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Original Article

Extracorporeal Cardiopulmonary Resuscitation for Out-of-Hospital Cardiac Arrest in Asian Patients: A Meta-Analysis

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Abstract: Objectives: Out-of-hospital cardiac arrest (OHCA) is a major cause of mortality and morbidity, and the survival rates differ across regions. Although numerous studies have investigated the effectiveness of extracorporeal cardiopulmonary resuscitation (ECPR) in Asian populations, few thorough meta-analyses have focused on this population. We aimed to address this research gap through a meta-analysis. Methods: PubMed, the Cochrane Library, Airiti Library, and China National Knowledge Infrastructure (CNKI) were systematically searched from 2000 to 2026 for studies conducted on Asian patients with out-of-hospital cardiac arrest (OHCA) receiving extracorporeal cardiopulmonary resuscitation (ECPR) or conventional cardiopulmonary resuscitation (CCPR). The primary endpoint was mortality (death) at the longest available follow-up. Subgroup analysis was performed based on the initial cardiac rhythm (shockable vs. non-shockable). Quantitative synthesis and meta-analysis were conducted using Review Manager 5.4 (Cochrane organization, London, UK).Results: A total of six cohort studies involving 158,235 patients were included, comprising three retrospective cohort studies and three prospective cohort studies. ECPR was associated with a significantly lower risk of death compared with CCPR (RR = 0.86, 95% CI: 0.81–0.91, $p < 0.00001$), indicating a 14% reduction in mortality risk. In the subgroup analysis, ECPR demonstrated a significant survival benefit in patients with initial shockable rhythm (RR = 0.90, 95% CI: 0.86–0.94, $p < 0.00001$) with zero heterogeneity ($I^2 = 0\%$), whereas no significant benefit was observed in the non-shockable subgroup (RR = 0.97, 95% CI: 0.84–1.12, $p = 0.65$). Conclusions: ECPR appears to improve survival-to-discharge in selected Asian patients

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with out-of-hospital cardiac arrest. However, the findings suggest that early initiation of ECPR and careful patient selection are crucial to maximizing its benefits. Further high-quality randomized controlled trials are warranted to validate these results and optimize clinical implementation strategies.

Keywords: Extracorporeal Membrane Oxygenation; Out-of-hospital cardiac arrest; Meta-analysis; East Asian.

1. Introduction

Out-of-hospital cardiac arrest (OHCA) remains a significant public health issue globally and accounts for a large proportion of sudden cardiac deaths. The incidence of OHCA varies widely. Moreover, the survival rates of individuals treated using conventional resuscitation techniques differ by region, and are influenced by factors such as the location of the arrest, time to resuscitation, and underlying health conditions [1-4]. Among patients who suffer OHCA, 6% to 22% are likely to survive with a positive neurological result [5]. This highlights the need for more effective interventions during the initial phases of cardiac arrest, particularly when conventional methods fail to achieve sustained return of spontaneous circulation (ROSC) [6].

Extracorporeal cardiopulmonary resuscitation (ECPR) has become an effective approach for OHCA, especially when traditional resuscitation fails. ECPR involves resuscitation using extracorporeal membrane oxygenation (ECMO), which offers a potential benefit by providing circulatory and respiratory support while reversible causes of cardiac arrest are addressed. The technique has been shown to improve outcomes for patients who experience refractory cardiac arrest; however, the implementation of ECMO requires specialized equipment, trained personnel, and a well-coordinated healthcare system [7].

Since its widespread adoption in clinical practice in East Asia, the use of ECPR has been the subject of numerous studies. The application of ECPR has been demonstrated to potentially improve survival and neurological outcomes compared to conventional CPR (CCPR) in East Asia [8, 9]. Research also indicates that ECPR may reduce reperfusion injury and secondary brain damage, which are common complications following conventional resuscitation [10, 11]. However, challenges remain regarding the generalizability of ECPR efficacy across different regions, as previous meta-analyses have predominantly aggregated data from Western populations and rarely focused on Asian cohorts [12]. To address this regional research gap, we conducted a meta-analysis of observational studies involving Asian patients with OHCA, comparing the overall survival impact of ECPR versus CCPR.

