

INPLASY

A Bayesian analysis of randomized trials evaluating extracorporeal cardiopulmonary resuscitation-based treatment for refractory out-of-hospital cardiac arrest

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ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023120060

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 December 2023 and was last updated on 14 December 2023.

INTRODUCTION

Review question / Objective What is the posterior probability of any effect, and a clinically relevant treatment effect of extracorporeal cardiopulmonary resuscitation (ECPR) in a meta-analysis of randomized trials comparing extracorporeal cardiopulmonary resuscitation (ECPR)-based therapy to conventional cardiopulmonary resuscitation (CCPR) in patients with refractory out-of-hospital cardiac arrest?

Rationale Out-of-hospital cardiac arrest carries a grim prognosis. Several randomized trials have been conducted with a specific emphasis on neurologically favorable survival. This Bayesian meta-analysis will focus on the posterior probability of a clinically relevant treatment effect.

Condition being studied Patients with refractory out-of-hospital cardiac arrest.

METHODS

Search strategy

PICO:

Patients: out-of-hospital cardiac arrest (and all alternative spelling)

Intervention: extracorporeal cardiopulmonary resuscitation (and all alternative spelling)

Control: conventional cardiopulmonary resuscitation (and all alternative spelling)

Outcome: neurologically favorable survival (and all alternative spelling)

A systematic search will be applied to MEDLINE & PubMed Central, EMBASE, and the Cochrane Library. The search will be defined based on the following terms: ECPR and all alternative spellings, CCPR and all alternative spellings, refractory OHCA and all alternative spellings, neurologically favorable survival and all alternative spellings (see Supplementary Material 1 for the full search strategy).

PubMed:

Disease associated search terms

#1 Out-of-hospital cardiac arrest[MeSH] 7.265

#2 Out-of-hospital cardiac arrest 12.868

#3 OHCA 4,440

#4 Ventricular fibrillation[MeSH] 17,942

#5 Ventricular fibrillation 46.941

#6 VF 17.540

#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 69.665

Intervention associated search terms

#8 Extracorporeal cardiopulmonary resuscitation 2.476

#9 ECPR 865

#10 Extracorporeal CPR 2.542

#11 Extracorporeal membrane oxygenation[MeSH] 15.551

#12 Extracorporeal membrane oxygenation 22.670

#13 ECMO 24.224

#14 Venous arterial extracorporeal membrane oxygenation 22.670

#15 Venous arterial ECMO 1.971

#16 V-A ECMO 255

#17 VA ECMO 2.422

#18 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR

#14 OR #15 OR #16 OR #17 24.921

Control treatment associated terms

#19 Cardiopulmonary resuscitation[MeSH] 22.602

#20 Cardiopulmonary resuscitation 33.123

#21 Conventional cardiopulmonary resuscitation 1.020

#22 CPR 39.960

#23 Advanced Life support 78.099

#24 ALS 58.319

#25 #19 OR #20 OR #21 OR #22 OR #23 OR #24 171.896

Combined search term

#26 #7 AND #18 AND #25 877

EMBASE:

Disease associated search terms

#1 Out-of-hospital cardiac arrest.af 17.870

#2 OHCA.af 8.201

#3 Ventricular fibrillation.af 28.860

#4 VF.af 39.026

#5 #1 OR #2 OR #3 OR #4 74.530

Intervention associated search terms

#6 Extracorporeal cardiopulmonary resuscitation.af 1.586

#7 ECPR.af 1.907

#8 Extracorporeal CPR.af 151

#9 Extracorporeal membrane oxygenation.af 27.294

#10 ECMO.af 29.939

#11 Venous arterial extracorporeal membrane oxygenation.af 2.039

#12 Venous arterial ECMO.af 5.203

#13 V-A ECMO.af 486

#14 VA ECMO.af 4.486

#15 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 39.493

Control treatment associated terms

#16 Cardiopulmonary resuscitation.af 28.858

#17 Conventional cardiopulmonary resuscitation.af 304

#18 CPR.af 31.255

#19 Advanced Life support.af 5.039

#20 ALS.af 84.856

#21 #16 OR #17 OR #18 OR #19 OR #20 133.682

Combined search term

#22 #5 AND #15 AND #21 1.153

Cochrane Library:

