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## Clinical Paper

Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial)<sup>☆</sup>

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## ABSTRACT

**Introduction:** Many patients who suffer cardiac arrest do not respond to standard cardiopulmonary resuscitation. There is growing interest in utilizing veno-arterial extracorporeal membrane oxygenation assisted cardiopulmonary resuscitation (E-CPR) in the management of refractory cardiac arrest. We describe our preliminary experiences in establishing an E-CPR program for refractory cardiac arrest in Melbourne, Australia.

**Methods:** The CHEER trial (mechanical CPR, Hypothermia, ECMO and Early Reperfusion) is a single center, prospective, observational study conducted at The Alfred Hospital. The CHEER protocol was developed for selected patients with refractory in-hospital and out-of-hospital cardiac arrest and involves mechanical CPR, rapid intravenous administration of 30 mL/kg of ice-cold saline to induce intra-arrest therapeutic hypothermia, percutaneous cannulation of the femoral artery and vein by two critical care physicians and commencement of veno-arterial ECMO. Subsequently, patients with suspected coronary artery occlusion are transferred to the cardiac catheterization laboratory for coronary angiography. Therapeutic hypothermia (33 °C) is maintained for 24 h in the intensive care unit.

**Results:** There were 26 patients eligible for the CHEER protocol (11 with OHCA, 15 with IHCA). The median age was 52 (IQR 38–60) years. ECMO was established in 24 (92%), with a median time from collapse until initiation of ECMO of 56 (IQR 40–85) min. Percutaneous coronary intervention was performed on 11 (42%) and pulmonary embolectomy on 1 patient. Return of spontaneous circulation was achieved in 25 (96%) patients. Median duration of ECMO support was 2 (IQR 1–5) days, with 13/24 (54%) of patients successfully weaned from ECMO support. Survival to hospital discharge with full neurological recovery (CPC score 1) occurred in 14/26 (54%) patients.

**Conclusions:** A protocol including E-CPR instituted by critical care physicians for refractory cardiac arrest which includes mechanical CPR, peri-arrest therapeutic hypothermia and ECMO is feasible and associated with a relatively high survival rate.

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## 1. Introduction

Out-of-hospital cardiac arrest (OHCA) is common affecting approximately 424,000 people in the USA and millions more around the world annually.<sup>1</sup> In-hospital cardiac arrest (IHCA) also carries a high mortality rate.<sup>2</sup> In many cardiac arrest patients, there is a failure to have a return of spontaneous circulation despite

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advanced cardiac life support and this is often in the setting of severe metabolic acidosis, acute blockage of a coronary artery or massive pulmonary embolism.<sup>3,4</sup> In refractory cardiac arrest, the use of veno-arterial extracorporeal membrane oxygenation (ECMO) assisted CPR (E-CPR) is proposed for both IHCA<sup>5-7</sup> and OHCA.<sup>8-10</sup> Whilst ECMO for patients with severe cardiac or respiratory failure is used in some tertiary hospitals in Australia,<sup>11,12</sup> there are no previous reports of E-CPR in the management of adult patients with refractory cardiac arrest in Australia.

Here, we report our preliminary experience with an E-CPR program that includes mechanical chest compressions, intra-arrest therapeutic hypothermia and cannulation by critical care physicians for the rapid commencement of veno-arterial ECMO in patients with refractory cardiac arrest.

## 2. Methods

### 2.1. Design

This is a prospective pilot study of a treatment protocol for selected patients with refractory cardiac arrest. The study protocol was approved by the Human Research and Ethics Committee of the Alfred Hospital, Melbourne, Victoria and Ambulance Victoria (NCT01186614). The requirement for informed patient consent was waived in accordance with Victorian Government regulations.

### 2.2. Setting and population

The study was performed at The Alfred Hospital in Melbourne, Victoria, Australia. This state has a population of approximately 5.5 million, with 75% of people located in the capital city of Melbourne. The Alfred Hospital Intensive Care Unit (ICU) is 45 beds and is the state referral center for ECMO, major trauma, major burns, hyperbaric oxygen, heart/lung transplantation and ventricular assist device insertion. The Alfred also has a significant case load in patients transported to hospital with return of spontaneous circulation (ROSC) post OHCA.<sup>13</sup>

