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REVIEW

Safety and Efficacy of Intra-Osseous versus Intravenous Vascular Access for Out-of-Hospital Cardiac Arrest: A Systematic Review and Meta-Analysis

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Background: The immediate administration of drugs and fluids is critical for successful resuscitation in out-of-hospital cardiac arrest (OHCA). Vascular access selection plays a pivotal role in ensuring timely delivery of therapeutic interventions during OHCA management. This study aims to compare the safety and efficacy of intraosseous (IO) and intravenous (IV) access in OHCA management.

Methods: We conducted a comprehensive search of PubMed, EMbase, Google Scholar, and the Cochrane Library databases to identify studies published up to February 20th, 2025, evaluating IO and IV access in OHCA patients. The outcomes of interest included return of spontaneous circulation (ROSC), survival from hospital admission to discharge, neurological outcome, comorbidities, and access time.

Results: Twenty-three studies, comprising 48945 cases of IO access and 188966 cases of IV access for OHCA management, were included. Overall, the rate of favorable neurological outcome was similar between patients with IO and IV access (odds ratio [OR] = 0.73; 95% confidence interval [CI] = 0.37 to 1.45, I^2=95.3%). IO access was associated with significantly lower odds of shockable rhythms in both adult (OR = 0.77; 95% CI = 0.70 to 0.85, I^2=86%) and pediatric (OR = 0.20; 95% CI = 0.12 to 0.33) patients. Additionally, IO access was linked to a lower rate of ROSC in pediatric OHCA patients (OR = 0.30; 95% CI = 0.21 to 0.42). Prospective studies and those with unadjusted time to intervention analysis demonstrated markedly lower rates of survival at discharge, favorable neurological outcome, and ROSC in the IO group compared to the IV group. It should also be noted that the interpretation of the results should take into account the high heterogeneity and potential biases, despite the corresponding subgroup analyses we conducted.

Conclusion: In OHCA management, IO access may be associated with less favorable outcomes in terms of survival, neurological function, and ROSC compared to IV access. Further research is needed to address limitations and provide more robust evidence regarding the comparative effectiveness of intraosseous and intravenous access in this clinical setting.

Keywords: intra-osseous access, intravenous access, out-of-hospital cardiac arrest, spontaneous circulation, hospital discharge

Introduction

Out-of-hospital cardiac arrest (OHCA) stands as a critical medical event with staggering mortality rates, necessitating swift and efficient interventions to enhance patient outcomes[1,2.] Nurses are pivotal in OHCA management, offering indispensable care during the prehospital phase and facilitating the administration of medications and fluids.[3] Among the crucial considerations for nurses in OHCA is the selection of vascular access, such as intraosseous (IO) or intravenous (IV) access, as it directly impacts the delivery of life-saving interventions.[4–6] While the European Resuscitation Council (ERC) guidelines[7] advocate for peripheral venous route utilization during cardiopulmonary resuscitation (CPR), they

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remain agnostic regarding a preference for drug administration. However, in instances where peripheral venous line catheterization proves arduous or after three unsuccessful attempts, the guidelines endorse the use of the intraosseous route.

Nurses are often responsible for establishing and maintaining vascular access routes, requiring a comprehensive understanding of their effectiveness and safety.[8] Although IV access has historically been the preferred route for medication and fluid administration, securing successful IV access in OHCA can pose challenges due to factors such as peripheral vasoconstriction, hypoperfusion, and vein identification difficulties in chaotic prehospital settings. In such scenarios, IO access offers an alternative route, facilitating direct access to the vascular system through the medullary space of a bone.[9,10] Given nurses' pivotal role in furnishing prehospital care and resuscitation for OHCA patients, it becomes imperative to assess the comparative merits and demerits of IO and IV access.[11] The study by Alilou et al[9] limited the population to adults, while the study by Ibrahim et al[10] restricted the study type to randomized controlled trials or observational studies with propensity score matching. Our study, however, includes all individuals who experienced out-of-hospital cardiac arrest and encompasses a variety of study types. This study aimed to summarize the existing data and to compare the effectiveness and safety of IO access vs IV access in OHCA.

Methods

Registration and Search Strategy

The study adhered to the Cochrane Handbook (version 5.1.0),[12] and followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA).[13] The review process was submitted to PROSPERO and assigned the registration number *CRD420250653034*.

Search Strategy

A comprehensive electronic search was conducted across four databases: PubMed, EMBASE, Cochrane Library, and Google Scholar for studies published up to February 20, 2025. We used structured and standardized Boolean logic to combine disease terms, intervention types, and population descriptors. An example of the complete search string used in PubMed is provided below:

("Cardiac Arrest"[Mesh] OR "cardiac arrest"[tiab] OR "out-of-hospital cardiac arrest"[tiab] OR "OHCA"[tiab])
AND ("Intraosseous Infusion"[Mesh] OR "intraosseous"[tiab] OR "IO access"[tiab])
AND ("Intravenous Infusions"[Mesh] OR "intravenous"[tiab] OR "IV access"[tiab])
AND (adult[tiab] OR pediatric*[tiab])

Google Scholar was used solely as a supplementary source to identify potential gray literature and was not considered part of the systematic search. In addition, we manually screened reference lists of all included articles for further eligible studies. The search was limited to studies involving human subjects.

Study Selection

Inclusion Criteria:

1. Studies comparing IO and IV access for OHCA.
2. Studies reporting any of the relevant outcome measures such as ROSC, survival to hospital admission and to hospital discharge, neurological outcomes, complications, and time to access.

Exclusion Criteria:

1. Non-English language articles and studies without full-text availability.
2. Case reports, editorials, conference abstracts, and reviews.

All title/abstract screening and full-text selection were conducted by two independent reviewers. Discrepancies were resolved through consensus discussion or adjudication by a third reviewer.

Data Extraction

Independent screening of titles and abstracts for eligibility was done by two reviewers. Selected studies were then undergoing full-text review. A standardized data extraction form was used to retrieve the following information: author, publication year, country, study design, sample size, Intervention: IO access or IV access for OHCA management, outcome measures including neurological outcomes, ROSC, survival to hospital discharge, bystander CPR, emergency medical services, witnessed cardiac arrest etc.Specifically, first-attempt access refers to the initial attempt to establish vascular access, regardless of success. Actual access refers to the vascular access method that was ultimately successfully established and used for drug administration.

Quality Assessment

Risk of bias was assessed using two tools appropriate for different study designs. For non-randomized observational studies, we applied the Newcastle–Ottawa Scale (NOS),[14] which scores studies on selection, comparability, and outcome (0–9 scale), and the results are summarized (Table 1). For randomized controlled trials (RCTs), we used the Cochrane Risk of Bias 2.0 (RoB 2) tool, which evaluates five domains:[1] randomization process,[2] deviations from intended interventions,[3] missing outcome data,[4] measurement of outcomes, and[5] selection of reported results; the detailed domain-specific ratings and overall bias assessments are summarized (Table 2). All assessments were conducted independently by two reviewers, with disagreements resolved by discussion or adjudication by a third reviewer when necessary.

