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Neurological outcome predictors after extracorporeal cardiopulmonary resuscitation: a systematic review

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Abstract

Background To consolidate current evidence on predictors of neurological outcome following extracorporeal cardiopulmonary resuscitation (eCPR) in patients with cardiac arrest.

Methods We conducted a systematic review of the literature across databases including PubMed, MEDLINE, Embase, CINAHL, the Cochrane Library, and Web of Science. Studies assessing neurological outcomes post-eCPR were identified, with a total of 10 studies eligible for individual assessment of which 8 comprising 4353 patients allowed to perform collective statistical analysis.

Results Favorable neurological outcomes were associated with age < 65 years (OR = 6.17), shockable rhythm at extracorporeal membrane oxygenation initiation (OR = 6.67) or hospital arrival (OR = 3.68), and initial pH ≥ 7.0 (OR = 2.01). Other factors involved the presence of any life sign (gasping, positive pupillary light reaction, or increased level of consciousness before or throughout cardiopulmonary resuscitation) (OR = 9.63; Se 0.89, Sp 0.46, PPV 0.22, NPV 0.96), transient return of spontaneous circulation, non-hypoxic mechanism of occurred hepatitis, public location, and hypothermic etiology of cardiac arrest; however, each of those findings was supported by only one study. Unfavorable outcomes were linked to hypoxic brain injury on computed tomography (OR = 12.40; Se 0.366, Sp 0.955, PPV 0.767, NPV 0.787) and elevated serum creatinine (OR = 2.22). The TiPS65 scale showed high predictive accuracy in two studies when the cut-off point was set at 4 points (88.4% and 88.6%; Se 0.172, Sp 0.971, PPV 0.423, and NPV 0.906, and Se 0.193, Sp 0.985, PPV 0.646, and NPV 0.896, respectively). Some predictors, like call-to-hospital time and bystander cardiopulmonary resuscitation, had mixed results across studies.

Conclusion Neurological prognostication in eCPR patients is a complex problem requiring the consideration of multiple variables regarding patient's and cardiac arrest characteristics. Future research should focus on the determination of outcome-affecting factors and assessment of their applicability in clinical settings. New knowledge on this ground will help to create recommendations for eCPR initiation and termination, consequently contributing to treatment results improvement.

Trial registration PROSPERO CRD42024530305.

Keywords Extracorporeal membrane oxygenation, Cardiac arrest, Functional outcome, Prognostic factors, Clinical decision-making

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Introduction

Extracorporeal membrane oxygenation (ECMO) is a method of automated lung (veno-venous ECMO) or both lung and heart (veno-arterial ECMO) function replacement. Its clinical deployment can be seen in an almost tenfold increase in the number of procedures with the use of ECMO between 2001 and 2021 [1]. The examples of diseases where ECMO constitutes an acknowledged form of treatment are hypothermia, acute respiratory distress syndrome, refractory cardiogenic shock, heart failure, pulmonary embolism, intoxication (e.g., beta-blockers, calcium channel blockers), and extracorporeal cardiopulmonary resuscitation (eCPR). Research results of post-cardiac arrest mortality and neurological outcomes regarding conventional cardiopulmonary resuscitation (CPR) and eCPR remain ambiguous. Both out-of-hospital and in-hospital cardiac arrest publications show no statistical differences or superiority of eCPR over CPR [2–5]. These discrepancies may be a reason for the short eCPR history in clinical practice and consequently small study groups in previous research. On the other hand, current literature does not show data about the superiority of CPR. This is an argument for further investigation of eCPR application results [6]. Each CPR instance requires defining start and end criteria due to potential harm in patients unlikely to survive. In such cases, futile therapy diminishes the quality of life, prolongs suffering, fosters false hope among families, and poses organizational and economic challenges for healthcare systems. Therefore, the European Resuscitation Council Guidelines 2021 highlight the importance of the aforementioned criteria statement [7]. Additionally, eCPR underscores the significance of cautious treatment cessation to mitigate increased mortality and complications risk. Existing research underscores the pivotal role of prognostication advantages post-eCPR, particularly in determining survival with favorable neurological outcomes [8, 9]. The articles published in recent years present the multidirectional approach to this topic. They evaluate the correlation between neurological outcome assessment and factors such as data from medical history and physical examination, laboratory test results, brain injury biomarkers, imaging results, or scores obtained in already validated diagnostic scales [10–13]. There are also several studies proposing original scales for neurological outcome prediction after employment of the Ecpr; nevertheless, none of them is sufficiently explored to determine its clinical utility [14]. Parameters such as age and shockable rhythm demonstrate particular usefulness as prognostic factors due to their widespread and immediate availability. Consequently, their potential for supporting therapeutic decision-making in cases of cardiac arrest is significantly greater compared to laboratory or diagnostic tests, which require additional organization, staff support, and valuable time to obtain results.

A primary concern in the use of eCPR is its availability. The procedure requires specialized equipment (extracorporeal membrane oxygenation, ECMO) and highly trained medical staff, both of which are not uniformly available across healthcare settings. ECMO systems are most commonly found in large academic medical centers and specialized cardiac or intensive care units, but their availability is far more limited in smaller hospitals, rural settings, or low-resource environments. As a result, patients in areas with less access to advanced medical technology and expertise may not be candidates for eCPR, potentially limiting their chances for survival and favorable neurological recovery following cardiac arrest.

Furthermore, the application of eCPR often requires a well-coordinated, rapid response, involving specialized teams and the transportation of patients to institutions where ECMO services are available. This logistical challenge can lead to disparities in treatment access, particularly for patients in more remote or underserved areas. Disparities in healthcare access, particularly between urban and rural populations, may contribute to inequities in the outcomes of cardiac arrest treatment, including eCPR. Patients from higher socioeconomic backgrounds are more likely to be treated in well-resourced settings, increasing the likelihood of receiving eCPR and potentially improving their outcomes. Conversely, patients from disadvantaged or marginalized communities may face barriers such as financial constraints, lack of transportation, or inadequate healthcare infrastructure, which can significantly reduce their chances of receiving the intervention.

In recent years, eCPR has been gaining popularity, leading to a steady rise in the number of publications on the topic, including those related to neurological outcome prediction. The continuous growth of knowledge in this area not only provides new information but also obligates the revision of previous findings and the conclusions drawn from them. This systematic review is aimed at summarizing current knowledge on potential factors utilized in predicting neurological outcomes after eCPR. To the best of our knowledge, this is the only review that excludes studies in which additional interventions were applied that could influence the final neurological outcome of patients, consequently preventing a reliable comparison of results obtained by the same predictive factors across different studies. We believe that the conclusions drawn from this study will support clinicians in making therapeutic decisions for patients with cardiac arrest and will indicate the direction for further research on the identification of prognostic factors.

Methods

This systematic review was conducted following the Cochrane Handbook for Systematic Reviews of Interventions and reported following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Additional file 1) [15, 16]. We registered the protocol in the International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42024530305).

Criteria for considering studies for this review

Types of studies

The review considered both observational and experimental study designs that provide relevant information regarding the neurological outcomes of patients undergoing eCPR. Inclusion criteria for types of study were observational studies such as cohort studies, case–control studies, and cross-sectional studies that investigate neurological outcomes following eCPR; experimental studies including randomized controlled trials and quasi-experimental studies assessing the neurological outcomes of patients undergoing eCPR; and studies utilizing prospective or retrospective designs. Exclusion criteria for types of study were studies lacking information on neurological outcomes following eCPR; studies with inadequate study design or methodology to assess neurological outcomes effectively; and studies not providing relevant data or outcomes related to eCPR or neurological assessment, case reports, or case series without broader generalizable findings. To address potential overlap in study populations, studies with overlapping datasets were carefully examined. When multiple studies reported on the same cohort, priority was given to the study with the most comprehensive data, the longest follow-up, or the largest sample size. If different studies from the same dataset provided unique or complementary analyses, they were included with a careful notation of their overlap to avoid duplicate patient contributions in pooled analyses.

Types of participants

The review considered studies involving adult patients (both men and women, ≥ 18 years old, and being part of all ethnic groups), who have experienced either in-hospital or out-of-hospital cardiac arrest of any etiology and subsequently underwent eCPR. The ability to predict neurological outcomes based on information gathered from medical history, physical examination, laboratory tests, and/or imaging studies also was evaluated. Exclusion criteria for participants were studies involving patients younger than 18 years of age and studies incorporating concurrent use of additional treatment methods alongside eCPR, such as target temperature management.

Types of interventions

The intervention of interest was eCPR, utilizing ECMO to support lung and/or heart function during cardiac arrest. Specifically, studies examining the neurological outcomes of patients who have undergone eCPR were included.

Types of outcome measures

The pre-specified main outcomes of the review primarily focus on neurological status following eCPR and its predictors. These outcomes were assessed using standardized neurological scales such as the Cerebral Performance Category (CPC), modified Rankin Scale (mRS), or Glasgow Outcome Scale (GOS). Additionally, factors contributing to neurological outcome prediction were examined.

