   | <b>n = 113</b>                       | <b>n = 3 (3%)</b>              | <b>n = 61</b>                    | <b>n = 24 (40%)</b>            | <0.001 |
| <b>Major Trauma</b>                                     | <b>n = 117</b>                       | <b>n = 60 (51%)</b>            | <b>n = 64</b>                    | <b>n = 22 (34%)</b>            | 0.03   |
| <b>Intoxication</b>                                     | <b>n = 47</b>                        | <b>n = 14 (30%)</b>            | <b>n = 41</b>                    | <b>n = 15 (37%)</b>            | 0.65   |

|                              |           |                    |           |                     |        |
|------------------------------|-----------|--------------------|-----------|---------------------|--------|
| <b>pH</b>                    | <b>81</b> | <b>7.19 ± 0.17</b> | <b>50</b> | <b>6.89 ± 0.33</b>  | <0.001 |
| <b>pCO<sub>2</sub> (kPa)</b> | <b>34</b> | <b>6.1 ± 2.8</b>   | <b>33</b> | <b>8.2 ± 2.8</b>    | 0.002  |
| <b>pO<sub>2</sub> (kPa)</b>  | <b>32</b> | <b>26.8 ± 17.7</b> | <b>33</b> | <b>29.1 ± 24.6</b>  | 0.657  |
| <b>BE (mmol/L)</b>           | <b>32</b> | <b>-12.8 ± 7.7</b> | <b>29</b> | <b>-21.72 ± 7.8</b> | <0.001 |
| <b>Potassium (mmol/L)</b>    | <b>86</b> | <b>3.9 ± 1.0</b>   | <b>59</b> | <b>5.3 ± 2.5</b>    | <0.001 |
| <b>Lactate (mmol/L)</b>      | <b>37</b> | <b>8.1 ± 11.8</b>  | <b>39</b> | <b>13.7 ± 5.7</b>   | 0.010  |
| Normalized thrombin time (%) | <b>61</b> | <b>73 ± 23</b>     | <b>29</b> | <b>47 ± 28</b>      | <0.001 |
| <b>ACT (seconds)</b>         | <b>2</b>  | <b>298 ± 53</b>    | <b>13</b> | <b>443 ± 311</b>    | 0.533  |
| <b>Coagulopathy [n(%)]*</b>  | <b>63</b> | <b>26 ± 41</b>     | <b>36</b> | <b>29 ± 81</b>      | <0.001 |

\*ACT > 150 sec and/or Quick < 70%



TABLE 3:

