Research letters

Resuscitation from accidental hypothermia of 13·7°C with circulatory arrest

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In a victim of very deep accidental hypothermia, 9 h of resuscitation and stabilisation led to good physical and mental recovery. This potential outcome should be borne in mind for all such victims.

Mortality from deep accidental hypothermia with circulatory arrest remains high, despite improved prehospital survival, rewarming techniques in hospital, and new types of heart and lung assistance.[1,2] The lowest temperature reported in a survivor of accidental hypothermia is 14·4°C in a child.[3] Long-term survival of up to 33% with minimum cerebral impairment after accidental deep hypothermia (core temperature <28°C) with circulatory arrest has been reported in young healthy adults.[4]

Our hospital uptake area in Norway is sparsely populated and subarctic. In several cases of accidental deep hypothermia we have used continuous prehospital cardiopulmonary resuscitation (CPR), air-ambulance evacuation, and rewarming with emergency cardiopulmonary bypass. No adult patient has yet survived to discharge, despite initial re-establishment of a perfusing cardiac rhythm and normalised organ function. Death has been due to progressive uncontrollable systemic oedema with pulmonary insufficiency and fatal brain swelling.

On May 20, 1999, at 1820 h, an experienced female off-piste skier aged 29 years fell while skiing down a waterfall gully. She and her two companions were junior registrars at the local hospital, trained in CPR, and equipped for extreme conditions. The woman became wedged between rocks and overlying thick ice, and the space was continuously flooded by icy water. Her skis prevented her from sliding and served as a grip by which her two companions tried to extract her. 7 min later, her friends called the emergency medical dispatch centre at Narvik Hospital by mobile telephone. The woman struggled under the ice for 40 min. At 1900 h she had stopped moving.

At 1939 h rescue teams arrived. They cut a hole in the ice downstream and removed her from the water, at which time she was clinically dead. Basic CPR was started immediately. An air ambulance arrived at 1956 h, bringing a rescuer and an anaesthesiologist who performed oral endotracheal intubation, ventilated her with 100% oxygen, and winched her into the helicopter. CPR and positive-pressure manual ventilation bag-to-tube was continued during the 1 h flight to Tromsø University Hospital. They arrived at 2110 h.

The patient was immediately taken to the operating room. She had no spontaneous respiration or circulation, her pupils were widely dilated and unresponsive to light. Electrocardiography was isoelectric. Separate electronic pharyngeal and rectal temperature probes measured initial temperature as 14·4°C. An arterial blood sample showed normal serum potassium and oxygenation, moderate hypercarbia, and severe metabolic acidosis (table). Foamy pink fluids streamed from the endotracheal tube. A team of cardiac surgeons, anaesthesiologists, perfusionists, and specialised nurses continued CPR with 100–120 external chest compressions and 15–20 ventilations per min, while the patient was prepared for cardiopulmonary bypass by femoral access, using a fully heparin-coated system. Systolic arterial blood pressure was around 75 mm Hg measured at a femoral-artery catheter during CPR. Full cardiopulmonary bypass bloodflow was reached at 2150 h. Rectal temperature decreased to 13·7°C at 2152 h. Mean arterial pressure was kept at 50 mm Hg; cardiopulmonary bypass flow started at 0·5 L/min and increased to 3·5 L/min as the venous return improved.

A maximum temperature gradient of 10°C was maintained between the woman's venous blood and the heat exchanger of the cardiopulmonary-bypass machine. At 2200 h, ventricular fibrillation started, which converted spontaneously to a pulse-generating cardiac rhythm after 15 min. Rectal tempurature remained at 14·2°C, whereas pharyngeal and oesophageal temperature had increased to 25·0°C and 31·5°C, respectively. We performed chest drainage followed by a median sternotomy because of bleeding from a lesion in the left subclavian artery caused by previous cannulation of the subclavian vein. The lesion was sutured directly.

We disconnected the patient from cardiopulmonary bypass after 179 min. At 170 min, the patient's rectal temperature had reached 36·0°C. Because of increasing cardiorespiratory insufficiency, we placed new cannulas in the patient's femoral vein and artery and she was

	On admission to operating room	After 5 min on CPB	On CPB with cardiac perfusing rhythm	Just before CPB stopped	Just after CPB stopped	Worst values without CPB	First values on connection to ECMO	First values in intensive care
Time	2120 h	2155 h	2215 h	0028 h	0049 h	0322 h	0445 h	0600 h
pH	6·65	6·54	6·64	7·14	7·10	7·00	7·30	7·29
$PaCO_2$ (kPa)	7·7	11·4	8·7	4·6	6·7	12·0	4·5	4·5
PaO_2 (kPa)	64·8	11·0	10·2	26·5	6·0	7·06	70·1	73·0
Base deficit	27	27	27	15	14	8	8	8
Haemoglobin (g/L)	15·7	13·1	12·2	7·4	9·6	8·1	10·2	9·3
Glucose (mmol/L)	. .	. .	30·9	. .	. .	. .	15·3	. .
Potassium (mmol/L)	4·3	8·2	6·7	4·2	4·0	3·4	3·6	3·1
Pharyngeal temperature (°C)	14·4	18·2	25·0	37·6	37·4	. .	. .	. .
Rectal temperature (°C)	14·4	13·7	14·2	36·0	36·4	. .	. .	. .

CPB=cardiopulmonary bypass; ECMO=extracorporeal membrane oxygenator; $PaCO_2$=partial pressure of carbon dioxide; PaO_2=partial pressure of oxygen.

