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REVIEW

Extracorporeal Cardiopulmonary Resuscitation: Reviewing the Evidence and Exploring Its Equitable Implementation in the UK National Health Service

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Abstract

Extracorporeal cardiopulmonary resuscitation offers a potentially revolutionary improvement in the historically poor outcomes for refractory cardiac arrest. Current evidence has only demonstrated efficacy in single high volume centres in Europe and the USA and important logistical and health economic considerations remain for a country wide roll out. In this article we will review the evidence and equitable delivery of extracorporeal cardiopulmonary resuscitation in the context of the principles of the United Kingdom healthcare system for a general medical audience.

Key words: extracorporeal membrane oxygenation; cardiopulmonary resuscitation; resuscitation

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Introduction

Cardiac arrest outcomes remain historically poor with survival to hospital discharge less than 2.2% in the UK (Perkins et al, 2018). Refractory cardiac arrest is characterized by a persistent loss of circulation despite resuscitation, with each additional minute of cardiopulmonary resuscitation (CPR) leading to increased mortality and poorer functional outcomes in survivors (Chai et al, 2023). With limited progress in interventions to improve outcomes, extracorporeal cardiopulmonary resuscitation (ECPR) offers a potentially revolutionary treatment for this condition. In this article we will review the evidence and equitable delivery of ECPR in the context of the principles of the United Kingdom healthcare system for a general medical audience.

Basic Principles of ECPR

Extracorporeal membrane oxygenation (ECMO) is a form of artificial mechanical support for the acutely failing respiratory or cardiac system. Utilising a centrifugal pump accessing the circulation through one or more large cannulae, blood is passed through an oxygenator membrane that adds oxygen and removes carbon

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dioxide. The type of support delivered depends on which circulatory system is accessed for drainage and return of blood. Respiratory support focusses on the venous system only and is termed veno-venous ECMO (VV ECMO). Cardiac support involving drainage from venous side and return of blood to the arterial system is termed veno-arterial (VA ECMO). There are however many different configurations including central surgical chest access as well as range of different devices available that can offer similar cardiac support (Low et al, 2024a).

ECPR is the commencement of VA ECMO during refractory cardiac arrest, which is defined as failure to achieve the return of spontaneous circulation (ROSC) after three cycles of advanced life support. The stability from ECMO can then allow the team days to weeks to resolve the underlying cardiac dysfunction, wean off mechanical support, consider bridging to long term mechanical support or transplantation. This process is influenced by the degree of neurological and multi-organ injury sustained during the cardiac arrest, particularly by periods of no CPR (no flow) and CPR (low flow) prior to institution of ECMO flow.

Current Clinical Evidence

Outcomes of out of hospital cardiac arrest remain poor with an approximate survival of 2–3% at 30 days in the UK (Perkins et al, 2018). Negative outcomes of cardiac arrest, such as death or major disability from hypoxic-ischaemic encephalopathy, are strongly linked to the duration of CPR until ROSC is achieved (Goto et al, 2016). A recent review of in-hospital cardiac arrest (IHCA) outcomes found that there was only a 5% chance of a neurologically favourable outcome after 10 minutes of CPR and less than 1% chance of a neurologically intact survival after 32 minutes (Okubo et al, 2024).

ECPR has long be proposed as a potential intervention in cardiac arrest with the first reported case in 1957 (Kennedy, 1966). Observational studies from across the world have signalled for potential benefit (Low et al, 2024b), notably the 2015 CHEER trial in Australia (Stub et al, 2015).

The first randomised trial (RCT) comparing ECPR to ongoing standard advanced life support (ALS) for out-hospital cardiac arrest (OHCA) transported to hospital in Minneapolis reported in 2020 (Yannopoulos et al, 2020). This showed a striking survival at 6 months benefit in refractory ventricular fibrillation (VF) or ventricular tachycardia (VT) cardiac arrest at from 0% in standard ALS compared to 43% in the ECMO arm. Survivors also all had a good cerebral performance category score of 1 or 2. The main criticism of this phase 2 trial was that is was designed to assess safety and deliverability and only included 30 patients. This was in part due to the use of bayesian analysis leading to the group reaching their pre-specified outcome and terminating the trial early for benefit to patients. The inclusion criteria included adults aged 18–75 years old however subsequent cohort data from the group has demonstrated that although absolute survival benefit reduces with age, survival associated with ECPR is significant for even older patients (Chahine et al, 2023).

