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REVIEWS

PREHOSPITAL EXTRA-CORPOREAL CARDIOPULMONARY RESUSCITATION: A SYSTEMATIC REVIEW OF PATIENT SELECTION CRITERIA AND DISPATCH PROTOCOLS

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ABSTRACT

Introduction: Out-of-hospital cardiac arrest remains a global health problem. There is emerging evidence that the use of extra-corporeal membrane oxygenation during resuscitation [ECPR], may help to improve outcomes. Several prehospital services around the world are now able to provide on-scene ECPR. However, the early identification of patients is a key factor in enabling this level of response to OOHCA. This systematic review aims to identify prehospital ECPR systems and describe their patient selection criteria and dispatch processes.

Methods: A systematic literature search of the MEDLINE and Embase databases was performed between the dates of 4th April 2024 and 11th April 2024. Study registries were also reviewed to identify the protocols of ongoing or planned studies. Additionally, forwards and backwards reference tracing of eligible literature was performed to identify further articles.

Results: A total of ten studies were identified. When combined, criteria involving premorbid conditions were the most frequently utilised, present in eight out of ten included studies. Age, the requirement for a witnessed cardiac arrest, resuscitation-related factors and ECPR-related factors were used in seven studies. The use of an aetiology or presenting rhythm related criteria were reported in five studies. The dispatch processes for ECPR teams were varied and included both helicopter and ground-based services. ECPR was planned to be performed on scene in nine systems, and one described the use of a rendezvous strategy.

Conclusions: Variability in the selection criteria and dispatch processes used by the identified ECPR services is likely to be reflective of the variation in geographical distribution, team composition and transport modes of prehospital EPCR services. Many eligibility criteria can be determined during emergency call receipt or shortly after resource arrival, highlighting the potential for improved screening by emergency medical dispatchers and non-specialist resources. The simple mnemonic 'PACE' (presenting rhythm, age, comorbidities, ECMO possible within 60 mins) to aid in evaluating key criteria on arrival is provided.

INTRODUCTION

Out-of-hospital cardiac arrest [OOHCA] remains a global health problem and significant cause of mortality (Chin et al., 2022). In the United Kingdom, just 7.8% of patients survive to 30 days following OOHCA (Resuscitation Council UK, 2024). There

is emerging evidence that the use of extra-corporeal membrane oxygenation [ECMO] during resuscitation, also known as extra-corporeal cardiopulmonary resuscitation [ECPR], may help to improve outcomes in patients requiring prolonged resuscitation, or those who do not respond to standard therapy (Adams et al., 2022; Low et al., 2023). The time from onset of cardiac arrest to initiation of ECPR has been demonstrated to be a contributing factor in outcomes (Sim et al., 2024). To reduce this timeframe, several prehospital services around the world are now able to provide ECPR on scene or at a rendezvous point before hospital arrival. However, the logistics involved in providing ECPR-capable teams to OOHCA are complex and require a proactive approach to dispatch to minimise delays (Stretch and Singer, 2024). Therefore, the early identification of patients who may benefit from on-scene ECPR is a key factor in enabling this level of response to OOHCA.

During cardiac arrest there is an immediate decrease and cessation of blood flow. This causes significant cellular hypoxia and systemic metabolic dysfunction (Gilhooley et al., 2019). Initiating ECPR via venous-arterial ECMO [VA-ECMO] offers a medium to deliver blood flow during resuscitation and thus mitigates against the harms from an abrupt cessation of perfusion whilst reversible causes are addressed (Inoue et al., 2020). VA-ECMO is the most common method of delivering ECPR, in which cannulation of a large vein and artery is undertaken either by a percutaneous ultrasound and Seldinger approach, or a direct surgical approach (De Charrière et al., 2020). In the setting of resuscitation, the femoral vein and artery are commonly used. Blood is extracted via a cannula in the femoral vein into the ECMO circuit. It then passes through an oxygen exchange membrane prior to being warmed and re-circulated into the systemic circulation via the femoral artery (Figure 1). This essentially bypasses the function of the patient's own heart and lungs.