Publication Bias

Publication bias was assessed by funnel plot[38] and Egger's regression test.[39,40] A p-value < 0.05 in Egger's test was considered indicative of potential publication bias.

Statistical Analysis

STATA version 12.0 (Stata Statistical Software, Release 12; StataCorp LP, College Station, TX) was used. Fixed/random-effects models were used to calculate the pooled odds ratios (OR) with 95% confidence intervals (CI). All odds ratios (ORs) were calculated as intravenous access relative to intraosseous access (IV/IO). Thus, an OR > 1 indicates a higher likelihood of the outcome in the IV group compared to the IO group. Restricted maximum-likelihood estimation and I^2 statistics were used to assess heterogeneity. I^2>50% was considered to indicate significant heterogeneity. We addressed confounding by indication through subgroup analyses based on study design, population, and adjustment for time to intervention. Publication bias was assessed by funnel plots and Egger's regression test. $P<0.05$ was considered statistically significant.

Results

Literature Search

In accordance with rigorous scientific methodology, our systematic search yielded a total of 2616 references. Following a meticulous screening process, 2394 duplicates were identified and subsequently eliminated. Further scrutiny of titles and abstracts led to the exclusion of 193 studies that did not meet the predetermined eligibility criteria. Subsequently, the full texts of 29 remaining studies were thoroughly examined. Ultimately, after a comprehensive evaluation, 23 studies were deemed eligible for inclusion in our analysis. These selected studies provided data from 48945 cases utilizing intraosseous (IO) access and 188966 cases utilizing intravenous (IV) access in the management of out-of-hospital cardiac arrest (OHCA). The study selection process is summarized in a PRISMA flow diagram [Figure 1], which illustrates the number of records identified, screened, assessed for eligibility, and included in the meta-analysis, along with reasons for exclusions.

General Characteristics

In our scientific investigation, we meticulously analyzed a total of 23 studies[15–25,27–32,33–37,26] to comprehensively assess the comparative effectiveness and safety of IO and IV access in the management of OHCA. Of these studies, thirteen

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Table 1 Quality Assessment of Non-Randomized Observational Studies Based on Newcastle-Ottawa Scale (NOS)

S. No	Selection					Comparability	Outcome			Result
	First Author, Publication Year	**Representativeness of the Exposed Cohort**	**Selection of the Non-Exposed Cohort**	**Ascertainment of Exposure**	**Demonstration That Outcome of Interest Was Not Present at Start of Study**	**Comparability of Cohorts on the Basis of the Design or Analysis**	**Assessment of Outcome**	**Was Follow-Up Long Enough for Outcomes to Occur**	**Adequacy of Follow Up of Cohorts**	**Total Score**
1.	Clemency et al 2017[15]	1	1	1	1	0	1	0	1	6
2.	Feinstein et al 2017[16]	1	1	1	1	2	1	1	1	9
3.	Kawano et al 2018[17]	1	1	1	1	2	1	1	1	9
4.	Mody et al 2019[18]	1	1	1	1	2	1	1	1	9
5.	Nguyen et al 2019[19]	1	1	1	1	0	1	0	1	6
6.	Baert et al 2020[20]	1	1	1	1	2	1	1	1	9
7.	Zhang et al 2020[21]	1	1	1	1	2	1	1	1	9
8.	Monaco et al 2023[22]	1	1	1	1	2	1	1	1	9
9.	Recher et al2021[23]	1	1	1	1	2	1	1	1	9
10.	Hamam et al 2021[24]	1	1	1	1	2	1	1	1	9
11.	Besserer et al 2021[25]	1	1	1	1	0	1	0	1	6
12.	Nilsson et al2023[26]	1	1	1	1	0	1	0	1	6
13.	Yang et al2023[27]	1	0	1	1	0	1	1	0	5
14.	Lee et al2024[28]	1	1	1	1	1	1	0	1	7
15.	Brebner et al 2024[29]	1	1	1	1	1	1	0	1	7
16.	Benner et al 2024[30]	1	1	1	1	0	1	0	1	6
17.	Vadeyar et al2023[31]	1	1	1	1	0	1	0	1	6
18.	Yang et al2024[32]	1	1	1	1	0	1	0	1	6

Table 2 Quality Assessment of Randomized Controlled Trials Based on Cochrane Risk of Bias 2.0 (RoB 2.0)

S. No	First Author, Publication Year	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of Outcome	Selection of Reported Results	Overall Risk of Bias
1.	Daya et al 2020[33]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
2.	Nolan et al 2020[34]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
3.	Couper et al 2025[35]	Some concerns	Low risk	Some concerns	Low risk	Low risk	Some concerns
4.	Vallentin et al 2025[36]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
5.	Ko et al 2024[37]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns

were retrospective in nature,[15–17,19–21,23,27,28,30–32,26] five were prospective cohort studies,[18,22,24,25,27] and five were randomized controlled trials (RCTs).[33–37] All studies included in our analysis were conducted within the timeframe spanning fro0m 2017 to February 20th, 2025. Geographically, five studies originated from the United States, while four were from Taiwan, Canada, or collaborative efforts between the USA and Canada. Additionally, two studies were conducted in France, Denmark, or the United Kingdom, with one study each in England, Poland, and Germany. The included studies encompassed a wide range of cases, from 22 to 43660. Moreover, twenty-two studies focused on adult populations, while two specifically targeted pediatric populations. Notably, seven studies incorporated adjustments for the time to intervention in their analyses. Furthermore, the number of actual attempts made for vascular access was reported in thirteen studies, while ten studies specifically evaluated the outcomes of the first attempt at vascular access (Table 3). The majority of non-randomized studies received high scores on the Newcastle–Ottawa Scale, indicating strong methodological quality (Table 1). In addition, the five included randomized controlled trials were assessed using the Cochrane RoB 2.0 tool. The domain-specific ratings and overall bias assessments for each RCT are summarized in Table 2.