Subsequently two further RCTs have been published. The largest single centre study of 264 patients from Prague included pulseless electrical activity (PEA) as well as VF/VT cardiac arrest. The primary results of the Prague ECPR trial did not demonstrate a benefit for ECPR with 31.5% in the ECPR group and 22.0% in the standard strategy group surviving to 180 days with good neurologic outcome (odds ratio [OR], 1.63 [95% CI, 0.93 to 2.85] $p = 0.09$) (Belohlavek et al, 2022). In sub-analysis, benefit of ECPR was seen when the duration of CPR was longer than 45 minutes. This apparent benefit for longer duration of CPR has also been reported in observational data (Mandigers et al, 2022). This highlights the balance of potential for ROSC versus early insertion of ECMO with its inherent risks including a 1–21% risk of intracranial haemorrhage (Fletcher-Sandersjöö et al, 2018). When the Prague data was analysed for VF and VT in a pooled analysis with the Minneapolis data there was a clear survival advantage to ECPR (Belohlavek et al, 2023). This effect was less evident with PEA which may be due to the heterogenous aetiology in this group and poses important question about future design of patient selection criteria.

The Prague trial substantially improved its standard ALS survival to 22%, more than double their predicted baseline survival. This raises an important question around whether the delivery of standard ALS is as optimised as possible for cardiac arrest (Belohlavek et al, 2022). Retrospective observational data suggests that transporting patients in OHCA reduces likelihood of survival (Grunau et al, 2020), likely secondary to reduced quality of ALS delivered enroute. However in the Prague trial randomisation occurred on scene so patients were not transported to hospital unless they were in the ECMO arm. In a secondary analysis of patients who did not achieve pre-hospital ROSC, the 180-day survival was 1.2% in patients without prehospital ROSC treated with conventional CPR and 23.9% in patients without prehospital ROSC treated with ECPR (log-rank $p < 0.001$) (Rob et al, 2022).

The third and only multi-centre ECPR RCT was performed in the Netherlands for 160 OHCA patients and demonstrated no survival benefit compared to ALS, 20% vs. 16% (Suverein et al, 2023). This was a pragmatic trial exploring ECPR in a wider healthcare setting in 10 centres across the Netherlands each of which is served by an emergency medicine service. The trial randomised patients after 15 minutes of cardiac arrest who presented with a shockable rhythm and had received bystander CPR. Following randomisation emergency services transferred all patients to hospital and subsequent management was either ECPR or continuation of conventional care. One area of concern was that all but two centres in the study recruited less than 5 patients per year on average and low flow times were longer with a mean of 74 minutes compared to 59 & 61 minutes in the ARREST and Prague OHCA trials respectively. There was also no standardisation of cannulation technique, post resuscitation care or neuro-prognostication across centres. This study highlighted the difficulty in forming a network of ECPR centres to provide care for the whole community and therefore the difficulties in providing an equitable service.

The available data suggests that there may be some benefit of ECPR for patients, especially those who have cardiac arrest without pre-hospital ROSC, however further research needs to be undertaken.

Current UK Practice

The UK National Health Service (NHS) constitution core mandates that the NHS provides a comprehensive service available to all (UK Government, 2023). ECPR is not currently commissioned within the NHS and is provided ad-hoc by 13 centres that mostly perform VV ECMO and heart transplantation (Singer et al, 2025; Akhtar et al, 2025). These centres are not equally distributed across the UK with, for example, no such facility in the entire of Wales or Northern Ireland. This introduces significant regional variation of practice and inequity as well as a cost burden to hospital Trusts.