2. Materials and Methods

2.1. Selection Criteria and Eligibility

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, this study established eligibility through the PICO framework: the population (P) comprised adults experiencing OHCA; the intervention (I) was extracorporeal cardiopulmonary resuscitation (ECPR); the comparator (C) was conventional cardiopulmonary resuscitation (CCPR); and the primary clinical endpoint (O) was the mortality rate. To ensure the inclusion of high-quality, vetted evidence, the analysis was restricted to peer-reviewed original research published between 2000 and 2026. Grey literature, such as conference abstracts and unpublished manuscripts, was excluded to maintain methodological integrity.

2.2. Data Sources and Search Strategy

A systematic and comprehensive literature search was executed across four major electronic databases including PubMed, the Cochrane

Library, China National Knowledge Infrastructure (CNKI), and Airiti Library, covering studies published from January 2000 to March 2026. The retrieval process utilized a strategic combination of Medical Subject Headings (MeSH), database-specific subject terms, and free-text keywords, employing Boolean operators such as AND and OR to optimize search sensitivity and specificity.

The search strategy was constructed around three core components including (1) Out-of-hospital cardiac arrest (OHCA), (2) Extracorporeal cardiopulmonary resuscitation (ECPR) or extracorporeal membrane oxygenation (ECMO), and (3) Asian populations or specific regional identifiers. For regional databases, translated search terms for ECPR, ECMO, and OHCA were employed to capture relevant studies. Additionally, the reference lists of all identified articles and prior systematic reviews were manually audited to identify any additional eligible studies that might have been missed in the initial electronic search.

2.3. Study Selection and Data Extraction

The screening process was conducted systematically to eliminate redundant entries and verify alignment with predefined inclusion criteria. Reviewers initially assessed titles and abstracts independently, followed by an in-depth full-text appraisal to finalize inclusion. Any discrepancies during the selection phase were adjudicated through consensus-based discussions. We utilized a standardized data extraction template to gather essential information, including the primary author, year of publication, study design, cohort size, patient demographics, the timing of ECPR initiation, and relevant clinical outcomes.

2.4. Methodological Quality Assessment

The risk of bias and methodological quality of the included trials were evaluated independently by three reviewers using the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) instrument. This appraisal covered multiple domains, including confounding, participant selection, intervention classification, deviations from intended protocols, missing data, and selective reporting. Following this rigorous evaluation, six studies were identified as meeting the criteria for quantitative synthesis (Figure 1, Table 1) [13-18].

2.5. Statistical Synthesis

Quantitative analysis was performed using Review Manager (RevMan) version 5.4 (Cochrane Collaboration, London, UK). To accommodate potential within-study and between-study variance, we employed a random-effects model to calculate pooled Relative Risks (RR) and their associated 95% confidence intervals (CIs). Statistical significance was established at a p-value < 0.05. Forest plots were generated to provide a visual representation of the effect sizes. Due to substantial clinical and methodological heterogeneity ($I^2 = 77\%$), we conducted a subgroup analysis stratified by the initial cardiac rhythm (shockable vs. non-shockable) using the random-effects model to explore potential sources of this heterogeneity. Available stratified data from Choi et al., (2023) and Okada et al., (2023) were extracted and pooled for this clinical subgroup synthesis.

3. Results

The PRISMA flow chart for the meta-analysis is shown in Figure 1 [19]. A total of six eligible observational studies with 158,235 patients were included in the meta-analysis to evaluate the effectiveness of ECPR in Asian OHCA patients. The methodological quality of the six included studies was evaluated using the Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) tool. Overall, four studies-Maekawa et al., (2013), Kim et al., (2014), Okada et al., (2023), and Choi et al., (2023)-were classified as having a moderate risk of bias. In contrast, two studies, Choi et al., (2016) and Shin et al., (2020), were judged to carry a serious risk of bias (Figure 4) [13-18].

The studies included in the meta-analysis have confidence intervals (CIs) that are relatively narrow and do not overlap 1. To assess the impact of all included studies on the overall meta-analysis results and to enhance the validity of the findings, we performed a comprehensive meta-analysis (Figure 2).