AIMS AND OBJECTIVES

To help inform the dispatch protocols of future prehospital ECPR systems, the aims and objectives of this review are:

- To identify ongoing or planned prehospital EPCR programmes
- To describe the patient selection criteria of ongoing or planned prehospital ECPR programmes
- To describe the dispatch processes utilised for prehospital ECPR teams

METHODS

This systematic review is structured using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). A systematic literature search of the MEDLINE and Embase databases was performed between the dates of 4th April 2024 and 11th April 2024. The search terms utilised are displayed in Table 1. MEDLINE was searched using the PubMed advanced search platform and Embase was searched using Ovid. Study registries were also reviewed to identify the protocols of ongoing or planned studies. Additionally, forward and backward reference tracing of eligible literature was performed to identify further articles. The inclusion and exclusion criteria are displayed in Table 2. Two reviewers undertook title and abstract screening to identify articles suitable for full-text review. A third reviewer was available to provide a final decision in the event of discrepancies. Data abstraction was performed by both

reviewers. The following data items were collected: reference details, location, case identification process, team composition, mode of transport, site of ECPR initiation, inclusion criteria and exclusion criteria.

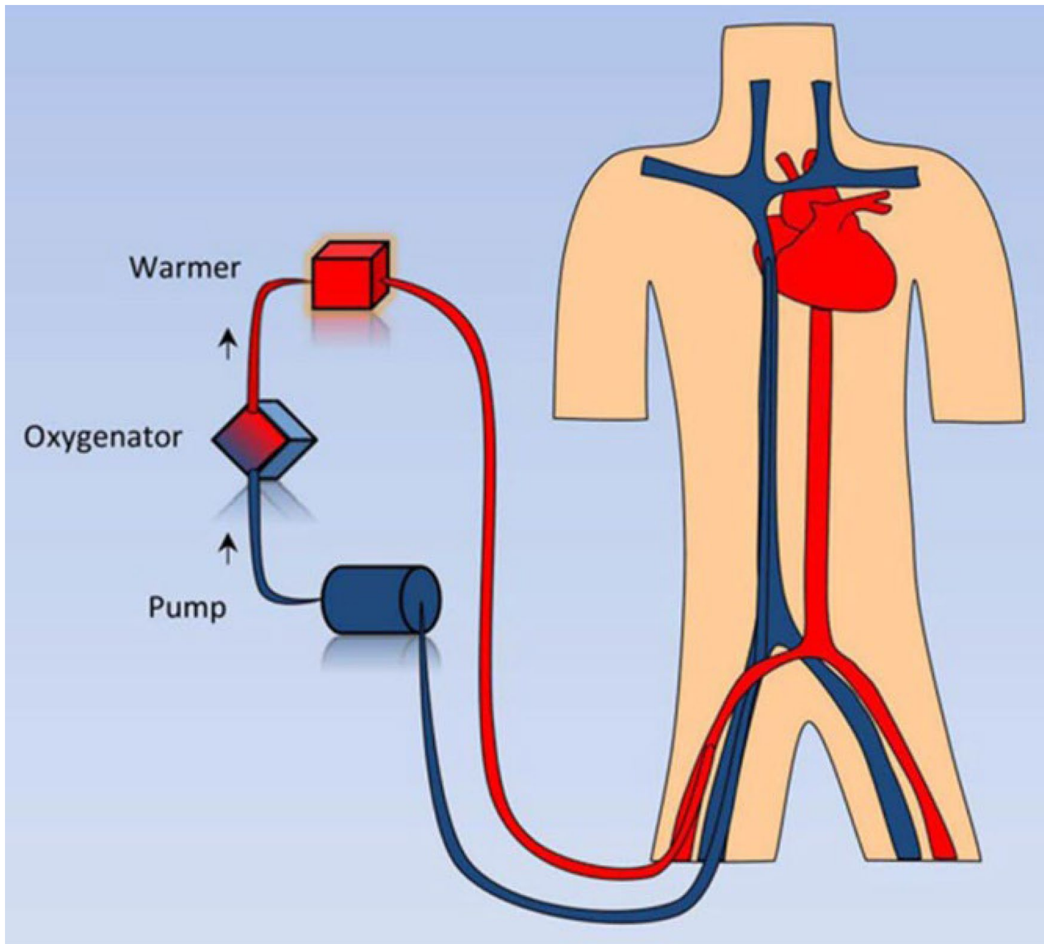

Figure 1: VA-ECMO via femoral arterial and venous cannula. Reproduced from Lawler et al. (2015).