Ambulance Victoria is the provider of the Emergency Medical Service (EMS) for Victoria. Paramedics operate under Ambulance Victoria Clinical Practice Guidelines, which for cardiac arrest resuscitation follow the Australian Resuscitation Council Guidelines. For patients with suspected cardiac arrest, basic life support trained fire-fighters, equipped with automatic defibrillators, co-respond across parts of Melbourne.<sup>14</sup> Prior to this trial, paramedics were authorized to cease resuscitation in the field after 30 min of CPR unless compelling reasons to continue such as hypothermia were present.<sup>15</sup>

Patients with refractory OHCA were eligible for the CHEER protocol if the following criteria were met: (a) aged 18-65 years; (b) cardiac arrest due to suspected cardiac etiology; (c) chest compressions commenced within 10 min by bystanders or EMS; (d) initial cardiac arrest rhythm of ventricular fibrillation (VF); and (e) mechanical CPR machine available.

Patients with IHCA were eligible for E-CPR at the discretion of the attending critical care physician when it was considered likely that the cardiac arrest would be reversible if veno-arterial ECMO and definitive treatment could be provided immediately. Patients with IHCA were excluded if they were known to have known significant pre-existing neurological disability, non-cardiac co-morbidities that cause limitations in activities of daily living such as severe chronic airways disease, cirrhosis of the liver, renal failure on dialysis and terminal illness due to malignancy.

Patients with cardiac arrest and ROSC followed by cardiogenic shock who were later treated with veno-arterial ECMO are not included in this report.

### 2.3. Treatment protocol

Patients who met the above inclusion criteria and who did not have exclusion criteria were eligible for the CHEER protocol after 30 min of persistent cardiac arrest. Patients with refractory OHCA were transported to the Alfred Hospital with mechanical chest compressions using the Autopulse™ (ZOLL Inc., Chelmsford, MA, USA). A rapid infusion of 2 L ice-cold saline was commenced en-route to hospital. Patients with IHCA also received mechanical chest compressions with the Autopulse™ and cooling during CPR using ice saline infusion. In all patients, standard advanced cardiac life support was continued with ventilation via an endotracheal tube with 100% oxygen and injection of intravenous adrenaline (1 mg every 4 min).

The E-CPR team consists of two critical care physicians for femoral vessel cannulation, an additional physician for ultrasound imaging of the inferior vena cava, an ECMO nurse coordinator for initiation of the ECMO circuit and management of the mechanical CPR machine. Another member of staff was allocated to rapidly infuse the cold saline infusion. A senior physician was allocated the role of team leader to continue management of the resuscitation. The E-CPR team responds with a dedicated E-CPR trolley that contains all materials for cannulation.

Once refractory cardiac arrest is confirmed, two critical care physicians percutaneously cannulate the femoral artery and vein with ultrasound guidance using a Seldinger technique. A 15Fr arterial cannula and a 17Fr venous cannula (Medtronic, Minneapolis, MN, USA) are inserted. Once cannulation is achieved, 5000 units of unfractionated heparin are administered intravenously and blood flow at 3 L min<sup>-1</sup> with oxygen gas flow 3 L min<sup>-1</sup> is commenced. The ECMO consists of a Rotaflow™ pump and Quadrox™ oxygenator with Bioline-coated™ circuits (Maquet, Rastatt, Germany) without venous saturation monitoring. During cannulation, chest compressions are paused briefly for the needle puncture of the blood vessel and passage of the guidewire. Imaging of the venous guidewire in the inferior cava and arterial guidewire in the descending aorta is required prior to dilatation of the vessels. No defibrillations are permitted during the cannulation attempt. An arterial blood gas is analyzed early after ECMO commencement. A chest X-ray is performed immediately after cannulation to check placement of the venous access cannula and endotracheal tube. Further details on the specific team roles during E-CPR are available on <http://edecmo.org/evidence-ecls/protocols/>.

Once satisfactory ECMO flows are achieved, a mean arterial perfusion pressure of 70 mmHg is targeted with intravenous administration of an adrenaline infusion. If the cause of the refractory cardiac arrest is suspected to be coronary artery occlusion, the patient is transported to the cardiac catheterization laboratory for coronary angiogram. This is performed via the non-cannulated femoral, brachial or radial artery and coronary intervention is performed as required. Patients with suspected pulmonary embolism undergo computerized tomographic pulmonary angiography and then thrombolysis or thrombectomy. Subsequently, the patient is transported to the ICU.

