Might rapid implementation of cardiopulmonary bypass in patients who are failing to recover after a cardiac arrest potentially save lives?

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Received 18 September 2012; received in revised form 20 May 2013; accepted 11 June 2013

Abstract

The question addressed was whether it might be beneficial to have a rapid-response emergency cardiopulmonary bypass service for patients who suffer an in-hospital or an out-of-hospital cardiac arrest of any aetiology. Eighty-five papers were reviewed using the reported search, of which 15 represented the best evidence to answer the clinical question. The authors, journal, date, country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. The concept of using emergency cardiopulmonary bypass (ECPB) for the management of cardiogenic shock and refractory cardiac arrest was developed in the late 1990s. Since this time, a large number of centres worldwide have reported success with use of ECPB for cardiac arrest refractory to conventional resuscitation techniques and for cardiogenic shock. This is a relatively new advancement in resuscitative strategy and is expanding in clinical practice. Clinical studies and experimental data reveal that ECPB is a very effective tool in the return of spontaneous circulation following refractory cardiac arrest. Resuscitation with this technique demonstrated survival benefit when compared with patients having conventional cardiopulmonary resuscitation for >10 min after witnessed in-hospital arrest, especially if the cause of arrest is of cardiac origin. The reported finding from a systematic review of 1494 patients treated with ECPB noted that the overall survival rate was 47.4%; their results indicate that the application of ECPB in cardiac arrest improves survival and the likelihood of a satisfactory neurological outcome. An additional review revealed that acceptable survival rate and neurological outcomes (30%) can be achieved with extracorporeal cardiopulmonary resuscitation in children after prolonged cardiac arrest (up to 95 min) refractory to standard resuscitation. However, no study has provided clear-cut evidence of the merits of ECPS in patients with out-of-hospital cardiac arrest, although many case reports and case series have concluded that it is an effective method. We conclude that institution of emergency cardiopulmonary bypass may save the lives of patients in whom routine attempts at resuscitation after a cardiac arrest fail, especially after >10 min. The likelihood of success is much higher for patients who have in-hospital witnessed cardiac arrest.

Keywords: Emergency cardiopulmonary bypass • Sudden cardiac arrest • Cardiopulmonary resuscitation

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in ICVTS [1].

CLINICAL SCENARIO

A 42-year-old man is brought by ambulance into the accident and emergency department after a witnessed out-of-hospital cardiac arrest with good cardiopulmonary resuscitation (CPR) for the last 40 min. The accident and emergency department staff feel that they cannot offer any further treatment and call you to consider emergency cardiopulmonary bypass (ECPB). You institute ECPB and successfully obtain a change of rhythm to sinus rhythm after 30 min and are able to wean him off ECPB 48 h later. You wonder whether everyone should have ECPB available for refractory cardiac arrest.

THREE-PART QUESTION

In [patients with refractory cardiac arrest] does [the institution of cardiopulmonary bypass] provide any benefit over [advanced life support alone in improving survival].

SEARCH STRATEGY

Medline 1966–2012 was searched using the OVID interface: [Exp Heart Arrest/OR exp life support care/OR cardiac arrest. mp OR cardiac massage. mp OR CPR. mp] AND [exp Cardiopulmonary Bypass/OR Cardiopulmonary Bypass. mp OR Cardiopulmonary support. mp].

SEARCH OUTCOME

A total of 85 papers were found using the above search, from which 15 represented the best evidence papers used to answer the question. These are documented in Table 1.

