International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Comparison of Prehospital Vascular Access Methods and Their Association with Survival in Out-of-Hospital Cardiac Arrest

Sheng-Min Lin[1,*], Cheng-Yu Chien[1–4,*], Chip-Jin Ng[1,2,4], Liang-Tien Chien[5,6], Hsin-Tzu Yeh[1,2,4], Pang-Ting Hsu[1,2,4,7], Ming-Fang Wang[1,2,4,8], Hsiao-Jung Tseng[1,2], Kuei-Chen Feng[3,*], Chien-Hsiung Huang[1,2,4]

[1]Department of Emergency Medicine, Chang Gung Memorial Hospital, Linkou and College of Medicine, Chang Gung University, Taoyuan City, Taiwan; [2]Department of Emergency Medicine, Chang Gung Memorial Hospital Taipei Branch, Taipei City, Taiwan; [3]Department of Emergency Medicine, Ton-Yen General Hospital, Zhubei City, Hsinchu County, Taiwan; [4]Department of Nursing, Chang Gung University of Science and Technology, Taoyuan City, Taiwan; [5]Graduate Institute of Management, College of Management, Chang Gung University, Taoyuan City, Taiwan; [6]Taoyuan Fire Department, Taoyuan City, Taiwan; [7]Department of Emergency Medicine, Chang Gung Memorial Hospital Keelugi Branch, Keelung City, Taiwan; [8]Division of Emergency Medicine, Saint Paul's Hospital, Taoyuan City, Taiwan

*These authors contributed equally to this work

Correspondence: Chien-Hsiung Huang, Department of Emergency Medicine, Chang Gung Memorial Hospital, Linkou and College of Medicine, Chang Gung University, Taoyuan 333, No. 5 Fushing St., GuiShan District, Taoyuan City, Taiwan, Tel +886-3-3281200 # 2505, Email innoto86@gmail.com

Purpose: Out-of-hospital cardiac arrest (OHCA) remains a critical emergency with low survival rates despite advanced prehospital interventions. Emerging evidence suggests that early administration of epinephrine is associated with improved outcomes compared to delayed epinephrine administration, particularly in non-shockable rhythms. While intravenous (IV) access is the standard route for drug delivery, it is often difficult to obtain in the prehospital setting. Intraosseous (IO) access offers a viable alternative, but its comparative survival benefit remains unclear. Few studies have examined the association of IO access on outcomes relative to patients who received no prehospital vascular access. This study aims to assess survival outcomes among OHCA patients receiving different prehospital vascular access strategies.

Patients and Methods: This retrospective cohort study included adult patients with non-traumatic OHCA in Taoyuan, Taiwan (June 2021–June 2024). Patients were grouped based on the final attempted route: IV, IO, failed IV, or no-access attempt. The primary outcome was survival to discharge; secondary outcomes were prehospital ROSC, survival over 2 hours, and favorable neurological outcome. Multivariable logistic regression was performed, with sensitivity analyses including early treatment (≤15 min), EMT-P–level providers, and epinephrine stratification.

Results: Among 5093 adult OHCA patients, compared with the no-access attempt group, IO access was associated with higher survival to discharge (aOR 1.44; 95% CI 1.08–1.91). IV access also showed increased survival to discharge (aOR 1.25; 95% CI 1.01–1.58). However, in the subgroup analysis of patients treated by EMT-P providers, IV access demonstrated a stronger association with survival to discharge (aOR 3.65; 95% CI 1.16–11.49) compared to IO access (aOR 2.29; 95% CI 1.28–7.24). Failed IV attempts yielded the poorest outcomes. Sensitivity and stratified analyses demonstrated that early vascular access (≤15 min) significantly improved survival for both IO (aOR 2.03; 95% CI 1.45–2.85) and IV (aOR 1.25; 95% CI 1.11–1.49) routes, with treatment timing, provider level, and epinephrine use modifying these associations.