After admission to the ICU, the target temperature of 33 °C is maintained for 24 h, followed by slow rewarming at 0.25 °C per hour. As soon as possible after arrival in the ICU, an 8.5F distal perfusion ("backflow") cannula (Mayo, Rochester, MN, USA) is inserted into the femoral artery immediately below the return ECMO cannula to prevent distal limb ischemia.

Weaning of ECMO is based on echocardiographic assessment of cardiac function and hemodynamic measurement, whilst ECMO flows are reduced to 1 L min<sup>-1</sup>. Successful weaning was defined as separation from ECMO support without subsequent mortality in the next 48 h. Once ECMO support is no longer needed, the arterial

and venous cannulae are removed by a vascular surgeon in the operating room.

Palliative care is instituted early in patients with uncontrollable bleeding and later if poor neurological prognosis is diagnosed after 96 h.

#### 2.4. Outcomes

The ongoing feasibility of the treatment protocol was determined by survival with good neurologic recovery, defined as a cerebral performance score (CPC) of 1-2 at hospital discharge.<sup>16</sup> Other reported outcomes included rates of ROSC, successful weaning from ECMO support and ICU and hospital length of stay. Recorded major complications included cannulation failure, bleeding with blood transfusion requirement, cerebral hemorrhage as reported on computerized tomography brain scan, the requirement for early vascular surgery for femoral arterial repair, limb fasciotomy and/or embolectomy either during or after ECMO.

#### 2.5. Analysis

Analyses were performed using SPSS (Version 19.0, SPSS Inc., Chicago, IL, USA). Numerical data were analyzed using Student's *t*-test or Mann-Whitney test as appropriate. Proportions were analyzed with chi-square test. Statistical significance was considered when  $p < 0.05$ .

### 3. Results

#### 3.1. Baseline and cardiac arrest characteristics

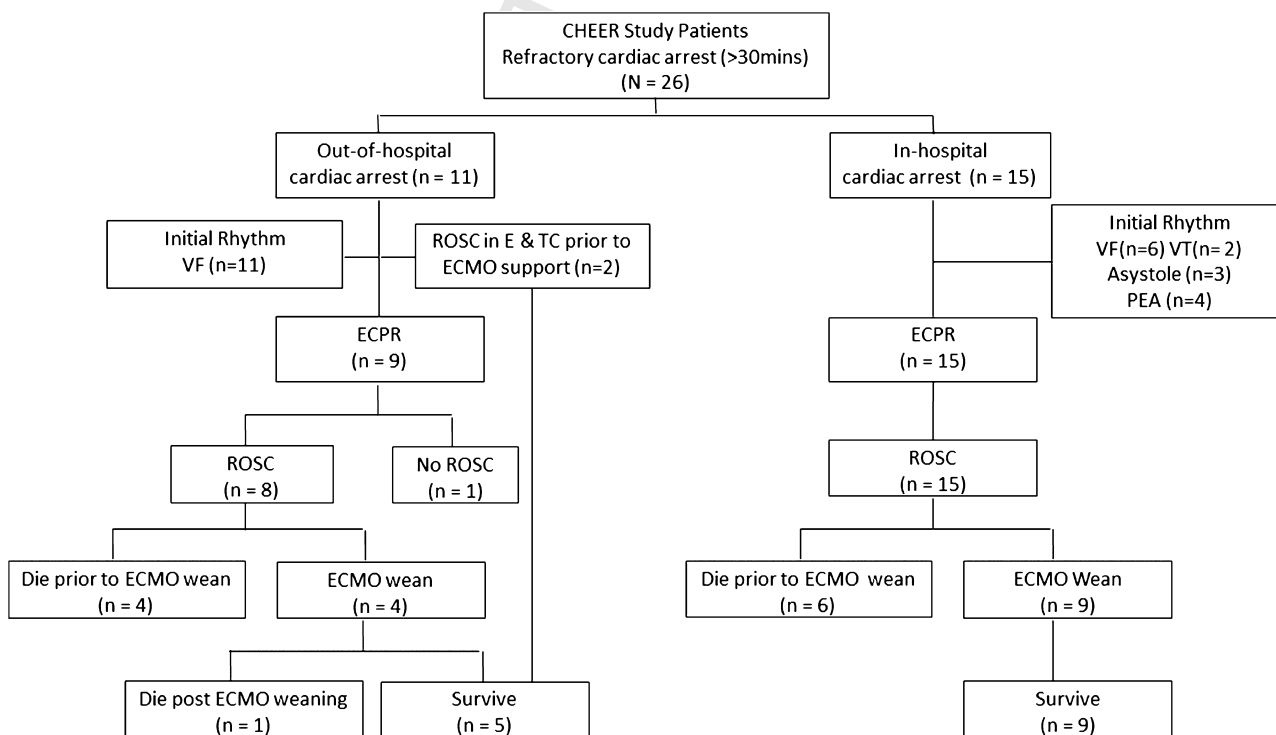
Over the 32 month period, the ECMO service at The Alfred treated 128 patients with ECMO, of whom 28 had veno-venous ECMO for respiratory failure and 100 had veno-arterial ECMO.