The VV ECMO service for severe respiratory failure in the UK was commissioned in 2011 in response to the influenza pandemic (Warren et al, 2020). Through 5 centres positioned across the UK the service has delivered good short term outcomes for patients in the UK with undifferentiated respiratory failure refractory to conventional management. The service has subsequently been increased to 8 centres. The skill set developed by this service is the transferable to deliver a VA ECMO and ECPR service. However the reality is that although these 8 centres are able to provide IHCA services and OHCA services to ambulance networks who deliver patients within 1 hour of cardiac arrest, they are only able to do so on an ad hoc basis given the lack of commissioning. The VV ECMO service does provide a national network for mobile ECMO, however the time taken to travel to different hospitals means a centralised model of ECPR is effectively underliverable.

The six adult heart transplant centres in the UK (NHSBT, 2024) also deliver VA ECMO for cardiac arrest but this is a small ad hoc section of work which is otherwise predominantly focused around advanced heart failure interventions. None of these units have a retrieval ECMO service attached.

Considerations for National ECPR Models

The Japanese ECPR service utilises a network of ECPR capable hospital with triage from the ambulance service and in a cohort study have demonstrated that 14.1% of patients survive to leave hospital with favourable neurology (Inoue et al, 2022). This is similar to the models used in both the Dutch multicentre study and Prague single centre studies (Suverein et al, 2023). The closest comparable UK service that is able to provide rapid vascular intervention across geographical boundaries is the primary percutaneous coronary intervention (PCI) service. In this model ambulance services triage the patients to the regional heart attack centre when inclusion criteria are met. Despite now being established for over two decades more than 25% patients have a call to balloon time of greater than 150 minutes from home and which rises to more than 60% of patients when inter-hospital transfer is required (Health Quality Improvement Partnership, 2021). Although this model could be developed to provide rapid access to OHCA in urban areas with ready access to tertiary hospitals, rural and smaller urban areas will struggle with access. To apply an ambulance service triaged, hospital based ECPR service model nationally would be achievable, with the advantage that existing Heart Attack Centres could be upskilled to provide cannulation. Depending on the patient volume, these patients could be managed in local ICUs or transferred into specialist ECMO centres. Given the Japanese experience, although this would not provide truly equitable care, such a model could cover a large proportion of the population.

One of the other models in use globally is the provision of on-scene ECPR. In Paris (Lamhaut et al, 2017) this is provided by the mobile intensive care unit of the emergency medical system. In this model a specialist team with the ability to provide ECPR is available 24/7 to assess patients in cardiac arrest and where appropriate cannulate on scene. A similar system is available in Regensburg (Philipp et al, 2023) in Germany where the ambulance and the ECPR service (road or helicopter) are simultaneously dispatched to cardiac arrests within a defined geographical area. In the UK trauma services include helicopter emergency medical services and this could be utilised to provide ECPR. There are 20,000 major trauma cases in the UK each year and approximately 70,000 cardiac arrests and 30,000 where CPR is commenced (NHS National Statistics, 2024). Should the Helicopter Emergency Medical Service (HEMS) model be used it would be essential to link into a network of cardiac arrest centres, although this would likely have to be different to the major trauma centres depending on patient volume. Currently this model is under evaluation for OHCA through the on scene ECPR trial in the Netherlands (Ali et al, 2024). The provision of equitable ECPR services nationally would very much depend on investment into HEMS services as at present HEMS delivery is inequitable in the UK with services being concentrated in more affluent areas (McHenry et al, 2024).

To date there is no system or study that is able to demonstrate the equitable delivery of a service across an entire country. Although OHCA can be conceivably managed by an appropriate structure and/or triage in pre-hospital care, IHCA poses significant challenges. Conceivably this could involve in-reach of pre-hospital services into hospitals however with approximately 10,000 IHCA annually in the UK, this would pose a significant logistical problem to deliver within a 45–60 minute timeframe (Intensive Care National Audit & Research Centre, 2023). An alternative would be to provide the skills required embedded within each hospital's arrest team, although with 515 hospitals in England, 220 of which are acute hospitals there is an average of only 20 cardiac arrests per hospital per annum. The acquisition of expertise able to provide large bore arterial access and confidently/competently manage ECPR will be a challenge in most hospitals. The exception to this may be hospitals with a primary PCI service where ECPR could be commenced in the cardiac catheter laboratory with subsequent transfer to an ECMO centre for ongoing care.