Prehospital OR out of hospital
AND
ECMO OR extracorporeal membrane oxygenation OR extracorporeal cardiopulmonary resuscitation OR ECPR

Table 1. Search terms.

Inclusion	Exclusion
Published since 01/01/2014	Studies or protocols for in-hospital ECPR
Published in English language	Full-text unavailable
Studies or protocols for EPCR performed on scene or at a rendezvous point prior to hospital admission	
Full-text availability	

Table 2. Literature inclusion and exclusion criteria.

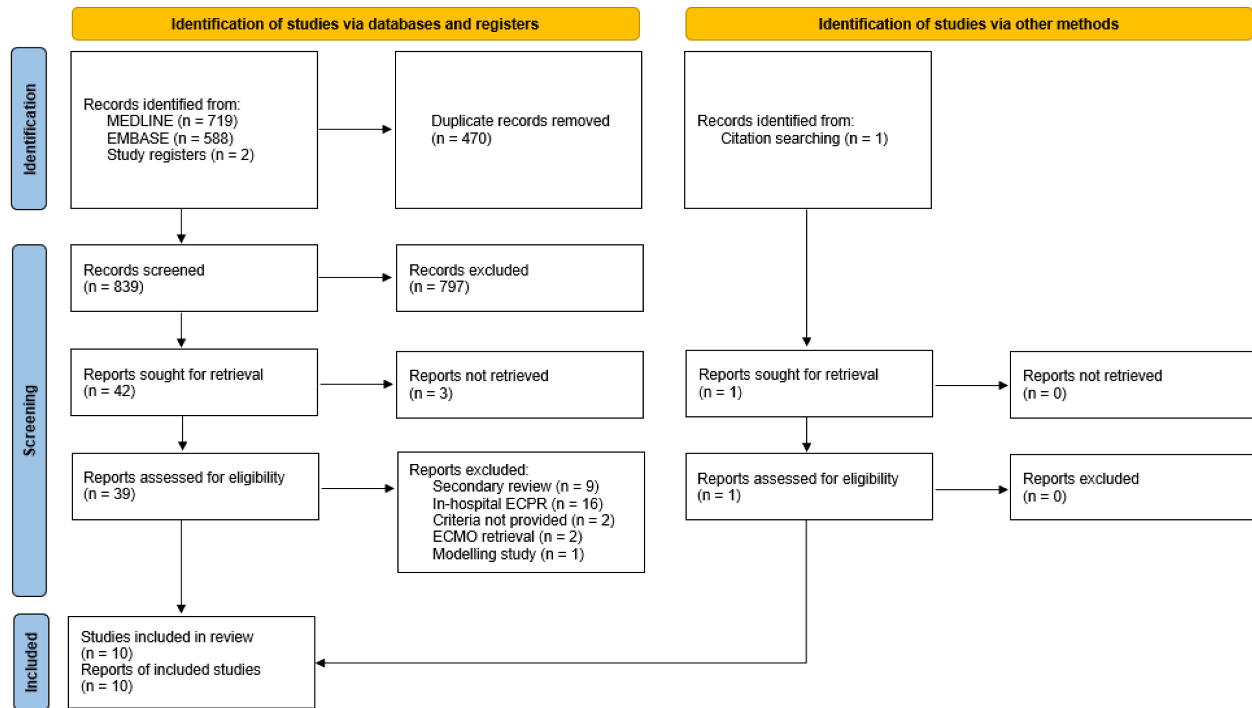

Figure 2: PRISMA flowchart

Reference	Age	Presenting rhythm	Witnessed OHCA	Bystander CPR	Aetiology	Resuscitation duration	Absence of comorbidities	Arrest-ECPR initiation time	Other
Lamhaut et al., 2017	18-65				Medical	>20 mins	Yes	ECMO team on site before 40th minute of resuscitation	ETCO2 >10mmhg
Singer et al., 2020 'Sub30'	>18		Yes	Yes	Presumed cardiac	>20mins or failure to sustain ROSC			
Bartos et al., 2020	18-75	VF/VT				No ROSC following 3 shocks		Transfer to RVP <30mins	LUCAS available
Petermichl et al., 2021			Yes	Yes				<60mins ALS	
Hutin et al., 2022	18-65					>20 mins	Yes	ECMO team on site before 40th minute of resuscitation	ETCO2 >10mmhg
Pozzi et al., 2022		VF/VT	Yes	Yes					
Leivaditis et al., 2023			Yes				Yes		Patients with primary hypothermia or intoxication also eligible
Richardson et al., 2023 'CHEER3'	18-65	VF/VT/ PEA	Yes					<45mins unless periods of ROSC or signs of life during resuscitation	<5mins no flow
Richardson et al., 2024 'PACER'	18-70	VF, VT, PEA	Yes	Yes		>20mins & <45mins			Within ECPR team hours (Mon-Fri 0900-1700), within 25 mins of EMS response
Ali et al., 2024 'ON-SCENE'	18-50	VF/VT OR high suspicion of PE	Yes OR signs of life (gasping/ movement)			>20mins & <45 mins			

Table 3. Inclusion criteria.

Reference	Major/ life-limiting comorbidities	Presenting rhythm	Advanced directive/ DNAR	Percutaneous cannulation not possible	Unwitnessed OHCA	Sustained ROSC	ETCO2	Other