Included in the latter group were 26 patients with refractory cardiac arrest (11 OHCA and 15 IHCA) who were treated with the CHEER protocol and who are the subject of this report (Fig. 1). Baseline characteristics of these patients are shown in Table 1. Patients were predominantly male (77%) with a median age of 52 (IQR 38-60) years. Major cardiovascular risk factors for ischemic heart disease occurred in less than 50% of patients.

The initial cardiac arrest rhythm was VF in the 11 OHCA patients. Median collapse to arrival to hospital was 62 min (IQR 45-73) overall but in the survivors, was 48 min (IQR 23-64) compared with 70 min (IQR 50-90) in non-survivors ( $p = 0.06$ ). The underlying cause of the refractory arrest in these patients was acute coronary syndrome in 8/11 (73%) patients, primary channelopathy in 2 patients and aortic dissection with acute aortic valve regurgitation in 1 patient. One of these 11 patients achieved ROSC in the Emergency Department during cannulation and did not require ECMO prior to transfer to the cardiac catheterization laboratory. Another patient failed cannulation but achieved ROSC en-route to the cardiac catheterization laboratory. All other OHCA patients were cannulated in the Emergency Department.

The initial cardiac arrest rhythm in the IHCA patients was VF in 11/15 (73%) cases, asystole in 3 cases and pulseless electrical activity in 1 case. The underlying cause of the refractory cardiac arrest in the IHCA patients was acute coronary syndrome in 5/15 (33%), pulmonary embolism in 2 patients, channelopathy in 2 patients and 1 patient each with idiopathic cardiomyopathy, Eisenmengers Syndrome, end-stage cystic fibrosis, heart transplant rejection, left ventricular aneurysm and left ventricular perforation. Eight patients with refractory IHCA were cannulated in the intensive care unit, five in the Emergency Department and two in the cardiac catheterization laboratory.

The cardiac arrest and E-CPR time intervals are shown in Table 2. Median time between arrival of the E-CPR team and ECMO flow initiation was 20 (IQR 15-30) min, with the median cardiac arrest



**Fig. 1.** Outcome of 26 non-postcardiotomy patients with refractory cardiac arrest. CHEER – Mechanical CPR, Hypothermia, ECMO and Early Reperfusion, E&TC – Emergency and Trauma Center, VF – ventricular fibrillation, ROSC – return of spontaneous circulation, ECMO – extracorporeal membrane oxygenation, ECPR – extracorporeal membrane oxygenation facilitated cardiopulmonary resuscitation.

**Table 1**  
Baseline characteristics.

Baseline	All N=26	Survivors N=14	Non-survivors N=12	P value
Age, years (IQR)	52(38-60)	52(37-57)	54(38-62)	0.75
Male, n (%)	20(77)	11(79)	9(75)	0.83
Cardiac risk factors				
Hypertension, n (%)	11(42)	5(36)	6(50)	0.46
Dyslipidemia, n (%)	11(42)	4(29)	7(58)	0.13
Diabetes mellitus, n (%)	2(8)	0(0)	2(17)	0.11
Congestive cardiac failure, n (%)	5(19)	1(7)	4(33)	0.09
Prior ischemic heart disease, n (%)	4(15)	1(7)	3(25)	0.21
Location of cardiac arrest				
Out of hospital, n (%)	11(42)	5(36)	6(50)	0.46
In hospital, n (%)	15(58)	9(64)	6(50)	
Initial rhythm				
VF, n (%)	19(73)	12(86)	7(58)	0.51
Asystole, n (%)	3(12)	0(0)	3(25)	
PEA, n (%)	4(15)	2(14)	2(16)	
Arrest etiology				
Ischemic heart disease, n (%)	14(54)	7(50)	7(58)	0.43
Cardiomyopathy, n (%)	2(8)	1(7)	1(8)	
Channelopathy, n (%)	3(12)	3(21)	0(0)	
Pulmonary embolism, n (%)	2(8)	1(7)	1(7)	
Respiratory, n (%)	2(8)	0(0)	2(16)	
Other, n (%)	3(12)	2(14)	1(7)	

