Hypothermic Cardiac Arrest With Full Neurologic Recovery After Approximately Nine Hours of Cardiopulmonary Resuscitation: Management and Possible Complications

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We describe full neurologic recovery from accidental hypothermia with cardiac arrest despite the longest reported duration of mechanical cardiopulmonary resuscitation (CPR) and extracorporeal life support (8 hours, 42 minutes). Clinical data and blood samples were obtained from emergency medical services (EMS) and the intensive care department. A 31-year-old man experienced a witnessed hypothermic cardiac arrest with a core temperature of 26°C (78.8°F) during a summer thunderstorm; he received mechanical CPR for 3 hours and 42 minutes, followed by 5 hours of extracorporeal life support. The use of a standard operating procedure that integrates a technical mountain rescue performed by EMS, optimizes prolonged CPR to the hub hospital, and enables prompt placement of extracorporeal life support is described and discussed. Three months postaccident, the patient had recovered completely (Cerebral Performance Category score of 1) and resumed normal daily life. Neurologically intact survival from hypothermic cardiac arrest is common, suggesting that aggressive resuscitation measures are warranted. There is a need for the establishment of a clear standard operating procedure and multiteam education and training to further optimize the patient survival chain from on-site triage and treatment to inhospital extracorporeal life support and postresuscitation care. [Ann Emerg Med. 2019;73:52-57.]

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INTRODUCTION

We report survival without neurologic impairment in a 31-year-old male climber, who underwent the longest recorded combination of mechanical cardiopulmonary resuscitation (CPR) and extracorporeal life support (8 hours, 42 minutes plus 28 minutes of suspected no/low flow) after presenting with hypothermic cardiac arrest with a core temperature of 26°C (78.8°F). Herein we highlight the need for the clear definition and use of a standard operating procedure[1] that integrates a technical mountain rescue performed by emergency medical services, optimizes prolonged CPR from the scene of the accident to the hub center during transport, and enables prompt placement of extracorporeal life support at admission.[2] The aim of implementing this standard operating procedure is to substantially improve survival and outcome of hypothermic cardiac arrest patients through multiteam education training and advanced operational cohesion.

CASE REPORT

On-Site Treatment and Triage

Two healthy male rock climbers (26 and 31 years old) were caught at an altitude of 2,800 m by a thunderstorm on the vertical wall of Marmolada, Dolomites, Italy (Figure 1), in the late afternoon on a summer day (day 0). The ambient temperature suddenly decreased to approximately 0°C (32°F) and one of the climbers quickly became trapped by a large cascade of runoff. The trapped climber was secured on the wall without any form of waterproof clothing and reportedly had already lost consciousness in the few minutes it took his companion to reach him. The companion signaled for help, using a light on his smartphone device directed toward a nearby mountain hut. The local helicopter emergency medical system was called (7:20 PM) (Figure 2).

A physician-staffed helicopter (EC-145T2; Airbus Helicopters, Marignane, France) reached the scene at 7:42 PM, and the unconscious patient was immediately evacuated with a 30-m winch operation before any resuscitation effort (Figure 1). The helicopter landed nearby; the initial rhythm was a low-voltage ventricular fibrillation (7:48 PM). Resuscitation maneuvers started immediately with manual CPR, followed after a few seconds by an electrical shock (200 J biphasic); mechanical CPR was started after one complete cycle of manual resuscitation. Despite another 2 defibrillation attempts (200 J biphasic), 1-mg epinephrine administration, and intubation, ventricular fibrillation