Lamhaut et al., 2017	Yes							> 5 mins no flow, cardiac arrest during transportation
Singer et al., 2020 'Sub30'	Yes						<1.3kPa	Known or visibly pregnant, no signs of life & evidence of ineffective CPR suggested by absence of electrical activity at 20mins
Bartos et al., 2020	Yes		Yes					Significant bleeding, nursing home resident
Petermichl et al., 2021	Yes		Yes		Yes			Traumatic injury with uncontrolled bleeding
Hutin et al., 2022	Exclusion criteria not described							
Pozzi et al., 2022		Non-shockable						
Leivaditis et al., 2023	Yes		Yes		Yes			
Richardson et al., 2023 'CHEER3'	Yes			Femoral cannulation not possible		Sustained ROSC with haemodynamic recovery		<20mins ALS
Richardson et al., 2024 'PACER'	Yes	Asystole	Yes	Yes		Yes		
Ali et al., 2024 'ON-SCENE'	Yes		Yes	No clear echographic visualisation of femoral artery or vein			<1.2kPa	Able to transfer to EPCR capable centre <30mins

Table 4. Exclusion criteria.

Reference	Age related	Witnessed event	Presenting rhythm	Premorbid condition	Aetiology	Resuscitation factors*	ECPR factors**
Lamhaut et al., 2017	Yes			Yes	Yes	Yes	Yes
Singer et al., 2020 'Sub30'	Yes	Yes		Yes	Yes	Yes	
Bartos et al., 2020	Yes		Yes	Yes	Yes	Yes	Yes
Petermichl et al., 2021		Yes		Yes	Yes		Yes
Hutin et al., 2022	Yes			Yes		Yes	Yes
Pozzi et al., 2022		Yes	Yes				
Leivaditis et al., 2023		Yes		Yes	Yes		
Richardson et al., 2023 'CHEER3'	Yes	Yes	Yes	Yes		Yes	Yes
Richardson et al., 2024 'PACER'	Yes	Yes	Yes	Yes		Yes	Yes
Ali et al., 2024 'ON-SCENE'	Yes	Yes	Yes	Yes		Yes	Yes

Definitions:

*Minimum resuscitation or ALS duration, absence of ROSC after a defined point, sustained ROSC, minimum ETCO2 value

**ECPR team availability, percutaneous cannulation not possible, ECPR initiation not possible within a defined timeframe

Table 5. Combined selection criteria.