Conclusion: Prehospital vascular access, either IV or IO, was associated with improved survival compared with no access attempt. Failed IV attempts were linked to the poorest outcomes, underscoring the potential harm of procedural delays. Early transition to IO may serve as an effective rescue strategy when IV access is difficult; however, successful IV or humeral IO should be preferred when feasible.

Keywords: prehospital vascular access strategies, intravenous access, intraosseous access, out-of-hospital cardiac arrest

https://doi.org/10.2147/IJGM.S579765
Received: 21 November 2025
Accepted: 3 February 2026
Published: 11 February 2026

Introduction

Out-of-hospital cardiac arrest (OHCA) remains a significant public health challenge. Despite extensive efforts, survival rate to hospital discharge remains low, typically under 8%, with fewer than 3% of survivors experiencing favorable neurological outcomes.[1–4] Early cardiopulmonary resuscitation (CPR), defibrillation, and administration of epinephrine by emergency medical services (EMS) are associated with favorable outcomes in OHCA.[5–8] In non-shockable OHCA patients, earlier epinephrine administration is associated with higher rates of return of spontaneous circulation (ROSC) and survival, whereas each minute of delay reduces the odds of survival by approximately 4%.[7,8]

Intravenous (IV) access is the preferred route for drug delivery during resuscitation; however, prehospital IV placement is often challenged by patient factors and scene constraints. Reported IV access success rates exhibit substantial variation, ranging from 73.5% in a Korean study to a 49% first-attempt success rate reported in a US cohort.[9,10] When IV access is difficult, updated guidelines recommend intraosseous (IO) access, which provides rapid access and higher success rate (reaching 97% for the humeral site and 98% for the tibial site on the first attempt).[9–11] Comparative effectiveness remains uncertain: several studies found no differences in sustained ROSC or neurological outcomes between IO and IV — even across insertion sites[12,13] — whereas one study reported lower odds of ROSC with tibial or humeral IO than with IV.[14] Yang et al likewise observed no difference in survival or neurological outcomes between routes, with better results for upper-extremity access.[15]

Recent large-scale randomized controlled trials, including PARAMEDIC-3 and IVIO, as well as a systematic review published in 2025, have demonstrated no significant difference in 30-day survival between IO-first and IV-first strategies and suggest that IO-first strategies may reduce the odds of sustained return of spontaneous circulation. However, these trials analyzed outcomes based on intention-to-treat protocols. The specific impact of "failed IV" attempts—a scenario carrying high risk of resuscitation interruption—and the comparison against a "no-access" baseline remain critical knowledge gaps that this study aims to address.[16,17] In Taiwan's current EMS practice, IV access is typically attempted first unless the patient presents with apparent difficulty in IV cannulation, in which case emergency medical technicians (EMTs) proceed directly to IO access. In situations involving multiple failed IV attempts, EMTs may prioritize expedited transport to the hospital, occasionally bypassing the establishment of alternative vascular access.

Importantly, most prior work is constrained by only including patients in whom vascular access was ultimately achieved. Furthermore, few studies have rigorously investigated how IO accessibility influences patient survival and neurological outcomes, particularly when contrasted with patients who received no prehospital vascular intervention.[18] To accurately reflect real-world clinical decision pathways, this study is uniquely designed to compare outcomes across four distinct groups: IV, IO, Failed IV, and No-access attempt. Therefore, the objective of this investigation is to provide critical insights for optimal prehospital practice by assessing survival and neurological outcomes in OHCA patients based on their vascular access strategy.

Materials and Methods

Study Design and Setting

This study was a retrospective cohort analysis conducted in Taoyuan City, Taiwan, from June 2021 to June 2024. Chang Gung Memorial Hospital (Linkou and Taipei branches) and the College of Medicine, Chang Gung University, are affiliated institutions under the Chang Gung Medical Foundation. The study protocol was reviewed and approved by the Chang Gung Medical Foundation Institutional Review Board, which serves as the central IRB for these institutions (IRB No. 202400158B0), and the retrospective nature of the study, the requirement for informed consent was waived. All data were anonymized and analyzed in de-identified form. Only authorized study personnel had access to the dataset, and confidentiality was maintained in accordance with IRB and institutional privacy regulations. The clinical trial number was not applicable.