PEA – pulseless electrical activity, VF – ventricular fibrillation.

to initiation of ECMO support being 56 (IQR 40–85) min. After initiation of ECMO, 22 (85%) patients underwent subsequent intervention to treat their underlying pathology (Table 2). The initial arterial blood gases after initiation of ECMO support are also shown in Table 2 and these show the presence of severe metabolic acidosis and mild respiratory acidosis.

### 3.2. Survival and neurological recovery

Overall, ROSC was achieved in 25/26 (92%) of patients. Median duration of ECMO support in the 24 cannulated patients was 2 (IQR 1–5) days, with 13/24 (54%) patients successfully weaned from ECMO. Survival to hospital discharge occurred in 14/26 (54%)

**Table 2**  
Cardiac arrest and treatment details.

Arrest characteristics	All N=26	Survivors N=14	Non-survivors N=12	P value
ECMO inserted, n (%)	24(92)	12(86)	12(100)	0.41
Median time from ECPR team arrival to initiation of ECMO, min (IQR)	20(15-30)	16(15-19)	30(24-35)	0.01
Median time from collapse to initiation ECMO, min (IQR)	56(40-85)	40(27-57)	78(48-101)	0.02
Location of ECMO (n = 24)				
Emergency Department, n (%)	13(50)	6(43)	7(58)	0.40
Intensive Care Unit, n (%)	7(27)	3(21)	4(33)	
Coronary catheterization laboratory, n (%)	3(12)	2(14)	1(8)	
Hospital ward, n (%)	1(4)	1(7)	0(0)	0.75
ST elevation on initial ECG, n (%)	9(35)	5(36)	4(33)	
Initial post arrest laboratory values				
pH	6.9(6.7-7.1)	7.0(6.8-7.1)	6.8(6.7-7.0)	0.02
PCO <sub>2</sub> mmHg	57(43-85)	52(32-69)	77(48-91)	0.23
PO <sub>2</sub> mmHg	112(83-211)	114(101-159)	97(68-350)	0.51
HCO <sub>3</sub> mEq/L	10(6-16)	15(8-16)	8(6-13)	0.23
Lactate mEq/L	10(7-14)	8(6-12)	13(9-14)	0.18
INR	1.3(1.2-1.4)	1.3(1.1-1.4)	1.3(1.2-3.1)	0.40
Troponin µg/mL	1.5(0.12-19)	0.16(0.07-5.8)	3.5(1.4-39)	0.02
Creatinine µmol/L	119(107-132)	114(97-123)	127(110-146)	0.24
Subsequent intervention				
Coronary angiogram, n (%)	21(81)	13(93)	4(33)	0.61
PCI, n (%)	11(42)	6(43)	5(42)	
Pulmonary thrombectomy, n (%)	1(4)	1(7)	0(0)	0.02
AICD, n (%)	5(19)	5(36)	0(0)	
Extent of coronary disease				
No significant disease, n (%)	6(23)	6(43)	0(0)	0.07
Single vessel disease, n (%)	6(23)	3(21)	3(25)	
Multivessel disease, n (%)	9(70)	4(29)	5(42)	
LMCA involvement, n (%)	2(16)	0(0)	2(17)	
Culprit vessel				
Left anterior descending, n (%)	4(15)	2(14)	2(17)	0.71
Left circumflex, n (%)	4(25)	2(14)	2(17)	
Right coronary artery, n (%)	3(8)	2(14)	1(8)	

OHCA – out-of-hospital cardiac arrest, ECMO – extra corporeal membrane oxygenation, PCI – percutaneous coronary intervention, LMCA – left main coronary artery, AICD – automatic implantable cardiac defibrillator.