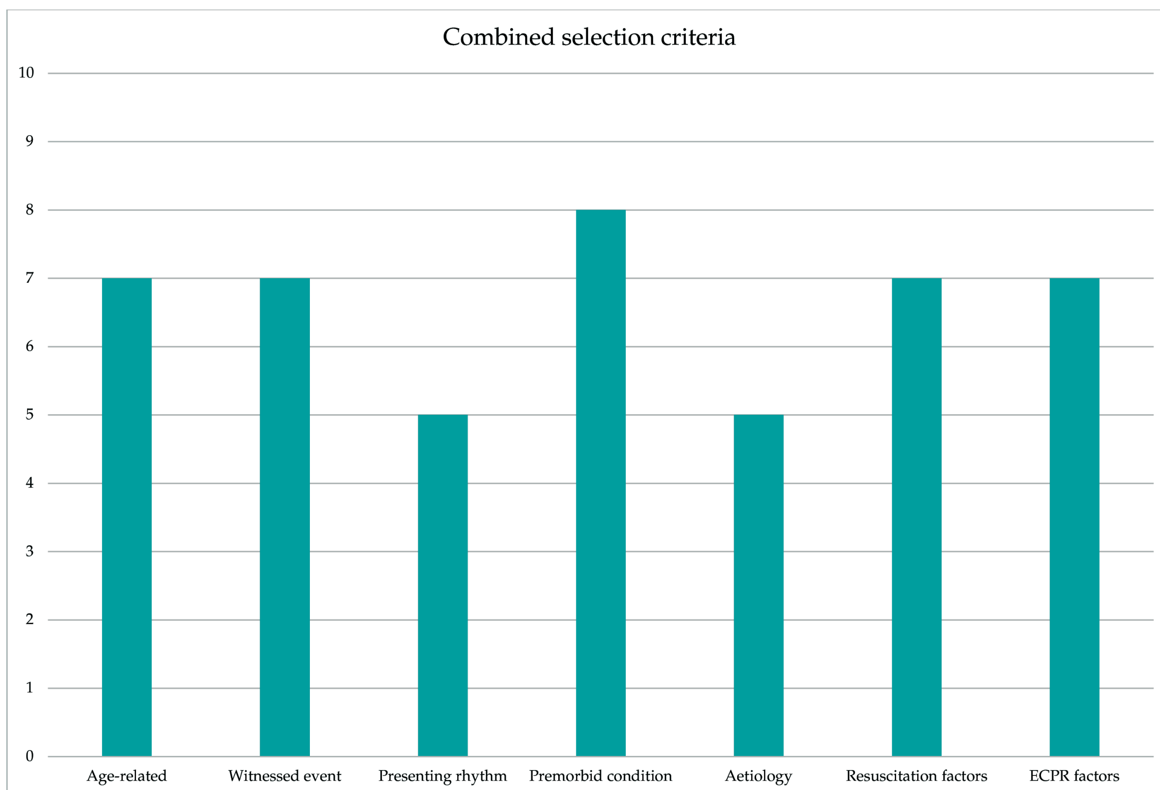

Figure 3: Combined selection criteria.

Reference	Location	Team composition	Case identification	Mode of transport	Site of EPCR initiation
Lamhaut et al., 2017	Paris, France	Dedicated ECPR team (emergency physician/intensivist, nurse anaesthetist and paramedic)	Proactively dispatched to all witnessed OHCA under 70 years old	Ground	On scene
Singer et al., 2020 'Sub30'	London, United Kingdom	Dedicated ECPR team (Advanced Paramedic, senior physician in prehospital care, two senior physicians in ECMO)	Calls screened by Advanced Paramedic Practitioner Desk	Ground	On scene
Bartos et al., 2020	Minnesota, USA	Dedicated 'mobile ECMO team'. One senior cannulating physician (interventional cardiology, emergency medicine or critical care), one sterile assistant, and one non-sterile assistant (critical care experienced Paramedics, nurses or physicians)	Central dispatcher notified by attending EMS Paramedic team. Mobile ECMO team and EMS rendezvous at agreed ED for ECMO initiation.	Ground	Following RVP with EMS at three pre-planned ED sites
Petermichl et al., 2021	Regensburg, Germany	Hospital-based ECPR team.	Simultaneous activation of ECPR team alongside EMS response to potentially eligible cases.	Ground	On scene
Hutin et al., 2022	Paris, France	Dedicated ECPR team (emergency physician/intensivist, nurse anaesthetist and paramedic)	Dispatched in conjunction with other EMS to witnessed OHCA	Helicopter	On scene
Pozzi et al., 2022	Lyon, France	Dedicated EPCR team (EMS physicians who had completed an 18-month period of surgical training with a cardiac surgery team)	Not stated	Ground	On scene
Leivaditis et al., 2023	Kaiserslauten, Germany	'Medical Intervention Car' (Anaesthesiologist, cardiac surgeon and clinical perfusionist)	MIC team notified within 5 minutes of arrival of EMS	Ground	On scene
Richardson et al., 2023 'CHEER3'	Melbourne, Australia	Dedicated three-person team consisting of two intensive care physicians (trained in US-guided femoral cannulation and ECMO initiation), and an experienced ICP (trained in ECMO circuit priming and pump management)	Automatic dispatch to suspected OHCA. Screening of potentially eligible cases by ICP using call data and situation reports from scene.	Ground	On scene
Richardson et al., 2024 'PACER'	Victoria, Australia	Not stated	Not stated	Ground	On scene
Ali et al., 2024 'ON-SCENE'	Nationwide, The Netherlands	Physician-led HEMS team	HEMS team activated by dispatcher using details from initial 112 call	Helicopter	On scene
ICP = Intensive Care Paramedic, EMS = Emergency Medical Services, OHCA = Out-of-hospital cardiac arrest, HEMS = helicopter emergency medical service					