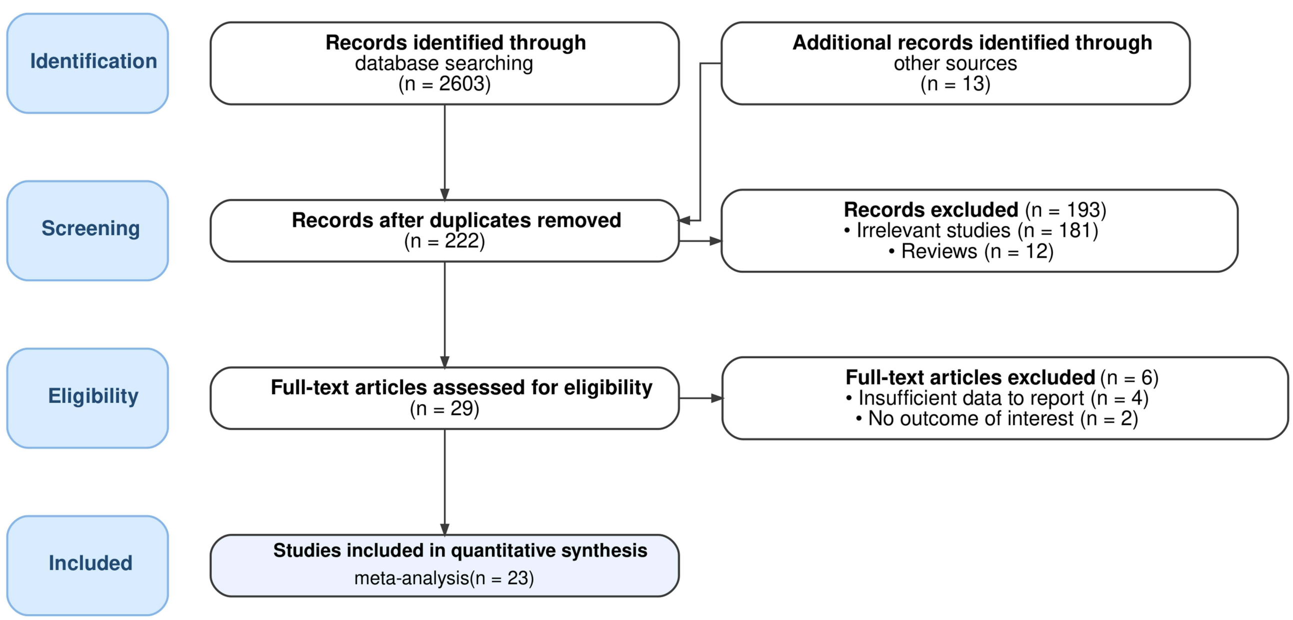

Figure 1 Flow diagram for the selection of studies and specific reasons for exclusion from the present meta-analysis.

Good Neurological Outcome

The pooled results for the primary outcome revealed no significant correlation between access type and neurological outcome (OR= 0.73, 95% CI: 0.37 to 1.45, I^2 = 95.3%). However, upon conducting a stratified analysis based on study design, time to intervention adjusted analysis, and population type, intriguing findings emerged. Specifically, prospective studies demonstrated a notably superior neurological outcome with IO access compared to IV access (OR = 0.58, 95% CI: 0.36 to 0.95). Moreover, studies that remained unadjusted for time to intervention also indicated favorable neurological outcomes favoring IO access (OR = 0.55, 95% CI: 0.34 to 0.88) [Figure 2; Tables S1–S3 for additional details]. It is noteworthy that no studies were specifically available for the pediatric subgroup, and all included studies exhibited a considerable degree of heterogeneity necessitating the adoption of a random effects model for analysis.

ROSC

Eighteen studies involving adults provided ROSC data. The type of vascular access did not correlate with ROSC (OR = 1.06; 95% CI: 0.65 to 1.73), with a high degree of heterogeneity of 94.9% (Figure 3). A single study that reported this outcome in pediatric patients, had a significant association (OR = 0.30; 95% CI: 0.21 to 0.42).

Further stratification based on study design elucidated intriguing nuances. Specifically, analysis of ten retrospective cohort studies failed to identify a significant link between access type and ROSC (OR = 1.26; 95% CI: 0.46 to 3.42). In contrast, findings from four prospective cohort studies suggested that patients with IO access experienced improved ROSC compared to those with IV access (OR = 0.67; 95% CI: 0.28 to 1.59). Notably, no significant correlation was observed in the five RCTs (OR = 1.12; 95% CI: 0.58 to 2.16). Conversely, analysis of twelve unadjusted studies revealed a noteworthy improvement in ROSC rates among the IO group (OR = 0.80; 95% CI: 0.70 to 0.91) [refer to Tables S1–S3 for comprehensive data].

Survival at Hospital Discharge

Fourteen studies in adults reported the survival at discharge. There was no association (OR= 0.76; 95% CI: 0.44 to 1.29) between the type of vascular access and the survival at discharge with a degree of heterogeneity of 97.0% (Figure 4). No studies were available for the pediatric subgroup. Further stratification based on study design unveiled intriguing insights. Specifically, among six retrospective cohort studies, no significant association was found (OR = 0.89; 95% CI: 0.21 to 3.73). Conversely, findings from prospective cohort studies demonstrated a noteworthy association, indicating improved survival at discharge in the IO group compared to IV group (OR = 0.62; 95% CI: 0.38 to 1.00). However, among the RCTs, a non-significant association was observed (OR = 0.76; 95% CI: 0.26 to 2.16), albeit with a higher degree of heterogeneity (83%) [Tables S1–S3]. Additionally, findings from nine unadjusted studies also revealed a significant association, suggesting improved survival at discharge in the IO group (OR = 0.57; 95% CI: 0.40 to 0.80).

Bystander Cardiopulmonary Resuscitation

Twenty-two studies reported the association of vascular access type with the bystander Cardiopulmonary Resuscitation (CPR). No significant association was found in adult patients (OR= 1.01; 95% CI: 0.90 to 1.14) with a moderate degree of heterogeneity (I^2 = 84.9%) as shown in Figure 5. Similarly, no significant association (OR = 1.33; 95% CI: 0.62 to 2.83) was detected in the pediatric subgroup (two study). The combined analysis for bystander CPR had a non-significant odd of 1.00 (95% CI: 0.96 to 1.03). Considering the study design, non-significant associations were observed in retrospective cohort studies (OR = 1.00; 95% CI: 0.92 to 1.09), prospective cohort studies (OR = 1.21; 95% CI: 0.60 to 2.43), and randomized controlled trials (OR = 0.93; 95% CI: 0.79 to 1.10), as summarized in Table S1–S3.

Shockable Rhythms

Nineteen studies reported data of the shockable rhythms, revealing a significant association (OR = 0.74; 95% CI: 0.67 to 0.82) in the adult group of patients. In the pediatric subgroup, a single study also showed a significant association (OR = 0.20; 95% CI: 0.12 to 0.33). The combined analysis for shockable rhythms, including both adults and pediatric patients, resulted in an OR of 0.77 (95% CI: 0.70 to 0.85) [Table–S1].

Table 3 Characteristics of Included Studies Investigating for Comparison of Intra-Osseous vs Intravenous Access for Out-of-Hospital Cardiac Arrest

