OUTCOME OF SURVIVORS OF ACCIDENTAL DEEP HYPOTHERMIA AND CIRCULATORY ARREST TREATED WITH EXTRACORPOREAL BLOOD WARMING

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ABSTRACT

Background Cardiopulmonary bypass has been used to rewarm victims of accidental deep hypothermia. Unlike other rewarming techniques, it restores organ perfusion immediately in patients with inadequate circulation. This study evaluated the long-term outcome of survivors of accidental deep hypothermia with circulatory arrest who had been rewarmed with cardiopulmonary bypass.

Methods Deep hypothermia (core temperature, <28°C) with circulatory arrest was found in 46 of 234 patients with accidental hypothermia. In 32 of the 46 patients, rewarming with cardiopulmonary bypass was attempted, resulting in 15 long-term survivors. In most of these patients, deep hypothermia developed after mountaineering accidents or suicide attempts. After an average (±SD) of 6.7±4.0 years of follow-up, we obtained the patients' medical histories and performed neurologic and neuropsychological examinations, neurovascular ultrasound studies, electroencephalography, and magnetic resonance imaging of the brain.

Results The average age of the patients was 25.2±9.9 years; seven were female and eight were male. The mean interval from discovery of the patient to rewarming with cardiopulmonary bypass was 141±50 minutes (range, 30 to 240). At follow-up there were no hypothermia-related sequelae that impaired quality of life. Neurologic and neuropsychological deficits observed in the early period after rewarming had fully or almost completely disappeared. One patient had cerebellar atrophy on magnetic resonance imaging with mild clinical signs, a condition that may have been caused by hypothermia. Other clinical abnormalities were either preexisting or due to injuries not related to hypothermia.

Conclusions This clinical experience demonstrates that young, otherwise healthy people can survive accidental deep hypothermia with no or minimal cerebral impairment, even with prolonged circulatory arrest. Cardiopulmonary bypass appears to be an efficacious rewarming technique. (N Engl J Med 1997;337:1500-5.)

DEEP accidental hypothermia (core temperature, <28°C) causes circulatory and neurologic disturbances.[1-8] Even with immediate treatment, mortality rates are high.[9-13] Successful management has been reported only in isolated cases.[14,15] The long-term outcome of patients with accidental deep hypothermia and cardiac arrest has not been assessed in a larger series.

In a retrospective multicenter study, 234 patients with accidental hypothermia of various degrees were identified. Forty-six of these had deep hypothermia with circulatory arrest.[11] Rewarming with cardiopulmonary bypass was attempted in 32 at three hospitals. The 15 long-term survivors, who were treated between 1977 and 1993, were healthy young people who had suffered deep hypothermia in most cases after mountaineering accidents or suicide attempts. The aim of this study was to assess the late outcome of these patients after rewarming with cardiopulmonary bypass.

METHODS

Characteristics of the Patients

We studied 15 young patients without cardiovascular disease (7 female and 8 male; mean [±SD] age, 25.2±9.9 years; range, 9 to 43) who had suffered accidental deep hypothermia with circulatory arrest after mountaineering accidents, a boating accident, or murder or suicide attempts (Table 1). At rescue all patients were comatose. Nine initially had vital signs such as respiration, a pulse, or regular electric cardiac activity. The other six patients had neither respiration nor a pulse. In all nine patients who initially had vital signs, cardiopulmonary arrest occurred a mean of 14.8±18.6 minutes after the rescue operation was begun. All patients were intubated and ventilated and received ongoing cardiac massage during transportation to the hospital. At the time of admission, all 15 patients had documented circulatory arrest (ventricular fibrillation in 10 and asystole in 5) and fixed, dilated pupils. The mean interval from discovery of the patient to rewarming with cardiopulmonary bypass was 141±50 minutes (range, 30 to 240).

