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Extracorporeal membrane oxygenation (ECMO) assisted cardiopulmonary resuscitation or uncontrolled donation after the circulatory determination of death following out-of-hospital refractory cardiac arrest—An ethical analysis of an unresolved clinical dilemma☆

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ABSTRACT

Background: The availability of extracorporeal membrane oxygenation (ECMO) assisted cardiopulmonary resuscitation (E-CPR), for use in refractory out-of hospital cardiac arrest (OHCA), is increasing. In parallel, some countries have developed uncontrolled donation after circulatory determination of death (uDCDD) programs using ECMO to preserve organs for transplantation purposes.
Aim: When facing a refractory OHCA, how does the medical team choose between initiating ECMO as part of an E-CPR protocol or ECMO as part of a uDCDD protocol?
Methods: To answer these questions we conducted a literature review on E-CPR compared to uDCDD protocols using ECMO and analyzed the raised ethical issues.
Results: Our analysis revealed that the inclusion criteria in E-CPR and uDCDD protocols are similar. That there may be a non-negligible risk of including patients in a uDCDD protocol, when the patient might have been saved by the use of E-CPR.
Conclusion: In order to avoid the fatal error of letting a saveable patient die, safeguards are necessary. We recommend: (1) the development of internationally accepted termination of resuscitation guidelines that would have to be satisfied prior to inclusion of patients in any uDCDD protocol, (2) the choice regarding modalities of ongoing resuscitation during transfer should be focused on the primary priority of attempting to save the life of patients, (3) only centers of excellence in life-saving resuscitation should initiate or maintain uDCDD programs, (4) E-CPR should be clinically considered first before the initiation of any uDCDD protocol, and (5) there should be no discrimination in the availability of access to E-CPR.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death in developed countries, with an incidence varying between 2 and 17 per 10,000 inhabitants.[1] The prognosis of OHCA remains poor, with a rate of survival to discharge estimated at 9.5% in the U.S. in 2013,[2] and survival with good neurological outcome estimated at 6%.[3]

Extracorporeal membrane oxygenation (ECMO) assisted cardiopulmonary resuscitation (E-CPR) has been used to treat refractory cardiac arrest since 1976.[4] E-CPR is a recognized therapy for refractory cardiac arrests after severe accidental hypothermia, heart surgery and cardiotoxic intoxications.[5] Studies show promising results principally when E-CPR is used as a rescue therapy for

Abbreviations: ECMO, extracorporeal membrane oxygenation; CPR, cardio-pulmonary resuscitation; E-CPR, extracorporeal membrane oxygenation assisted cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; IHCA, in-hospital cardiac arrest; DCDD, donation after circulatory determination of death; uDCDD, uncontrolled donation after circulatory determination of death; ROSC, return of spontaneous circulation; WIT, warm ischemia time; TOR, termination of resuscitation; VF, ventricular fibrillation; VT, ventricular tachycardia; TP, torsade de pointes; PEA, pulseless electrical activity; ACLS, advanced cardiac life support; DBDD, donation after brain death determination; ETCO2, end tidal CO2.

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in-hospital cardiac arrest (IHCA).[6–9] Results for OHCA are more controversial but remain encouraging[10–14] with E-CPR increasingly available in large emergency departments.

Uncontrolled donation after circulatory determination of death (uDCDD) programs[15] (also known as Maastricht Category II donations) have been developed, principally in Spain since the late 1980s, in France since 2006 and in the Netherlands, USA and the UK more recently. Typically, in such programs, patients in refractory cardiac arrest who meet the criteria for inclusion in a uDCDD protocol, have CPR continued until arrival at a uDCDD center. At this point either cold renal perfusion[16] or ECMO regional perfusion is implemented.[16,17] Both these techniques minimize warm ischemic damage until the organs, most commonly the kidneys, can be surgically recovered for donation and transplantation. ECMO regional perfusion usually involves the insertion of a supra-diaphragmatic aortic balloon,[18] in order to avoid cardiac and brain perfusion following the initiation of ECMO circulation.[19]

In cases of refractory cardiac arrest, how should the treating physician choose between initiating ECMO as part of an E-CPR protocol in an attempt to save the life of the patient or initiating ECMO as part of a uDCDD protocol in an attempt to preserve the organs for donation and transplantation? Which ethical issues are raised by this choice? Without robust and defensible clinical practices there is a risk of providing a standard of resuscitation below that expected in wealthy western countries, even as the donation practice is of the highest and most technologically advanced standard.

To answer these questions, we chose to conduct a review of existing recommendations on E-CPR and uDCDD, which included a comparison of protocols and outcomes. Our focus is ECMO assisted uDCDD protocols rather than other uDCDD protocols that use cold perfusion. We then analyze the ethical issues and propose several recommendations to guide policy in this currently unresolved clinical dilemma.