As shown in Figure 2, the mortality rates of the CCPR groups ranged from 83.68% to 96.01%, whereas the mortality rates of the ECPR groups ranged from 66.67% to 88.11%. It should be noted that the crude mortality rates appear higher in the ECPR group in some individual studies, which likely reflects baseline differences in patient severity, as ECPR is typically applied to more critically ill or refractory OHCA patients. Overall, the meta-analysis indicated that ECPR led to significantly higher survival rates compared to the control groups. ECPR was associated with an overall risk ratio (total RR) of 0.86 [95% CI: 0.81–0.91], which indicates that ECPR is associated with a 14% relative reduction in mortality risk compared with CCPR. The fact the 95% CI does not overlap 1 indicates the result is statistically significant ($Z = 5.29$, $P < 0.00001$). Despite variability among individual studies, the weighted pooled analysis demonstrated a consistent survival benefit for ECPR.

While there was significant variation among individual studies, ECPR was associated with better survival outcomes in most studies. More specifically, Choi et al., (2016) and Choi et al., (2023) reported RR values of 0.88 and 0.89, respectively, which suggest that ECPR leads to higher survival rates. Kim et al., (2014) reported an even higher RR of 0.47, which indicates that the ECPR group had a significantly greater probability of surviving than the patients who received CCRP. Maekawa et al., (2013) obtained a moderate RR of 0.73. In the study by Okada et al. (2023), ECPR was associated with higher survival rates in both the shockable (RR = 0.90) and non-shockable (RR = 0.90) subgroups. Similarly, Shin et al., (2020) obtained a RR of 0.78, indicating that the ECPR led to a small benefit.

The I^2 value was 77%, which indicates significant heterogeneity between the studies included in the meta-analysis. Despite this, the significance of the pooled data (RR = 0.86, $P < 0.00001$) support the robustness of the findings of the meta-analysis that ECPR leads to a significantly lower risk of mortality in Asian OHCA patients compared to CCPR.

To systematically address the substantial overall heterogeneity, we conducted a subgroup analysis stratified by the initial cardiac rhythm (Figure 3). In the shockable rhythm subgroup (comprising Choi et al., [2023] and the shockable cohort of Okada et al., [2023]), ECPR was associated with a highly significant 10% relative reduction in hospital mortality compared with CCPR (pooled RR = 0.90, 95% CI: 0.86–0.94, $P < 0.00001$). Notably, statistical heterogeneity within the shockable subgroup was completely resolved ($I^2 = 0\%$, $P = 0.80$), confirming initial rhythm as a primary source of overall heterogeneity. Conversely, in the non-shockable rhythm subgroup (comprising Choi et al., [2023] and the non-shockable cohort of Okada et al., [2023]), no statistically significant difference in mortality was observed between ECPR and CCPR (pooled RR = 0.97, 95% CI: 0.84–1.12, $P = 0.65$), with persistent high heterogeneity ($I^2 = 95\%$, $P < 0.00001$). The test for subgroup differences did not demonstrate a statistically significant difference between the two rhythm strata ($Chi^2 = 0.78$, $df = 1$, $P = 0.38$, $I^2 = 0\%$).

4. Discussion

Our meta-analysis, encompassing over 158,000 Asian patients, provides compelling evidence that ECPR significantly reduces mortality risk by 14% compared to conventional CPR in OHCA cases. This survival advantage is particularly noteworthy within the context of Asian regional healthcare systems, where the integration of advanced life support and specialized resuscitation centers provides a unique landscape for refractory cardiac arrest management.

In the cohort study by Choi et al., (2016), ECPR was not associated with an increase in the rate of survival to discharge with preserved

neurological function (adjusted OR = 0.65; 95% CI: 0.41-1.04). However, that study noted that early initiation of ECPR was positively associated with favorable neurological outcomes in adult patients OHCA with medical causes, which suggests that the timing of initiation of ECPR could influence recovery in specific patient populations [14]. The cohort study by Okada et al. (2023) employed risk-set matching by using time-dependent propensity scores (despite a number of constraints) and observed a higher 30-day survival rates among OHCA patients with initially shockable and non-shockable rhythms. Specifically, the odds ratio for 30-day survival in the ECPR group was 1.76 (95% CI: 1.38–2.25) for patients with shockable rhythms and 5.37 (95% CI: 2.53–11.43) for those with non-shockable rhythms, compared to controls. Additionally, the same study demonstrated that ECPR was linked to favorable neurological outcomes in individuals whose initial rhythms were not shockable (OR = 4.25, 95% CI: 1.43-12.63). However, no such association was observed for patients with initially shockable rhythms (OR = 1.11, 95% CI: 0.82-1.49), which suggests that the efficacy of ECPR may vary depending on the type of rhythm during cardiac arrest [17]. It is important to contextualize these findings within the methodological quality of the evidence; our ROBINS-I assessment identified a serious risk of bias in the study by Choi et al., (2016), particularly regarding confounding and deviations from intended interventions [14]. Such methodological disparities may partially explain the divergence in clinical outcomes reported across these major cohort studies. These findings further support the notion that patient selection plays a crucial role in determining the benefits of ECPR, as some patients may survive due to the intervention but still suffer from severe neurological impairment due to prolonged hypoxic injury before ECPR initiation [20, 21].