EMS System in Taoyuan

Taoyuan City is the fourth largest metropolitan area, Taiwan (2.3 million residents; 1853 persons/km^2), covering urban, rural, and mountainous districts. Coordinated by a single dispatch center, the EMS system comprises 41 EMS stations and 13 designated first-aid hospitals and responds to approximately 2000 non-traumatic OHCA cases annually; EMS protocols adhere to the 2020 American Heart Association (AHA) Advanced Cardiovascular Life Support (ACLS) guidelines. Taiwan employs a three-tier EMS system comprising, Emergency Medical Technician–Intermediate (EMT-2), and Emergency Medical Technician–Paramedic (EMT-P) personnel. Within this system, vascular access may be established by EMT-2 and EMT-P, who are authorized to perform IV and IO cannulation. Medication administration—including epinephrine—is permitted only for EMT-P under medical director's orders. Epinephrine is administered in OHCA to support perfusion and facilitate ROSC. However, its prehospital use is constrained by scope-of-practice and staffing: when a response unit is not staffed with an EMT-P, epinephrine cannot be administered even if IV/IO access has been successfully obtained. Consequently, prehospital epinephrine use is not universal across OHCA encounters in this setting. Within the Taoyuan Fire Department (TYFD), every EMT-P and EMT-2 completed a standardized 4-hour IO course that combined lectures and hands-on practice with EZ-IO® on task trainers. The curriculum covered indications/contraindications, anatomical landmarks, step-by-step technique, and demonstrations; after training, skills were evaluated, and paramedics were certified before field use. System-level quality assurance (QA) includes Utstein-based run sheets reviewed by a QA team and, for time metrics, body-camera video auditing by two independent reviewers under privacy regulation. Training and competency are organized and verified by the fire department and its medical supervisors/education faculty.

Study Population

The study population consisted of adult patients (≥18 years old) who experienced non-traumatic OHCA during the study period and received prehospital resuscitation attempts by EMS personnel. Non-traumatic etiology was ascertained from EMS dispatch and the on-scene primary impression documented on EMS run sheets. Cases with an obvious traumatic mechanism (eg, motor vehicle collision, fall from height, penetrating injury) are excluded from the Taoyuan OHCA registry at the time of data entry according to Utstein-based definitions and were therefore not present in our initial dataset; when the etiology was uncertain or not explicitly documented, EMS narratives and hospital records were reviewed to adjudicate the cause prior to analysis. Patients were excluded if they had a pre-existing do-not-resuscitate (DNR) order, exhibited signs indicating death at the scene (eg, rigor mortis, decapitation, decomposition), or if OHCA was caused by drowning, hanging, or intoxication. Additionally, cases with pregnancy, missing essential prehospital or hospital data were excluded.

Study Groups

All included patients were classified into four groups based on their prehospital vascular access. The No-access attempt group included patients who did not receive or try to set a peripheral line or epinephrine during EMT resuscitation until arrive emergency department (ED). The IV Group consisted of patients who successfully received IV access. The IO Group comprised patients who received intraosseous access (including both humeral and tibial sites). The Failed IV Group included patients in whom IV access attempts were unsuccessful in the field, and peripheral access was not successfully established until hospital arrival. The selection of vascular access was determined by EMS (EMT-P and EMT-2) personnel based on the clinical conditions at the scene. For analysis purposes, classification was based on the final attempted vascular access route, reflecting the last route attempted before arriving ED. Because occasional crossovers occurred (eg, failed IV followed by IO or vice versa), we defined exposure per protocol by the final attempted prehospital route before ED arrival. Accordingly, crossover cases were classified under their final route (IO or IV).