S. No	Author, Year	Country	Ethnicity	Study Design	Study Duration	Inclusion Criteria	IO (n)	IV (n)	Age_IO	Age_IV	M/F_IO	M/F_IV	Time to Intervention Adjusted in Analysis	Selection of Intervention & Comparator
1.	Clemency et al 2017[15]	USA	Caucasian	RC	2013-2015	Adult OHCA	552	788	59.8	63	340/212	552/236	No	First Attempted IO and IV access
2.	Feinstein et al 2017[16]	USA	Caucasian	RC	2012-2014	Adult non-traumatic OHCA	275	1525	61.5 ± 16.1	64.3 ± 16.7	142/133	984/541	Yes (time to establishment of vascular access adjusted)	Actual IO and IV access for drug use
3.	Kawano et al 2018[17]	USA & Canada	Caucasian	RC	2007-2009	Adult non-traumatic OHCA	660	12,495	64 (52–77)	68 (55–80)	351/309	8284/4211	No	First Attempted IO and IV access
4.	Mody et al 2019[18]	USA & Canada	Caucasian	PC	2011-2015	Adult non-traumatic OHCA	3068	16,663	65 (53–77)	68(56.7–81)	1743/1325	11,064/5599	Yes (Time to medications administration adjusted)	First Attempted IO and IV access
5.	Nguyen et al 2019[19]	USA	Caucasian	RC	2013-2017	Adult non-traumatic OHCA	342	453	66	64.7	202/140	292/161	No	First Attempted IO and IV access
6.	Baert et al 2020[20]	France	Caucasian	RC	2011-2017	Adult non-traumatic OHCA	1576	27,280	64 (52–75)	67 (56–78)	601/975	27,280/19207	Yes (Time to medications administration adjusted)	Actual IO and IV access for drug use
7.	Daya et al 2020[33]	USA & Canada	Caucasian	RCT	2012-2015	Adult non-traumatic OHCA	661	2358	62.3 ± 14.8	62.7 ± 14.3	481/180	1935/423	Yes (Time to establishment of vascular access adjusted)	Actual IO and IV access for drug use
8.	Nolan et al 2020[34]	UK	Caucasian	RCT	2014-2017	Adult non-traumatic OHCA	2237	5080	67.5 ± 17.5	70.9 ± 15.9	1355/882	3364/1716	No	Actual IO and IV access for drug use
9.	Zhang et al 2020[21]	USA & Canada	Caucasian	RC	2011-2015	Adult non-traumatic OHCA	7975	27,758	65	67	4664/3311	19,007/8751	Yes (Time to establishment of vascular access adjusted)	First Attempted IO and IV access
10.	Monaco et al 2023[22]	Germany	Caucasian	PC	1989-2020	Adult OHCA	1303	29,688			812/491	19,802/9886	No	Actual IO and IV access for drug use
11.	Recher et al2021[23]	France	Caucasian	RC	2011-2018	Pediatrics non-traumatic OHCA	351	252	7.4 (5.5 −11.3)	12.4 (7.4–21.5)	204/147	157/95	No	First Attempted IO and IV access
12.	Hamam et al 2021[24]	USA	Caucasian	PC	2015-2017	Adult OHCA	2603	4293	65.2 ± 17.9	64.5 ± 18.2	1155/1448	1599/2694	No	Actual IO and IV access for drug use
13.	Besserer et al 2021[25]	Canada	Caucasian	PC	2011-2015	Pediatric non-traumatic OHCA	601	160	0-3	14 (3–16)	344/257	109/51	No	Actual IO and IV access for drug use
14.	Couper et al 2025[35]	UK		RCT	2021-2024	Adult OHCA	3030	3034	67.8±16.3	68.3±15.9	1941/1063	1951/1048	Yes (We performed two post-hoc sensitivity analyses to mitigate any causal association between time of drug administration and outcome, namely replacing time to drug administration with response time and removal of time to drug administration).	Actual IO and IV access for drug use

(*Continued*)

Table 3 (Continued).

S. No	Author, Year	Country	Ethnicity	Study Design	Study Duration	Inclusion Criteria	IO (n)	IV (n)	Age_IO	Age_IV	M/F_IO	M/F_IV	Time to Intervention Adjusted in Analysis	Selection of Intervention & Comparator
15.	Vallentin et al 2025[36]	Denmark		RCT	2022	Adult OHCA	731	748	69±15	70±14	517/214	516/232	No	Actual IO and IV access for drug use
16.	Ko et al 2024[37]	Taiwan, China		RCT	2020-2023	20-80years OHCA	741	991	64.0 (54.0–72.0)	66.0 (56.0–74.0)	521/220	713/278	No	First Attempted IO and IV access
17.	Nilsson et al 2023[26]	Denmark		RC	2016-2020	Adult OHCA	773	5979	67±16.71	70±15.30	503/270	3956/2023	No	Actual IO and IV access for drug use
18.	Yang et al 2023[27]	Taiwan, China		RC	2020-2021	Adult nontraumatic OHCA	22	90	61.5(52.75–77.0)	69.0(51.0–82.0)	5/17	32/58	No	First Attempted IO and IV access
19.	Lee et al 2024[28]	Taiwan, China		RC	2019-2022	Adult OHCA	401	1602	71 (59–83)	71 (59–83)	246/155	1088/514	Yes (We used the Kaplan-Meier Method to demonstrate the time frompatient approach to epinephrine administration in different subgroups)	Actual IO and IV access for drug use
20.	Brebner et al 2024[29]	British Columbia		PC	2019-2023	Adult OHCA	537	1575	63 (49–75)	66 (51–78)	379/158	1147/428	No	First Attempted IO and IV access
21.	Benner et al 2024[30]	Portland		RC	2018–2021	Adult OHCA	1171	822	62 (50–72)	67 (53–77)	739/432	589/233	No	First Attempted IO and IV access
22.	Vadeyar et al2023[31]	England		RC	2015-2020	Adult OHCA	18288	43,660	68.9 (54.8–79.0)	72.6 (60.3–82.0)	11,270/7018	28,657/15003	No	Actual IO and IV access for drug use
23.	Yang et al 2024[32]	Taiwan, China		RC	2021-2023	Adult OHCA	840	840	67.39±15.95	67.45±16.56	581/259	582/258	No	Actual IO and IV access for drug use

Abbreviations: OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; IO, intraosseous; IV, intravenous; EMS, emergency medical service; PC, Prospective Cohort; RC, Retrospective Cohort; RCT, Randomized Controlled Trials.