Rewarming was performed by a cardiovascular surgeon using femoro-femoral cannulation and standard cardiopulmonary-bypass equipment (two patients were treated in Lausanne, four in Zurich,

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and nine in Bern). In two children sternotomy was necessary for cannulation. The mean rectal or esophageal temperature at referral was 21.8±2.5°C (range, 17.1 to 25.0) and rose to 35.6±1.8°C (range, 32.0 to 38.0) within 97.9±47.2 minutes (range, 60 to 240) after rewarming. After rewarming and arrival in the intensive care unit, 14 patients had a cardiac sinus rhythm and 1 had a transient nodal rhythm. Their pupils reacted normally to light. Seven patients were able to communicate within the first 12 hours after rewarming, five could communicate within 24 hours, and three required up to 30 days to regain consciousness. The mean duration of intubation and ventilation was 7.3±11.5 days (range, 8 hours to 44 days). The patients remained in the intensive care unit for an average of 10.5±13.1 days (range, 2 to 46).

The main problems at discharge were pulmonary in 11 patients, neurologic in 9, neuropsychological in 10, cardiac in 4, and renal in 5. Four patients had fractures, one had a burn caused by an inadequate rewarming attempt, one had pancreatitis, and one had deep venous thrombosis (cardiopulmonary-bypass cannulation site). Five patients were sent home directly from the hospital after 7.8±2.2 days (range, 5 to 10). Ten patients were transferred to other hospitals after 22.7±19.5 days (range, 2 to 55) for further treatment or rehabilitation, where they stayed for 40.2±58.9 days (range, 7 to 228).

Assessment

All patients or their parents were contacted and gave informed consent for the study. All agreed to a follow-up examination. This was performed at the hospital in Bern 6.7±4.0 years (range, 5 days to 179 months) after the accident.

At follow-up, physical and neurologic examinations and special tests described below were performed. The results were categorized as normal, borderline (abnormal without clinical relevance), or pathologic (abnormal with clinical relevance).

Neurovascular Ultrasound Studies

A duplex system for color coding (Acuson XP10, Mountain View, Calif.) was used to visualize the extracranial vessels (internal, external, and common carotid and vertebral arteries on both sides), and a 2-MHz pulsed Doppler system (TC2-64B or TC2-2000, Eden Medical Electronics, Ueberlingen, Germany) was used for flow-velocity measurements of the intracranial vessels (anterior, middle, and posterior cerebral arteries on both sides and basilar artery). These examinations were performed to rule out an extracranial or intracranial macroangiopathy, which could influence the results of other neuropsychological and neurophysiologic studies. Flow velocities were compared with those in a control group of healthy subjects matched for age and sex.

Electroencephalography and Neuropsychological Tests

Electroencephalography was performed on all patients. Standard electrode positions were used according to the 10–20 method. Adult patients underwent comprehensive neuropsychological testing with a standardized battery of clinical tests.[16] Patient 6 underwent an equivalent test battery for children on the fifth day after the accident. Functioning in all patients was assessed on the basis of each patient's ability to provide personal information, orientation, mental control, attention span, memory, higher cognitive functions, spatial performance, and language abilities. A score of 0 was assigned if there was no impairment, a score of 1 in the case of slight impairment, a score of 2 in the case of moderate impairment, and a score of 3 in the case of severe impairment. The results were compared with existing values in age-matched controls.[16] The patients' overall neuropsychological performance was scored with the same scale.

Magnetic Resonance Imaging of the Brain

Magnetic resonance imaging of the brain was carried out on a 1.5-T system with a circularly polarized head coil (Signa, General Electric, Milwaukee). T_1-weighted sagittal and axial multislice scans (single spin–echo) and T_2-weighted axial (double spin–echo) sequences covering the entire brain were obtained. Two neuroradiologists independently assessed the images with respect to global or focal atrophy and the presence of lesions. They were told the patients' age and sex but not clinical details.

Statistical Analysis

Descriptive statistics were generated when appropriate. Unless otherwise stated, values are expressed as means (±SD) and ranges. When the results were compared with those in age-matched control subjects, the differences were calculated by the nonparametric Wilcoxon signed-rank test.

RESULTS

History and Physical Examination

Fourteen patients reported complete recovery and one patient (Patient 10) satisfactory recovery from the accident. Despite persistent deficits due to accident-related injuries but not to the hypothermia, none of the patients felt handicapped. They all resumed their former lifestyles. Only one patient (Patient 4) required medical treatment for preexisting psychiatric problems. The general physical examination showed normal findings in all patients.

