Complete neurologic recovery after ten minutes of absent cerebral blood flow at normothermia

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Abstract

Prolonged normothermic cardiac arrest is associated with a high incidence of neurological morbidity and mortality1. Whole body temperature-controlled perfusion has been applied to limit reperfusion injury and minimize ischemia2. We describe the full recovery of a patient after the application of rapid hypothermia following an intraoperative aortic rupture with ten minutes of absent cerebral blood flow.

Clinical Case

A 57-year-old male presented for coronary artery bypass grafting (CABG) following missed anterior STEMI (Trop-T 254ng/L). The patient described a three-week history of crescendo angina with a baseline NYHA-I. The only clinically relevant risk factor was obesity (BMI 35kg/m^2). Coronary angiography confirmed proximal triple vessel coronary artery disease with moderate left-ventricular function (LVEF 35%) with antero- and posterior hypokinesia.

Cardiopulmonary bypass (CPB) was established via central cannulation (34°C) and intermittent cold (4°C) ante- and retrograde blood cardioplegia was given. Following uneventful distal grafts (LIMA to LAD, Radial to D1 and SV to PDA) the resident completed two proximal anastomoses on a single cross clamp (90min). The patient rapidly weaned from CPB (0.04µg/kg/min adrenalin) with a final on pump PO_2 of 236mmHg. The aortic cannula was removed upon confirmation of stability after protamine administration. At aortic decannulation, a transverse aortic rupture extended outside the double purse-string snare progressing posteriorly, most likely due to high systolic pressures (145mmHg) and a fractured snare tip. No post CPB blood gas had been drawn yet, however an FiO_2 of 0.36 assumes that the PO_2 at the time of arrest was not supranormal.

Digital pressure was applied to the aorta whilst the right groin was exposed, but progression of the rupture prevented pursuing this strategy. The patient was immediately heparinized (30,000IU), a further 10,000IU were added to the pump reservoir. The patient was allowed to completely exsanguinate into the CPB circuit until the aortic edges could be identified. Meanwhile venous re-cannulation was performed via the right atrium. An aortic cannula was inserted into the defect after a large non-pledgeted single purse string was sutured around the ruptured aortic edges. After 10 mins of normothermic circulatory arrest (absent cerebral flow) CPB could be re-established. The patient was rapidly cooled to 18°C and ice packs were placed around the head. Although the aorta had been significantly narrowed, there was adequate flow into the root. Following a telephonic discussion with the University Heart Centre in Freiburg, Germany, parts of the concept of "Controlled Reperfusion of the Whole Body" were instituted[1,3]: The pO_2 was lowered to <150mmHg, the alkalosis was avoided and calcium kept as low as possible (target 0.7mmol/L). Once cooled to 18°C for 23min CPB was stopped for 6mins to insert a leukocyte depleting filter and switch over to a

femoral cannula, and for a further 8mins after a period of reperfusion whilst the edges of the aorta were debrided. The aorta was primarily repaired in a double layer at 10% flow (9mins). The superior vena cava (SVC) was cannulated and 5mins of retrograde cerebral perfusion was established at 30% of full flow, after the SVC was clamped centrally and the antegrade CPB was stopped for 5 mins in order to wash out any debris or air from the cerebral circulation that might have entered during the aortic arch repair. During retrograde cerebral perfusion, high suction was maintained on the aortic root vent with the patient in Trendelenburg position, following which, the patient was rewarmed. Osmolality was kept high (not measured) by adding 200ml of 20% albumin and 250ml of mannitol 20% to the circuit. Once warm, the patient was weaned uneventfully from CPB on 0.03μg/kg/min adrenalin.

The patient had an uneventful course in ICU with a peak creatinine of 1.2mg/dL but was kept intubated for 36 hours due to massive perioperative transfusion, and although not actively managed, temperatures remained below 36.5°C for the first 24 hrs. in ICU. Subsequently, the patient has made a complete recovery with no neurological deficit and was discharged home on the 14th postoperative day. Histology of the aorta only revealed atheromatous plaque.