Table 6. ECPR team dispatch process.

RESULTS

Identification of Eligible Studies

The study identification process is displayed by a PRISMA flowchart (Figure 2). Application of the search strategy yielded 1,307 articles and two studies within study registries. 470 duplicates were removed, leaving 839 for title and abstract screening. 39 reports were selected for full text review. One additional article was identified via citation searching. Nine articles were excluded as they were secondary reviews of an existing ECPR system, sixteen described selection criteria for in-hospital ECPR, two did not provide any inclusion or exclusion criteria, two described the use of ECMO retrieval teams and one was a modelling study with hypothetical selection criteria. A total of ten studies were selected for final inclusion.

Inclusion Criteria

The total number of selection criteria utilised ranged from three to six. Age-related criteria were the most frequently included and were specified in seven (70%) articles. Upper age cut-offs ranged from 50 (Ali et al., 2024) to 75 years (Bartos et al., 2020), with 65 years being the most frequently utilised (n=3). All systems with age criteria required patients to be aged 18 or older. The requirement for the cardiac arrest being witnessed was also reported in seven articles (70%). Bystander CPR was only required in four. Presenting shockable rhythms (ventricular fibrillation or pulseless ventricular tachycardia) were reported in five inclusion criteria, and two of these studies also included PEA. A minimum duration of conventional resuscitation was required in six articles. Five articles had inclusion criteria for the onset of cardiac arrest to ECPR initiation. Additional criteria described included ETCO2 >10mmHg (n = 2), the availability of mechanical CPR (n = 1), the presence of primary hypothermia or intoxication (n = 1) and cases occurring during the operating hours of the ECPR team (n = 1).

Exclusion Criteria

The absence of major or life-limiting comorbidities was the most frequently described eligibility criteria identified within this review, with eight articles requiring this. Examples of comorbidities included advanced heart failure, COPD, terminal illness, advanced malignancy and severe frailty (Richardson et al., 2023; Singer et al., 2020). Similarly, the presence of an advanced directive or DNAR was listed as an exclusion criteria five times. Two ECPR systems excluded patients with unwitnessed OHCA, and two listed trauma or significant bleeding as exclusion criteria.

Combined Selection Criteria

When combined, patient selection criteria involving premorbid conditions were the most frequently utilised, in eight out of ten included studies (Table 5 and Figure 3). Age-related, the requirement for a witnessed cardiac arrest, resuscitation-related factors and ECPR-related factors were used in seven studies. The use of an aetiology or presenting rhythm related criteria were reported in five studies.

