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ORIGINAL ARTICLE

Therapeutic Hypothermia May Improve Neurological Outcomes in Extracorporeal Life Support for Adult Cardiac Arrest

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Background Limited data exists on patients receiving therapeutic hypothermia during extracorporeal life support (ECLS). We investigated outcomes and prognostic factors in these patients.

Methods A retrospective review was conducted for 225 consecutive adult patients treated with ECLS between July 2003 and January 2016. Extracorporeal life support was initiated for refractory cardiac arrest (>10 mins) in 79 patients (35.1%). Patient demographics, ECLS-related complications, in-hospital mortality and neurological outcomes were analysed.

Results The mean age was 49.9 ± 12.4 years. Sixty-two patients (78.5%) were male. The mean duration of CPR and ECLS were respectively, 32.0 ± 23.3 mins and 5.4±4.0 days. Therapeutic hypothermia (34°C) was maintained for 24 hours in 14 patients (17.7%). Thirty-five patients (44.3%) were weaned off ECLS. Twenty-one patients (26.6%) survived to hospital discharge with 16 (20.3%) recovering good neurological function. Compared to ECLS at normothermia, neurologically favourable survival was higher in the hypothermia group (42.9% vs 15.4%, P=0.020). Multivariable analysis identified a non-shockable rhythm [odds ratio (OR) 5.1, confidence interval (CI) 1.5–16.8], ischaemic hepatitis (OR 6.2, CI 1.1–33.6) and hypoxic ischaemic encephalopathy (OR 5.1, CI 1.5–17.1) as predictors of in-hospital mortality. Therapeutic hypothermia (OR 4.9, CI 1.2–20.4) and acute renal failure (OR 0.19, CI 0.05–0.70) were predictors of neurologically favourable survival.

Conclusions In this report of patients treated with ECLS, in-hospital survival and survival with good neurological performance were 26.6% and 20.3% respectively. A non-shockable rhythm, ischaemic hepatitis and hypoxic

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ischaemic encephalopathy were predictors of in-hospital mortality. Therapeutic hypothermia during ECLS was associated with improved neurological outcomes.

Keywords Cardiac arrest • Therapeutic hypothermia • Extracorporeal life support

Introduction

Despite advances in resuscitative care, the survival rate after cardiac arrest remains poor at <20% [1]. Extracorporeal cardiopulmonary resuscitation (E-CPR) has shown a survival benefit over conventional CPR in patients with in-hospital cardiac arrest (IHCA) of cardiac origin [2]. Amongst patients resuscitated with extracorporeal life support (ECLS), the rate of neurologically favourable survival remains low, ranging from 4% to 45% [2–11].

This study was conducted to evaluate the impact of peri-resuscitative variables and adjunct measures such as therapeutic hypothermia on early outcomes in patients receiving ECLS for refractory cardiac arrest at a tertiary referral centre. With an increasing number of high-risk patients being considered for ECLS, identification of prognostic factors will be useful for risk assessment and decision-making.

Materials and Methods

Following approval from the local institutional review board (reference: 2011/144/C, 2013/153/C), a retrospective review was performed to investigate the outcomes of patients who received E-CPR for cardiac arrest at our tertiary referral centre between July 2003 and January 2016.

Definitions

In-hospital mortality was defined as all-cause mortality during the hospital stay for ECLS. Renal failure was defined as serum creatinine clearance levels lower than 60 ml/min as calculated with the Cockroft–Gault formula, or the need for renal replacement therapy. Ischaemic hepatitis was defined as an acute reversible elevation in transaminases of at least 20 times the upper limit of normal, excluding other known causes of acute hepatocellular injury. The cerebral performance category (CPC) is a commonly used five-category scale which has been the historical gold standard for measuring neurological status after cardiac arrest [12]. The five categories are: CPC 1, conscious and alert with good cerebral performance; CPC 2, conscious and alert with moderate cerebral performance; CPC 3, conscious with severe cerebral disability; CPC 4, comatose or in persistent vegetative state; and CPC 5, brain dead, circulation preserved. Good (neurologically favourable) and poor neurological outcomes were defined as a CPC of 1–2 and 3–5, respectively.

Patients

During the period July 2003 to January 2016, 225 patients received venoarterial ECLS at our institution. This study focussed exclusively on patients receiving E-CPR for refractory cardiac arrest, with conventional CPR ongoing for more than 10 mins. Patients receiving ECLS for cardiogenic shock without CPR and post-cardiotomy support for failure to wean from cardiopulmonary bypass were excluded. In 79 patients (35.1%), the indication for ECLS was refractory cardiac arrest necessitating E-CPR. All patients had ECLS initiated during continuous external cardiac massage. From 2013 onwards, as part of an ongoing study, patients receiving E-CPR who remained unconscious after return of spontaneous circulation were randomly selected (odd-day admissions) to receive therapeutic hypothermia at 34°C for the first 24 hrs of ECLS. Analysis of outcomes focussed on ECLS-related complications, in-hospital mortality and neurological performance.

ECLS Setup and Management

Implantation of ECLS was considered under conditions of prolonged arrest after CPR for more than 10 mins without return of spontaneous circulation. Contraindications to ECLS included irreversible medical conditions limiting life expectancy to less than one year, severe coagulopathy with clinical evidence of bleeding, advanced age (>70 years) and poor premorbid functional status (bedbound or uncommunicative). The ECLS circuits were preassembled in preparation for rapid setup and priming.

Extracorporeal life support was instituted by a qualified cardiovascular surgeon via percutaneous cannulation of the common femoral artery and vein using the Seldinger technique. Standard ECLS components consisting of an extracorporeal centrifugal pump, oxygenator and heat exchanger were utilised. In patients who received therapeutic induced hypothermia, cooling to a target core body temperature of 34 °C was performed in the intensive care unit by modulating the heat exchanger component of the ECLS circuit. The temperature was maintained at 34 °C for 24 hrs. Core body temperature readings were obtained by measuring the tympanic and nasopharyngeal temperatures, as well as via sensors of the Allon 2000 (Allon, MTRE, Israel) temperature regulating console. After 24 hrs, gradual rewarming towards a temperature of 36.5 °C was commenced at a rate not exceeding 0.5 °C/hr.

An intra-aortic balloon pump was inserted in the majority of patients (85%) to augment unloading of the left ventricle. Intravenous heparin was administered to prevent thrombosis within the ECLS circuit, targeting an activated clotting time of 180 to 200 secs, unless contraindicated by existing