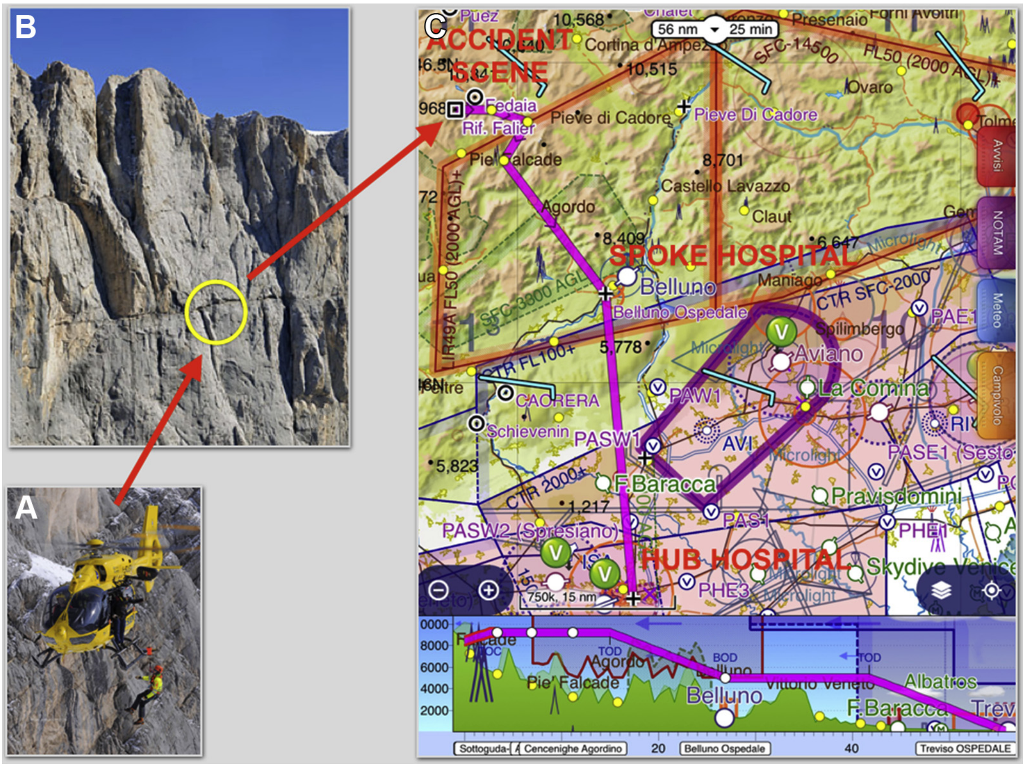

Figure 1. Winch operation by a physician-staffed helicopter (*A*), scene of the accident (*B*), and map showing the accident, spoke, and hub center locations (*C*). Altitudes are reported in feet.

degenerated into pulseless electrical activity and asystole (8:10 PM).

Prolonged CPR During Transport

After intubation, an esophageal temperature probe was placed and a core temperature of 26°C (78.8°F) was measured, and the diagnosis of hypothermic cardiac arrest made. CPR was continued with a mechanical chest compression device (LUCAS 2; Physio Control, Redmond, WA); initial end-tidal carbon dioxide ($ETCO_2$) level ranged between 14 and 22 mm Hg. At 8:20 PM, the patient was transferred by helicopter under continuous mechanical CPR to the spoke Hospital of Belluno, Italy (43 km; arrival at 8:34 PM), because a direct flight to the hub Hospital of Treviso, Italy, was impossible because of the darkness (Figure 1). On arrival, the patient's core temperature was stable (26.6°C [79.9°F]) and cardiac output under continuous CPR was considered sufficient ($ETCO_2$ 22 mm Hg); therefore, in accordance with the local protocol for refractory hypothermic cardiac arrest, the patient was transferred to a road ambulance and transported to the hub hospital (Treviso, Italy; 83 km) under ongoing mechanical CPR; meanwhile, the extracorporeal life support team was alerted.