Dispatch Processes

Nine articles described prehospital ECPR systems operating in large urban populations, with just one nationwide service identified (Ali et al., 2024). Eight articles described the use of ground-based teams, and two reported on the use of helicopter-based teams (Hutin et al., 2022; Alli et al., 2024). The process for case identification was available in eight articles, with six utilizing a proactive approach to dispatch upon receipt and screening of the emergency call. Two systems dispatched an ECPR team following an initial update from attending resources (Bartos et al., 2020; Leivaditis et al., 2023). The use of a dedicated ECPR team was described in six articles, with one reporting the provision of ECPR by a physician-led HEMS team (Alli et al., 2024) and one reporting the dispatch of a hospital-based team (Petermichl et al., 2021). ECPR was planned to be performed on scene in nine systems, while one described the use of a rendezvous strategy (Bartos et al, 2020).

DISCUSSION

In this review, an age-based criterion was frequently utilised, with 7 out of 10 articles including this requirement. Age is a well-established prognostic factor in cardiac arrest and may serve as a surrogate measure of comorbidities, decreasing cardiac or pulmonary physiological reserve, and frailty (Wissenberg et al., 2015; Fernando et al., 2020). This review identified a wide heterogeneity of ages eligible for ECPR between 18 and 75 years with various upper age cut-offs utilised (50, 65, 70, and 75 years). This may suggest a disparity or paucity of evidence regarding the age criterion for ECPR. Several studies have examined age and the association between survival and neurological outcomes following cardiac arrest and ECPR. Chahine et al. (2023) identified age as a dependent factor associated with favourable neurologically intact survival, with those aged 20-39 years having a reported survival rate of 51% (n = 21/41), whereas a significant decline in favourable survival was seen in those aged 70-79 years (22.6% n= 12/53). These findings were echoed within a systematic review examining 29 ECPR protocols and associated outcomes by Tran et al. (2023). Despite the higher rates of favourable survival seen in younger patients, Kikuta et al. (2021) demonstrated than ECPR could be successfully applied in older patients if careful prognostic and selection criteria are applied. Prognostic factors such as a lack of comorbidities, agonal breathing, and short cannulation times were associated with more favourable outcomes in older patients. This may suggest ECPR may be a useful tool if applied in carefully selected patients without the use of age cut-offs.

The presence of major or life-limiting comorbidities was the most frequently utilised exclusion criterion, featuring in eight protocols. Determining the presence and prognosis of comorbidities may be difficult in the prehospital setting, due limited access to patient records and the need to prioritise expedient resuscitative interventions in eligible patients. The remote review of electronic patient clinical records during the response phase, prior to provider arrival, may expedite and inform decision making. Additionally, the use of validated comorbidity assessments may aid the creation of standardised assessment criteria, and thus guide clinicians in making eligibility decisions. The Charlson Comorbidity Index [CCI] may represent a suitable option, and has been found to accurately predict the long-term outcomes of patients in medical, surgical, trauma and intensive care settings (Charlson et al., 2022). The CCI assigns a value to the presence of each of

eighteen conditions to provide a numerical score, all of which can be rapidly established by prehospital clinicians through clinical assessment and history taking.

The case identification and dispatch processes for prehospital ECPR teams, and subsequent location of ECPR initiation, appear to be variable and require careful system-specific considerations. These factors are highly influenced by team composition, prehospital systems and geography. Currently three locations for initiating ECPR currently exist within the literature: at scene, after moving the patient to a rendezvous location, or following transfer directly to an ECPR centre (Song et al., 2023). One factor which has significant influence over ECPR outcome is the time from collapse to cannulation (Downing et al., 2022; Tran et al., 2023). Experienced ECMO teams require approximately fifteen to twenty minutes to perform cannulation and establish flow, and the benefit of ECPR is lost after low flow periods of one hour. Therefore the current consensus is to initiate ECPR within 40 minutes of cardiac arrest. Teams should select and refine case identification processes that minimise the time from dispatch to cannulation to maximise the efficacy of ECPR (Leung et al., 2024). Early dispatch processes, such as simultaneous activation of an ECPR team with first responders, while carrying the risk of a potentially high stand-down rate, may be necessary to reach patients in a quick timeframe. This approach is not without risk, as over dispatch may result in missed ECPR patients if the team is committed to delivering care for non-ECPR eligible patients, or initiating ECPR too early when ROSC could have been established with conventional ALS (Richardson et al., 2023).