In the development of a national ECPR system that can manage both IHCA and OHCA it is likely we will need a mixture of models that are adapted to regional geographical variations. In large cities such as London where there are multiple ECPR capable centres a rapid primary transfer of patients who meet criteria to specific ECMO institutions could be facilitated. In urban areas which lack any current

ECMO infrastructure heart attack centres could be upskilled to provide ECPR services through the PCI network. In large rural areas a pre-hospital HEMS model could overcome distance and time factors for reaching specialist centres. Importantly these models are still vulnerable to underyling inequity in delivery of care to socio-economically deprived areas that are prexisting in the NHS for both the delivery of ECPR and the provision of care to prevent cardiac arrest. There is unlikely to be any model that will lead to universal equitable cover that will be affordable to the country, as we have been unable to achieve this to date even for both PCI and HEMS services.

Organ Donation & Normothermic Regional Perfusion

Even with ECPR most patients will continue to die following out of hospital cardiac arrest. Where ECPR is used death may be delayed but perfusion of vital organs can be adequately managed in the post cardiac arrest shock state. This increases the likelihood that patient and family wishes for consideration of organ donation can be can be considered, either as donation after brainstem death (DBD) (22% of cases (Casadio et al, 2017)) or donation after circulatory death (DCD). The Prague RCT demonstrated a significant increase in organ donation in the ECPR arm, with 29 organs donated compared to 7 in the standard ALS arm (Smalcova et al, 2023). Organ donation from both ECMO (Rajsic et al, 2024) and ECPR (Raphalen et al, 2023) have initially shown matched outcomes in transplantation comparable to those from donors not treated with mechanical support. Although this does not necessarily speak to the equitable distribution of ECPR in the community, it does raise wider community benefits which may accrue from such programmes.

Normothermic regional perfusion (NRP) is used in Europe during uncontrolled organ retrieval whereby a VA ECMO circuit is placed after confirmation of death with a clamp or a balloon placed in the thoracic aorta to maintain perfusion or abdominal organs while donation is considered. A model which allowed generalised access to ECPR would also allow access to NRP, which in Spain has resulted in increased access to organ donation with matched outcomes (del Río et al, 2019) from kidneys transplanted from NRP uncontrolled donation. As over 60% (Linde et al, 2023) of refractory cardiac arrests admitted to hospital will not be suitable for inclusion to ECPR, particular due to long low flow times pre-hospital, there is potential significant benefit for transplant programmes in the UK.

NRP remains contentious in the UK with unresolved ethical concerns about how to ensure that the dead donor rule and the consenting donor rule are maintained (Gardiner et al, 2021). There must be certainty of no blood flow to the brain from ECMO after the confirmation of death. Also measures to ensure the coroner is in agreement on the cause of death and the family are given sufficient explanation and consideration of donation must be robust.

Cost Effectiveness Analysis of ECPR

The health economics of ECPR is unique to each country's baseline management of cardiac arrest, reimbursement systems and the country's willingness to pay. In the Netherlands the INCEPTION trial found the cost of ECPR was €121,643 per additional quality adjusted life year (QALY) (Delnoij et al, 2024). However, the difference in mean costs after 1 years from conventional CPR group and ECPR was €5109 (ECPR was higher). In Australia, assuming an additional 3 QALYs, the cost was assessed to be lower with ECPR with an incremental cost effectiveness ratio of €16,890 per QALY (Dennis et al, 2019). These analyses have not included the longterm impacts of patients either returning to economically productive work or the care needs for persistent morbidity. Looking for comparable interventions in the NHS, mechanical thrombectomy for stroke which has been commissioned in the UK costs £14,362 (≈ €16,085, 2020) per patient for care at the thromectomy service (Balami et al, 2020). Whereas longerterm left ventricular assist device therapy has not been commissioned at a cost of £47,631 (≈ €56,205, 2022) per QALY (Lim et al, 2022). A review of the limited publications suggest that hospital based ECPR for OHCA may be cost effective for healthcare systems (Addison et al, 2022).