Methodology

As our goal is to conduct an ethical analysis by identifying and comparing the inclusion criteria for E-CPR protocols with those for uDCDD protocols, we conducted a review of E-CPR and uDCDD protocols.

Review of E-CPR prospective studies for OHCA

A Pubmed search was conducted using the following keywords: extracorporeal cardiopulmonary resuscitation OR extracorporeal life support OR extracorporeal membrane oxygenation AND cardiac arrest NO pediatric. We found 544 papers, with 424 published in the last 10 years. After a detailed analysis, we selected eight studies that had a prospective design either observational studies[10,11,13,20–22,53] or pilot study,[12] that concerned OHCA and excluded poisoning, accidental hypothermia, or drowning. See flow Diagram 1. We also made reference to a recent systematic review on the outcomes of E-CPR by Ortega-Deballon et al.[52]

The search highlighted that E-CPR for OHCA has been used in many countries: USA,[22] Australia,[12] France,[5] Germany,[9] Japan,[13] Belgium,[11] Taiwan,[8] Italy,[23] Korea,[6,24] Austria,[25] Canada (IHCA),[26] the Netherlands[27] and Czech Republic.[28]

From the eight identified studies (Table 1) we extracted the inclusion criteria for E-CPR, the initial rhythm and the no-flow period for survivors and the outcomes in terms of survival and neurological outcome, including the number of patients who became brain dead and any resultant organ donations (if mentioned).

We also reviewed the available recommendations on E-CPR.

Review of uDCDD protocols

We conducted a literature search on Pubmed using the keywords: donation after circulatory determination of death (DCDD); non-heart beating donation; or donation after cardiac death (DCD); and selected only studies concerning uncontrolled DCDD protocols (i.e., Maastricht I or II). Our goal in this review was to identify exemplifier protocols of uDCDD practice to allow comparison with the E-CPR literature.

Our research enabled us to confirm that several countries reported experience in uDCDD. Countries with substantial experience in uDCDD include France[17,31] and Spain,[15,32] with some experience in Belgium,[33] The Netherlands,[34] Austria,[35] Mexico,[36] Russia,[37] Italy,[38] Korea,[39] Taiwan,[40] the U.S.,[41,55] and more recently the U.K.

We chose to focus our analysis on French and Spanish uDCDD protocols, as other countries have reported limited experience with uDCDD. For instance, in New York City, the pilot study performed between 2010 and 2011 failed to recruit any patients.[55]

In France, there are 13 uDCDD centers, 'with a unique national protocol issued by the Agency of Biomedicine, the French national regulatory authority for organ and tissue procurement and transplantation'.[17,31] In Spain, there are two centers in Madrid, one in Barcelona, one in Grenada, one in Coruna and one in Alicante.[16] We analyzed the clinical steps in two uDCDD protocols (France[17,31] and Madrid[15,32]) that potentially compete with E-CPR. See Table 2.

Results

A review of E-CPR prospective studies for OHCA over the last ten years

Of the eight identified studies all but one measured functional outcome by the use of the cerebral-performance category (CPC) score. LeGuen et al. used the Glasgow outcome scale (GOS).[20] Most studies used a protocol which as well as E-CPR included mechanical CPR, hypothermia for 24 h, and coronary angiography if necessary.[10–12,20]

Survival with good neurological outcome in OHCA varied broadly among these studies between 2%[21] and 45%.[12] The neurological outcome depended on the duration of no-flow and low flow period. Thus, Fagnoul et al. included OHCA in an E-CPR protocol after only 10 min of CPR,[11] and Lamhaut et al. initiated E-CPR pre-hospital.[10]

E-CPR has the risk of saving the life of patients but leaving them with irreversible and catastrophic anoxic brain damage[13] sometimes of a severity that will result in subsequent brain death. Brain death might allow donation after brain death determination (DBDD), and this has been reported in some studies.[10,11,20,21] None of the studies mentioned controlled donation after circulatory death (Maastricht III—donation after withdrawal of life-sustaining therapy), a potential donation option in patients with catastrophic brain damage who are not brain dead.

Available recommendations for E-CPR

In 2009, various French medical societies proposed indications for the use of E-CPR based on expert consensus: intoxications; severe hypothermia (<32 °C); signs of life during CPR; and any refractory cardiac arrest with a no-flow period ≤5 min, an initial shockable rhythm (VF; VT; TP) or a low-flow period ≤100 min with an ETCO2 ≥10 mmHg.[29]

The 2010 European Resuscitation Council Guidelines do not mention the use of E-CPR for the management of refractory cardiac arrest.[30]

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