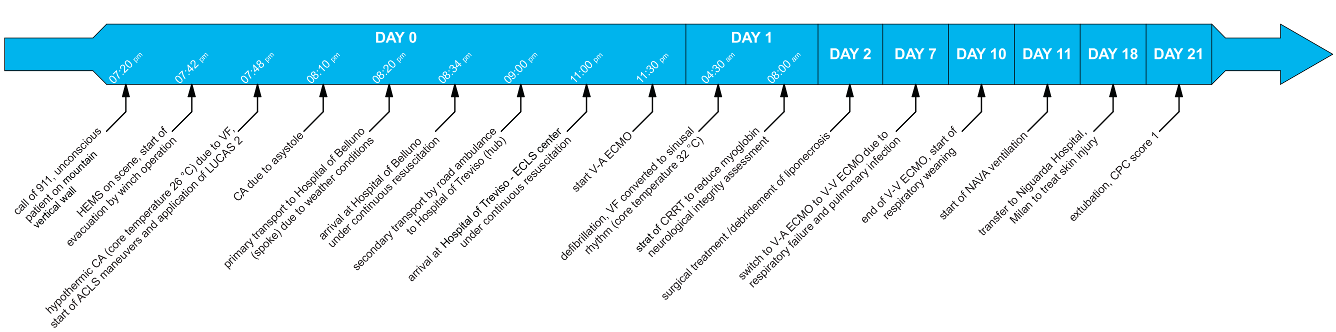

Figure 2. Course of treatment. *HEMS*, Helicopter emergency medical system; *CA*, cardiac arrest; *VF*, ventricular fibrillation; *ACLS*, advanced cardiac life support; *ECLS*, extracorporeal life support; *CRRT*, continuous renal replacement therapy; *NAVA*, neurally adjusted ventilatory assist; *CPC*, Cerebral Performance Category.

Hospital Admission and Extracorporeal Life Support Placement

After the patient's arrival (11 PM), venous-arterial extracorporeal membrane oxygenation was commenced (11:30 PM). Core temperature (esophageal) was 26.1°C (78.9°F); venous blood gas and serum analyses indicated pH 6.97, PaO_2 40.8 mm Hg, $PaCO_2$ 98 mm Hg, potassium 4.8 mmol/L, lactate 14.9 mmol/L, and other key laboratory values per the Table. Extracorporeal rewarming was performed at 1°C/hour, with a perfusion goal of 2.0 to 2.2 L/min per meter squared according to the local protocol. At 4:30 AM, a core temperature of 32°C (89.6°F) was reached and the cardiac rhythm turned from asystole to ventricular fibrillation. After one electrical shock (200 J biphasic), ventricular fibrillation was converted to sinus rhythm, and return of spontaneous circulation was achieved after 8 hours and 42 minutes of cardiac arrest (Figure 2).

Postresuscitation Care

The initial left ventricular ejection fraction was 5%; therefore, venous-arterial extracorporeal membrane oxygenation was continued with a blood flow of 3 L/min, FiO_2 0.55, and sweep gas flow of 6 L/min. Concurrently, mean arterial blood pressure was kept between 70 and 80 mm Hg with intravenous norepinephrine at 0.1 µg/kg per minute; anticoagulation with unfractionated heparin was maintained (target activated clotting time 180 to 220 seconds), as was pressure-regulated volume-controlled ventilation with FiO_2 0.4, tidal volume 480 mL, respiratory rate 15 breaths/min, and positive end expiratory pressure 8 cm H_2O. The first arterial blood gas analysis after return of spontaneous circulation showed pH 7.25, PaO_2 221 mm Hg, $PaCO_2$ 33.7 mm Hg, potassium 4.5 mmol/L, and lactate 9.5 mmol/L. Neurologic evaluation showed mental alertness with full motor response to command in all extremities (8:00 AM of day 1). Because of the release of inflammatory metabolites, myoglobin, and creatine phosphokinase (Table), continuous renal replacement therapy (multiFiltrate; Fresenius GmbH, Bad Homburg, Germany) with the EMiC2 (Fresenius GmbH) filter was started, and the cytokine absorption filter Cytosorb (CytoSorbents Corporation GmbH, Berlin, Germany) was subsequently placed into the extracorporeal membrane oxygenation circuit. Creatine phosphokinase peaked at 160,000 U/L, together with a progressive decrease of glomerular filtration rate, followed by a progressive recovery. On day 7, there was a partial recovery of the ventricular function (left ventricular ejection fraction 40%), but because of persistent respiratory failure, venous-arterial extracorporeal membrane oxygenation was replaced by a venous-venous extracorporeal membrane oxygenation up to day 10. On day 21, the patient was extubated; cerebral performance category score was 1, with only mild retrograde amnesia at day 28. Three months and 10 days after the accident, the patient left the rehabilitation unit and resumed normal daily life activities, with only minimal impairment of short-term verbal memory. Written informed consent for publication of the case report was obtained from the patient.