The neurological status was measured and assessed at specific time points post-eCPR, including hospital discharge, 30 days post-resuscitation, or at longer-term follow-up periods such as 90 days or 1 year post-resuscitation. Assessment variables included neurological outcome assessment using standardized scales (CPC, mRS, GOS) and variables related to neurological outcome prediction, such as factors examined (e.g., medical history, physical examination, laboratory tests, imaging studies), time of assessment, examiner, proportion of patients with favorable and unfavorable outcomes, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and cut-off points.

Search methods for identification of studies

Electronic search

The last electronic search was conducted in January 2024. In the searches, the following databases were used: PubMed, MEDLINE, Embase, CINAHL Ultimate, the Cochrane Library, and Web of Science. The search included references that have been published till the end of December 2023. Studies had to be published in English. A list of research terms used for the present review is reported in Additional file 2.

Searching other resources

For non-indexed conference proceedings, the review team searched relevant conference proceedings and websites (e.g., Google Scholar). In addition, the review team hand-searched bibliographies of relevant systematic reviews, narrative reviews, and meta-analyses found, as well as relevant citations in bibliographies of the articles included in the review.

Data collection and analysis

Selection of studies

The search resulted in 288 records after removing duplicates. The references were imported into the Excel software spreadsheet to conduct screening by titles and abstracts. First, a random sample of 40 records was independently double-screened by one of the authors to assess inter-rater agreement. The inter-rater agreement was assessed using Cohen's K was satisfactory, $K = 87.5\%$. Any conflicts and questions related to the eligibility criteria were resolved by discussion with the co-authors before proceeding with the screening. At this stage, two different authors (one being the first author, the rest being distributed among the remaining authors) independently screened a random sample of 60% of the records. The inter-rater agreement with Cohen's K was good ($K = 85\%$). Questions and conflicts were discussed and resolved among the authors.

Data extraction and management

Any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer. Data quality checks were conducted to ensure accuracy and consistency in recording.

Data was extracted from included studies using a standardized data extraction form. The following data was extracted: author(s), year of publication, country, and study design; inclusion and exclusion criteria; number of patients included in the study; mean age of patients and female-to-male ratio; characteristics of cardiac arrest (location, shockable rhythm); key time intervals (mean no-flow time, mean low-flow time, mean eCPR duration, mean hospital stay duration); outcome measures (survival to eCPR withdrawal, 24-h survival rate, survival-to-discharge rate, 30-day survival rate, mean time of follow-up); neurological outcome assessment details (used scale, time of assessment, examiner, the proportion of patients with favorable and unfavorable outcomes); examined factors for neurological outcome prediction; measures of effect (relative risks, odds ratios, risk differences, number needed to treat); and measures of accuracy (sensitivity, specificity, PPV, NPV).

Assessment of risk of bias in included studies

The risk of bias was assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool, which is specifically designed to evaluate bias in non-randomized studies, including cohort studies, case–control studies, and quasi-experimental designs. This tool provides a structured framework for assessing bias across seven key domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results. Confounding was evaluated to determine whether other variables might have influenced the observed association between the intervention and outcome. The selection of participants was assessed to ensure appropriate comparability between groups. The classification of interventions was examined to determine whether intervention classification was accurate and free from misclassification bias. Deviations from intended interventions were identified to detect any systematic departures from the intervention protocol that could introduce bias. The extent of missing data was analyzed to assess its potential impact on study results, whereas the measurement of outcomes was evaluated for objectivity and reliability. The selection of reported results was assessed to identify any evidence of selective outcome reporting that might influence study findings.

Each included study was systematically evaluated across these domains, with an emphasis on identifying potential sources of bias that could affect internal validity and overall reliability. Bias assessments were conducted independently by two reviewers to ensure a rigorous and objective evaluation process. Any discrepancies in judgment were resolved through discussion, and when necessary, a third reviewer was consulted to reach a consensus. The overall risk of bias for each study was determined based on the cumulative impact of biases identified across the domains, with studies categorized as having low, moderate, serious, or critical risk of bias according to ROBINS-I criteria. Several challenges were encountered during the assessment process. One common difficulty was distinguishing between confounding and selection bias, particularly in observational studies where baseline differences between intervention and control groups were not always adequately accounted for. To address this, we closely examined the statistical methods used for confounder adjustment, giving preference to studies employing propensity score matching, inverse probability weighting, or multivariable regression models with comprehensive covariate adjustments. Another challenge was the potential for misclassification bias, especially in studies relying on administrative databases or self-reported measures. In such cases, we assessed whether the studies validated their exposure and outcome classifications against objective clinical criteria or independent verification methods.

The handling of missing data presented additional complexity, as many studies lacked explicit descriptions of how missing values were addressed. We classified studies with high rates of missing data and inadequate handling methods (e.g., complete case analysis without justification) as having a higher risk of bias. When studies employed appropriate imputation techniques or

sensitivity analyses to account for missing data, the risk of bias was downgraded accordingly.

In cases where studies included overlapping populations, additional steps were taken to prevent duplication of data and ensure the integrity of the analysis. When multiple studies were identified as using the same or substantially overlapping patient cohorts, priority was given to the study with the most comprehensive dataset, longest follow-up, or highest methodological quality. If studies reported different but complementary outcomes from the same population, they were included in a way that minimized redundancy while preserving the breadth of relevant findings. Sensitivity analyses were performed to assess whether the inclusion or exclusion of overlapping studies affected overall conclusions. Decisions regarding the handling of overlapping populations were transparently documented to enhance reproducibility and methodological rigor.

To ensure full transparency, all bias assessments were comprehensively documented (see Additional file 3), including the rationale for each judgment, considerations regarding domain-specific risks, and any uncertainties encountered during the evaluation. Graphical representations of bias distribution across studies were generated using Robvis, allowing for a clearer understanding of potential biases influencing the overall findings of the review.

Measures of treatment effect

The effect measures for the main outcomes, focusing on neurological status following eCPR) and its predictors, included relative risk (RR), odds ratio (OR), risk difference (RD), and number needed to treat (NNT).

RR compared the risk of a neurological outcome (e.g., favorable vs. unfavorable) between patients who underwent eCPR with favorable neurological outcomes and those who did with unfavorable neurological outcomes. OR assessed the odds of a particular neurological outcome (e.g., favorable vs. unfavorable) in patients who underwent eCPR compared to those who did not or between different predictor groups. RD quantified the absolute difference in the risk of a neurological outcome (e.g., favorable vs. unfavorable) between patients who underwent eCPR and those who did not or between different predictor groups. NNT estimated how many patients need to undergo eCPR to prevent one unfavorable neurological outcome or to achieve one favorable neurological outcome, compared to alternative interventions or exposures.

Effect size calculation

Effect sizes were computed for each study based on relevant outcome measures and sample sizes. Variance estimates were derived from reported standard errors, confidence intervals, or calculated from raw data.

Meta-analysis

A random-effects model with inverse variance weighting and Hartung-Knapp adjustment was employed to pool effect sizes across studies. Forest plots were generated to visualize individual study effects and the pooled estimate with 95% confidence intervals (CI). Heterogeneity was assessed using Cochran's Q statistic and Higgins & Thompson's I^2 statistic. Publication bias was examined using funnel plots and tested using Egger's regression test or Begg's rank correlation test.

Statistical software

All statistical analyses were performed using Python (version 3.14, libraries: pandas, numpy, statsmodels). *P*-values less than 0.05 were considered statistically significant. Sensitivity analyses were conducted to assess the findings, exploring study quality, sample size, and methodological differences.

Data synthesis

For data synthesis in this systematic review, a multifaceted strategy was implemented. Firstly, a narrative synthesis approach was adopted, grouping studies by design, patient characteristics, interventions, and outcomes. Key findings were qualitatively summarized, with an emphasis on identifying patterns and discrepancies. Subgroup analyses were conducted to explore heterogeneity, examining factors such as study design and patient demographics.

Results

Description of studies

The initial search across different databases yielded a total of 616 citations. After screening, a total of 10 studies on 7968 patients were included (Fig. 1) [14, 17–25]. Due to the possible overlap of patient population in 5 of them (3 using the SAVE-J II registry and 2 using the JAAM-OHCA registry), further summary and statistical analysis were decided to be obtained with data of research with the largest study group regarding each registry. Consequently, the results presented below were based on 8 studies on 4353 patients.