Two review articles published in 2025 give substantial evidence for the effectiveness of ECPR in OHCA patients [22, 23]. A meta-analysis of four RCTs found that ECPR enhanced the likelihood of survival with positive neurological outcomes by 72% compared to conventional CPR (OR = 1.72, 95% CI: 1.09-2.70), particularly among patients with initial shockable rhythms (OR = 1.90, 95% CI: 1.16-3.13) [24]. In addition to these findings, a larger meta-analysis of 13 studies and 14 control groups revealed that ECPR significantly reduced overall in-hospital mortality (OR = 0.63, 95% CI: 0.50-0.79), with high certainty of evidence. Specifically, OHCA patients showed a significant reduction in mortality (OR = 0.62, 95% CI: 0.45-0.84) [25]. Our meta-analysis, which primarily focused on Asian patients, also presents a positive stance towards ECPR. These data demonstrate that, despite differences between individual studies, the accumulated evidence eventually supports the survival advantage of ECPR in selected OHCA patients.

Previous meta-analyses have predominantly included data from Western populations and have rarely conducted subgroup analyses specific to Asian patients [23]. Our study, which includes a meta-analysis focused on Asian populations, contributes to closing this information gap. Unlike previous meta-analyses that primarily aggregated Western data, our study specifically focuses on the Asian population, providing a more tailored evidence base for regional healthcare policies [23, 25]. The robust survival benefit observed in our study may be partially attributed to the specific organizational characteristics of Emergency Medical Services (EMS) and the high density of ECMO-capable facilities in several Asian regions. These systemic factors facilitate a more rapid transition from conventional resuscitation to extracorporeal support, which differs from the logistical landscapes analyzed in previous Western-centric meta-analyses [25-27].

The scientific literature supports prioritizing ECPR for younger patients with reversible causes of cardiac arrest and without severe comorbidities, as these individuals have better survival prospects and are more likely to benefit from extracorporeal support [28, 29]. A recent 2025 study demonstrated that increasing age

independently reduces the likelihood of survival after out-of-hospital cardiac arrest treated with ECPR. Moreover, the effective therapeutic window for ECPR initiation was found to be substantially shorter in older patients (less than 21 minutes), whereas younger patients retained survival potential even with delays of up to approximately 73 minutes. These findings highlight the importance of age-tailored and rapid initiation of ECPR to optimize outcomes [30].

ECPR may offer limited benefit and even pose unnecessary risks in older patients, those with multiple organ failure, or individuals with severe underlying conditions that significantly compromise post-recovery quality of life [31]. The combination of a shorter therapeutic window and reduced survival rates with advancing age underscores the need for careful patient selection to avoid futile interventions. [30, 32] This result raises the possibility that ECMO may not consistently have a substantial impact for all patients. Therefore, more accurate patient selection methods must employed for initiation of ECMO, in accordance with the Extracorporeal Life Support Organization's (ELSO) guidelines [33]. The ELSO lists a number of related contraindications that might impact the decision to use ECMO [34]. One crucial factor is whether the patient could achieve sufficient quality of life if they survive and recover. For instance, if recovery would result in severe disability or an inability to live independently, ECMO may not be the best option [35, 36]. It is also important to consider any preexisting diseases that may impact the patient's quality of life, such as frailty, end-stage cancer, or impaired central nervous system function. Moreover, the age and size of the patient need to be considered, as both of these factors influence the success of ECMO [37]. Thus, the decision to apply ECPR should be carefully considered on the basis of our data and prior research, and in accordance with the AHA, ELSO, and expert consensus recommendations [38].