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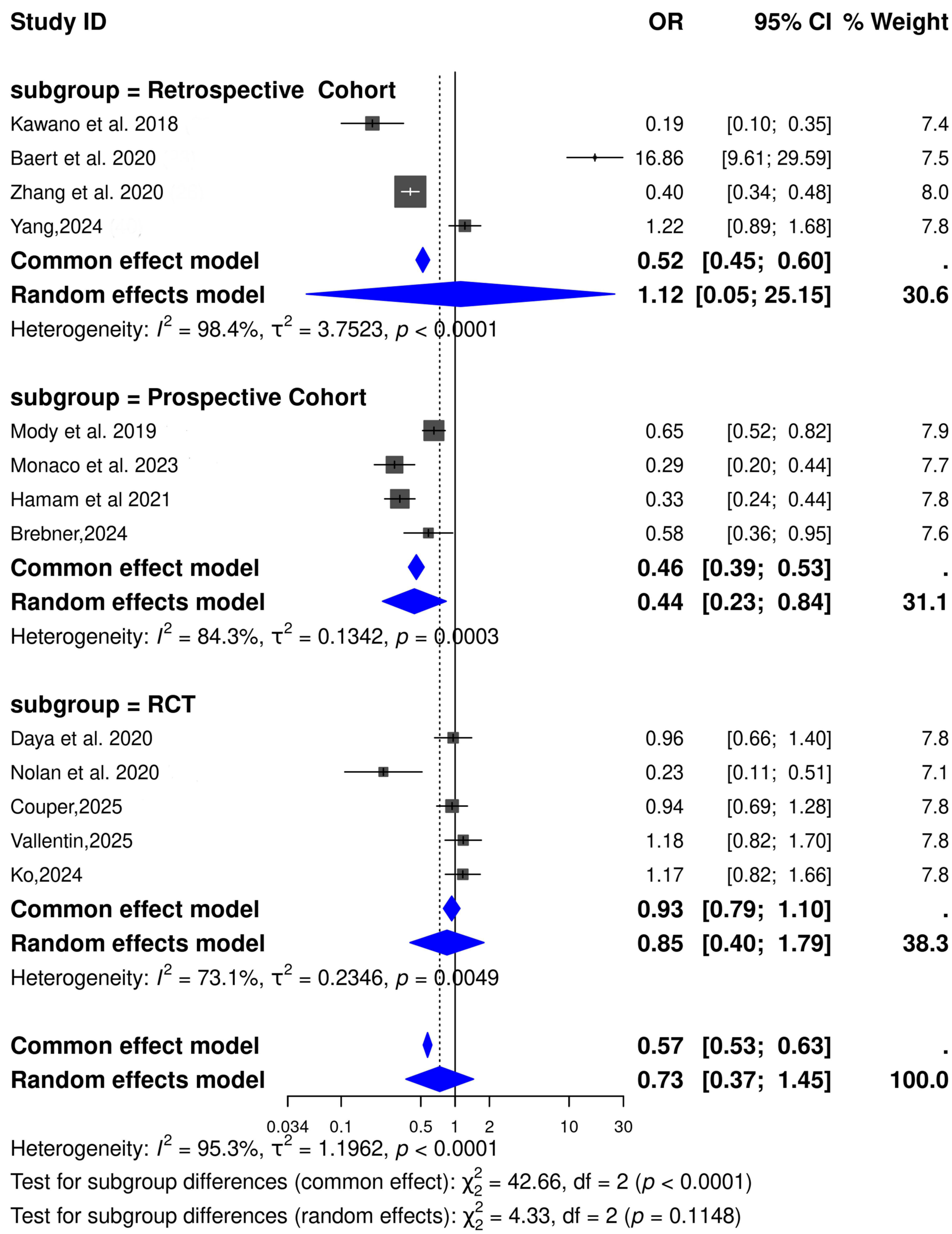

Figure 2 Forest plot for pooled odds ratio of good neurological outcome at hospital discharge between IO and IV access. Odds ratio shown as IV vs IO (ie, OR > 1 favors intravenous access).

Abbreviations: IO, intraosseous; IV, intravenous; RCT, randomized controlled trials.

In terms of study design, eleven retrospective cohort studies showed a significant association (OR = 0.71; 95% CI: 0.64 to 0.80). Three prospective cohort studies also showed a significant association (OR = 0.48; 95% CI: 0.28 to 0.84). Five RCT demonstrated a non-significant association (OR = 0.92; 95% CI: 0.76 to 1.10). Six adjusted studies demonstrated an OR of 0.77 (95% CI: 0.66 to 0.90) with heterogeneity of 88.2% ($p < 0.0001$) for shockable rhythms. Conversely, for thirteen unadjusted studies, a significant association was found (OR = 0.72; 95% CI: 0.62 to 0.84) [Table S2–S3].

Emergency Medical Services

Eleven studies reported data of the association between the type of vascular access and Emergency Medical Services (EMS) in adult patients, with a non-significant odd of 1.00 (95% CI: 0.79 to 1.28). No studies were available for the

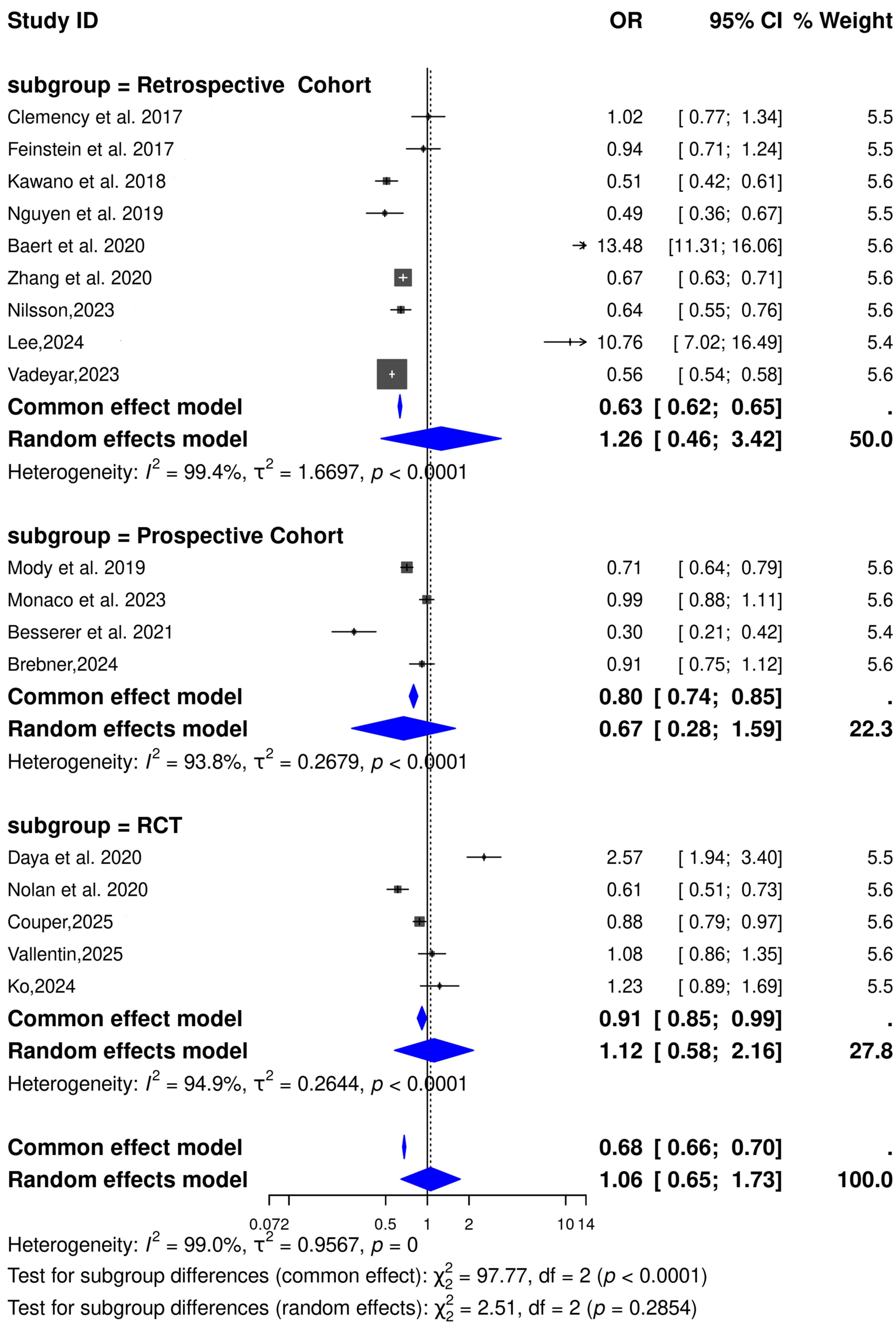

Figure 3 Forest plot for pooled odds ratio of ROSC between IO and IV access. Odds ratio shown as IV vs IO (ie, OR > 1 favors intravenous access).
Abbreviations: ROSC, Return of Spontaneous Circulation; IO, intraosseous; IV, intravenous; RCT, randomized controlled trials.

pediatric subgroup. Subgroup analysis, based on study design, showed that 6 retrospective cohort studies had an OR of 0.88 (95% CI: 0.58 to 1.33). Two prospective cohort study showed an OR of 1.09 (95% CI: 0.55 to 2.18). Three RCTs had an OR of 1.24 (95% CI: 0.91 to 1.69). Subgroup analysis based on time to intervention analysis for emergency medical services (EMS) showed that 3 adjusted studies had an OR of 0.93 (95% CI: 0.78 to 1.12), and 8 unadjusted studies had an OR of 1.05 (95% CI: 0.74 to 1.49).

