

References / Literature Review and Grading

ECMO in ED for Out of Hospital Cardiac Arrest

(4/23/2022)

We followed the AAEM procedure for literature review. We first reviewed relevant guideline statements and then proceeded with a search of pubmed.

Guideline statements

AHA - ACLS -

https://www.ahajournals.org/doi/10.1161/CIR.0000000000000732?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20pubmed

Literature review

Pubmed

ECMO AND “cardiac arrest” AND systematic[sb] (last 5 years, human) 35 total citations 13 potentially relevant

“ECPR” AND “cardiac arrest” clinical trials (since 2020) - 9 studies, 2 presenting primary results that are relevant (ARREST and Nakashima), 1 referring to design of relevant study (EROCA, first author HSU)

Note: Some additional literature was cited in the CPC Committee peer review process and is referenced, but not graded in this table as it was not identified by the literature search procedures.

Publication	GradeK	QualityK	GradeM	QualityM	Year	Comments	Additional Comments
Ooweneel, et al ¹⁹	A	Adequate	A	Adequate	2016	Systematic review from 2016 of ECPR for OHCA, IHCA, and cardiogenic shock. 10 cohort studies with a control arm were included. Standardized outcome measures for both 30 day and 6 month survival. 13% higher long-term survival and 14% higher neurologically-intact survival in ECPR than in propensity-matched controls.	Included in and out of hospital, and refractory cardiogenic shock in MI (pre-arrest) - (positive - i.e. supports ECPR)
Holmberg, et al ²⁰	B	Poor	C	Poor	2018	Systematic review, including 15 observational studies of OHCA. Heterogeneity of outcome measures among studies. Overall low study quality. Meta-analysis could not be performed due to high risk of bias and heterogeneity of studies.	Meta-analysis of observational studies of OHCA and IHCA; adults and children - overall the authors rated this literature as inconclusive (neutral).
Twohig, et al ²¹	A	Adequate	C	Adequate	2019	Systematic review of 17 studies of ECPR but only 9 observational studies compared ECPR to CCPR, 1 of which was prospective. Odds ratio favoring 30 day survival/hospital discharge in patients treated with ECPR with moderate to high risk of bias.	Meta-analysis of observational studies, generally at high risk of bias, but did have a strong signal in favor of ECPR (positive)

Miraglia, et al⁶	A	Good	B	Adequate	2020	Systematic review of 6 propensity-matched cohort studies of adult IHCA and OHCA. ECPR was associated with better 30 day and long-term neurological outcomes and survival when pooled IHCA and OHCA arrest data were used. No benefit for ECPR was seen for 30 day survival and neurologic outcomes in OHCA. Long-term survival and neurologic outcome may be better in OHCA.	ECPR of OHCA and IHCA, but only included studies with propensity score matching. Had a strong signal in favor of ECPR, but limited by lack of randomization. (Supportive)
Hsu, et al (EROCA)⁹	C	Adequate	C	Adequate	2021	Prospective single center University of Michigan feasibility trial randomizing OHCA patients to standard vs expedited transport and measuring arrival to ED within 30 minutes and frequency of initiation of ECPR. Included non-shockable rhythms. 12/15 eligible pts randomized to expedited transport. 5/15 pts received ECPR, with 0% survival.	Studied feasibility of early transport to an ECPR center. Did not directly randomize to ECPR versus control. Did not demonstrate feasibility. There was only one survivor in the whole study, who did not receive ECPR. (Not Supportive)

Yannopoulos, (ARREST) ³	A	Outstanding	A	Outstanding	2020	Randomised open-label single center trial from University of Minnesota. Enrolled 30 adults with OHCA with initial rhythm of v fib or pulseless v tach and no ROSC after three shocks and transfer time of less than 30 min. Survival to hospital discharge: 6/14 in ECPR and 1/15 in standard ACLS group. CPC category 1 in 5/6 survivors in ECPR group. Study stopped early due to prespecified stopping criteria being met.	Trial was strongly positive, but the model required interventional cardiologists able to cannulate for ECMO 24-7 and only included shockable arrests out of hospital (supportive)
Nakashima, et al ²²	C	adequate	C	adequate	20199	Prospective multicenter observational study in Japan. < 45 min after emergency call, 15 min of CPR in ED then cannulation. Primary endpoint 6 month favorable neurologic outcome, defined CPC 1 or 2. 407 total patients, 250 with ECPR. Significantly higher number with VF/pVT in the ECPR group. Primary endpoint reached in VF/pVT group. No statistical benefit if conversion from VF/pVT to PEA before ECPR.	Basically compared sites that did ECPR to those that did not. As such, relatively high risk of bias (other site effects). (Supportive)