Our performed subgroup analysis successfully identified the initial cardiac rhythm as a major source of overall heterogeneity (Figure 3). When stratified by cardiac rhythm, ECPR demonstrated an exceptionally robust and completely homogeneous survival benefit in patients presenting with shockable rhythms (RR = 0.90, I^2 = 0%). This complete absence of intra-group heterogeneity suggests that patients with refractory ventricular fibrillation or pulseless ventricular tachycardia represent the most consistent and optimal candidates for ECPR across different clinical registries. This is physiologically plausible, as shockable rhythms are highly associated with reversible acute coronary etiologies (e.g., acute myocardial infarction) that can be definitively treated via percutaneous coronary intervention once hemodynamic support is secured by extracorporeal circulation. In contrast, the lack of benefit in the non-shockable subgroup (RR = 0.97, P = 0.65) highlights the potential clinical futility of ECPR in patients presenting with asystole or pulseless electrical activity (PEA). These cases often involve prolonged low-flow or no-flow times, leading to irreversible hypoxic-ischemic brain injury before cannulation can be successfully established. These findings strongly advocate for an initial rhythm-tailored triage strategy when selecting adult OHCA candidates for ECPR initiation in Asian healthcare settings.

In our study, the proportion of male patients was higher than that of female patients. This observation aligns with previous research indicating that OHCA occurs more frequently in men than in women. Potential explanations for this disparity include differences in cardiovascular risk factors, hormonal influences, and variations in bystander response rates between sexes [39]. Understanding these sex-based differences in OHCA incidence may help refine resuscitation strategies and improve patient outcomes [40].

Our meta-analysis highlights the potential survival benefit of ECPR over conventional CPR in Asian OHCA patients. However, appropriate patient selection, timely initiation, and adherence to evidence-based guidelines are essential to maximize outcomes. Future large-scale, multicenter trials are needed to establish

standardized indications and improve the clinical applicability of ECPR.

5. Limitation

Several limitations of this meta-analysis warrant consideration. First, residual confounding in studies utilizing propensity score matching remains a significant concern, as unmeasured variables excluded from these models may influence the observed outcomes. Furthermore, the lack of standardized eligibility criteria for ECPR across institutions introduces inherent selection bias. Additionally, the overall quality of the included studies was variable. Our appraisal using the ROBINS-I tool categorized two of the six studies as having a serious risk of bias, primarily driven by confounding factors and issues in outcome measurement. The significant heterogeneity (I2 = 77%) observed in our results underscores the importance of implementing standardized ECPR protocols across Asian medical centers. This clinical variance likely stems from discrepancies in the definitions of ECPR initiation timing (low-flow time) and differences in the proportion of initially shockable versus non-shockable rhythms across the included cohorts. The presence of these methodological risks suggests that the observed heterogeneity may be attributed to study-level biases rather than purely clinical differences. The inconsistent reporting in the included studies also precluded more granular subgroup or sensitivity analyses beyond the initial cardiac rhythm stratification, further limiting the interpretability of our pooled estimates. Nevertheless, current evidence suggests that ECPR offers a meaningful survival advantage over CCPR for Asian OHCA patients regarding survival to discharge.

6. Conclusion

Our meta-analysis of 158,235 Asian patients provides robust evidence that ECPR significantly reduces the relative risk of mortality by 14% (RR = 0.86) compared to conventional CPR in OHCA cases. These findings fill a critical information gap by focusing specifically on the Asian population, where ECPR adoption is rapidly increasing. However, our results emphasize that ECPR is a high-stakes intervention and should be utilized selectively rather than indiscriminately.

To maximize survival benefits, ECPR prioritization should be directed toward younger patients with reversible etiologies and short downtime, with a focus on rapid therapeutic initiation. Conversely, the potential for futility is high in patients with advanced age or multi-organ failure. Given the substantial heterogeneity and varying methodological quality of current non-randomized evidence, clinical implementation must strictly adhere to established international guidelines, such as those from the AHA and ELSO, to ensure both evidence-based practice and resource efficiency.

Future research, particularly large-scale randomized controlled trials, is essential to refine patient selection criteria. Such research will help transition Asian resuscitation practices from a one-size-fits-all approach toward a precision-based model tailored to individual patient profiles.