Disease associated search terms

#1 Out-of-hospital cardiac arrest[MeSH] 665

#2 Out-of-hospital cardiac arrest 1.614

#3 OHCA 618

#4 Ventricular fibrillation[MeSH] 630

#5 Ventricular fibrillation 4.424

#6 VF 2.476

#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 7.777

Intervention associated search terms

#8 Extracorporeal cardiopulmonary resuscitation 104

#9 ECPR 99

#10 Extracorporeal CPR 49

#11 Extracorporeal membrane oxygenation[MeSH] 303

#12 Extracorporeal membrane oxygenation 1.001

#13 ECMO 1.010

#14 Venous arterial extracorporeal membrane oxygenation 78

#15 Venous arterial ECMO 95

#16 V-A ECMO 7

#17 VA ECMO 117

#18 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 1.495

Control treatment associated terms

#19 Cardiopulmonary resuscitation[MeSH] 1.484

#20 Cardiopulmonary resuscitation 3.021

#21 Conventional cardiopulmonary resuscitation 229

#22 CPR 2.848

#23 Advanced Life support 4.143

#24 ALS 3.263

#25 #19 OR #20 OR #21 OR #22 OR #23 OR #24 11.208

Combined search term

#26 #7 AND #18 AND #25 58

#27 Filter: clinical trials 51.

Participant or population Patients enrolled in randomized studies with refractory out-of-hospital arrest, either randomized to ECPR or CCPR.**Intervention** Extracorporeal cardiopulmonary resuscitation (ECPR).

Comparator Conventional cardiopulmonary resuscitation (ECPR).

Study designs to be included Randomized controlled trials.

Eligibility criteria Randomized studies will be included when comparing and ECPR-based treatment to CCPR in patients with refractory OHCA and reporting on the primary outcome (neurologically favorable survival). Studies will be excluded when they applied a non-randomized design, or did not report results on the outcome of neurologically favorable survival.

Information sources Electronic databases:

- PubMed
- MEDLINE
- Cochrane Library.

Main outcome(s) The primary outcome is 6-month neurologically favorable survival, preferably reported by the Cerebral Performance Category (CPC). A CPC of 1 and 2 is deemed neurologically favorable, and CPC 3-5 is considered neurologically unfavorable. Alternatively, neurological performance can be assessed by the modified Rankin scale (mRS), in which an mRS of 0-3 indicates neurologically favorable survival.

Additional outcome(s) No additional outcomes.

Data management Data extraction will be performed by 2 reviewers using a predefined worksheet in Microsoft Excel.

Quality assessment / Risk of bias analysis Risk of bias will be independently assessed with the Risk of Bias 2.0 tool (RoB 2.0), by two reviewers. The domains include risk of bias due to the randomization process, due to deviations from intended interventions, due to missing outcome data, due to measurement of the outcome, and due to selection of the reported result. The final judgment can range from 'high' to 'low' risk of bias.

Strategy of data synthesis – Conversion of continuous non-normally distributed data to mean and standard deviation by Wan's method.

- The assumed control risk (ACR) will be calculated for the CCPR group, after which absolute risk differences can be calculated, according to the proposal of the Cochrane collaboration.
- Data will be expressed as relative risks (RRs), absolute risk differences (ARDs), numbers needed to treat (NNTs) and posterior probabilities of various effect sizes in Bayesian analyses.

- These effect size thresholds include: ARD >0%, ARD >5%, ARD >10%, ARD >15%, ARD >20%
- Primary analyses will be performed under a vague prior for all patients.
- Secondary analyses will be performed under a vague prior for patients with shockable rhythms.
- Sensitivity analyses will be performed under informed literature-based priors.
- JASP software will be used for statistical analyses.

Subgroup analysis A subgroup analysis will be performed for patients with shockable rhythms.

Sensitivity analysis Sensitivity analyses will be performed using literature-based priors in an additional Bayesian analysis.

Language restriction English language.

Country(ies) involved Netherlands, Czech Republic, United States.

Other relevant information None.

Keywords Extracorporeal cardiopulmonary resuscitation; Conventional cardiopulmonary resuscitation; Out-of-hospital cardiac arrest; randomized controlled trials; Bayesian inference.

Dissemination plans After completion of the study we aim to publish this in a medical peer-reviewed journal.

Contributions of each author

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