The median sample size was 590 (IQR 365–916) patients. The majority of patients were male, with a median percentage of 82.7% (IQR 71.8–84.6%), and the median age was 59 years (IQR 54–60.5). Over half of the patients presented with a shockable cardiac rhythm, with a median of 58.8% (IQR 32.1–66.2%). The survival-to-discharge rate varied widely, with a median of 24.5%

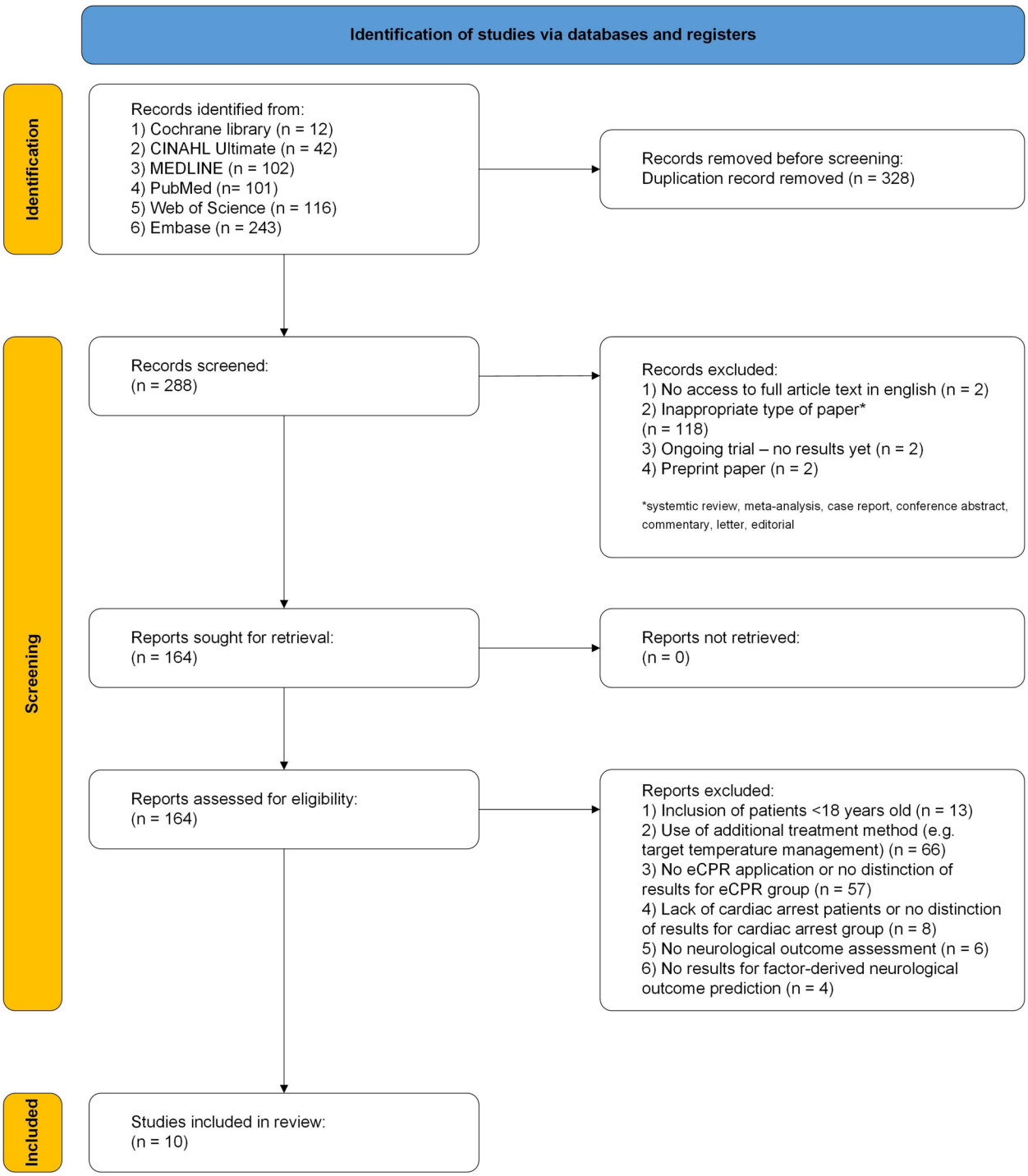

Fig. 1 Flow diagram of the search and inclusion of references. This diagram visually represents the process of study selection for this systematic review. The search process began with a comprehensive review of databases, resulting in an initial pool of articles. After screening for relevance and applying inclusion and exclusion criteria, the number of studies included in the review was reduced. The diagram highlights the key stages of study selection, including the number of studies excluded at each step due to factors such as irrelevance, methodological issues, and lack of outcome data

(IQR 10.4–45.2%). A favorable outcome was achieved in a median of 12.4% of patients (IQR 6.4–25.7%).

Results of individual studies

The final synthesis of 10 eventually included studies that identified several factors regarding clinical, laboratory, and radiological data examined on utility in neurological outcome prediction. One of the most frequently assessed factors was age suggesting a higher prevalence of favorable outcomes in younger patients especially < 65 years old (OR = 6.17; $p = 0.014$); however, two studies showed no significant differences [17–20]. The presence of shockable rhythm at ECMO implementation or hospital arrival implicated in OR = 6.67 ($p = 0.044$) and OR = 3.68 ($p < 0.001$), respectively [17, 19]. The research performed by Takiguchi et al. [20] did not support the value of both rhythms on hospital arrival and was consistent with Okada et al.'s [19] initial cardiac rhythm at the scene. The initial value of pH on hospital arrival ≥ 7.0 was connected with a moderately higher incidence of favorable outcomes (OR = 2.01 and OR = 1.12). One study demonstrated the relevance of call-to-hospital arrival interval reaching ≤ 25 min (OR = 2.96; $p < 0.001$); nevertheless, the other one opposed that finding (OR = 0.85). A similar situation was noticed concerning bystander CPR presence [19–21]. The rest factors revealed to be statistically correlated with unfavorable neurological outcomes were hypoxic brain injury on computed tomography scans (OR = 12.40, $p = 0.001$; Se 0.366, Sp 0.955, PPV 0.767, NPV 0.787) and higher initial serum creatinine level (OR = 2.22, $p = 0.002$). Favorable outcome was more often observed in case of any life sign presence (OR = 9.63; Se 0.89, Sp 0.46, PPV 0.22, NPV 0.96) such as gasping (OR = 2.33), positive pupillary light reaction (OR = 6.21) or increased level of consciousness before or throughout CPR (OR = 6.05), transient return of spontaneous circulation (OR = 2.76, $p < 0.001$), non-hypoxic mechanism of occurred hepatitis ($p = 0.013$), public location (OR = 1.37), and hypothermic etiology of cardiac arrest (OR = 2.54, $p < 0.001$). Unfortunately, each of the aforementioned factors was evaluated by only one of the included papers [18, 20, 22–25]. Besides individual factors, three studies investigated the prognostic application of the TiPS65 scale that consists of four factors each scoring 1 point (time from call to hospital ≤ 25 min, initial pH on hospital arrival ≥ 7.0, shockable rhythm on hospital arrival, < 65 years old). The result of two of them allowed to assess scale accuracy reaching 88.4% and 88.6% (Se 0.172, Sp 0.971, PPV 0.423, and NPV 0.906 and Se 0.193, Sp 0.985, PPV 0.646, and NPV 0.896 respectively) when the cut-off point was set at 4 points [14, 19, 21].

The complete description of each reviewed study was summarized in Additional file 4. Its shortened version was displayed in the main text as Table 1. The study performed by Okada et al. (2020) is divided into two parts due to its methodology, which distinguished the development and validation cohort in the TiPS65 scale creation process [19].

Statistical analysis

A meta-analysis was conducted to assess the pooled effect size of favorable outcomes across 8 studies. The pooled effect size of favorable outcomes was analyzed using a random-effects inverse variance model with Hartung-Knapp adjustment. Forest plots were constructed to display probabilities with 95% confidence intervals (95% CI) for individual studies as well as the meta-analytic averages (Figs. 2, 3, 4, and 5).

The percentage of male patients showed a pooled effect size of 78.5%, highlighting the proportion of males in the patient population. Shockable rhythm demonstrated a pooled effect size of 56.1%, indicating the prevalence of this condition. Lastly, favorable outcomes had a pooled effect size of 14.6%, illustrating the overall proportion of favorable outcomes observed.

The combined estimate of the proportion of favorable outcomes across all included studies was 14.6%. This indicates that, on average, 14.6% of patients experienced favorable outcomes. The 95% confidence interval for the pooled effect size ranged from 12.50 to 16.90%. This suggests that the true proportion of favorable outcomes is likely to lie within this range, although the relatively wide interval reflects some uncertainty around the precise pooled effect size. Heterogeneity among the studies was significant, as assessed by Cochran's Q test ($Q = 153.73$, $p < 0.001$). The heterogeneity variance (τ^2) was calculated, and Higgins & Thompson's I^2 statistic was 94.80%, indicating that 94.80% of the observed variation in effect sizes is attributable to differences between studies rather than random chance. Funnel plots were utilized to assess publication bias (Fig. 6).

Several factors contributed to the observed heterogeneity, impacting the interpretation of pooled effect estimates. A major source of heterogeneity was differences in patient demographics, particularly age and sex distribution. The pooled proportion of male patients (78.5%) suggests a substantial gender imbalance, potentially influencing outcome variability. Additionally, the prevalence of shockable rhythm, a key prognostic factor, varied across studies, further complicating cross-study comparisons.