Table 1: Best evidence papers

Author, date, journal and country, Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Le Guen <i>et al.</i> (2011), Crit Care, France [2] Prospective cohort study (level 2)	51 patients included in the study who experienced an out-of-hospital cardiac arrest from January 2008 to August 2010. Inclusion criteria: (i) witnessed out-of-hospital cardiac arrest; (ii) refractory cardiac arrest; (iii) CPR was pursued until the patient's arrival at ICU; (iv) a mobile cardiothoracic surgery team was available; and (v) lack of known, severe comorbidities that should have precluded admission into an ICU. Patients who experienced in-hospital cardiac arrest were excluded, as well as patients who were severely hypothermic (body temperature <32°C) before CPR	Failure to establish ECPS Time taken to establish ECPS Survival after 24 and 48 h Global survival rate Cause of death	In 9 patients (18%); in 1 patient aortic dissection. Prolonged no-flow duration Median, 3 min [IQR 0.5–6.5] vs 2.5 min (IQR 1–6); $P = 0.04$ and lower mean end-tidal CO ₂ levels (9 ± 3 min vs 12 ± 2 min; $P = 0.04$) 17 patients (40%) at 24 h 5 patients (12%) at 48 h 2 patients 4% at day 28 with good neurological outcome Multiple organ failure ($n = 23$; 45%), brain death ($n = 10$; 20%) and severe haemorrhage ($n = 7$; 14%)	Small number of patients included in the study. Children were excluded from study group. Absence of a control population of victims of cardiac arrest was ethically justified because the natural evolution of refractory cardiac arrest remains death
Sasson <i>et al.</i> (2010), Circ Cardiovasc Qual Outcomes, USA [3] Meta-analysis (level 1)	Data collected from 79 studies. Total number of patients included in this study was 142 740 Duration of studies extended from 1950 to 2008. All patients included in this study had witnessed OHCA of presumed cardiac aetiology	(i) Understanding the importance bystander CPR, critical shockable rhythms and value of ROSC; (ii) OHCA patients 40% are found. With VF/VF only, 22% achieve ROSC; (iii) Targeted CPR training; (iv) Survival from OHCA has not improved in almost 30 years	Survival rate to hospital admission 23.8% Survival rate to hospital discharge 7.6%	
Nagao <i>et al.</i> (2009), Circ J, Japan [4] Prospective cohort study (level 2)	Study was conducted from November 2000 to December 2007. 1145 patients with an out-of-hospital cardiac arrest were included. 974 patients were ineligible; only 171 (14.9%) patients met the eligibility criteria for this study, of whom 102 had hypothermia induced after ROSC (post-ROSC cooling group) and 69 had hypothermia induced during cardiac arrest (intra-arrest cooling group) Criteria for eligibility: (i) aged 18–74 years; (ii) cardiac arrest witnessed by bystanders; (iii) presumed cardiac aetiology of arrest; (iv) time interval from collapse to arrival of paramedics at patient's side within 15 min; (v) persistent cardiac arrest on arrival at the emergency department Exclusion criteria: (i) tympanic membrane temperature <30°C; (ii) on arrival at the emergency department, successful ROSC within 10 min of arrival with conventional ALS; (iii) non-cardiac aetiology of cardiac arrest or pregnancy; (iv) if families refused to give informed consent	Favourable neurological outcome at hospital discharge Outcome after collapse to CPB interval	21 patients (12.3%) 0.89 (95% CI 0.82–0.97) and after CPB-to-34°C interval, 0.99 (95% CI 0.98–0.99) when collapse-to-34°C interval was divided into two components Accuracy of a collapse-to-CPB interval at a cut-off of 55.5 min and CPB-to-34°C interval at a cut-off of 21.5 min was 85.4 and 89.5%, respectively	This was neither an RCT nor a multicentre study. Study period past the limit of the 2005 CPR guidelines. The use of extracorporeal CPR was limited to the hospital setting and was too invasive for use in most hospitals. Cooling was initiated after arrival at the ED, but if intravenous infusion of large-volume, ice-cold fluids was used for the pre-hospital induction of intra-arrest cooling, a favourable neurological outcome might ensue

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Table 1: (Continued)