Importantly, the assessments of the cost effectiveness in these studies have not included the benefits of increased organ donation through ECPR and NRP. When looking at chronic renal failure, renal replacement therapy alone costs the NHS in England over £700 (≈ €861, 2012) million each year (Kerr et al, 2012). For each renal transplant performed the cost benefit derived from saved costs on renal replacement versus transplant care was £241,000 (≈ €28,465, 2024) over 10 years for 1 patient.

When reviewing the health economics of ECPR it cannot be considered outside of the investment of earlier highly effective therapies in the chain of survival. An example of this is improving access and deliver of public access defibrillators (Buter et al, 2024). It would be inappropriate to fund ECPR without ensuring that there is widespread access to early defibrillation and an education programme to facilitate a broad knowledge of the bystander management of cardiac arrest—e.g., mandatory school based basic life support training.

Commissioning challenges also need to be overcome to institute a national programme of ECPR. This includes developing evidence of clinical benefit and cost-effectiveness which would allow ECPR to be recommended by the National Institute for Health & Care Excellence and be supported by the clinical reference groups and clinical priority advisory group. One avenue to producing the UK-based research required would be the development of an ECPR research programme co-finded by research funding agencies and commissioners. This was the approach taken for the studies into VV ECMO in the CESAR trial (Peek et al, 2009).

Ethical Considerations of ECPR

Due to the nature of cardiac arrest, there is no opportunity to obtain consent from patients for the invasive nature of ECPR and its subsequent sequqelae in the intensive care unit and rehabilitation phase. Indeed family members may also not be present at the time of cardiac arrest to allow context for an informed medical decision. This can lead to difficult decising making if the intervention was not the patients wish and it is important to have early involvement of palliative care specialists for the patient and family.

When establishing patient selection criteria, it is crucial to consider the evidence base and resource allocation while avoiding discriminatory practices based on simplistic measures like age, which may not accurately reflect a patient's true frailty.

Conclusion

ECPR offers a potentially revolutionary improvement in outcomes for refractory cardiac arrest and the potential for saving further lives through organ donation. The strongest evidence exists for utilisation of ECPR in refractory cases of VF and VT with onset of ECMO flow within 1 hour of CPR. However there are considerable health economic, logistical and ethical considerations to overcome in addition to further evidence of effectiveness to the UK healthcare system. It is likely that any equitable provision of ECPR in the NHS would need to differ between regions based on geography and underlying healthcare facilities. Given the highly disparate nature of studies into the health economic benefit, NHS based studies into both feasibility, cost-benefit and models of care are urgently required. A national review in collaboration with all stakeholders should be established to determine what further UK specific information is required and strategies for equitable national delivery of the service.

Key Points

- Extracorporeal cardiopulmonary resuscitation offers a potential revolutionary improvement in historically poor outcomes for refractory cardiac arrest.
- Current evidence has only demonstrated efficacy in single high-volume centres in Europe and the USA and important logistical and health economic considerations remain for a country wide roll out. No ECPR system in the world has demonstrated an equitable delivery of ECPR for its entire population.
- Learning can be taken from the national severe respiratory failure VV ECMO service, primary angioplasty for myocardial infarction and Helicopter Emergency Medicine services.
- Organ donation through ECPR offers further important benefits to consider from development of this service.
- Normothermic regional perfusion can offer further potential for organ donation however carries significant ethical dilemmas.
- Health economic data is lacking and has been difficult to assess longerterm economic impact and organ donation implications.

Availability of Data and Materials

Not applicable.

Author Contributions

NB and WA contributed to the conception of the manuscript. WA drafted the manuscript. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

WA has received educational grants from Abbott, Abiomed, Chalice, Medtronic and Resuscitec and speaker honoraria from Abiomed. NB declares no conflict of interest.

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