Neurologic Findings

Three patients had borderline abnormalities that were probably related to circulatory arrest during hypothermia (Table 1). Other abnormalities were preexisting or caused by injuries incurred during the accident but were not related to hypoxia or hypothermia. Patient 6 had mildly impaired coordination of his left arm and hand, which interfered minimally with function. Patient 7 had an impaired ability to make rapid alternating movements of his left hand (dysdiadochokinesia) at follow-up that did not affect his overall performance. He had resumed his profession as an engineer and his sports activities such as mountaineering and climbing. This patient showed the most remarkable recovery, since it took six months for him to be able to walk unaided and about one year for him to be able to read and write normally. Patient 9 had dysesthesia of his left foot.

Neurovascular Ultrasound Studies

All patients had normal carotid and vertebral arteries in the neck on duplex scanning. Flow velocities of the extracranial and intracranial vessels were within the normal range.

Electroencephalography

On visual assessment five patients had borderline results and one had pathologic results (Table 1). The borderline alterations consisted of focal abnormalities (slow waves and epileptiform discharges) in three patients and slowed background activity in two. Patient 12, who had the lowest core temperature at rescue, had an electroencephalogram with slowed background activity and sharp and theta

TABLE 1. CHARACTERISTICS OF THE PATIENTS AT REWARMING AND FOLLOW-UP.*

PATIENT NO.	SEX/AGE (YR)	CAUSE OF HYPOTHERMIA	ADDITIONAL INJURIES	CORE TEMPERATURE BEFORE REWARMING (°C)	NEUROLOGIC FINDINGS†		
					CNS	PNS	OVERALL
1	F/24	Fall into crevasse and ice water	Injury of left brachial plexus during rescue	24.0 (E)	Normal	Mild lesion of left-arm plexus with extension deficit of fingers due to injury during rescue	Borderline
2	F/25	Exposure while hiking	—	24.4 (E)	Normal	Normal	Normal
3	F/43	Avalanche	Shoulder fracture	19.6 (R)	Normal	Normal	Normal
4	F/31	Exposure after suicide attempt‡	—	25.0 (R)	Normal	Normal	Normal
5	M/42	Fall into crevasse and ice water	Femur fracture	20.0 (E)	Normal	Normal	Normal
6	M/9	Fall into crevasse and ice water	—	21.0 (E)	Mild abnormalities of coordination and fine finger movements	Normal	Borderline
7	M/25	Fall into crevasse	Frostbite	17.5 (E)	Mild abnormality of coordination of left hand, mild ataxia during tandem walking	Normal	Borderline
8	F/22	Exposure after suicide attempt‡	—	22.0 (E)	Normal	Normal	Normal
9	M/28	Fall into crevasse	—	22.1 (E)	Dysesthesia of left foot, reflex asymmetry, no motor impairment	Normal	Borderline
10	M/13	Exposure after attempted murder	Brain injury, bilateral anterior tibial compartment syndromes	24.0 (R)	Borderline (mild athetosis)	Bilateral foot drop and steppage gait after anterior tibial compartment syndromes	Pathologic
11	M/17	Exposure after suicide attempt‡	Rib fractures	20.0 (R)	Normal	Normal	Normal
12	M/13	Fall into crevasse	Injury of left brachial plexus during rescue	17.1 (E)	Normal	Mild lesion of left-arm plexus with extension deficit of fingers due to injury during rescue	Borderline
13	F/26	Exposure after suicide attempt‡	—	23.0 (R)	Normal	Normal	Normal
14	M/25	Prolonged immersion in cold water after boating accident	—	24.5 (R)	Preexisting hemicord syndrome on the right (no worsening after hypothermia)	Normal	Pathologic
15	F/35	Exposure after suicide attempt‡	—	23.5 (R)	Normal	Normal	Normal

*CNS denotes central nervous system, PNS peripheral nervous system, MRI magnetic resonance imaging, E esophageal, and R rectal.

†Borderline results refer to abnormal findings without clinical relevance. Pathologic results refer to abnormal findings with clinical relevance. Pathologic neurologic and neuropsychological findings were not due to hypothermia. Patient 10 had had a cerebral injury before hypothermia occurred, and Patient 14 had a preexisting Brown-Séquard's syndrome. Patient 12, who had pathologic findings on electroencephalography, did not have seizures.