7. Figures Legends

Through systematic searches of PubMed (n = 138), the Cochrane Library (n = 65), CNKI (n = 46), and Airiti Library (n = 46), a total of 295 records were identified. After removing five duplicate records, 290 reports were screened by title and abstract, which resulted in the exclusion of 226 records. The eligibility of the remaining 64 full-text publications was evaluated. A total of 58 studies were excluded for specific reasons including non-Asian populations (n = 41), patients not experiencing OHCA (n = 11), irrelevant study designs (n = 2), lack of relevant outcome measures (n = 1), insufficient data regarding ECPR (n = 2), and inclusion of pediatric subjects (n = 1). Ultimately, six studies that met all predefined inclusion criteria were included in the meta-analysis (Figure 1).

Table 1. Summary of included study characteristics

Study	Country	Settings	Study Design	Cardiac Arrest Location	ECPR Patients	CCPR Patients	Mean Age (ECPR)	Mean Age (CCPR)	Male Gender (ECPR)	Male Gender (CCPR)	In-Hospital Mortality (ECPR)	In-Hospital Mortality (CCPR)	Outcomes	Overall Bias (ROBINS-I tool)
Maekawa et al., 2013	Japan	Single-centre	PCS	OHCA	53	109	54 (47-60)	71 (59-80)	44	79	36	102	30-day neurological outcomes	Moderate risk
Kim et al., 2014	Korea	Single-centre	PCS	OHCA	55	444	53 (41-68)	69 (56-77)	41	285	25	426	30-day neurological outcomes	Moderate risk
Choi et al., 2016	Korea	Multi-centre	RCS	OHCA	320	36,227	56 (45-68)	67 (54-77)	258	24,143	263	33903	discharged neurological outcomes	Serious risk
Shin et al., 2020	Korea	Single-centre	RCS	OHCA	30	40	60 ± 9	61 ± 15	25	30	20	34	180-day and 30-day neurological outcomes; 180-day and 30-day survival	Serious risk
Okada et al., 2023 [Shockable]	Japan	Multi-centre	PCS	OHCA	913	913	58.3 ± 14.9	59.0 ± 16.3	784	778	688	764	30-day neurological outcomes; 30-day survival	Moderate risk
Okada et al., 2023 [Nonshockable]	Japan	Multi-centre	PCS	OHCA	370	370	58.7 ± 16.4	57.3 ± 17.9	284	278	326	361	30-day neurological outcomes; 30-day survival	Moderate risk
Choi et al., 2023	Korea	Multi-centre	RCS	OHCA	484	117,907	55.2 ± 14.2	70.1 ± 15.0	396	74611	415	113200	discharged neurological outcomes	Moderate risk

Abbreviations: ECPR: Extracorporeal Cardiopulmonary Resuscitation; CCPR: Conventional Cardiopulmonary Resuscitation; OHCA: Out-of-Hospital Cardiac Arrest; RCS: Retrospective Cohort Study; PCS: Prospective Cohort Study.