**Table 3**  
Outcomes and complications.

Outcomes	All N = 26	Survivors N = 14	Non-survivors N = 12	P value
Survival to hospital discharge, n (%)	14 (54)			
CPC 1–2, n (%)	14 (54)	14 (100)		
ROSC, n (%)	25 (96)	14 (100)	11 (92)	0.27
Wean off ECMO <sup>a</sup>	13/24 (54)	12/12 (100)	1 (7)	0.01
Median time on ECMO, days (IQR)	2 (1–5)	3 (1.8–5)	1 (1–5)	0.32
Median time in ICU, h (IQR)	134 (39–291)	230 (118–320)	30 (4–134)	0.01
Median hospital length of stay, days (IQR)	13 (1.3–22)	20 (12–26)	1 (1–8)	<0.01
Bleeding, n (%)	18 (70)	10 (71)	8 (67)	0.79
Renal replacement therapy, n (%)	10 (39)	4 (29)	6 (50)	0.29
Peripheral vascular issues, n (%)	10 (39)	5 (36)	5 (42)	0.75
Stroke, n (%)	6 (23)	2 (14)	4 (33)	0.25

ECMO – extra corporeal membrane oxygenation, CPC – cerebral performance category, ROSC – return of spontaneous circulation.

<sup>a</sup> From patients requiring ECMO.

patients comprising 9/15 (60%) of patients with IHCA and 5/11 (45%) patients with OHCA. All survivors were discharged directly home with full neurological recovery (CPC = 1). The difference in the median time of collapse to initiation of ECMO between survivors and non-survivors was 40 [IQR 27–57] min vs. 78 [IQR 48–101] min ( $p = 0.02$ ) (Table 2).

The causes of death in the 12 patients who died were severe anoxic brain injury in 4 patients (33%), multi-system organ failure in 3 patients (25%), cerebral hemorrhage in 2 patients, uncontrollable bleeding in 2 patients (one with intra-abdominal bleeding due to a ruptured liver and one with intra-thoracic bleeding due to fractures of the ribs). One patient with pre-existing chronic cardiac failure due to severe coronary artery disease awoke and was successfully weaned from ECMO but declined any further medical intervention and in the setting of progressive heart failure, had comfort measures instituted.

### 3.3. Complications

A blood transfusion was required in 16/26 (69%) of patients including the two patients who died primarily of major bleeding. Overall, the median packed red cell requirement was 3.5 (IQR 0–6) units. Vascular surgery intervention was required in 10/24 (42%) patients who underwent cannulation. This consisted of femoral artery repair and surgical placement of an arterial backflow cannula in 9/10 patients and fasciotomy of an ischemic limb in 1 patient (Table 3).

## 4. Discussion

This study reports the preliminary experience of an E-CPR protocol that includes mechanical chest compressions, intra-arrest therapeutic hypothermia and percutaneous cannulation for ECMO by critical care physicians for the treatment of patients with refractory cardiac arrest.

Our rates of survival to hospital discharge of 60% in patients with refractory IHCA and 45% with refractory OHCA are higher than in other reports. For example, Nagao et al. placed 50 patients with refractory OHCA on ECMO during CPR.<sup>9</sup> Therapeutic hypothermia was induced and maintained for 48 h with coronary angiography performed after establishment of ECMO support. That protocol achieved ROSC in 46/50 (92%) of patients but survival to discharge with good neurological recovery was only 12/50 (24%). Recently, a systematic review of the Japanese experience of 1282 cases of OHCA treated with E-CPR at over 30 centers, reported an overall survival rate of 26%.<sup>10</sup> Other centers have reported even lower survival rates with E-CPR for patients with OHCA. For example, a French study by Le Guen et al. of 51 patients with OHCA treated with E-CPR, found

that only 2 patients (4%) were alive at 28 days.<sup>17</sup> In that study, 90% of patients had died within 48 h of multi-organ failure (47%), brain death (20%) or hemorrhagic shock (14%). This very poor survival rate may be explained by the median time from collapse to establishment of ECMO support of 120 min (IQR 102–149 min).

Survival rates for E-CPR for refractory IHCA are higher than OHCA.<sup>8</sup> The Extracorporeal Life Support Organization (ELSO) registry reported on 297 adult patients who underwent E-CPR (11% of 2633 adult ECMO uses).<sup>18</sup> Median age was 52 years and 75% of patients had cardiac disease. Survival to hospital discharge in this registry was 27%. Similarly, a study of 85 patients by Haneya et al. reported a survival rate of 30% when the time between collapse and ECMO was less than 90 min.<sup>19</sup>