Author, date, journal and country, Study type (level of evidence)	Patient group	Outcomes	Key results			Comments
	Patients underwent emergency CPB plus intra-aortic balloon pumping, with subsequent PCI if needed. Mild hypothermia (34°C for 3 days) was induced during cardiac arrest or after return of spontaneous circulation					
Chen <i>et al.</i> (2008), Lancet, Taiwan [5] Prospective observational cohort study (level 2)	3-year study, 975 patients, age 18–75 years with in-hospital events cardiac arrest of cardiac origin who underwent CPR for more than 10 min. A matching process based on propensity score was done to equalize potential prognostic factors in both groups. In the study, 113 patients were enrolled in the conventional CPR group and 59 in the extracorporeal CPR group	Patients alive at various points	Time points	CPR + ECLS (%)	CPR alone (%)	No element of randomization and no confounding or selection factors were taken into account when results were presented
			24 h	65.2	41.3	
			3 days	52.2	34.8	
			14 days	37.0	23.9	
			30 days	34.8	17.4	
			6 months	32.6	15.2	
			1 year	19.3	13.0	
			HR 0.51, 95%			
		HR for survival based on propensity-score-matched groups ECPS + CPR vs CPR alone	CI 0.35–0.74, $P < 0.0001$, 30 day survival (HR 0.47, 95% CI 0.28–0.77, $P = 0.003$) and 1 year survival (HR 0.53, 95% CI 0.33–0.83, $P = 0.006$) favouring extracorporeal CPR over conventional CPR			
Masseti <i>et al.</i> (2005), Ann Thorac Surg, France [6] Retrospective and concurrent study (level 3)	40 patients were included in the study group after meeting the inclusion criteria from June 1997 to January 2003. Patients were included into the ECLS therapy if they presented with refractory cardiac arrest requiring external cardiac massage, could not be returned to spontaneous circulation within 45 min or received ECPS in the hospital. Three groups of ECPS-supported patients were selected	Survival after cardiac arrest	Out-of-hospital arrest, 1–5%; in hospital arrest, 17–25%			Small study sample
		Return of spontaneous circulation	Restored in 50% who receive CPR, among whom 10–30% have permanent brain damage			
		Survival to discharge	8 patients were alive and without any sequel at 18 month follow-up			
Alsoufi <i>et al.</i> (2007), J Thorac Cardiovasc Surg, Saudi and Canada [7] Retrospective cohort study (level 2)	80 children <18 years of age were included in this study from March 2000 to December 2005. Patients who were in a haemodynamically unstable condition and placed on ECMO urgently without active cardiac arrest were not included in this study	Successful weaning off ECLS	42 patients (54%; $n = 35$)			Selection bias and lack of randomization. There has been no complete or uniform appraisal of neurological function and deficit by an independent paediatric neurology specialist. Small cohort size, high incidence of patients with an unfavourable outcome and multiple variables in this heterogeneous group of patients
		Survival until hospital discharge	27 patients (34%)			
		Acceptable survival and neurological outcomes	24 patients (30%)			
Sung <i>et al.</i> (2006), Ann Thorac Surg, South Korea [8]	22 patients in cardiac arrest underwent emergency PCPS from November 2003 to July 2005. In 26 patients the cause of arrest was known, but in 6 patients there was no evident disease	Weaned from the PCPS	13 patients (57%)			Absence of a control group for comparison. Used only one PCPS system
		Discharged from hospital with no neurological or other complication	9 patients (39%)			

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Table 1: (Continued)

Author, date, journal and country, Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Retrospective and concurrent study (level 3)	diagnosed before PCPS. In 6 patients an IABP was inserted simultaneously during PCPS.	Hypoxic brain damage	One patient (4%)	
Athanasuleas <i>et al.</i> (2006), Resuscitation, USA [9]	34 sudden death victims were included in the study between 1992 and 2001. Mean age was 63 ± 9.3 years. Acute MI: 20 patients arrested in the catheterization laboratory; 17 patients operating room cardiac arrest; 4 patients ICU cardiac arrest; 10 patients put back on ECPS. 15 cardiogenic shock patients were excluded	Survival after cardiac arrest	27 patients survived (79.4%)	Small number of patients included in the study
Review (level 4)		Permanent neurological damage	2 patients (5.8%)	
Kurusz <i>et al.</i> (2002), Perfusion, USA [10]	Review of clinical reports of ECPS in cardiac arrest or cardiogenic shock. 13 papers found reporting ECPS after cardiac arrest and seven papers reporting ECPS after carcinogenic shock	Survival after cardiac arrest	88 of 407 reported in the literature (21%)	Systematic search strategies not reported. Some papers missed
Retrospective study (level 2)		Survival after cardiogenic shock	137 of 335 (41%)	
		Poor survival	Patients with witnessed cardiac arrest or CPR over 30 min	
Martin <i>et al.</i> (1998), Chest, USA [12]	10 patients attending the ED with out-of-hospital cardiac arrest unresponsive to conventional methods, placed on femoral artery and femoral vein for establishment of emergency cardiopulmonary bypass weaned after 2 h	Long-term survivors	No long-term survivors; mean survival 48 h	No definitive interventions attempted while on ECPS
Case series (level 4)		Weaning from CPB	Seven successfully weaned from CPB with spontaneous circulation	
		Cardiac arrest to CPB	Mean time 32 min	
Tisherman <i>et al.</i> (1990), Acta Anaesthesiol Scand Suppl, USA [13]	A 28-year old woman brought to the ED with recurrent VF. ECPS instituted after 46 min of CPR	CPB duration	15 h	Case report, low level of evidence
Case report (level 4)		Outcome	Survival to discharge, normal neurologically	
Rees <i>et al.</i> (1992), Lancet, UK [14]	PCPS initiated in four patients in cardiogenic shock, 4 patients in asystole and 1 patient in resistant VF. 4 asystolic patients arrested in catheter laboratory. A patient in VF arrested on the ward 24 h after angioplasty; PCPS established 25–40 min post-arrest	Survival in arrest group	All 5 patients reverted to sinus rhythm after angioplasty on PCPS, and 3 survived to discharge. One death due to aortic root rupture and one due to bronchopneumonia after 2 months (60% survival)	Small study. No patients with out-of-hospital arrest
Case series (level 4)		Survival in cardiogenic shock group	All 4 patients died. All had evidence of MI 5–24 h prior to PCPS. 3 had angioplasty on PCPS, 1 had AVR, and 1 had a large irreparable VSD	
		Duration of PCPS	40 min to 29 h of successful support	
Schwarz <i>et al.</i> (2003), Crit Care Med, USA [15]	46 patients supported with CPB, 25 because of cardiogenic shock unresponsive to pharmacological therapy and 21 because of	Successful weaning from CPB	28 of 46 patients weaned	Not out-of-hospital patients