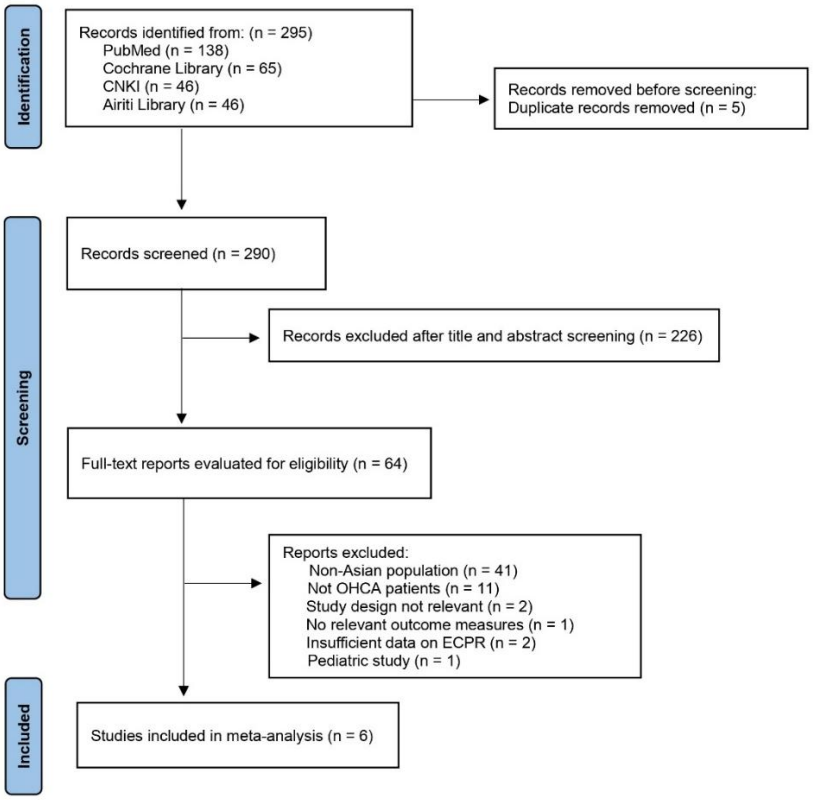


Figure 1. PRISMA flow diagram of study selection for the meta-analysis.

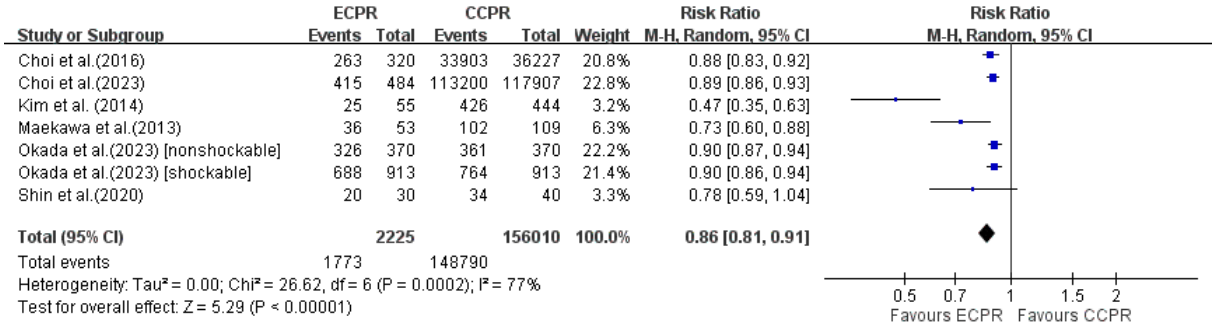


Figure 2. Forest plot depicting mortality outcomes after CPR with or without ECMO (pooled data from all studies).

Abbreviations: CI = confidence interval; event = number of deaths (mortality); total = number of participants at risk; df = degrees of freedom; I^2 = percentage of total variation across the studies due to heterogeneity rather than change; Chi^2 = Chi-squared test; Z = Z-score test. The pooled data shows a significant survival benefit in the experimental group (RR = 0.86, 95% CI: 0.81–0.91, $p < 0.00001$). An RR < 1 indicates a lower risk of mortality in the ECPR group compared with the CCPR group.