In addition to a shorter duration between collapse and ECMO support, the high rate of recovery found in our study compared with those reported previously may be explained by our multifaceted treatment approach during E-CPR. Firstly, mechanical chest compressions have not been shown to be superior to manual chest compressions,<sup>20</sup> but these trials of mechanical CPR were conducted during standard advanced cardiac life support treatment out of the hospital. We have found that continuous mechanical compressions with only brief pauses during needle puncture of the femoral vessels provide for better overall rates of compressions. Secondly, peri-arrest therapeutic hypothermia using a large bolus of IV ice-saline has been shown to decrease core temperature rapidly and may improve neurological outcomes.<sup>21</sup> Our protocol for therapeutic hypothermia targeting 33° was established prior to the recent large randomized trial indicating no difference between 33° and 36°. The ideal target temperature and duration of cooling, in this patient cohort of very prolonged low flow time, with potential benefit from a more aggressive neuroprotective strategy requires further study. Finally, the use of critical care physicians with considerable experience in ECMO cannulation provides for a relatively short time between presentation of the patient and ECMO support and a high success rate of cannulation during CPR.<sup>23</sup>

The target of 60 min to E-CPR initiation is a major challenge in patients with OHCA, if paramedics only consider leaving the scene at 30 min after collapse. The ongoing European study by Belohlavek and colleagues of a “Hyperinvasive approach to out-of-hospital cardiac arrest using mechanical chest compression device, pre hospital intraarrest cooling, extracorporeal life support and early invasive assessment compared to standard of care<sup>24</sup>”, will be very informative regarding developing systems of care that consider more rapid transfer of patients with OHCA to dedicated E-CPR capable hospitals.

One concern with the use of E-CPR in prolonged resuscitation is the possibility that patients suffer severe neurological deficits leading to protracted ICU and hospital length of stay. This would

have significant resource implications for hospitals with ECMO programs. We found that non-survivors with severe neurological insult, multiorgan failure and/or bleeding had a very short length of stay and, importantly, survivors were discharged with excellent neurological outcomes. This is similar to other recent E-CPR reports.<sup>19,25,26</sup>

Whilst complications of E-CPR are not unexpected in this high risk population, a major complication rate of 76% in our patients is significant. Our group has previously highlighted the association between bleeding, the requirement for blood transfusions and clinical outcomes of ECMO patients.<sup>23</sup> The systemic inflammatory response and associated coagulopathy of prolonged cardiac arrest coupled with antiplatelet therapy and anticoagulation for patients with coronary artery stents or pulmonary embolism need to be carefully balanced against the risk of bleeding. In addition, prolonged chest compressions in chest and/or abdominal injury as seen in two of our patients.

Another important consideration in E-CPR is the timing of backflow cannula insertion. We have adopted a protocol that delays the insertion of a arterial backflow cannula until completion of cardiac catheterization. However, placement of a backflow arterial cannula may be difficult once the 15F arterial ECMO cannula is in place, since there may be limited blood flow at that time and thus considerable difficulty in imaging the superficial femoral artery with ultrasound. Therefore, a number of our patients required transfer to the Operating Theater for surgical placement of the femoral arterial backflow cannula. In one case, an ischemic lower limb was diagnosed at that time and fasciotomy was required.

Nevertheless, our supportive results suggest that there should be increased availability of E-CPR, as part of a comprehensive multifaceted approach for select patients with refractory cardiac arrest. For patients with OHCA, that may require mechanical chest compressions to ensure safe transport by ambulance to an ECMO center as soon as possible in appropriate patients. For both OHCA and IHCA, a rapid response E-CPR team that has clearly defined roles and all equipment ready for immediate use is required. We also consider peri-arrest therapeutic hypothermia to be an important component of this protocol. With this approach, a high number of patients should be expected to recover with excellent neurological outcome.

## 5. Conclusions

The CHEER protocol appears to be a successful approach for the management of selected patients with refractory OHCA and IHCA. Whilst further research into the resource implications of E-CPR may be needed, we conclude that establishing an E-CPR program is feasible in a large city with a dedicated ECMO center.

## Conflict of interest statement

Mechanical chest compression devices (Autopulse™) donated by ZOLL Medical, Chelmsford, MA, USA. The company had no input into study preparation, analysis, results or publication. The authors have no other competing interests.

## Author contributions

SB and DS devised protocol. Approval of Ambulance protocol was provided by KS and TW. Training of Ambulance staff was provided by DS and SB. E&TC training provided by DeS. ECMO data maintained by VP and JS. DS performed statistical analysis. DS, SB, KS, VP, and DK analyzed the results. SB and DS wrote the manuscript. All authors revised and approved the final version of the manuscript.

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