Variability in study design also contributed to heterogeneity. Differences in follow-up duration, outcome definitions, and inclusion criteria resulted in inconsistent effect sizes. Some studies employed stringent selection criteria, focusing on specific subpopulations, whereas

Table 1 The summary of reviewed studies' characteristics

Ref	Inclusion criteria	Exclusion criteria	Number of patients	Location of cardiac arrest	Survival rate [%] [1]At discharge from hospital [2]After 30 days	Percentage of patients with a favorable outcome [%] assessed with Cerebral Performance Categories scale [1]At discharge from hospital [2]After 30 days	Examined factors
[17]	• witnessed, refractory OHCA or IHCA • patients hospitalized between January 2007 and December 2016	• cardiogenic shock after cardiac arrest receiving ECLS without cardiac massage • OHCA due to hypothermia (< 32 °C)	131	IHCA and OHCA	10.4[1]	6.4[1]	• age • sex • low-flow time > 30 min • pH • shockable rhythm
[18]	• OHCA • patients hospitalized between January 2006 and May 2019 • ≥ 18 years old	• eCPR performed in another institution • unwitnessed CA • incomplete follow-up data	136	OHCA	36.8[1]	25.7[1]	• hypoxic brain injury on CT • age • age > 75 years old • Charlson's comorbidity index • sex • low-flow time • low-flow time > 60 min • ECMO to CT time • dialysis • initial serum creatinine • initial eGFR • initial lactate level
[22]	• patients hospitalized between May 2004 and December 2018 • ≥ 18 years old	• lack of liver function laboratory data	365	IHCA and OHCA	45.2[2]	32.9[1]	• presence of hypoxic hepatitis Definition: increased > 20 times upper the normal range ALT or AST serum level (ALT > 820 IU/l, AST > 800 IU/l) occurring from day 0 to day 2

Table 1 (continued)

Ref	Inclusion criteria	Exclusion criteria	Number of patients	Location of cardiac arrest	Survival rate [%] [1]At discharge from hospital [2]After 30 days	Percentage of patients with a favorable outcome [%] assessed with Cerebral Performance Categories scale [1]At discharge from hospital [2]After 30 days	Examined factors
[19]	• patients hospitalized between June 2014 and December 2017 (JAAM-OHCA registry) • ≥ 18 years old • shockable rhythm (VF or pVT)	• traumatic cause of CA • no resuscitation attempt in hospital • DNR order • patients transported to the participating hospitals after receiving any treatment at other hospitals • ROSC at hospital arrival • no pre-hospital data	Development cohort: 458	OHCA	-	Development cohort: 12.4[2]	• age 18–64 / ≥ 75 years old • age 65–74 / ≥ 75 years old • witnessed CA • bystander CPR • shockable initial rhythm • shockable rhythm on hospital arrival • time from call to hospital arrival ≤ 25 / > 25 min • time from call to hospital arrival ≤ 30 / > 30 min • time from call to hospital arrival ≤ 35 / > 35 min • initial pH on hospital arrival ≥ 7.0 / < 7.0 • initial pH on hospital arrival ≥ 6.9 / < 6.9 • initial pH on hospital arrival ≥ 6.8 / < 6.8
			Validation cohort: 458			Validation cohort: 12.4[2] TiPS65 score = 0: 1.6 TiPS65 score = 1: 4.4 TiPS65 score = 2: 12.5 TiPS65 score = 3–4: 30.8	TiPS65 score values*: • 1 point • 2 points • 3 points • 4 points *1 point for each: time from call to hospital ≤ 25 min; initial pH on hospital arrival ≥ 7.0; shockable rhythm on hospital arrival; < 65 years old

Table 1 (continued)

Ref	Inclusion criteria	Exclusion criteria	Number of patients	Location of cardiac arrest	Survival rate [%] [1]At discharge from hospital [2]After 30 days	Percentage of patients with a favorable outcome [%] assessed with Cerebral Performance Categories scale [1]At discharge from hospital [2]After 30 days	Examined factors
[23]	• ≥ 18 years old • refractory CA (lack of ROSC after 20–30 min of conventional CPR)	• CA caused by trauma, severe hypothermia (< 32 °C) • cardiogenic shock after ROSC • pregnancy	434	OHCA	15.9[2]	14.5[2]	Sign of life before or throughout CPR: • gasping (any abnormal breathing pattern) • pupillary light reaction (presence or recovery of any pupillary response assessed visually by pen light examination by a physician, other than bilateral non-reactive dilated pupils) • increased level of consciousness (spontaneous eye opening, increased jaw tone, swallowing, speech, or other body movement) • any sign of life before or throughout CPR
[24]	• patients hospitalized between January 2013 and December 2018 (SAVE-J II registry) • ≥ 18 years old	• patients transferred from another hospital • sustained ROSC when ECMO was initiated • non-cardiac etiology of CA such as acute aortic syndromes, hypothermia, primary cerebral disorders, infection, drug intoxication, trauma, suffocation, drowning • hospital arrival to ECMO initiation time > 60 min • missing data on transient ROSC, timing of ROSC, CA to ECMO initiation time interval, and outcomes	1501	OHCA	29.0[1]	14.7	• presence and timing of transient ROSC Definition: any palpable pulse or measurable blood pressure ≥ 1 min before ECMO initiation either before or after hospital arrival

Table 1 (continued)

Ref	Inclusion criteria	Exclusion criteria	Number of patients	Location of cardiac arrest	Survival rate [%] [1]At discharge from hospital [2]After 30 days	Percentage of patients with a favorable outcome [%] assessed with Cerebral Performance Categories scale [1]At discharge from hospital [2]After 30 days	Examined factors
[14]	• patients hospitalized between January 2018 and December 2019 (JAAM-OHCA registry) • ≥ 18 years old • shockable rhythm (VF or pVT confirmed by paramedics at the scene or at hospital arrival, defibrillated by bystander with AED or by paramedics before hospital arrival)	• traumatic cause of CA • no resuscitation attempt in hospital • DNR order • patients transported to the participating hospitals after receiving any treatment at other hospitals • ROSC at hospital arrival • no pre-hospital data	590	OHCA	26.0[2]	Total: 10.8[2] TiPS65 score = 0: 0.0 TiPS65 score = 1: 3.1 TiPS65 score = 2: 12.2 TiPS65 score = 3: 18.2 TiPS65 score = 4: 42.3	TiPS65 score cut-off values*: • > 0 points • > 1 point • > 2 points • > 3 points *1 point for each: time from call to hospital ≤ 25 min; initial pH on hospital arrival ≥ 7.0; shockable rhythm on hospital arrival; < 65 years old
[21]	• patients hospitalized between June 2014 and December 2021 (JAAM-OHCA registry) • ≥ 18 years old • non-shockable initial rhythm	• traumatic cause of CA • not in CA at the initial contact by EMS • patients who were not resuscitated by paramedics • no resuscitation attempt in hospital • ROSC at hospital arrival • no pre-hospital data	370	OHCA	11.1[2]	Total: 4.1[2] TiPS65 score = 0: 5.2 TiPS65 score = 1: 4.2 TiPS65 score = 2: 0.9 TiPS65 score = ≥ 3: 11.4	TiPS65 score elements: • time from call to hospital ≤ 25 min • initial pH on hospital arrival ≥ 7.0 • shockable rhythm on hospital arrival • < 65 years old
[25]	• patients hospitalized between January 2013 and December 2018 (SAVE-J II registry) • ≥ 18 years old	• implementation of ECMO after admission to ICU • ECMO withdrawn after cannulation because of ROSC • ROSC on hospital arrival or at ECMO initiation • CA started in an ambulance or after arriving at the hospital • unknown CA location • patients transferred from another hospital	1744	OHCA	25.0[1]	13.0[1]	• location of OHCA (residential vs. public)

Table 1 (continued)

Ref	Inclusion criteria	Exclusion criteria	Number of patients	Location of cardiac arrest	Survival rate [%] [1]At discharge from hospital [2]After 30 days	Percentage of patients with a favorable outcome [%] assessed with Cerebral Performance Categories scale [1]At discharge from hospital [2]After 30 days	Examined factors
[20]	• patients hospitalized between January 2013 and December 2018 (SAVE-J II registry) • ≥ 18 years old	• implementation of ECMO after admission to ICU • all cases with ROSC • ECMO withdrawn after cannulation because of ROSC • patients transferred from another hospital • unknown outcome	1781	OHCA	24.5[1]	12.7[1]	• age • sex • witnessed CA • bystander CPR • initial cardiac rhythm at the scene • pre-hospital intervention (defibrillation, adrenaline administration) • initial cardiac rhythm on hospital arrival • ambulance call to hospital arrival time • hospital arrival to ECMO time • ambulance call to ECMO time • CA to ECMO interval • emergency coronary angiograph • percutaneous coronary intervention • Intra-aortic balloon pump • CA etiology (cardiac causes, acute aortic dissection/aneurysm, pulmonary embolism, primary cerebral disorders, infections, other medical causes, accidental hypothermia, poisoning, trauma, suffocation, other nonmedical causes)

Factors that showed statistically significant correlation with neurological outcome were underlined

AED automated external defibrillator; *ALT* alanine aminotransferase; *AST* aspartate aminotransferase; *CA* cardiac arrest; *CPR* cardiopulmonary resuscitation; *CT* computed tomography; *DNR* do not resuscitate; *ECMO* extracorporeal membrane oxygenation; *eCPR* extracorporeal cardiopulmonary resuscitation; *eGFR* estimated glomerular filtration rate; *EMS* emergency medical service; *ICU* intensive care unit; *IHCA* in-hospital cardiac arrest; *OHCA* out-of-hospital cardiac arrest; *pVT* pulseless ventricular tachycardia; *ROSC* return of spontaneous circulation; *VF* ventricular fibrillation

