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Title: Portable ECMO in the pre-hospital setting

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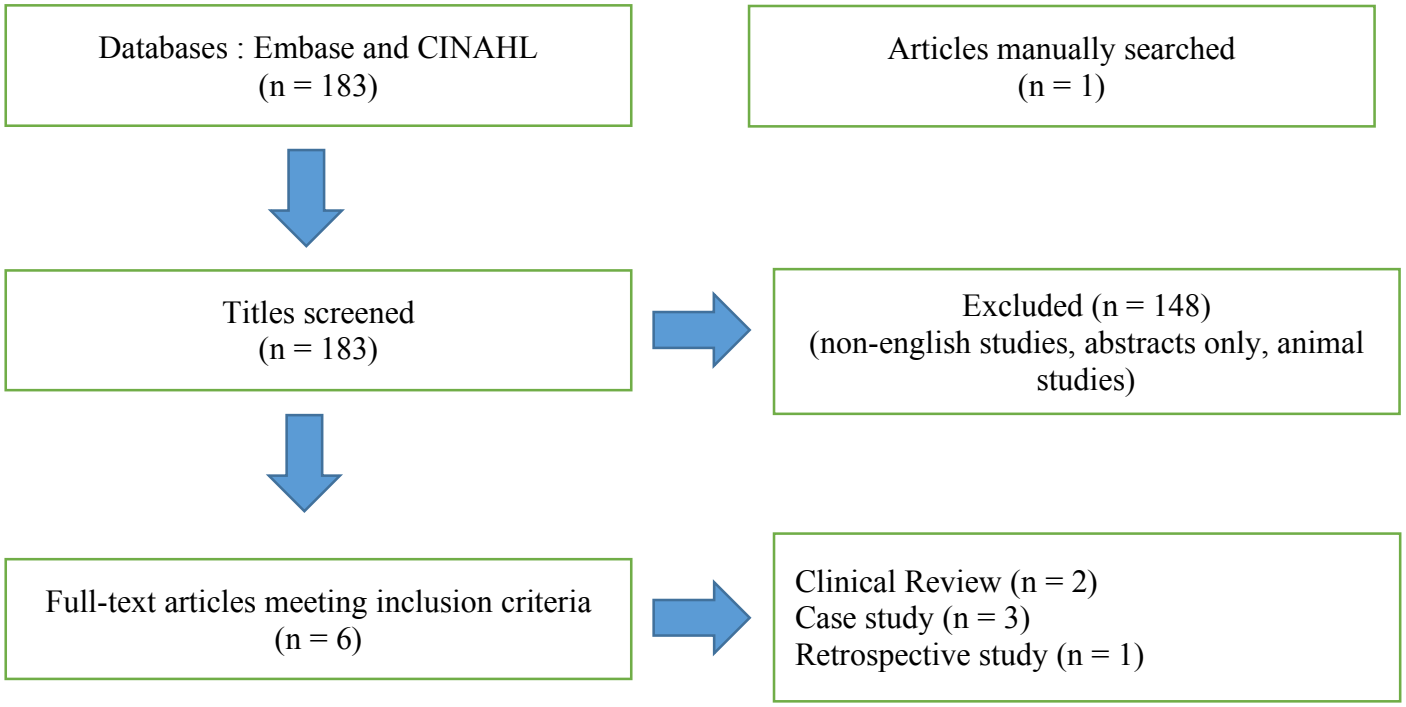
Title: Does pre-hospital Extracorporeal Membrane Oxygenation (ECMO) improve patient outcomes in civilian population?

PICO: In all refractory cardiac arrest patients, does portable ECMO in the pre-hospital setting improve patient outcome?

Rationale: ECMO was first introduced in 1965 to aid in the treatment of cardiopulmonary failure. Since then, ECMO has largely become a speciality within hospitals where patients are transferred to these centres to be treated. Its growing involvement in patients in refractory CA has resulted in the evolution of portable ECMO (P-ECMO) machines into the emergency departments (ED). However, the rise in emergency medicine has identified the importance of "no-flow" time in these patients and acknowledging the need for pre-hospital ECMO as a critical life-saving intervention. A search will be performed to analyse its application and outcomes in the pre-hospital setting.