Comment

The role of post cardiac arrest-induced hypothermia as a protective neurological strategy has been investigated for over six decades[4]. Although the use of targeted temperature management (TTM) has become standard of care in ICUs and resuscitation guidelines[5], there remains equipoise on the nadir temperature and duration of this therapy. The International Liaison Committee on Resuscitation (ILCOR) initially recommended lower targeted temperatures (32-34°C), the data for which hinged primarily on two clinical trials published in 2002[6,7]. These studies compared moderate TTM versus uncontrolled temperature management and confirmed an improved survival in the hypothermic treated shockable arrhythmia patients. More recently however, the ILCOR recommendations have expanded the treatment range (32-36°C) following a clinical trial that showed that a lower temperature is not superior to a control of the peak temperature below 36°C[8].

These strategies do however rely on an extended period of hypothermia (12-28hrs) with slow rewarm (0.5°C/hr.). A subsequent animal study has shown that it may not be necessary for long duration cooling for neurological benefit. Thirty minutes of cooling to approximately 33°C in conjunction with "controlled automated reperfusion of the whole body" (CARL) following 20 minutes of normothermic cardiac arrest was sufficient to significantly improve survival and neurologic outcome in a porcine model[1,3].

In the clinical case presented above, the patient was rapidly cooled to a nadir temperature of 18°C. This strategy was partially neuroprotective following normothermic arrest as well as providing sufficient time to address the arch as the full extent of the tear was not initially evident. It is not clear what the optimum nadir temperature is as there is no evidence to support deep- over moderate hypothermia as part of a post arrest strategy. Our rewarming strategy of 11°C/hr. far exceeded the <1°C recommendations of clinical studies[6]. However, the potentially beneficial effects of slower rewarming on neurological recovery must be offset against the prolonged bypass time.

Together with the hypothermic strategy, reperfusion injury was limited by including parts of the CARL strategy, that could be implemented in this special case, e.g. maintaining a *normal* pO_2, aiming for a low calcium (although citrate was not available to us at the time to reduce the free serum calcium, no calcium supplementation was given, which would have been our standard of practice prior to weaning from bypass), increase osmolarity (limit cerebral edema), prevent alkalosis and add a leucocyte filter to reduce free radical formation[2].

Thus, rapid short-term deep hypothermia with standard rewarming (11°C/hr. – Gradient of 10°C) and applying parts of the reperfusion concept of CARL resulted in complete neurological recovery following 10 minutes of normothermic no flow cardiac arrest. Although it may appear futile to continue support a patient following a catastrophic event as described, clinicians should consider the above described aggressive targeted strategy in a post circulatory arrest.

References

1. Trummer G, Benk C, Beyersdorf F. Controlled automated reperfusion of the whole body after cardiac arrest. J Thorac Dis 2019;11:S1464–70.

2. Beyersdorf F. The use of controlled reperfusion strategies in cardiac surgery to minimize ischaemia/reperfusion damage. Cardiovasc Res 2009;83:262–8.

3. Taunyane IC, Benk C, Beyersdorf F, Foerster K, Cristina Schmitz H, Wittmann K, et al. Preserved brain morphology after controlled automated reperfusion of the whole body following normothermic circulatory arrest time of up to 20 minutes. Eur J Cardiothorac Surg 2016;50:1025–34.

4. Williams GR, Spencer FC. The clinical use of hypothermia following cardiac arrest. Ann Surg 1958;148:462–8.

5. Howes D, Gray SH, Brooks SC, Boyd JG, Djogovic D, Golan E, et al. Canadian Guidelines for the use of targeted temperature management (therapeutic hypothermia) after cardiac arrest: A joint statement from The Canadian Critical Care Society (CCCS), Canadian Neurocritical Care Society (CNCCS), and the Canadian Critical Care Trials Group (CCCTG). Resuscitation 2016;98:48–63.

6. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–63.

7. Holzer M, Sterz F, Darby JM, Padosch SA, Kern KB, Böttiger BW, et al. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med 2002;346:549–56.

8. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33°c versus 36°c after cardiac arrest. N Engl J Med 2013;369:2197–206.