## REWARMING METHODS [n\* (%)]

| REWARMING METHOD                               | EXTERNAL REWARMING<br>total n =115 |                                  | ECLS<br>total n = 53  |                                   | Internal Rewarming<br>Total n = 21 |                                  | NOT WARMED<br>total n = 4 |                      | p      |
|--|------------------------------------|----------------------------------|-----------------------|-----------------------------------|------------------------------------|----------------------------------|---------------------------|----------------------|--------|
|  | <i>data Available</i>              |                                  | <i>data Available</i> |                                   | <i>data Available</i>              |                                  | <i>data Available</i>     |                      |        |
| <b>Glasgow Coma Scale median [IQR]</b>         | <i>n = 115</i>                     | <b>10</b><br>[3; 15]             | <i>n =53</i>          | <b>3</b><br>[3; 3]                | <i>n =21</i>                       | <b>3</b><br>[3; 3]               | <i>n =4</i>               | <b>3</b><br>[3; 3]   | <0.001 |
| <b>Cardiac Arrest</b>                          | <i>n =115</i>                      | <i>n =9</i>                      | <i>n =53</i>          | <i>n =43</i>                      | <i>n =21</i>                       | <i>n =13</i>                     | <i>n = 4</i>              | <i>n = 4</i>         | <0.001 |
| <b>Temperature pre-rewarming median [IQR]</b>  | <i>n =43</i>                       | <b>28.0°C</b><br>[26.0;<br>30.7] | <i>n =41</i>          | <b>25.4 °C</b><br>[22.6;<br>27.0] | <i>n =14</i>                       | <b>27.1°C</b><br>[25.7;<br>28.6] |                           | -                    | <0.001 |
| <b>Temperature post-rewarming median [IQR]</b> | <i>n =32</i>                       | <b>35.4°C</b><br>[35.0;<br>36.6] | <i>n =41</i>          | <b>36.0°C</b><br>[34.0;<br>36.5]  | <i>n =11</i>                       | <b>34.0°C</b><br>[32.0;<br>35.0] |                           | -                    | 0.40   |
| <b>Rewarming rate mean +/- SD</b>              | <i>n =23</i>                       | <b>2.0°C/h</b><br>± 1.6          | <i>n =36</i>          | <b>3.1°C/h</b><br>± 1.7           | <i>n =9</i>                        | <b>1.3°C/h</b><br>± 1.2          |                           | -                    | 0.003  |
| <b>Stay in ICU (days) (median [IQR])</b>       | <i>n =28</i>                       | <b>2.0</b><br>[1.0 ;<br>4.0]     | <i>n =27</i>          | <b>4.0</b><br>[2.0;<br>11.0]      | <i>n =11</i>                       | <b>3.0</b><br>[1.0; 5.0]         |                           | -                    | 0.10   |
| <b>Survival Rate</b>                           | <i>n =115</i>                      | <i>n = 107</i><br>(93%)          | <i>n =53</i>          | <i>n = 21</i><br>(40%)            | <i>n =21</i>                       | <b>15</b><br>(71%)               | <i>n = 4</i>              | <i>n = 0</i><br>(0%) |        |

N\* = 8 Missing data on rewarming method

TABLE 4

## POST-REWARMING COMPLICATIONS &amp; OUTCOME [n (%)]

| n   | NO CARDIAC ARREST<br>n = 128 |                            | CARDIAC ARREST<br>n = 73 |                            | p      |
|---|------------------------------|----------------------------|--------------------------|----------------------------|--------|
|   | <i>data available</i>        |                            | <i>data available</i>    |                            |        |
| <b>Survival to hospital discharge *</b>         | 128                          | <b>121 (95%)</b>           | 73                       | <b>26 (36%)</b>            | <0.001 |
| - <b>Respiratory failure</b>                    | 45                           | <b>16 (36%)</b>            | 30                       | <b>22 (73%)</b>            | 0.002  |
| - <b>Cardiovascular collapse</b>                | 43                           | <b>15 (35%)</b>            | 32                       | <b>19 (59%)</b>            | 0.060  |
| - <b>Neurologic dysfunction</b>                 | 42                           | <b>16 (38%)</b>            | 30                       | <b>19 (63%)</b>            | 0.055  |
| - <b>Renal failure</b>                          | 44                           | <b>15 (34%)</b>            | 29                       | <b>13 (45%)</b>            | 0.462  |
| - <b>Glasgow Outcome Score**</b><br>(mean [SD]) | 121                          | <b>4.2 ± 6.6</b>           | 26                       | <b>3.6 ± 5.9</b>           | 0.53   |
| <b>ICU stay (days)</b> (median [IQR])           | 41                           | <b>2.0 (1.0; 4.0)</b>      | 28                       | <b>4.0 (1.8; 11.3)</b>     | 0.048  |
| <b>Hospital stay** (days)</b> (median [IQR])    |                              | <b>10.5</b><br>[5.0, 79.2] |                          | <b>17.5</b><br>[1.3, 31.5] | 0.38   |

\*All patients with pre-hospital or hospital cardiac arrest. If only the 60 patients who were still in cardiac arrest at hospital admission are counted, the survival rate would only be 22%.