‡These patients attempted suicide by intoxication with various substances and were exposed to cold after losing consciousness.

§Patient 4 refused to complete neuropsychological testing; however, on the basis of data obtained from the interview and the history there were no findings to indicate clinically significant cognitive impairment.

¶Patient 6 underwent testing with a neuropsychological test battery for children.

‖Patient 7 had cerebellar atrophy that was presumably related to the hypothermia and calcification of the basal ganglia that was presumably unrelated to the hypothermia. Patient 10 had post-traumatic lesions of the right frontal and temporal lobes.

**Cognitive performance in this patient was evaluated on the basis of data obtained from the history and the interview, because there were neither test material nor test norms available in her native language of Swedish.

Table 1. Continued.

Electroencephalography			Neuropsychological Testing†	MRI of Brain†
Background Frequency (Hz)	Abnormalities	Overall Results†		
10	Asymmetry of left retrotemporal area	Normal	Normal	Normal
9–10	Frontal theta waves	Normal	Normal	Normal
10–12	—	Normal	Normal	Normal
7–8	Focal epileptiform discharges	Borderline	Normal§	Normal
9–10	—	Normal	Normal	Normal
8–9	—	Normal	Normal¶	Normal
7–11	Slow waves in left frontotemporal area	Normal	Normal	Pathologic‖
9–10	Focal epileptiform discharges, left temporal slowing	Borderline	Normal	Normal
7–8	Slowed background activity	Borderline	Normal	Normal
9	—	Normal	Pathologic	Pathologic‖
9–10	Left temporal slowing	Borderline	Normal	Normal
7–8	Focal sharp waves, right temporoparietal slowing	Pathologic	Normal	Normal
8	Dysrhythmic background activity	Borderline	Normal	Normal**
9	—	Normal	Normal	Normal
10	—	Normal	Normal	Normal

waves in the right temporoparietal region. However, he had no history of seizures and did not require antiepileptic medication. All documented electroencephalographic changes were probably related to hypothermia.

Neuropsychological Findings

Thirteen of the 15 patients completed neuropsychological testing. Patient 4 refused to complete testing, but interview data did not indicate partial or global cognitive impairment. Patient 13 was interviewed in her native language of Swedish and did not show any neuropsychological impairment; however, neither test material nor norms were available in her native language.

Patient 6, who could not be tested at follow-up, made a good recovery and resumed attending school. Patient 7, who had very severe neuropsychological deficits on discharge from the hospital, including aphasia, apraxia, and emotional problems, recovered completely. Patient 10 had slightly impaired orientation and memory and a moderately impaired attention span, corresponding to the traumatic brain damage seen on imaging. Despite severe brain injury, which required rehabilitation for seven months, he attended a regular school and did not require special tutoring. Overall, no patient had any hypothermia-related impairment.

Magnetic Resonance Imaging of the Brain

Findings on magnetic resonance imaging were normal in 13 patients and pathologic in 2 patients. Patient 7 had a global cerebellar atrophy, symmetrically involving both cerebellar hemispheres and the vermis. In addition, T_2-weighted images showed a low signal intensity of the basal ganglia due to bilateral calcifications. The calcifications, but not the cerebellar atrophy, were already apparent on a computed tomographic scan obtained 10 days after the accident. Therefore, the cerebellar atrophy was most likely related to the hypothermia, and the calcifications were not. Magnetic resonance imaging of Patient 10 showed cortical and subcortical defects of the right frontal and temporal lobes as a result of a sustained head injury, which was not related to the hypothermia. Twelve of the 15 magnetic resonance scans showed subtle enlargements of basal perivascular spaces, which were considered within the limits of normal.