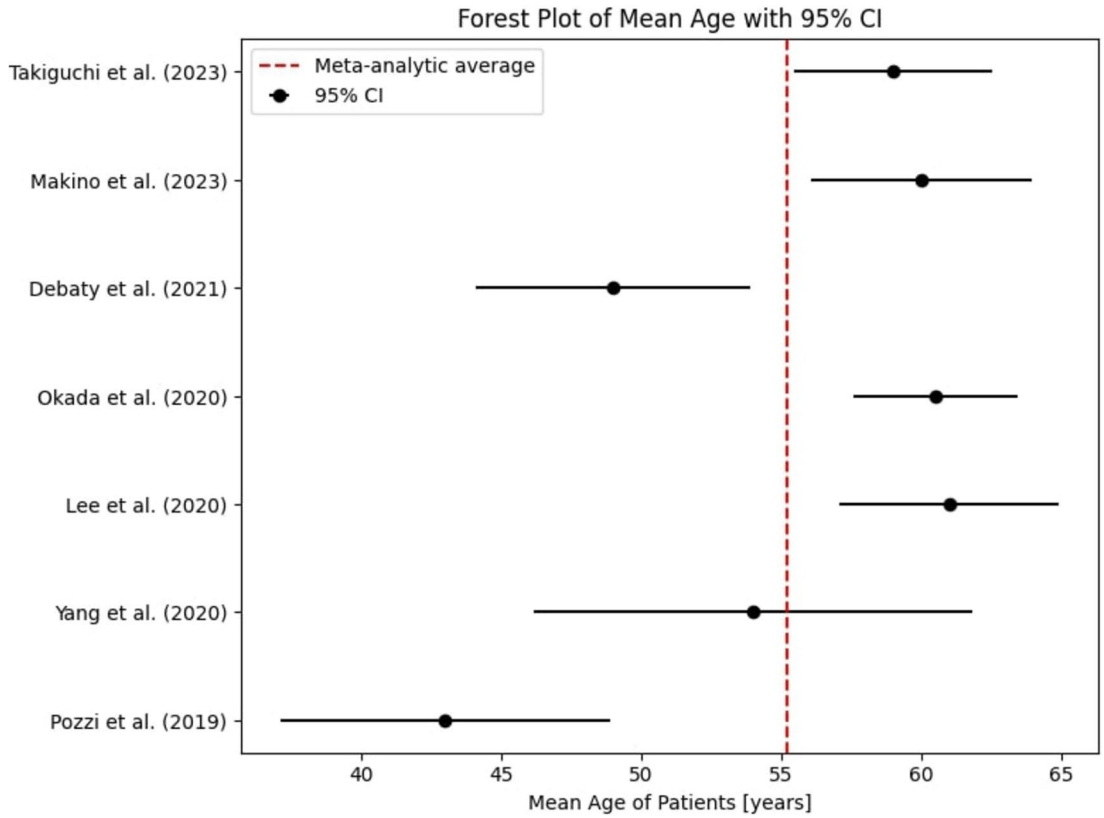

Fig. 2 Forest plot of mean age. This forest plot displays the mean age of patients across the studies included in the systematic review. Each horizontal line represents the 95% confidence interval (CI) for the mean age in each study, whereas the square markers indicate the pooled estimate of the mean age for each study. The plot shows variability in the age distribution across studies, highlighting how age might influence neurological outcomes after eCPR. The overall estimate is provided as a combined measure across studies

others had broader inclusion criteria, leading to a more heterogeneous patient pool. These discrepancies affected the comparability of findings and introduced variability in treatment response.

Furthermore, differences in healthcare settings and treatment protocols influenced observed outcomes. Variations in post-resuscitation care, including the use of targeted temperature management and extracorporeal life support, may have contributed to discrepancies in survival and neurological recovery. Additionally, differences in emergency medical services, hospital resources, and regional clinical practices likely played a role in the heterogeneity of treatment effects.

Given the small number of studies, Peters' linear regression test for funnel plot asymmetry was not performed. Due to the magnitude of heterogeneity, further data synthesis was discontinued. The subgroup analysis was discussed in the discussion section.

The forest plot illustrates the effect sizes of all included studies in Fig. 7. The subgroup analysis based on age groups reveals varying pooled effect sizes and variances across different cohorts. Patients aged less than 50 years exhibited a pooled effect size of 0.135 (variance: 0.025), indicating a modest proportion of favorable treatment outcomes. In contrast, patients aged 50–60 years showed a slightly lower pooled effect size of 0.130 (variance: 0.041), suggesting a more variable benefit from the treatment within this age bracket. Those aged 60 years and older demonstrated the highest pooled effect size at 0.215 (variance: 0.060), indicating a significant proportion experiencing favorable outcomes, though with considerable variability.

These subgroup differences have important clinical implications. The lower pooled effect size observed in patients younger than 50 years suggests that this group may have unique physiological or pathological factors influencing their response to treatment. One possible explanation is that younger patients may experience more severe primary insults, such as traumatic cardiac arrests or cardiac arrests due to underlying structural heart disease, which could reduce their likelihood of achieving favorable outcomes despite aggressive treatment. Additionally, their relatively lower burden of

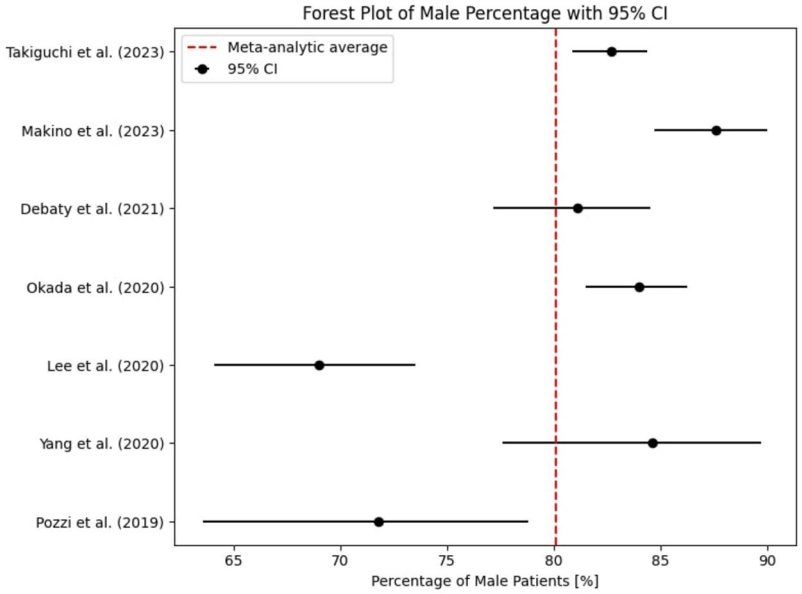

Fig. 3 Forest plot of male percentage. This forest plot illustrates the percentage of male patients included in each study. The percentage of male patients is plotted on the *x*-axis, and each study's estimate is represented by a square marker with corresponding 95% CI bars. The figure shows variation in male representation across studies, which could potentially impact the interpretation of gender-related effects on neurological outcomes post-eCPR

chronic comorbidities may influence the aggressiveness of treatment strategies applied in this cohort.

For patients aged 50–60 years, the slight decrease in pooled effect size (0.130) compared to the younger group, coupled with increased variance (0.041), suggests a more heterogeneous response to treatment. This variability may be attributed to the presence of age-related risk factors such as hypertension, diabetes, and cardiovascular disease, which influence both the baseline prognosis and response to interventions. While some patients in this group may retain sufficient physiological resilience to benefit from treatment, others may have a higher burden of comorbidities that negatively impact their recovery potential. The wider variance highlights the need for individualized clinical decision-making within this age group, with careful consideration of preexisting health conditions and functional status.

In contrast, patients aged 60 years and older demonstrated the highest pooled effect size (0.215), indicating a greater proportion of favorable outcomes. This finding may be counterintuitive, as advanced age is often associated with poorer prognoses. However, this could be explained by the fact that older patients are more likely to experience in-hospital cardiac arrests, where immediate medical intervention and standardized post-resuscitation care protocols may contribute to improved survival rates. Furthermore, the higher pooled effect size in this group may reflect a selection bias, where older patients who survived the initial event and were included in the studies had inherently better health statuses than the general elderly population.

However, the considerable variance observed in this group (0.060) suggests that outcomes are highly variable, likely influenced by factors such as frailty, cognitive function, and preexisting do-not-resuscitate (DNR) orders. While some older patients may benefit significantly from treatment, others may have poorer functional recovery due to preexisting conditions. The observed variability highlights the importance of personalized treatment approaches, with decisions guided by comprehensive geriatric assessments rather than age alone.

Overall, these findings suggest that age is an important factor in predicting treatment outcomes, but it should not be considered in isolation. The variability observed within each age group underscores the need for individualized approaches to patient care. Clinicians should integrate age-specific risk factors, comorbidities, and patient preferences when making treatment decisions. Additionally, future research should focus on refining prognostic models that incorporate age-related markers to improve risk stratification and optimize treatment strategies across different age cohorts.