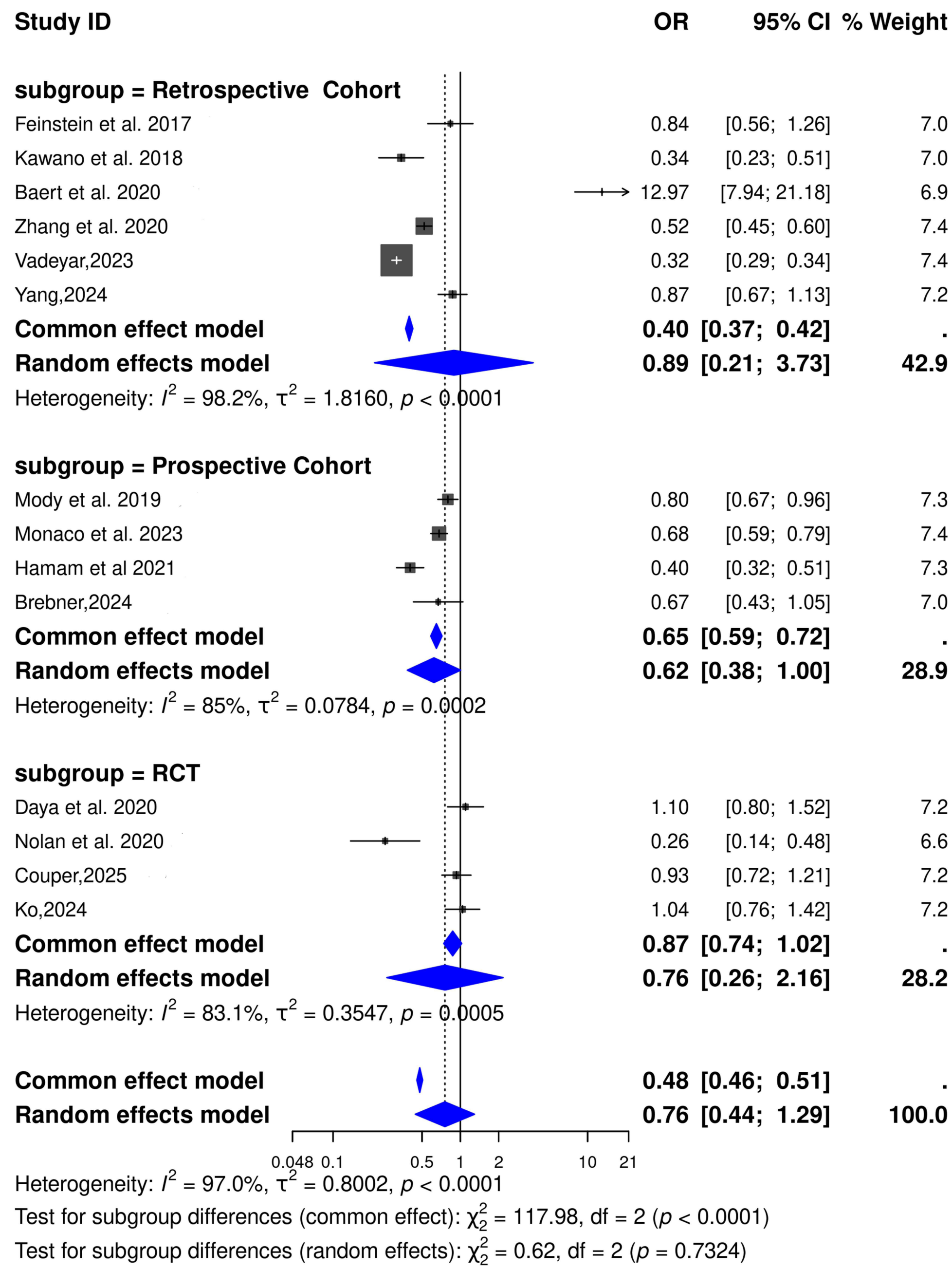

Figure 4 Forest plot for pooled odds ratio of survival at hospital discharge between IO and IV access. Odds ratio shown as IV vs IO (ie, OR > 1 favors intravenous access).
Abbreviations: IO, intraosseous; IV, intravenous; RCT, randomized controlled trials.

Witnessed Cardiac Arrest

There was a non-significant association between the type of vascular access and witnessed cardiac arrest (OR=0.97; 95% CI: 0.90 to 1.04) in the adult group. In the pediatric subgroup, there were 2 studies with an OR of 0.91 (95% CI: 0.70 to 1.19). Twelve retrospective cohort studies showed a significant association between witnessed cardiac arrest in IO as compared to IV access groups (OR=0.93; 95% CI: 0.88 to 0.98) [Table S1–S3].

Publication Bias

Funnel plots were generated for all six outcomes and are presented in Figure 6 (panels a–f). Visual inspection showed general symmetry for most outcomes. Egger's test indicated no significant publication bias for bystander CPR (p =