Search Strategy: Medical search databases was used included EMBASE and Clinical Key. The following terms were used in the search: mobile, portable equipment, trauma, pre-hospital paramedic, EMS, cardiac arrest, cardiac arrest, ECMO, extracorporeal membrane oxygenation device. One article was manually searched.



Authors and Year	Study Design	Population	Study Aims	Results	Strengths and Limitations
Saxena, P., Shehatha, J., Boyt, A., Newman, M., & Konstantinov, I. (2009)	Case study	15 year old female (n = 1)	To compare different methods of active re-warming of a hypothermic CA patient, including ECMO, cardiopulmonary bypass (CPB) and thoracic lavage	CPB is the standard therapy but is associated with higher rates of multi-organ failure in hypothermic CA pts Long term outcome (15 yrs) of CPB pts have satisfactory neurological outcome ECMO has a 6.6 times higher chance of survival compared to CPB as it provides prolonged circulatory support, decreasing risk of multi-organ failure	(-) case study (-) limited population (-) inability to generalise to wider population (-) susceptible to research bias (-) difficult to replicate (+) in-depth analysis of the patient/outcome and associated variables/risk factors
Arlt, M., Philipp, A., Graf, B., Schmid, C., & Hilker, M.	Case study	9 year old female (n = 1)	To discuss the first use of portable ECMO in the pre-hospital setting for CA	Advanced life support remained unsuccessful (50minutes) Veno-arterial ECMO occurred on scene and resulted in	(-) case study (-) limited population (-) susceptible to research bias (-) difficult to replicate

(2011)				ROSC and transport to hospital for further examination Patient found to have poor cerebral perfusion and multiple-organ dysfunction	(-) lacks information regarding neurological impairment, which could provide more information about the importance of P-ECMO (+) in-depth and detailed analysis of the patient/outcome and associated variables/risk factors (+) specifically discusses portable ECMO and its implications for future emergency medicine practice (+) prompting further investigation into the use of pre-hospital ECMO on a wider population
Latimer, A., McCoy, A., & Sayre, M. (2018)	Clinical review	N/A	To analyse different emerging technologies, including ECMO, that may benefit OHCA patients	ECMO allows clinicians to investigate underlying/reversible cause of CA ECMO CA pts increased survival rates with favourable neurological outcome between 14%-54%	(-) susceptible to over-interpretation of information (-) retrospective design (-) lack of generalisability (-) lacks pre-hospital evidence (+) discusses portable ECMO

				Reduce collapse to ECMO flow time via portable ECMO increases survival rate Further research required for ECMO patient selection	for pre-hospital setting, which is a new emerging concept (+) identified the importance of no-flow time and the time criticality of these patiens (+) discussed the importance of ensuring ECMO insertion time was within the 60mins (+) rigorous review and analysis of research (+) analysed the neurological effects post-ECMO
Kwak, J., Majewski, M., & Jellish, W. (2020)	Clinical review	Anesthesiologists	To discuss the rapidly emerging use of ECMO and its impact on neurological outcomes	Patients with underlying cause of CA have better survival when placed on ECMO Factors associated with worse outcomes on ECMO include comorbidities, acidosis and end-organ failure at time of insertion	(-) inability to establish cause-effect relationship (-) susceptible to over-interpretation of information (-) retrospective design (-) lack of generalisability (+) in-depth analysis of method, procedure, pathophysiology of complications

				OHCA survival without ECMO (2%-11%) OHCA survival with ECMO (15%-25%) ECMO patient selection criteria: <60years, no flow time <5min, shockable rhythm, adequate CPR, ECMO implantation time frame of 60 minutes High mortality remains due to neurological complication(s) (13.3%) resulting in long-term mortality Difficult to assess ECMO complication pre-hospitably as it requires CT imaging Further research identifying ECMO-related neurological injuries is required	(+) discusses pre-hospital intervention (+) discusses patient selection criteria for ECMO (+) thoroughly analyses neurological complications in ECMO patients (+) identifies patient risk factors and how it correlates with their outcome