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Table 1: (Continued)

Author, date, journal and country, Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Case series (level 4)	cardiopulmonary arrest unresponsive to ALS	Survival to discharge	19 of 25 patients with cardiogenic shock, 3 of 21 patients with cardiopulmonary arrest; 14% survival after cardiac arrest	
Karmy-Jones <i>et al.</i> (1999), Resuscitation, Canada [16]	29-year-old woman whom, while undergoing an elective gynaecological procedure, acutely arrested. ALS ineffective. ECPS was instituted	Outcome	Restoration of sinus rhythm after 40 min of ECPS and discharge home after 2 months	Case report, low level of evidence
Case report (level 4)				
Fujimoto <i>et al.</i> (2001), Artif Organs, Japan [17]	9 patients suffering circulatory collapse after acute MI refractory to ALS resuscitation, placed on ECPS. All in-hospital patients	Long-term survival	Four survivors, although one had a poor neurological outcome	
Case series (level 4)		Procedure under CPB	All patients required a surgical procedure, including VSD repair in four and free wall rupture in two	

ALS: advanced life support; AVR: aortic valve replacement; CI: confidence interval; CPB: cardiopulmonary bypass; ECMO: extracorporeal membrane oxygenation; ECSL: extracorporeal life support; ED: emergency department; HR: hazard ratio; IABP: intra-aortic balloon pump; ICU: intensive care unit; IQR: interquartile range; MI: myocardial infarction; OHCA: out-of-hospital cardiac arrest; PCI: percutaneous coronary intervention; PCPS: percutaneous cardiopulmonary support; RCT: randomized controlled trial; ROSC: return of spontaneous circulation; VF: ventricular fibrillation; VSD: ventricular septal defect.

RESULTS

A best evidence topic was written according to a structured protocol. We aim to determine whether in patients with refractory cardiac arrest, the institution of cardiopulmonary bypass (CPB) provides any benefit over advanced life support (ALS) alone.

Le Guen *et al.* [2] assessed the use of ECPB following out-of-hospital refractory cardiac arrest in 51 patients and observed a low survival rate (4%).

Sasson *et al.* [3] published results of 79 studies involving 142 740 patients between January 1950 and August 2008. The findings of this study confirmed the value of bystander CPR, significance of 'shockable' rhythms and return of spontaneous circulation in out-of-hospital arrest. The survival rate to hospital admission was 23.8% and to hospital discharge it was 7.6%. Survival to hospital discharge was more likely among those witnessed by a bystander (6.4–13.5%), those witnessed by emergency medical service (4.9–18.2%), who received bystander CPR (3.9–16.1%), patients who had ventricular fibrillation (VF)/ventricular tachycardia (VT) (14.8–23.0%) or who achieved return of spontaneous circulation (15.5–33.6%). In out-of-hospital cardiac arrest patients, 40% had VF/VT and 22% achieved return of spontaneous circulation.