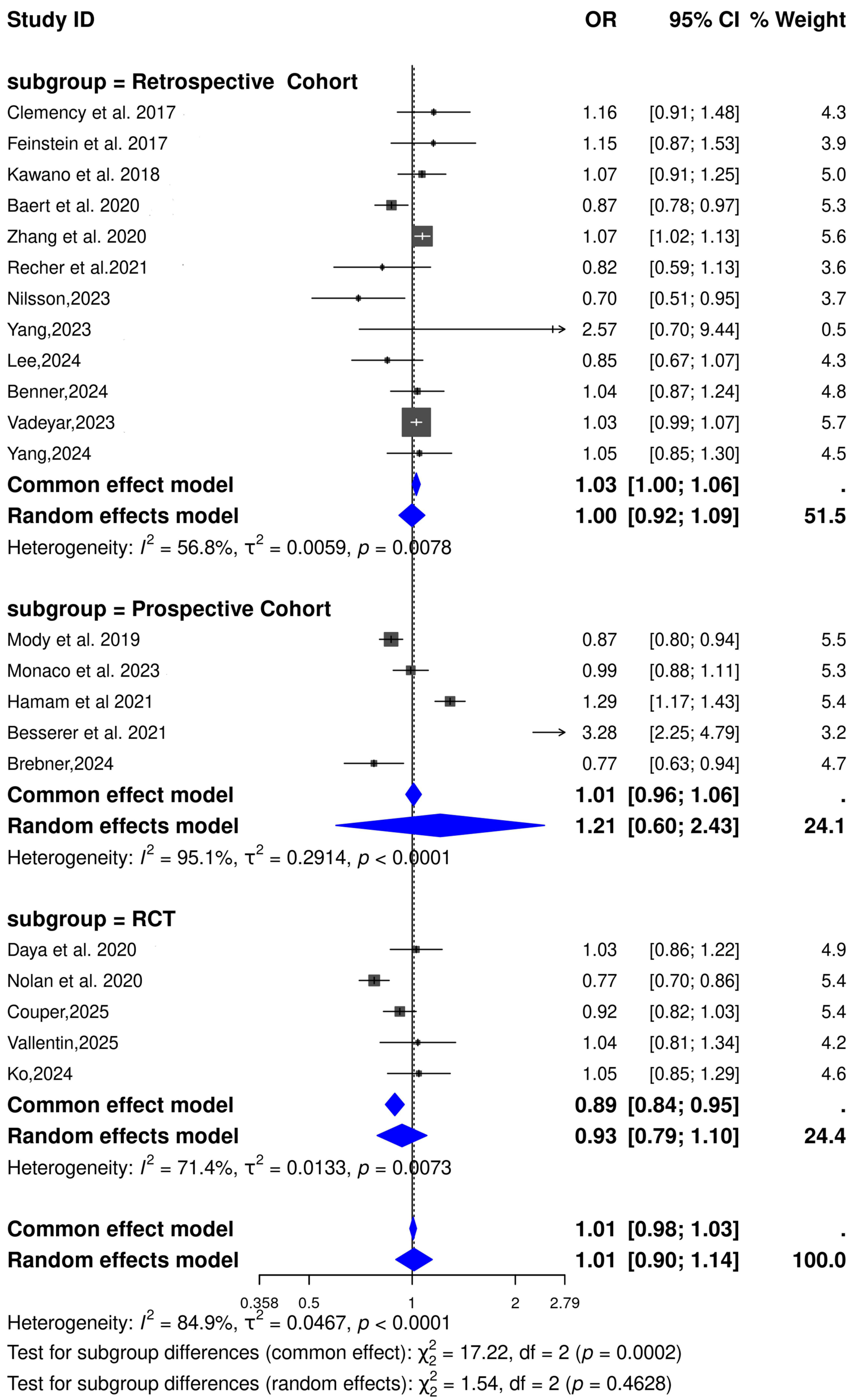

Figure 5 Forest Plot for the association of bystander cardiopulmonary resuscitation between IO and IV access. Odds ratio shown as IV vs IO (ie, OR > 1 favors intravenous access).

Abbreviations: IO, intraosseous; IV, intravenous; RCT, randomized controlled trials.

0.9569), EMS-witnessed arrests (p = 0.7582), favorable neurologic outcomes (p = 0.3610), and shockable rhythm (p = 0.0871). However, significant publication bias was detected for ROSC (p = 0.03996) and survival to hospital discharge (p = 0.0161).

Discussion

Our study compared the safety and efficiency of intraosseous and intravenous vascular access in OHCA patients. Our results, as shown in Table 4, indicate that patients who received intraosseous access had a lower rate of return of spontaneous circulation (ROSC) and a decreased survival rate to hospital discharge.This discrepancy may be attributed to the potentially better hemodynamic status of patients who achieved venous access compared to those who received intraosseous access. It's noteworthy that intraosseous access is typically considered a secondary option, often utilized when patients have overall worse hemodynamic status.[16] Importantly, no significant differences were observed in the time from prehospital care recognition or the emergency system call to vascular access, whether it was intraosseous or venous.

Overall, our subgroup analysis underscores the intricacy of comparing intraosseous and intravenous access for OHCA. While intraosseous access may offer advantages for certain subgroups, such as patients with shockable rhythms, consistent evidence supporting its superiority in terms of neurological outcome, survival at discharge, EMS, bystander