Blood chemistry values during CPR and rewarming

connected to an extracorporeal membrane oxygenator (ECMO). She was transferred to the intensive-care unit after 9 h of resuscitation, rewarming, and stabilisation, and remained there for 28 days. ECMO was needed for 5 days, during which time several organ dysfunctions developed that required, in addition to ECMO, haemodiafiltration and respiratory support. Transitory haemorrhagic diathesis, atrophic gastritis, ischaemic colitis, and polyneuropathy also occurred. After intravenous sedation was stopped, the patient was mentally alert with adequate responses and spontaneously moved three of four extremities. After an unsuccessful extubation on day 11, she was tracheotomised and remained on a ventilator for 35 days, partly because of critical illness polyneuropathy. She was transferred to her local hospital by air ambulance on day 28 and moved to a rehabilitation unit on day 60.

At follow-up, 5 months after the accident, she had residual partial pareses of the upper and lower extremities that was improving. Her mental function was excellent and she was gradually returning to work. She had also resumed hiking and skiing.

Victims of very deep accidental hypothermia with circulatory arrest should be seen as potentially resuscitable with a prospect of full recovery. Reliable prognostic markers are unclear after cold-water immersion.[5] An optimum mechanism of cooling (whole-body cooling with subsequent circulatory arrest instead of warm hypoxic arrest followed by cooling), rapid prehospital response, continuous CPR, and rapid extracorporeal blood rewarming may improve outlook.

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Sirolimus-tacrolimus combination immunosuppression

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A series of 32 recipients of liver, kidney, or pancreas transplants who were treated with sirolimus and low-dose tacrolimus experienced a low rate of rejection and excellent graft function without drug-related toxic effects.

Sirolimus is as effective as cyclosporin in preventing renal graft loss due to rejection while maintaining superior graft function.[1] Various studies have shown the safety and efficacy of the combination of sirolimus and cyclosporin, and the potential for cyclosporin dose reduction.[2] Sirolimus is effective when used alone or with cyclosporin after liver transplantation.[3] Sirolimus and tacrolimus have similar structures and compete for the same intracellular binding protein (FKBP12).[4] However, the sirolimus-FKBP12 complex does not inhibit calcineurin and T-cell activation as the tacrolimus-FKBP12 complex does, but it exerts its immunosuppressive effect by inhibiting mTOR, a protein essential for cytokine-driven T-cell proliferation. Experimental transplantation studies suggest synergism between sirolimus and tacrolimus.[5] We investigated whether sirolimus can be given safely to tacrolimus-treated transplant recipients and whether its addition allows the dose of tacrolimus to be decreased.

Between April, 1998, and May, 1999, we recruited 32 transplant recipients (16 female, 16 male) aged 16–69 years (mean 50). (Full details of the patients are available from the investigators.) Tacrolimus and sirolimus treatment was started on the day of transplantation via nasogastric tube at daily doses of 0·03 mg/kg (33% of the recommended dose) and 5 mg, respectively. Doses were subsequently adjusted to maintain trough concentrations of 3–7 μg/L and 6–12 μg/L, respectively. Prednisone was given as a 500 mg intravenous bolus during transplantation and subsequently at 25 mg/day tapering to 5–10 mg/day at 1 month. Steroids are being withdrawn from all patients beyond 3 months. Antithymocyte globulin was given to recipients of pancreas grafts for 3–7 days (mean 4·5). All patients received prophylaxis with trimethoprim and sulphamethoxazole against *Pneumocystis carinii*, and those at high risk of cytomegalovirus transmission received ganciclovir. Graft biopsies were done if there was biochemical or clinical evidence of graft dysfunction.

Indications for liver transplantation were cryptogenic cirrhosis (six), primary biliary cirrhosis (six), fulminant liver failure (four), hepatitis C (three), autoimmune hepatitis (two), α1-antitryspin deficiency (one), and primary sclerosing cholangitis (one). Two patients received liver and kidney grafts for polycystic disease and for alcoholic cirrhosis with IgA nephropathy. Seven patients received pancreas transplants for diabetic nephropathy, two of whom had previously undergone kidney transplantation; the other five received kidney grafts simultaneously. One patient received an ABO-incompatible liver and another received a cross-match-positive kidney-liver combination.

30 (94%) of the 32 recipients are alive and well with normal function in all grafts 43–450 days (mean 230) after transplantation. 23 (92%) of the liver recipients are alive; five (20%) of these were comatose and on mechanical ventilation at the time of transplantation. A 57-year-old man with alcohol-associated autoimmune hepatitis who remained dependent on mechanical ventilation after liver transplantation died of a subarachnoid haemorrhage 66 days after transplantation. He did not have thrombocytopenia or hypertension. Necropsy showed cytomegalovirus infection of the lung and a normal liver. A 54-year-old woman with primary sclerosing cholangitis who was on treatment for intrahepatic abscesses at the time of transplantation died from hepatic-artery haemorrhage at home 28 days later. An abscess adjacent to the artery was found; the liver was normal.

Only one episode of rejection has occurred. A 52-year-old recipient, of her own volition, stopped all medications, including tacrolimus and sirolimus, for 1 week, because of transient malaise, 233 days after transplantation. She developed grade 1 rejection that was reversed by a 3-day course of prednisolone (500 mg/day) and the resumption of sirolimus and tacrolimus. At the time of rejection, sirolimus and tacrolimus concentrations in her blood were undetectable.