Yoshida, T, et al., (2020)	Retro-spective study	(n = 531)		Underlying CA cause, time from CA to ECMO insertion are independent prognostic factors for favourable outcomes Median time (MT) from CA to hospital arrival (10.5min) MT from CA to ECMO insertion (37.5min) 1 and 3 month survival rates higher in ECMO then non-ECMO (23.7% and 16.7%; 6.0% and 3.7%, respectively) Favourable cerebral function at 1 and 3 month in ECMO and non-ECMO pts (15.8% and 13.9% ; 1.9% and 1.7%, respectively)	(-) retrospective study, causality cannot be established (-) study inclusion criteria as it is unclear whether these results are applicable to all CA pts (-) lacks pre-hospital evidence, only discusses ECMO in emergency department (ED) (-) weaker level of evidence (-) prone to recall bias (+) cost-effective study (+) can be used as initial study to build a foundation for future research (+) identified timeframes regarding on-scene, transport and ECMO insertion (+) in-depth analysis of patient selection criteria for ECMO and patient outcome, particularly neurological outcomes

					(+) results identified major impact of early ECMO on CA patients
Marinaro, J., et al., (2020)	Case report	65 year old male (n = 1)		P-ECMO in pre-hospital environment is uncommon outside of Paris (survival-to-discharge rate 38%) P-ECMO screening criteria is the same as in-hospital Arrest-to-hospital time is >35min, ECMO team dispatched to scene to achieve arrest-to-cannulation time <60min ECMO insertion <60min associated with better survival Hand-crank used to provide circuit flow removes the need for ECMO specialist, easily	(-) case study (-) limited population (-) inability to generalise to wider population (-) susceptible to research bias (-) difficult to replicate (+) first reported P-ECMO in North America for refractory CA (+) foundation for further research to be conducted in P-ECMO in pre-hospital setting (+) identified selection criteria, which allowed for a better understanding of potential future patients (+) discusses pre-hospital ECMO and its effectiveness on patient outcome

				transferable to hospital equipment and is more feasible	(+) discusses pre-hospital ECMO feasibility and its cost-effectiveness

Comments: P-ECMO has been found to be beneficial in patients in refractory CA as it allows earlier establishment of ROSC and gives treating clinician's time to identify the underlying condition. The insertion of ECMO should be aimed to be done within 60 minutes from the patient's initial arrest/collapse. This time-frame is correlated with increased survival rates as it allows adequate organ perfusion, particularly the brain. If there is a delay, results have shown that patients may obtain ROSC but later die from multi-organ failure or removal of life support due to neurological impairment causing their vegetative state. ECMO is not solely responsible for survival, but plays an important role in providing the correct support until other facilities can be reached, such as catheter lab, as it can significantly reduce the time of "no-flow" which can be fatal. The selection criteria for ECMO is still evolving and has not yet been identified which can impact the ability to generalise findings to other populations. Hence, majority of the research that practices pre-hospital ECMO is limited to Europe, specifically France. France has produced successful results of pre-hospital ECMO and illustrate promising evidence for the future development of portable ECMO in emergency medicine.

Consider: There lacks appropriate selection criteria for portable ECMO in ED and pre-hospital setting. The timeframe of 60minutes has found to be beneficial to patient outcome, however mainly pre-hospital studies have been able to maintain this timeframe. Further research is required in order to establish more data on specifically pre-hospital ECMO and patient selection criteria in order to measure how these variables affect patient outcome and potentially reduce "no-flow" time. Current literature is weak and lacks validity. Hence, despite ethical complications, randomised controlled trials should be conducted in the future in order to make a more robust conclusion regarding the use of portable ECMO.

Clinical Bottom Line: The current availability of literature regarding pre-hospital ECMO for CA patients is limited and requires the reliance of "portable" ECMO in the ED rather than ECMO centres. In the absence of robust data, emergency medicine aiming to integrate P-ECMO into their service should do so with caution and ensure that the clinicians are appropriately trained or collaborating with on-call ECMO teams with skilled physicians.