DISCUSSION

Survival after accidental deep hypothermia (core temperature, <28°C) and prolonged cardiac arrest is rare.[7,9,12] Although there have been isolated case reports, the long-term outcome of such patients has not been described. The results of our study are encouraging. At follow-up all 15 patients who survived rewarming with cardiopulmonary bypass had resumed their former activities and lifestyles. There were either no hypothermia-related neurologic or neuropsychological deficits or only mild ones. Abnormal findings on examination were due to injuries sustained during the accident or rescue. Both the high survival rate (47 percent; 15 of 32 patients) and the long-term outcome of our patients are remarkable considering the severe neurologic problems in the early period after rewarming (prolonged coma, amnesia, aphasia, ataxia, or spasticity). Some patients needed long-term rehabilitation. Severe deficits soon after rewarming have also been documented in other studies.[6,12,17] The favorable outcome in our study is in contrast to resuscitation results in patients with normothermia and cardiac arrest, who have a poor outcome. Only 8 to 14 percent of patients with out-of-hospital or in-hospital cardiac arrest survive resuscitation and leave the hospital.[18,19] In other reports, 33 to 48 percent of survivors had persistent moderate-to-severe neurologic and neuropsychological impairment.[20,21]

Five main reasons may account for the relatively good survival rate and favorable long-term outcome in our patients with hypothermia. First, hypothermia was deep. Hypothermia increases the tolerance of the brain to ischemia. It slows metabolic processes and reduces oxygen consumption.[22,23] The protective effect of moderate hypothermia has been applied successfully in the treatment of traumatic brain injury.[24] In cardiac surgery deep hypothermia is routinely used for cerebral protection when circulatory arrest is required.[25-28] At a core temperature of 20°C cardiac arrest is tolerated for up to 30 minutes without clinically significant neurologic or neuropsychological deficits.[27,28] Second, none of our patients had asphyxia or hypoxic brain damage before hypothermia developed, problems that often occur in avalanche or drowning victims.[3,12,29-31] Asphyxia that precedes cooling of the body increases the risk of death.[11] Third, our surviving patients were young, were in good general health, and had no vascular risk factors. Unlike patients in other referral centers our patients were not homeless people, who are often malnourished and have other medical problems.[32] Fourth, the infrastructure and experience of rescue organizations in Switzerland may have influenced the outcome favorably.[33,34] Thirteen patients were rescued by helicopter with a professional team that included a physician. During transportation and at the hospital, hypothermia was maintained and the patients were rewarmed only after cardiopulmonary bypass was initiated.[6,11,35]

The fifth and potentially crucial factor responsible for the good outcome in this series may have been the rewarming technique.[6,35,36] Early rewarming with cardiopulmonary bypass has theoretical advantages as compared with other rewarming methods: it is the fastest method of rewarming; it provides adequate and immediate circulatory support; it may improve tissue perfusion by hemodilution; metabolic and toxic derangements can be corrected rapidly; and the heart is rewarmed before the rest of the body, thus preventing shock due to peripheral vasodilatation.[35] In the absence of such contraindications as asphyxia, severe traumatic injury, and extremely elevated serum potassium levels (exceeding 10 mmol per liter), cardiopulmonary bypass appears to be the rewarming method of choice for accidental deep hypothermia with circulatory arrest.[6,10,11,35] However, the value of this technique is doubtful for a patient with circulatory arrest but only moderate hypothermia.[13,29] The upper and lower limits of the core temperature at which rewarming attempts justify the use of extracorporeal circulation remain unclear.[12,13,17,29,34]

In patients with preserved circulation and a less severe hypothermia, other rewarming techniques can be used and may be preferable.[12,13,32,37,38] For instance, rewarming with warm air is noninvasive and technically easy to perform.[39] In addition, the availability of rewarming with cardiopulmonary bypass is limited to large medical centers. Another important goal is to establish predictors of poor outcome in deep accidental hypothermia.[8,11,13,17,29,40]

In conclusion, our study demonstrates that the long-term outcome of survivors of accidental deep hypothermia with prolonged circulatory arrest and rewarming with cardiopulmonary bypass is favorable. Severe hypothermia-related neurologic deficits observed in the early post-rewarming period had disappeared at follow-up. Permanent neurologic deficits of clinical relevance were either preexisting or due to injuries sustained during the accident or rescue. The long-term survival rate of 47 percent is higher than previously reported[9,12,29] and may be explained by the severity of hypothermia, the rewarming technique used, the rescue teams used, the patients' characteristics, and the absence of asphyxia before exposure to the cold.

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