Nagao *et al.* [4] reviewed 171 cases between November 2000 and December 2007 in patients with witnessed out-of-hospital cardiac arrest. Cardiopulmonary resuscitation was carried out whilst the patients were assessed for commencing ECPB. Once bypass was instituted, emergency percutaneous coronary intervention was performed. It was noted that using this approach, 19.3% of the patients

(44 of 171) survived to hospital discharge, and 12.3% (21 of 171) survived with favourable neurological outcomes.

Chen *et al.* [5] presented results of the use of ECPB for refractory in-hospital arrest patients ($n = 172$) against those treated conventionally. Out of these, 113 underwent conventional CPR and 59 received ECPB treatments. The ECPB group was noted to have cause-reverting interventions, such as percutaneous coronary intervention, coronary artery bypass graft and heart transplantation. One year survival was higher in the ECPB than the conventional CPR group (18.8 vs 9.7%; $P = 0.007$), and this survival was maintained in the propensity-matched comparison (19.6 vs 13.0%; $P = 0.006$).

Masseti *et al.* [6] published the results of 40 patients who suffered refractory cardiac arrest and managed with establishment of ECPB. Eighteen patients survived; six were weaned off the pump, nine were bridged to ventricular assist device, and two patients had direct bridging to cardiac transplantation. Overall, eight patients were alive and without any complications at 18 months of follow-up.

Alsoufi *et al.* [7] reviewed 80 children who had cardiac arrests refractory to conventional cardiopulmonary resuscitation. Emergency extracorporeal cardiopulmonary resuscitation with extracorporeal membrane oxygenation was established within 5–10 min of the initiation of CPR. Acceptable survival and neurological outcomes (30%) were achieved after prolonged refractory cardiac arrest (up to 95 min).

Sung *et al.* [8] published their experience with implementation of ECPB in 22 patients with refractory cardiac arrest. In the 13 patients (59%) who could be weaned from ECPB, 12 patients had

interventions to correct the cause of arrest, including four requiring percutaneous coronary interventions and two coronary artery bypass grafts. Ten of these patients (83%) were weaned from ECPB. Ten patients (44%) survived, and they were all noted to be neurologically intact except for one. In 2006, Athanasuleas *et al.* [9] published a 9 year analysis of patients ($n = 34$) with cardiac arrest. In 88% of these patients (30 of 34) CPB was commenced in the operating room via a median sternotomy approach. The length of cardiac arrest in this cohort of patients averaged 43–72 min, and transfer to the operating room for CPB was delayed in some cases. The survival rate in this patient cohort was 74% (27 of 34). All survivors except for two were in general neurologically intact.

A review of clinical reports by Kurusz and Zwischenberger [10] has delineated several indications for emergent applications, with the most frequent being cardiac arrest or cardiogenic shock. Survival is more likely in patients with cardiogenic shock (40%) in comparison to cardiac arrest (21%). A recent multicentre report from Japan compares the effectiveness of ECPB for refractory cardiac arrest vs conventional ALS. All hospitals used standardized ALS for the initial 15 min of cardiac arrest treatment and included hypothermia and haemodynamic optimization in their post-arrest management protocol. Out of the 134 patients treated, two survivors (1.6%) were assessed to have intact neurological function at 30 days, whereas with ECPB there were 22 survivors out of 183 patients treated (12%). This study is ongoing, but the large difference in survival is the first of its kind to directly compare ECPB vs standard ALS care.

Nichol *et al.* [11] published a systematic review of ECPB for cardiac arrest and refractory shock. They recognized 85 studies, with a total of 1494 patients treated with ECPB for refractory shock or cardiac arrest. The overall survival was shown to be 47.4%. Where ECPB was the only modality used to treat cardiac arrest, the investigators found 54 studies with 674 patients, and 44.9% of these patients survived to discharge.

Martin *et al.* [12] reported that percutaneous cardiopulmonary bypass could be initiated in the emergency department.

CLINICAL BOTTOM LINE

Emergency cardiopulmonary bypass resuscitation seem to be an effective tool in patients for whom cardiac arrest would not be expected to be reversed by conventional advanced life support. In haemodynamic collapse of cardiac origin, the emergency cardiopulmonary bypass would be the best treatment option. The use of ECPB in cardiac arrest secondary to non-cardiac medical conditions has been reported less frequently and has been associated with a worse outcome [18]. Further prospective multicentre randomized studies are needed to define the patient population with out-of-hospital refractory cardiac arrest who would benefit from ECPB.

Conflict of interest: none declared.

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