\*\*For rewarming hospital

TABLE 5:

## SURVIVORS VS. NON-SURVIVORS AFTER HYPOTHERMIC CARDIAC ARREST [n(%)]

| Variable                                       | Survivors<br>n = 26   |                   | Non-Survivors<br>n = 47 |                   | P     |
|--|-----------------------|-------------------|-------------------------|-------------------|-------|
|  | <i>data available</i> |                   | <i>data available</i>   |                   |       |
| N  |                       |                   |                         |                   |       |
| Sex male                                       | n = 26                | n = 20 (77%)      | n = 47                  | n = 38 (81%)      | 0.77  |
| Age, years (median [IQR])                      | n = 26                | 45 (16 -78)       | n = 47                  | 37 (13 -61)       | 0.02  |
| Accident type                                  | n = 26                |                   | n = 47                  |                   | 0.005 |
| - mountain                                     |                       | n = 11 (42%)      |                         | n = 37 (79%)      |       |
| - urban rural                                  |                       | n = 9 (34%)       |                         | n = 5 (11%)       |       |
| - water  |                       | n = 6 (23%)       |                         | n = 5 (11%)       |       |
| Aetiology of mountain accident                 | n = 10                |                   | n = 36                  |                   | 0.02  |
| - avalanche                                    |                       | n = 2 (20%)       |                         | n = 20 (56%)      |       |
| - crevasse                                     |                       | n = 2 (20%)       |                         | n = 10 (28%)      |       |
| - outdoor exposure                             |                       | n = 6 (60%)       |                         | n = 6 (17%)       |       |
| CPR duration, min (Mean +/- SD)                | n = 13                | 29 ± 387          | n = 15                  | 120 ± 101         | 0.16  |
| Temperature at hospital arrival (median [IQR]) | n = 26                | 24.9 [22.2, 25.5] | n = 47                  | 25.6 [23.0, 28.1] | 0.14  |
| ECG at hospital arrival                        | n = 24                |                   | n = 38                  |                   | 0.35  |
| - asystole                                     |                       | n = 1             |                         | n = 16            |       |
| - ventricular fibrillation                     |                       | n = 10            |                         | n = 19            |       |
| - PEA  |                       | n = 4             |                         | n = 2             |       |
| - Sinus  |                       | n = 9             |                         | n = 1             |       |
| Witnessed cardiac arrest                       | n = 24                | n = 17 (71%)      | n = 27                  | n = 8 (30%)       | 0.005 |
| Asphyxia confirmed                             | n = 22                | n = 5 (23%)       | n = 39                  | n = 19 (49%)      | 0.059 |
| ROSC before rewarming                          | n = 26                | n = 9 (35%)       | n = 42                  | n = 3 (7%)        | 0.007 |
| Successful defibrillation                      | n = 8                 | n = 4 (50%)       | n = 10                  | n = 1 (10%)       | 0.12  |
| Major trauma                                   | n = 26                | n = 11 (42%)      | n = 38                  | n = 11 (29%)      | 0.30  |
| Pre-rewarming lab findings                     |                       |                   |                         |                   |       |
| - Ph   | n = 17                | 6.96 ± 0.14       | n = 33                  | 6.85 ± 0.39       | 0.30  |
| - Potassium, mMol/L                            | n = 22                | 3.5 ± 0.9         | n = 37                  | 6.5 ± 2.5         | 0.001 |
| - Lactate, mMol/L                              | n = 19                | 11.1 ± 5.2        | n = 20                  | 16.2 ± 5.1        | 0.003 |
| - Coagulopathy*                                | n = 17                | n = 13 (77%)      | n = 19                  | n = 16 (84%)      | 0.68  |
| Rewarming method                               | n = 26                |                   | n = 44                  |                   | 0.30  |
| - " ECLS"                                      |                       | n = 16 (62%)      |                         | n = 27 (61%)      |       |
| - " External"                                  |                       | n = 3 (12%)       |                         | n = 7 (16%)       |       |
| - " Internal"                                  |                       | n = 7 (27%)       |                         | n = 6 (14%)       |       |
| - " Not rewarmed"                              |                       | n = 0 (0%)        |                         | n = 4 (9%)        |       |
| Rewarming rate, °C/h                           | n = 26                | 3.1 ± 2.1         | n = 47                  | 0.4 ± 0.5         | 0.93  |

\*ACT &gt; 150 sec and/or Quick &lt; 70%

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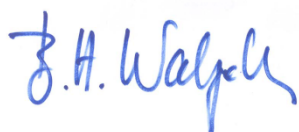
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