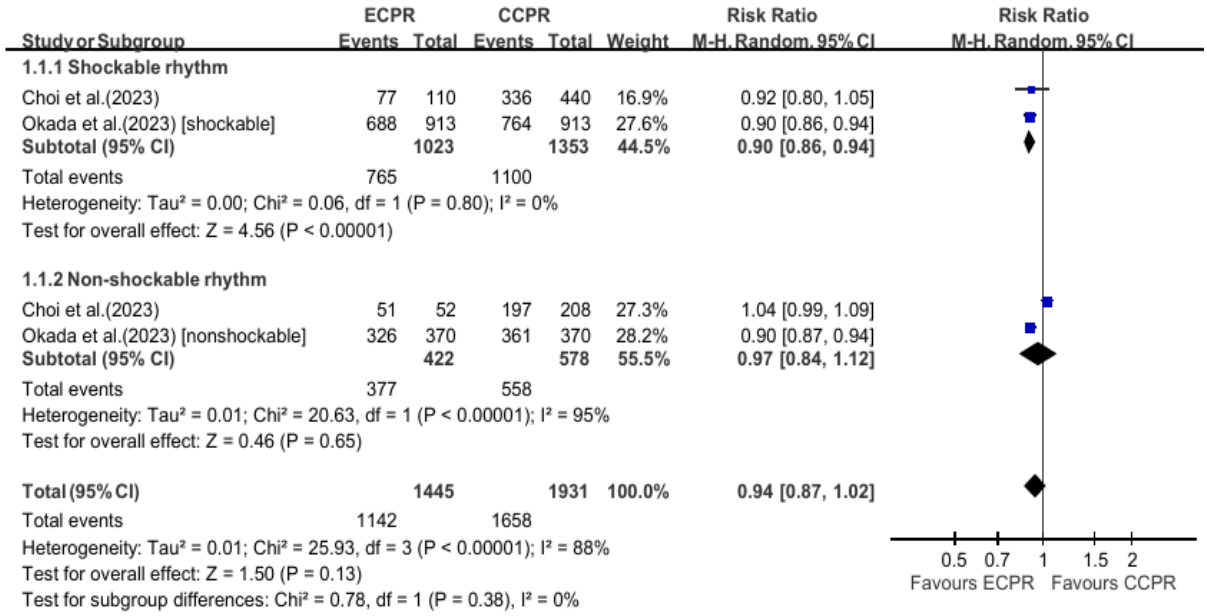


Figure 3. Forest plot of hospital mortality comparing ECPR and CCPR stratified by the initial cardiac rhythm (shockable vs. non-shockable).
Abbreviations: CI = confidence interval; M-H = Mantel-Haenszel method; Random = random-effects model; RR = risk ratio. The pooled data demonstrate a significant mortality reduction for ECPR exclusively in the shockable rhythm subgroup (RR = 0.90, 95% CI: 0.86 – 0.94, P < 0.00001), with a complete resolution of statistical heterogeneity (I^2 = 0%, P = 0.80). Test for subgroup differences: Chi^2 = 0.78, df = 1 (P = 0.38), I^2 = 0%.

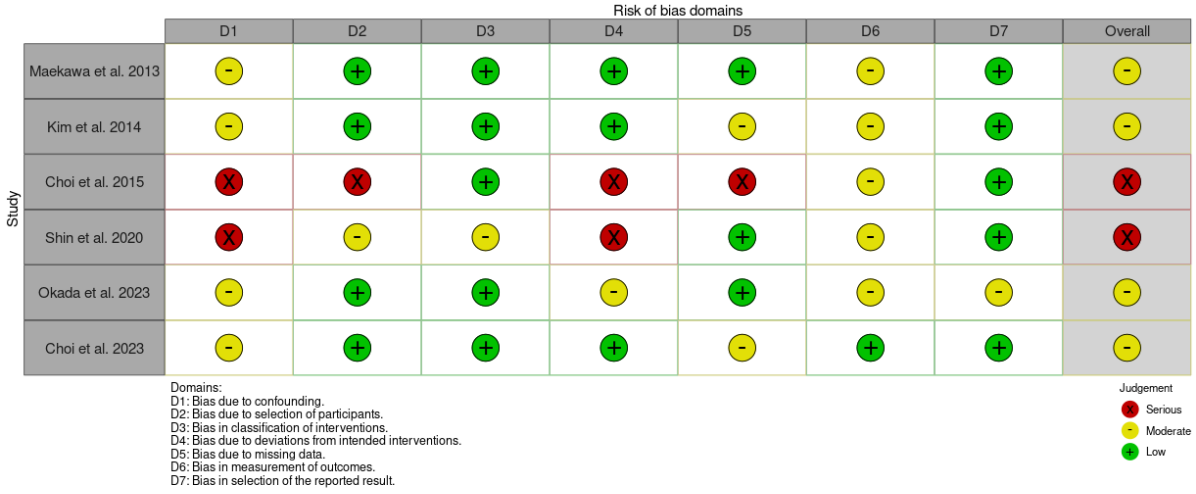


Figure 4. Risk of bias assessment summary for the included non-randomized studies using the ROBINS-I tool.
Abbreviations: D1 = bias due to confounding; D2 = bias in selection of participants; D3 = bias in classification of interventions; D4 = bias due to deviations from intended interventions; D5 = bias due to missing data; D6 = bias in measurement of outcomes; D7 = bias in selection of the reported result; ROBINS-I = Risk Of Bias In Non-randomized Studies - of Interventions.

Conflict of Interest

The authors declare that they have no conflicts of interest related to the research, authorship, or publication of this article.

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Ethical Declarations

As this work is a meta-analysis of previously published and anonymized data, institutional ethics committee approval and informed consent were not required.

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