The mode of ECPR team transport also warrants further consideration. Within this review, eight out of the ten included ECPR services utilised a ground-based response. This is likely to be influenced by the fact that ECPR services are often established in highly populated urban areas, with several articles describing dispatch of a dedicated ECPR team from a centralised hospital location. Within our review, just two systems described the use of a helicopter-based ECPR team. As systems aim to improve equity of care and provide ECPR coverage to a larger population over a larger geographical area, a helicopter-based ECPR service may be advantageous. As demonstrated by ter Avest et al. (2022), the air transfer of patients for in-hospital ECPR from semi-rural locations is not feasible. This has led to investigation into how bringing ECPR to the patient via a helicopter-based service may increase eligibility (Gottula et al., 2024). However, this approach has a significant impact on cost-effectiveness and requires additional logistical considerations. As highlighted by Hutin et al. (2022) in their description of a helicopter-borne ECPR team, just 30% (n = 12) of patients received ECPR, with the team being cancelled prior to arrival in 23 out of 40 activations. The 'On-Scene' trial, featuring a nationwide HEMS-based system in The Netherlands, described by Ali et al. (2024), is ongoing and its findings may influence further helicopter-based ECPR services.

Future Research

In the United Kingdom, the prehospital response to OOHCA often involves the dispatch of a specialist or advanced critical care paramedics with frequent exposure and experience in prehospital resuscitation. Due to the locality of these resources, they are often on scene prior to the arrival of HEMS based enhanced care teams. After initial identification of potentially eligible patients and dispatch of a HEMS-based ECPR team, advanced critical care paramedics may be able to confirm eligibility, establish ALS and begin to

'prepare' the patient and environment for ECPR initiation. This may also include the deployment of mechanical CPR to facilitate relocation of the patient to a rendezvous point where ECPR can be initiated. Additionally, similarly to the arrangements described by Singer et al. (2020), the presence of an advanced paramedic at scene to optimise cardiac arrest management allows ECMO/ECPR specialists to concentrate solely on establishing ECPR. Future research should explore the impact of co-deployment of specialist paramedics on ECPR selection and initiation. Furthermore, services should explore the feasibility of a process for facilitating direct communication between the attending clinicians and enroute ECPR team. This may help to reduce the time prior to committing to, or deciding against, ECPR initiation. Consequently, this may reduce the time spent on scene confirming eligibility or stand down resources from unsuitable cases at an earlier point, maximising their availability.

'PACE' Mnemonic

Our review has demonstrated that much of the information required to assess patient suitability for ECPR can be determined during initial emergency call receipt or following the arrival of first responders. A mnemonic has been created to aid dispatch staff and initial responders in identifying potentially eligible patients. Providing updates containing this information to dispatch centres may help improve the timeliness and accuracy of prehospital ECPR team dispatch.

Figure 4: 'PACE' mnemonic for initial assessment by non-specialists or first responders.

LIMITATIONS

Our review has several limitations. Firstly, the search strategy used may not have identified studies utilizing other terminology. To reduce the risk of missing relevant articles, search terms were decided by consensus between reviewers, and pilot tests to identify known literature were undertaken. Secondly, searches were only performed for articles published in the English language which may exclude relevant literature in other languages. However, the results indicate ECPR systems in a range of countries were identified. Thirdly, clinical outcomes were not identified. The decision not to include these was made as it was felt the heterogeneity of included studies would prevent meaningful comparison.

CONCLUSION

This review has identified common patient selection criteria across ten prehospital ECPR systems, including patient age, initial presentation characteristics, and the absence of comorbidities. Variability in the specific parameters of these is likely to be reflective of the variation in geographical distribution, team composition and transport modes of prehospital ECPR services. Many of the frequently utilized eligibility criteria can be determined during emergency call receipt or shortly after resource arrival, highlighting the potential for improved screening by emergency medical dispatchers and non-specialist resources

to reduce ECPR team dispatch times. A simple mnemonic to aid with evaluating key criteria on arrival is provided. Future research should evaluate the impact of prehospital screening tools on dispatch and ECPR initiation times.

ETHICS

Ethics approval was not sought for this study as it is a secondary review. All included studies received their own ethics approval.

REGISTRATION AND PROTOCOL

This review was not registered, and a protocol was not prepared prior to completion.

SUPPORT

No financial support was provided to the authors of this review.

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