The variance values reflect varying levels of consistency in treatment responses across studies within each age subgroup, with younger patients showing the least variability and older patients showing moderate

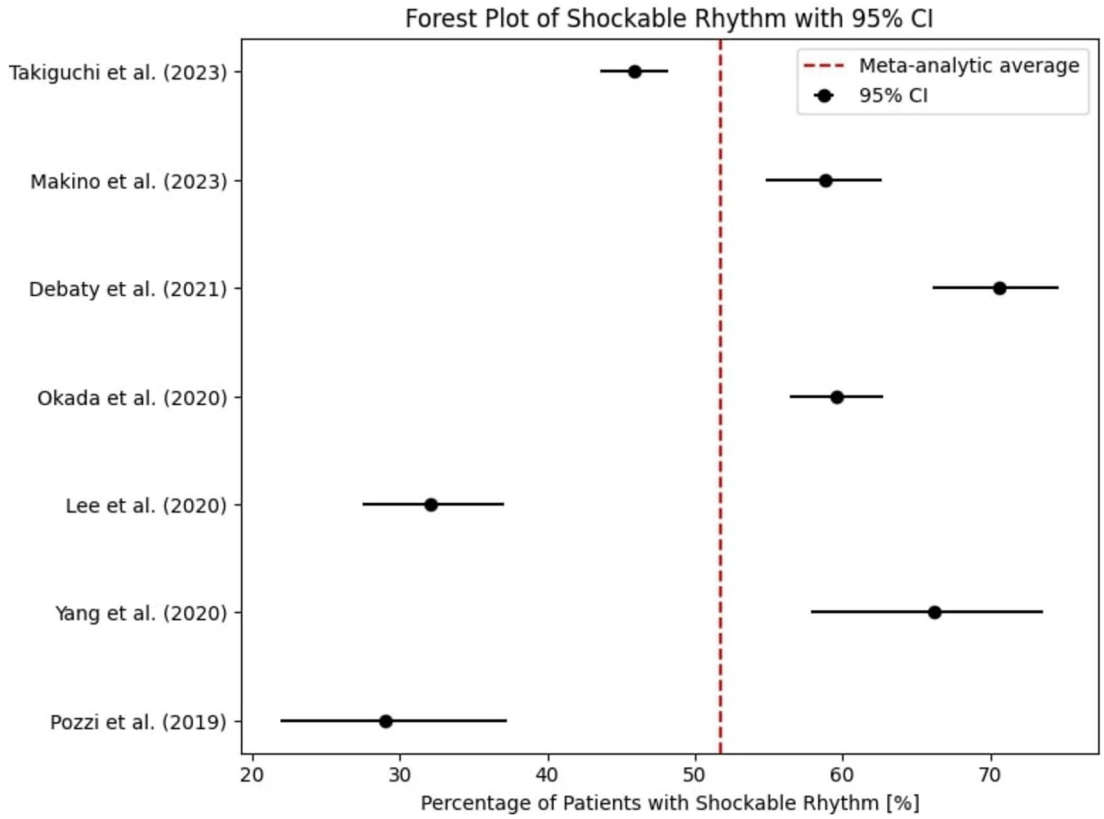

Fig. 4 Forest plot of shockable rhythm. This forest plot presents the proportion of patients in each study who experienced a shockable rhythm during their cardiac arrest event. The *x*-axis represents the percentage of patients with a shockable rhythm, with the squares indicating study-specific estimates and the CI bars representing the uncertainty around each estimate. A trend of variation in the proportion of patients with shockable rhythm is observed across studies, suggesting its potential as a predictive factor for neurological outcomes

consistency. These findings suggest that treatment efficacy may increase with age, highlighting the need for age-specific considerations in clinical management and further investigation into age-related treatment responses.

Bias assessment

Bias assessment was done using the ROBINS—I tool for non-randomized trials. The bias assessment of the included studies revealed that two studies had moderate overall bias primarily due to potential confounding and missing data risks [17, 18]. In contrast, eight studies exhibited serious overall bias, driven mainly by high risks associated with confounding and missing data [14, 19–25]. Despite these issues, all studies maintained low risk in the classification of interventions, measurement of outcomes, and reporting of results, indicating strong methodological approaches in these domains. Overall bias assessment with described domain titles is summarized in Figs. 8 and 9.

Discussion

The use of ECMO in cardiac arrest treatment was first proposed almost 60 years ago [26]. During this period, plenty of studies have been comparing eCPR to CPR; nevertheless, due to the lack of randomized controlled trials on large populations and following meta-analyses, its utility remains uncertain. The available data suggest a significantly higher incidence of survival with favorable neurological outcomes in short-term observation; however, less frequently described results of long-term follow-up are ambiguous [27, 28]. The promising outcome of eCPR application is even more encouraging when it is combined with supplementary interventions and strict monitoring. The research performed by Trummer et al. showed that the addition of cannulation at the scene in out-of-hospital cardiac arrest cases and real-time monitoring of temperature, hemodynamic, and metabolic parameters with their following adjustment to hypothermia-supported eCPR leads to a rarely observed percentage of favorable outcome (41% and 28% for in-hospital and out-of-hospital cardiac arrest

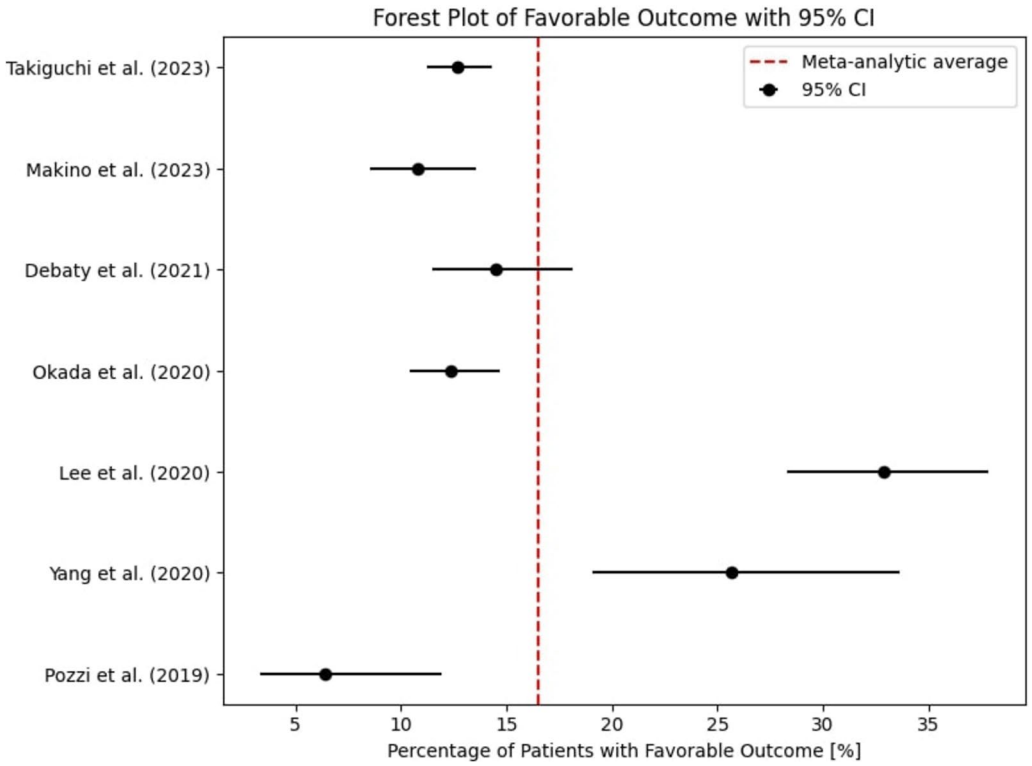

Fig. 5 Forest plot of favorable outcome. This forest plot shows the proportion of patients achieving a favorable neurological outcome following eCPR, as defined by each study. Each study's estimate of the proportion with favorable outcomes is depicted as a square with the corresponding 95% CI. The figure highlights the variability in the reported rates of favorable outcomes, which can be attributed to differences in patient populations, eCPR protocols, and outcome definitions across studies

after 3 months, respectively) [29]. It suggests there is still a potential for therapy improvement, which can be achieved via a multidirectional approach. An adequate example to confirm this statement is a study by Yannopoulos et al. aimed at refractory OHCA patients presenting with an initial shockable rhythm. Due to the high incidence of coronary artery disease in the described population, the research team created a conduct protocol involving the use of Lund University Cardiopulmonary Assist System (LUCAS) device and impedance threshold device, ECMO with following therapeutic hypothermia and early coronary angiography with percutaneous coronary intervention performance if necessary. Its application contributed to a 50% survival rate with favorable neurological outcomes assessed at discharge from the hospital and maintained in 1-month follow-up [30]. The presented data support the conclusions regarding the key role of therapy adjustment based on the analysis of the clinical situation. For this reason, it is crucial to determine reliable criteria for treatment implementation and termination based on patient and condition characteristics. This approach aims at avoiding premature termination or prolonged continuation both having harmful impact on patients [31]. To decide which patients can benefit from each conduct we try to assess the feasibility of survival with favorable neurological outcomes. Due to the multifaceted nature of cardiac arrest, resuscitation, and their subsequent implications, it is a challenging process that requires a wide range evaluation of existing correlations to establish clinical value [32–34]. The results of this systematic review provide critical insights into the factors influencing neurological outcomes following extracorporeal cardiopulmonary resuscitation.