Table. Time course of selected laboratory parameters related to critical care management and complications.

Parameter (Reference Range)	Day 0 (Admission)	Day 1 (VA ECMO Start)	Day 7 (VV ECMO Start)	Day 10 (Weaning From VV ECMO)	Day 18 (Last Day in Treviso ICU)
Platelet count (150–400×10^9/L)	199	76	73	104	317
WBC count (4–10×10^9/L)	6.50	11.06	20.96	17.59	13.46
Hemoglobin (13–17 g/dL)	8.1	8.9	9	11.4	9.4
INR (0.85–1.20)	3.16	1.35	1.21	1.18	1.26
aPTT (26.4–38.2 s)	41	33.3	78.9	25.9	25.3
Antithrombin III (75%–120%)	28	99	84	86	85
Albumin (3.4–4.8 g/dL)	3.0	3.4	3.3	2.6	3.0
Creatinine (0.7–1.20 mg/dL)	1.57	2.3	3.3	2.18	1.54
GFR (mL/min per 1.73 m^2)	52	33	39	35	53
CPK (20–200 U/L)	4,662	>25,300	34,735	1,673	56
LDH (240–480 U/L)	1,336	>3,000	3,340	1,825	1,043
Procalcitonin (0.00–0.50 ng/mL)	NA	78.9	52.0	35.9	10.6
Troponin T (0.00–0.06 ng/mL)	4.46	3.46	2.71	3.26	2.45

VA, Venous-arterial; *ECMO*, extracorporeal membrane oxygenation; *VV*, venous-venous; *ICU*, intensive care unit; *WBC*, white blood cell; *INR*, international normalized ratio; *aPTT*, activated partial thromboplastin time; *GFR*, glomerular filtration rate; *CPK*, creatine phosphokinase; *LDH*, lactate dehydrogenase; *NA*, not avaiable.

DISCUSSION

This case provides an example of a successful chain of survival with optimized on-site treatment and triage, transport decisions, and early integration of extracorporeal life support, despite adverse environmental and logistic conditions. Thanks to the application of our predefined standard operating procedure,[1] the hypothermic cardiac arrest patient received time-limited advanced life support measures at the scene, complete with early and continuous high-quality CPR both on initial assessment and throughout the transport operation to the closest extracorporeal life support center. To our knowledge, this case represents the longest reported duration of mechanical CPR (3 hours, 42 minutes) and extracorporeal life support (5 hours) with full neurologic recovery.

European Resuscitation Council guidelines for the management of hypothermic cardiac arrest clearly state that without an evident cause of death, such as lethal trauma or prolonged asphyxia, patients with hypothermic cardiac arrest should receive prolonged CPR and be transported to an extracorporeal life support hub center for extracorporeal rewarming.[3] There is, in fact, a decrease in oxygen consumption of approximately 6% for every 1°C reduction in core temperature[4] that is postulated to result in a neuroprotective effect. Our healthy patient was rapidly cooled by the ice-cold cascade: this water exposure led to fast cooling without hypoxemia because the patient's head was not submerged. CPR to treat the witnessed hypothermic cardiac arrest was started immediately after the technical evacuation and continued during helicopter emergency medical system and ground transport. Specifically, mechanical CPR was performed for a total of 3 hours and 42 minutes (222 minutes); before this case, the longest reported duration of successful mechanical CPR in a hypothermic cardiac arrest patient was 80 minutes.[5] Previously, large randomized controlled trials involving ground-based ambulances have failed to show better patient outcome with mechanical CPR devices compared with manual resuscitation.[6,7] Data on mechanical CPR use during helicopter transport are sparse; however, a mannequin study demonstrated superior CPR quality when mechanical resuscitation was compared with manual CPR during a helicopter rescue[8]; also, a Japanese study indicated a higher return of spontaneous circulation rate.[9] In short, mechanical chest compression devices can provide high-quality CPR safely during prolonged transport, given the limits of provider endurance capacity, vehicle design, and restraint systems.