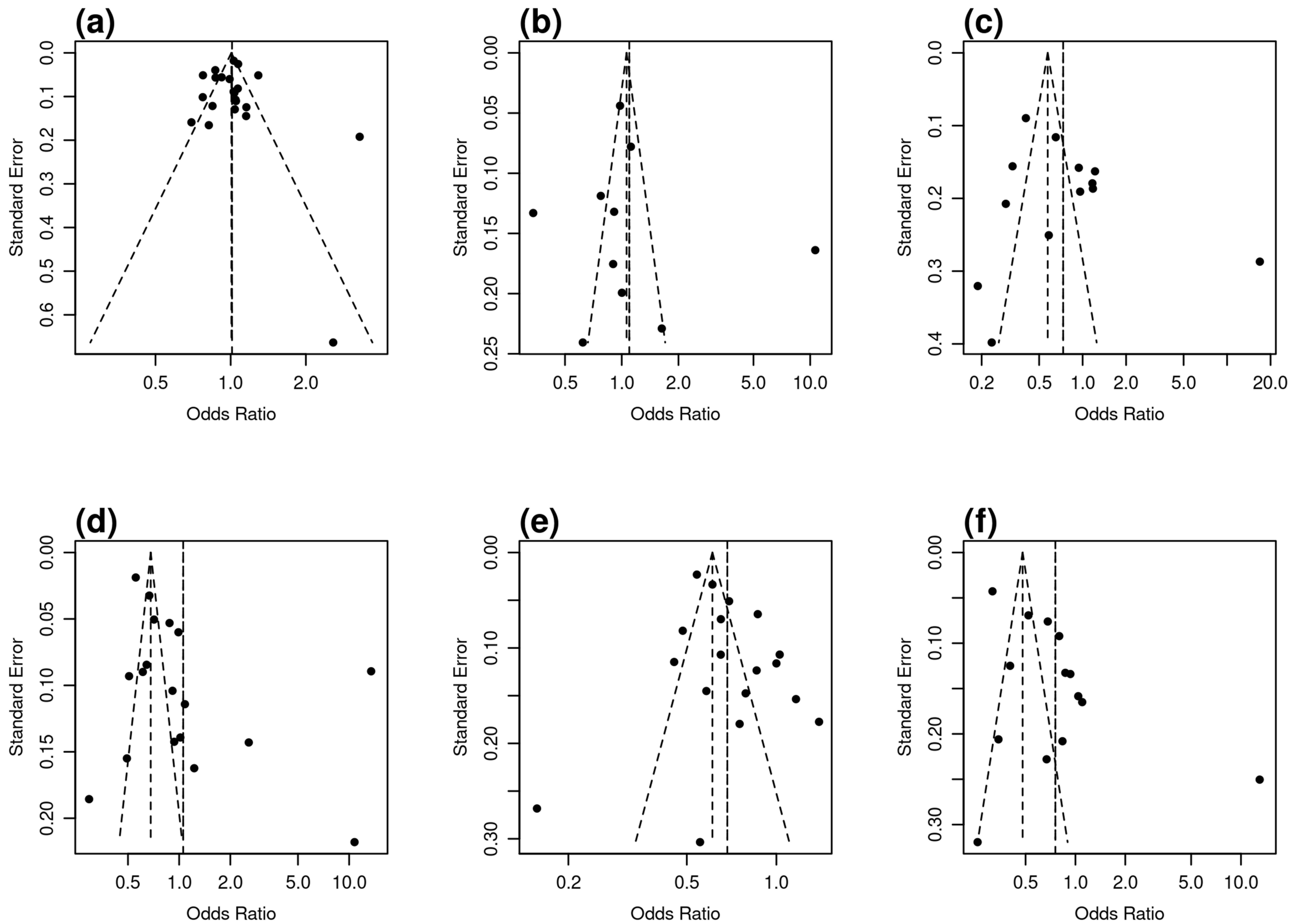

Figure 6 Funnel plot with pseudo 95% confidence limits (**a**) Funnel plot for the association of Bystander CPR; (**b**) Funnel plot for the association of ems; (**c**) Funnel plot for the association of good Neurological Outcome; (**d**) Funnel plot for the association of ROSC; (**e**) Funnel plot for the association of shockable rhythms; (**f**) Funnel plot for the association of survival at hospital discharge. Odds ratio shown as IV vs IO (ie, OR > 1 favors intravenous access). The vertical line represents the overall pooled OR; dashed lines represent pseudo 95% confidence intervals. Egger's test indicated statistically significant asymmetry for ROSC (p = 0.03996) and survival (p = 0.0161), suggesting potential publication bias.

Abbreviations: CPR, cardiopulmonary resuscitation; EMS, emergency medical service; PC, Prospective Cohort; RC, Retrospective Cohort; RCT, Randomized Controlled Trials.

Table 4 Summary of Pooled Outcomes for IV vs IO Access in Out-of-Hospital Cardiac Arrest

Variables	Number of Studies	Pooled Odds Ratio (OR) [95% CI]	I2
Neurological outcome	14	0.75 (0.49 to 1.13)	94.9%
Shockable Rhythms	19	0.74 (0.67 to 0.82)	87.4%
Survival at Discharge	15	0.78 (0.57 to 1.06)	96.5%
EMS	11	1.00 (0.79 to 1.28)	93.7%
Bystander CPR	22	1.00 (0.79 to 1.28)	58.1%
ROSC	19	1.11 (0.87 to 1.40)	98.6%
Witnessed Arrest	21	0.97 (0.90 to 1.04)	86.2%

Abbreviations: IO, intraosseous; IV, intravenous; ROSC, return of spontaneous circulation; EMS, emergency medical services; CPR, cardiopulmonary resuscitation.

CPR, ROSC, or witnessed arrest is lacking. Our findings emphasize the necessity for healthcare professionals to carefully consider individual patient conditions, available resources, and expertise when choosing between intraosseous or intravenous access in OHCA scenarios. Collaboration among prehospital care providers, emergency departments, and cardiologists is essential for optimizing patient outcomes and delivering effective interventions based on specific contexts and available resources. For example, when venous attempts fail or are impractical, IO remains a critical alternative—especially in patients with non-shockable rhythms or obesity.

It's important to note that our review identified only two relevant clinical outcome-directed studies in children, and the results showed that IO access was associated with significantly lower odds of shockable rhythms in pediatric patients (OR = 0.20; 95% CI = 0.12 to 0.33). Additionally, IO access was linked to a lower rate of ROSC in pediatric OHCA patients (OR = 0.30; 95% CI = 0.21 to 0.42). However, currently, most studies focusing on pediatric out-of-hospital cardiac arrest patients concentrate on chest compressions, mainly because of the low incidence rate in children and the fact that most cases are caused by respiratory asphyxiation.[41] Further clinical studies should specifically examine the balance between the practical benefits of intraosseous access for timely drug administration and the potentially diminished effects of medications administered via the intraosseous route. The findings from our subgroup analysis based on population type, study design, and time to intervention analysis provide valuable insights into the effectiveness of these interventions in different contexts.

We found comparable neurological outcomes for both types of access in both adult and pediatric populations. However, for shockable rhythms, intraosseous access correlated with significantly higher success rates of achieving ROSC compared to intravenous access across all age groups. Unadjusted studies suggested that intraosseous access correlated with higher odds of favorable neurological outcome and lower odds of survival at discharge. This disparity underscores the importance of considering confounding factors and potential biases when interpreting study results. The time to intervention analysis also yielded valuable insights. Adjusted studies demonstrated that both access types were associated with comparable outcomes for various variables, including neurological outcome, shockable rhythms, survival at discharge, EMS, bystander CPR, ROSC, and witnessed arrest.

Previous two meta-analyses[42,43] reported that IO access led to worse outcomes in OHCA patients compared to IV access. Morales-Cané et al[42] found a lower survival at hospital discharge in the IO group of patients. Granfeldt et al,[43] incorporating the study by Zhang et al,[21] showed that IO access correlated both with lower survival and poorer neurological outcome at discharge. In contrast to previous reviews, our study incorporated additional results from analyses of 14 studies. Although most included studies were of high quality and employed multiple statistical methods to address confounding factors, the retrospective observational study design has inherent limitations that may impact the interpretation of the current meta-analytic results. One limitation is the method of vascular access selection (first attempted versus actual access), which may introduce confounding by indication. Successfully cannulating an IV line during CPR can be challenging due to compromised peripheral vasculature. In some cases, intraosseous access may be pursued as a last resort due to its higher success rate during CPR. Patients who receive intraosseous access in such cases may have specific characteristics compared to those with easily established IV access, such as obesity, which itself is associated with worse outcomes.

Another limitation is the often unaccounted for time to intervention, which may introduce resuscitation time bias. Prolonged time to intervention, and subsequently longer CPR duration, may independently influence outcomes regardless of the type of access used. Furthermore, the main benefit for the patient lies in the medications administered via vascular access rather than the type of access itself. Therefore, adjusting for medication administration timing could improve the quality of comparative analysis. Emergency care providers should consider the impact of medication administration delays on outcomes when deciding on the particular type of access, especially in patients with non-shockable rhythms.[44] Additionally, although most outcomes demonstrated no evidence of publication bias, Egger's test revealed potential asymmetry for ROSC and survival to discharge. This suggests that studies with null or negative results may be underrepresented. Nonetheless, the consistency of findings across subgroups and effect models supports the robustness of our conclusions.

Finally, many of the included studies were retrospective in nature, which may introduce selection bias and unmeasured confounding factors. Future prospective studies should standardize vascular access attempts, document the timing of drug administration, and adjust for key covariates such as body mass index and CPR duration to minimize bias.

Conclusions

Our results suggest that IO access may be related to less favourable outcomes in terms of survival, neurological function, and ROSC compared to IV access in OHCA management. Further research is required to address limitations and provide more robust evidence regarding the comparative effectiveness of intra-osseous and intravenous access in this clinical setting.

Patient and Public Involvement Statement

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Data Sharing Statement

All data analysed in this study are included in this manuscript. No additional data are available beyond those presented in the manuscript. For additional queries, the corresponding author could be contacted through email.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare.

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