Bougouin, et al ¹⁰	C	Adequate	C	Adequate	2019	Prospective registry of OHCA in Paris area, 2011-2018. 8% survival in 525 patients given ECPR prehospital, vs. 8.6% for CCPR. No significant advantage of ECPR for survival to hospital discharge. Significant selection bias in pts treated with ECPR. Did not examine long term or neurologically intact survival.	Did matching to address differences in baseline characteristics. Shockable rhythm associated with higher likelihood of a good outcome, but interaction (shockable / ECPR) not formally tested. In patients without ROSC and shockable rhythm there were 28 survivors in ECPR group and 3 in conventional CPR group. (neutral on primary outcome, possibly supportive in shockable)
Stub, et al (CHEER) ^{10,23}	C	Adequate	C	Adequate	2014	Single center prospective observational study from Australia of IHCA and OHCA. Initial vfib rhythm, bystander cpr within 10 min for OHCA, after 30 min of CCPR. Included intra-arrest therapeutic hypothermia of 33 degrees. 26 pts (11 OHCA and 15 IHCA). Survival to hospital discharge 45% OHCA and 60% in IHCA all with full neurologic recovery. No case control and possible significant selection bias. No report of long term outcomes.	No control group, combination of OHCA and IHCA. They were able to get patients on ecmo within an hour of collapse about half the time (median time to ecmo 40 in survivors and 78 in nonsurvivors). Gives proof of concept (over half survived using this approach). (Supportive)
Mosca, et al ²⁴	D	Poor	D	Poor	2016	Single center retrospective chart review study in New York City of 31 patients who underwent ECPR after CCPR for IHCA. Multiple possible confounders, minimal chart review methods. 42% survival	Hard to interpret, but likely supportive of the concept in appropriately selected patients. (supportive)

						at 1 year. No significant difference in > 45 or < 45 minutes duration of CCR prior to ECPR.	
Shinar, et al ⁴	D	Adequate	D	Adequate	2019	Single community hospital in San Diego retrospective chart review study of combined 58 pts with IHCA and OHCA who had EP-initiated ECPR. 24% vs 14% adjusted survival to hospital discharge.	Seven year case series of community ED, with ED physician (no residents) initiated cannulation. In general provides some data that a motivated group of emergency physicians can initiate ECPR (supportive)
Lamhaut, et al ¹¹	C	Poor	C	Poor	2017	Prospective registry of OHCA in Paris area from 2011-2015 using mobile intensive care units and strict inclusion criteria. 154 total patients, 9% survival during early period and 28% during more stringent criteria in later period. Period 2 had initiation of ECPR after 20 min of no ROSC and with more favorable patient factors. No control group.	Survival improved during a quality improvement (involving ECPR and other components) however patient selection changed, which makes the improved survival harder to interpret. (supportive)

Reynolds, et al ¹³	C	Good	C	Good	2017 Prospective multicenter North American observational cohort study of OHCA (PRIMED) with analysis of hypothetically ECPR-eligible subgroup for natural history of survival and neurologic outcome with conventional CPR. 11% or 1237 met eligibility criteria. 38% of these survived to hospital discharge and 30% with a good neurologic outcome. 1/3 failed to achieve ROSC and half of those with ROSC died in the hospital or were discharged with poor neurologic outcome.	This study provides a potential number of patients who might be eligible for ECPR given prolonged arrest in spite of professional resuscitation. Interestingly about 30% of this hypothetical population survived with a good neurological outcome (which is much higher than zero), which is a higher than expected good outcome proportion and lower than control group survival in the recent ARREST trial. (neutral)
Alm-Kruse, et al ¹²	D	Adequate	D	Adequate	2021 Registry study of pre and post-ECPR protocol implementation at two Norwegian centers. No significant difference in survival pre vs post (30/48 vs 50/100 ECPR-eligible patients). In Post group, 14 actually received ECPR.	No difference in survival in this uncontrolled before and after study in Norway - but possible trend towards worse survival after implementing ECPR - low volume may have been a problem. (Negative, possibly harmful)

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