In the case of cardiac arrest, both the time from cardiac arrest to the beginning of CPR (no-flow time) and the low-flow time (time with manual or mechanical CPR) should be short and extracorporeal life support commenced as soon as possible, if indicated.[10] This can only be achieved by clear standard operating procedure definition, promotion, and education pertaining to how best to optimize a timely and cohesive multiteam treatment scenario in the case of hypothermic cardiac arrest in the mountains. Paramount is specific promotion of the benefits of extracorporeal life support within the helicopter emergency medical system crews and the directive for early patient arrival notification to hub hospitals to guarantee a timely preannouncement to the extracorporeal life support team and smooth operation. Since 2013, a dedicated standard operating procedure for the management of patients with refractory cardiac arrest has been implemented[1] in the mountainous Dolomites area of Italy, incorporating the helicopter emergency medical system and spoke and hub centers.

To our knowledge, with an overall duration of 8 hours and 42 minutes, this is the longest documented cardiac arrest resuscitation combining mechanical chest compressions, extracorporeal life support, and rewarming with extracorporeal membrane oxygenation in a hypothermic patient. Previously, Meyer et al[11] reported a patient in hypothermic cardiac arrest who was resuscitated with manual CPR for 4 hours and 48 minutes and rewarmed with cardiopulmonary bypass for 3 hours and 52 minutes. Despite that the core temperature at the scene was higher in our case compared with the case reported by Meyer et al[11] (26°C [78.8°F] versus 20.8°C [69.4°C]), the healthy condition of our patient, as well as the rapid cooling rate and uninterrupted chain of survival, could have played a role in this favorable outcome. Moreover, the low-dose use of epinephrine (notably, 1 mg during the total mechanical CPR time of 3 hours, 42 minutes) could have prevented excessive cerebral oxygen extraction. The use of advanced life support drugs in hypothermic patients remains controversial, and no benefit has been demonstrated in patients presenting with a core temperature below 30°C (86°F)[3]; moreover, in a recent animal experimental study epinephrine showed deleterious effects on cerebral oxygenation.[12] In this case study, the epinephrine dose was limited not only because of the lack evidence in humans but also because the relatively high $ETCO_2$ level indicated a sufficient cardiac output during mechanical CPR.

After hospital admission, extracorporeal membrane oxygenation enables controlled rewarming, avoiding excessive temperature excursions. However, the optimal rewarming rate is unknown and thus not currently standardized. In our case, the rewarming rate was set at approximately 1°C/h, according to the management protocol of our center for severely hypothermic patients in cardiac arrest. This leads to a gradual increase in flow, helping to avoid the formation of gas bubbles and to protect the brain from ischemia-reperfusion damage, in comparison with a high rate of rewarming (up to 4 to 10°C/h).[2] Moreover, appropriate critical care support is also essential after return of spontaneous circulation. For instance, acute renal failure is frequently observed after prolonged cardiac arrest.[2,13] In our case, in addition to continuous renal replacement therapy, a hemofiltration filter was incorporated into the extracorporeal membrane oxygenation circuit[14] to enhance the clearance of myoglobin[15] and the inflammatory cytokines released after reperfusion. Overall, postresuscitation treatment is challenging for critical care providers because of pathophysiologic alterations related to therapeutic choices (such as weaning from extracorporeal membrane oxygenation and mechanical ventilation) and the complexities related to neurologic monitoring in the unconscious patient.

Neurologically intact survival from hypothermic cardiac arrest has been previously observed, suggesting that aggressive resuscitation measures are warranted. There is a need for the establishment of a clear standard operating procedure with associated education and training integrating diverse expertise into a single seamless chain of survival. The ideal chain spans the realms of care from on-site triage and treatment to inhospital extracorporeal life support and postresuscitation care to optimize the survival of patients in refractory cardiac arrest due to accidental hypothermia, as well as other causes.

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