One of the most consistently reported predictors of favorable neurological outcomes was the presence of a shockable rhythm at the time of eCPR initiation or upon hospital arrival. The association between shockable rhythms and better outcomes is well-supported by existing literature, which attributes this to the generally more favorable response to defibrillation and the likelihood of a less prolonged no-flow state [35, 36]. However, the lack of consensus across all studies highlights the complexity of this predictor and suggests that shockable rhythm alone may not be sufficient to determine outcomes without considering other factors.

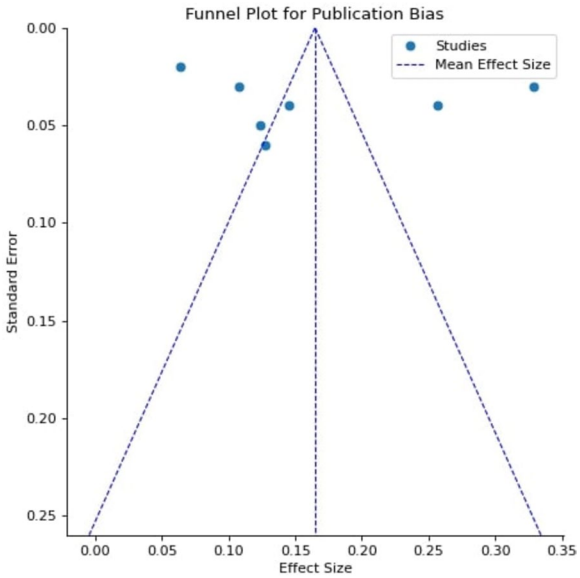

Fig. 6 Funnel plot for publication bias. This funnel plot visually assesses the potential presence of publication bias in the included studies. The plot represents study effect sizes on the *x*-axis and their corresponding standard errors on the *y*-axis. In an ideal scenario without bias, the studies should be symmetrically distributed around the combined effect size estimate. The figure shows the distribution of studies, with any asymmetry potentially suggesting publication bias, where studies with significant findings are more likely to be published than those with null results

Age also emerged as a significant predictor, with younger patients (< 65 years) generally showing better neurological recovery. This could be attributed to the greater physiological resilience of younger individuals and the lower likelihood of comorbidities that could complicate recovery [37]. However, the absence of significant findings in some studies underscores the need for cautious interpretation, as age-related outcomes may be influenced by other variables such as pre-existing health conditions or the quality of immediate post-resuscitation care.

Other factors, such as initial pH upon hospital arrival and the presence of hypoxic brain injury on computed tomography scans, demonstrated variable impacts on neurological outcomes. The findings suggest that while certain laboratory and imaging parameters can offer prognostic value, their reliability may be contingent on the timing of assessment and the specific clinical context [38].

The review identified the TiPS65 scale as a promising tool for predicting neurological outcomes post-eCPR. With a reported accuracy of approximately 88% when applied with a cut-off of 4 points, this scale could serve as a valuable adjunct in clinical decision-making [21]. However, given that the scale's validation is limited to a few studies, further research is necessary to establish its generalizability across diverse populations and settings.

Limitations

This systematic review of neurological outcome predictors after extracorporeal cardiopulmonary resuscitation has several notable limitations that impact the interpretation and generalizability of the findings. One of the most significant limitations is the substantial heterogeneity observed across the included studies, which arises from variations in patient populations, study designs, and eCPR protocols. Differences in inclusion criteria, resuscitation strategies, and post-resuscitation care contribute to variability in reported outcomes, making it difficult to draw definitive conclusions. This heterogeneity reduces the comparability of findings and limits the ability to identify consistent predictors of neurological recovery.

Small sample sizes and short follow-up durations further constrain the statistical power of the meta-analysis, impeding robust assessments of long-term neurological outcomes. Many studies included in this review lack sufficient patient numbers to generate precise effect estimates, increasing the risk of type II errors and reducing the reliability of pooled effect sizes. Additionally, the limited follow-up in most studies prevents comprehensive evaluation of long-term functional and cognitive recovery, which is critical for assessing the true impact of eCPR.

Bias also plays a considerable role in shaping the conclusions of this review. The risk of bias assessment using the ROBINS-I tool revealed moderate to serious risks in multiple domains, particularly regarding confounding and missing data. Many studies did not adequately adjust for confounding variables such as pre-existing comorbidities, duration of cardiac arrest, or severity of neurological injury, all of which could significantly influence outcomes. Missing data on key variables, including detailed neurological assessments and long-term follow-up results, further undermines the robustness of the findings. The presence of such biases reduces confidence in the reported associations between predictors and outcomes, necessitating cautious interpretation of results.

Publication bias and selective outcome reporting may also distort the overall conclusions. Studies with significant or favorable findings are more likely to be published, whereas those with null or negative results may remain unpublished, leading to an overestimation of the strength of associations between predictors and favorable neurological outcomes. The use of funnel plots to assess publication bias was limited by the small number of included studies, which restricts the ability to detect asymmetry and quantify its impact. Additionally, inconsistent outcome definitions and measurement

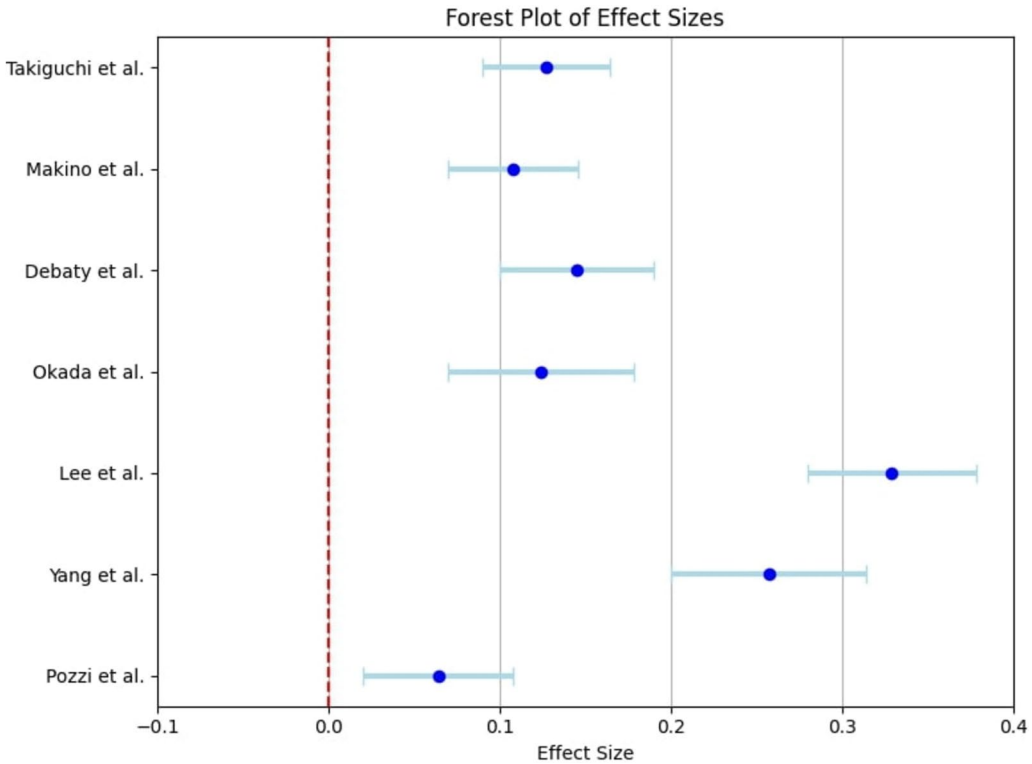

Fig. 7 Forest plot of effect sizes. This forest plot illustrates the effect sizes (e.g., odds ratios, mean differences) from each study included in the systematic review. Each square marker represents the effect size estimate for a specific study, with the corresponding horizontal line showing the 95% CI. The pooled overall effect size, depicted as a diamond, summarizes the magnitude of the relationship between eCPR and neurological outcomes. The plot highlights variability in effect sizes across studies, indicating the need for further research to better understand the impact of eCPR on patient recovery

tools across studies further complicate the synthesis of data. Variability in the assessment of neurological function, ranging from crude survival measures to detailed neurological scores, hinders direct comparisons and weakens the external validity of the findings.

Furthermore, the exclusion criteria applied in this review, which restricted the participant pool to adults and excluded patients receiving concurrent interventions such as target temperature management, limit the generalizability of the results. The omission of these patient groups reduces the applicability of the findings to broader clinical populations, as key treatment interactions and their influence on neurological outcomes remain unexamined.

Data extraction and synthesis posed additional challenges due to inconsistencies in the reporting of key metrics. The lack of standardized reporting across studies led to difficulties in aggregating and comparing findings, introducing potential inaccuracies in the meta-analyses and narrative synthesis. These discrepancies further highlight the urgent need for uniform guidelines in future research on eCPR outcomes.

To address the heterogeneity and biases in eCPR research, future studies should focus on larger, multicenter trials with diverse patient populations to improve statistical power and generalizability. Standardized reporting criteria for neurological outcomes and other key clinical endpoints should be established, enabling better comparisons across studies. Additionally, longer follow-up durations are crucial for assessing long-term neurological recovery, which many current studies overlook. Rigorous adjustment for confounding variables using advanced statistical methods will help reduce bias, whereas broader inclusion criteria will ensure more representative findings. Randomized controlled trials with blinded outcome assessments should be prioritized to minimize bias, and publication of both positive and negative results is essential to mitigate publication bias. Collaborative research networks can also help standardize protocols and enhance study quality. By implementing these strategies, future research will provide more reliable and applicable evidence to guide clinical decisions regarding eCPR.

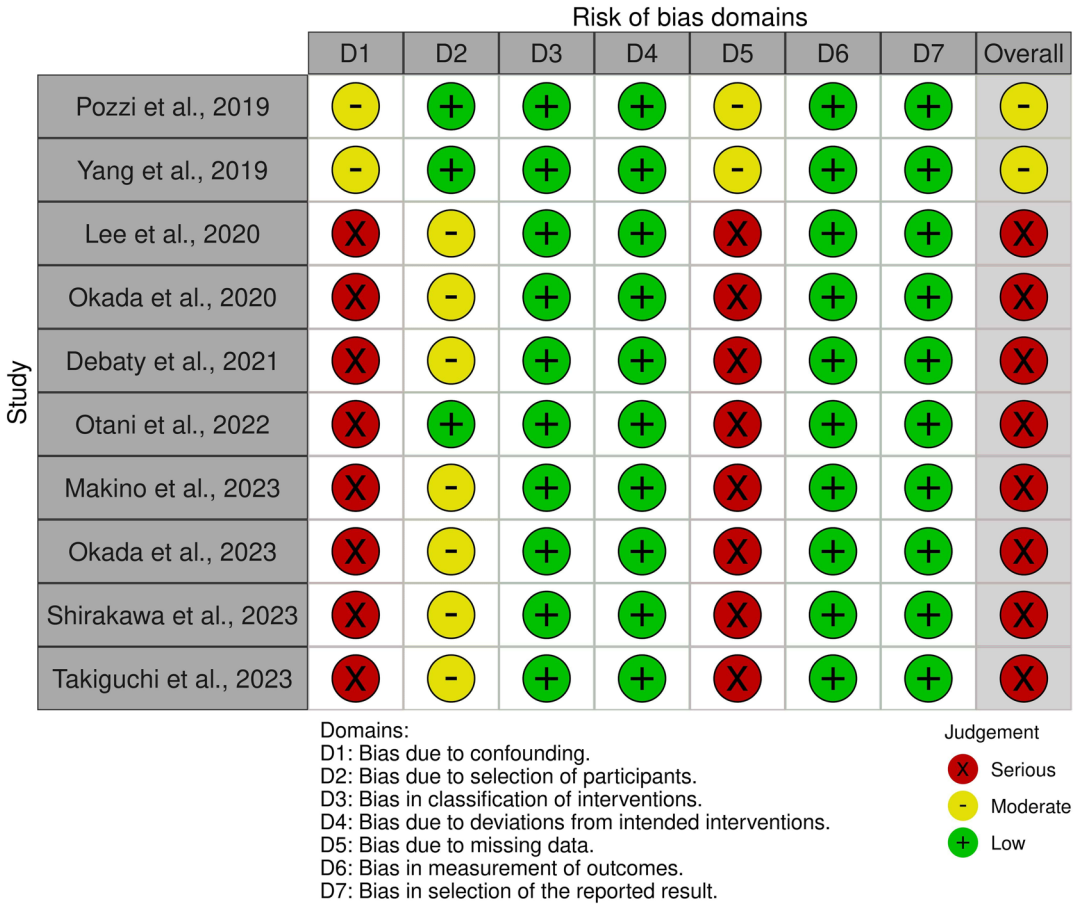

Fig. 8 Bias assessment "traffic light" plots of ROBINS—I protocol. This figure presents a traffic light plot used to assess the risk of bias in the included studies according to the ROBINS-I protocol. Each domain of bias assessment (such as confounding, selection bias, and missing data) is represented as a color-coded square: green indicates low risk of bias, yellow indicates moderate risk, and red indicates high risk. The plot provides a quick visual overview of the bias risks across different studies, helping to evaluate the quality of the evidence included in this review

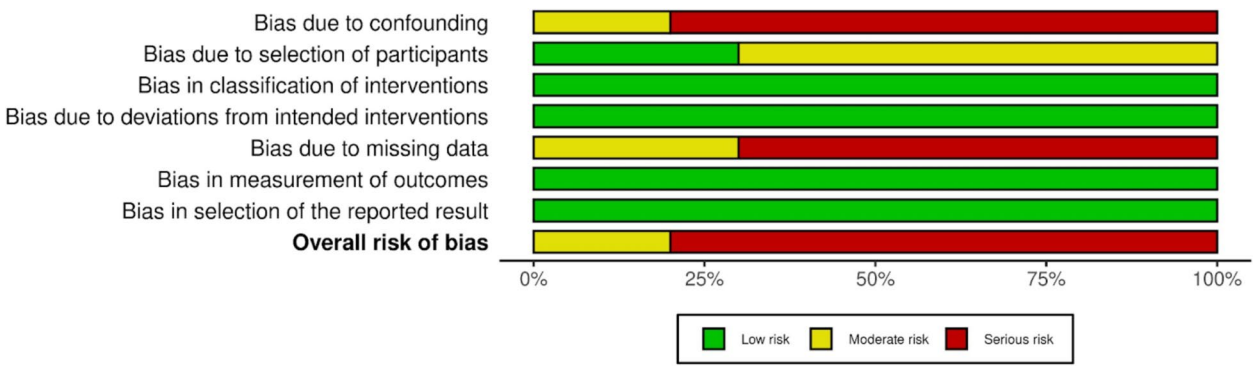

Fig. 9 Summary plot of ROBINS—I protocol for chosen studies. This summary plot presents the overall risk of bias for each study based on the ROBINS-I protocol. Each study is represented by a column, and the overall risk of bias for each study is color-coded according to the ROBINS-I scoring system (green for low risk, yellow for moderate risk, and red for high risk). This plot provides a comprehensive view of the methodological quality of the studies included in the systematic review, allowing for the assessment of how bias might have influenced the findings and conclusions drawn from the data

Given these limitations, the findings of this systematic review should be interpreted with caution. The significant heterogeneity, potential biases, and methodological inconsistencies underscore the necessity for more standardized, large-scale studies with rigorous methodologies. Future research should aim to minimize bias through better study design, ensure comprehensive follow-up to assess long-term neurological outcomes, and adopt standardized reporting criteria to enhance the reliability and applicability of findings in this critical area of clinical research.

Conclusions

The implementation of eCPR is undoubtedly a promising step towards improving post-resuscitation health aftermath. To take full advantage of this therapy, the creation of fair guidelines for eCPR application that will support decision-making in clinical settings seems to be indispensable. The decision about initiation and/or termination should be based on accurately predicted neurological outcomes. This systematic review presents an insight into the current state of knowledge about existing correlations between neurological outcomes and parameters obtained from clinical, laboratory, and imaging data. Due to the insufficient amount of data on this ground, further research ought to focus on the evaluation of previously examined factors in large population-based studies. The emphasis should first be placed on easily and quickly accessible clinical and laboratory data because of their simple applicability in clinical conditions. An investigation of novel factors, especially the ones specific to brain injury however more difficult to perform, may be crucial to find parameters characterized with better predictive value. For this reason, worth considering solutions for accuracy improvement are prognostic scales like the described TiPS65 consisting of several common factors.

Abbreviations

CI	Confidence interval
CPC	Cerebral performance categories scale
CPR	Cardiopulmonary resuscitation
ECMO	Extracorporeal membrane resuscitation
eCPR	Extracorporeal cardiopulmonary resuscitation
GOS	Glasgow outcome scale
mRS	Modified Rankin scale
NNT	Number needed to treat
NPV	Negative predictive value
OR	Odds ratio
PPV	Positive predictive value
RD	Risk difference
RR	Relative risk
Se	Sensitivity
Sp	Specificity

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-025-02818-y.

Additional file 1: PRISMA 2020 checklist.

Additional file 2: ECMO Search protocol for PROSPERO 2024.

Additional file 3: Bias Assessment.

Additional file 4: The detailed summary of reviewed studies characteristics.

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Authors' contributions
DW: conceptualization, methodology, investigation, resources, writing—original draft, and project administration; WZ: formal analysis, investigation, resources, data curation, writing—original draft, and visualization; HC: formal analysis, investigation, resources, data curation, writing—original draft, and visualization; TK: conceptualization, methodology, validation, writing—review and editing, and supervision; MP: validation, writing—review and editing, and supervision. All authors read and approved the final manuscript.

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