Outcome Measures

The primary study outcomes were survival to hospital discharge. The secondary outcomes included prehospital ROSC, survival for at least two hours post-arrest and favorable neurological outcomes, defined as a Cerebral Performance Category (CPC) score of 1 or 2 at discharge. Additionally, we conducted pre-specified exploratory analyses stratified by prehospital epinephrine administration and, within the epinephrine subgroup, route-level comparisons.

 https://doi.org/10.2147/IJGM.S579765

Data Collection and Variables

Data were extracted from the Taoyuan OHCA registry, a prehospital database that systematically records OHCA cases based on the Utstein reporting guidelines. Patient demographic and clinical data were obtained from EMS run sheets and hospital records, including patient characteristics, arrest-related factors (traumatic or non-traumatic) , EMS performance metrics, and patient outcomes. Patient characteristics included age, sex, hospital level and medical history. Arrest-related factors encompassed witnessed arrest, bystander CPR, use of public automated external defibrillators (AEDs), arrest location, and initial cardiac rhythm. EMS performance metrics comprised response time (from emergency call to EMS arrival), duration of on-scene resuscitation (scene time interval), transport time, airway management strategy, vascular access type, and time to epinephrine administration. Hospital outcomes were assessed based on survival status and the CPC score at discharge. The time to epinephrine administration was defined as the interval from the emergency call to the first administration of epinephrine.

Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics across study groups and are presented as mean ± standard deviation (SD) or median with interquartile range (IQR) for continuous variables, as appropriate, and as counts with percentages for categorical variables. Baseline characteristics are reported descriptively without formal statistical testing, consistent with recommended reporting practices for observational studies.

Multivariable logistic regression models were used to evaluate the association between prehospital vascular access groups and clinical outcomes. Epinephrine administration during resuscitation was included in the primary models as a covariate to account for differences in resuscitation context and treatment intensity. Given that epinephrine use may lie on the causal pathway between vascular access and outcomes, additional sensitivity analyses stratified by epinephrine administration were performed to assess the robustness of the associations. In multivariable models including "time to epinephrine" as a covariate, patients in the "No-access" and "Failed IV" groups (who did not receive epinephrine) were handled by excluding them from specific time-dependent sub-analyses, as appropriate, to avoid bias from undefined time intervals.

Covariates were selected a priori based on clinical relevance and prior literature, including age, sex, witnessed arrest, bystander cardiopulmonary resuscitation, arrest location, hospital level, airway management, emergency medical services (EMS) time intervals, and initial shockable rhythm. Additional variables identified as potential confounders in univariate analyses were also considered (Supplementary Table S1). Marginal predicted probabilities were subsequently estimated to facilitate interpretation of adjusted effects.

To assess the robustness of the primary findings and address potential sources of bias, several sensitivity analyses were performed. First, analyses were repeated after restricting the cohort to patients who received their first pharmacologic treatment within 15 minutes of EMS contact to mitigate resuscitation time bias. Second, analyses were restricted to cases attended by EMT-P–level providers, who were authorized to administer epinephrine, to reduce confounding related to provider capability and treatment eligibility. Third, stratified analyses by epinephrine administration status were conducted to examine the consistency of associations across treatment subgroups. These analyses were considered exploratory.

Statistical analysis was conducted using SAS version 9.4, and statistical plots were generated with the R package "ggplot2". All tests were two-sided, with a p-value less than 0.05 considered statistically significant.

Results

Between June 2021 and June 2024, a total of 13,051 OHCA cases were reported in Taoyuan City. Of these, 7765 cases were excluded due to on-scene death declarations or family-signed Do-Not-Resuscitate orders. An additional 193 cases were excluded due to specific criteria (eg, pregnancy (n=9), age <18 years (n=107), intoxication (n=13), incomplete data (n=64). The final study cohort comprised 5093 patients, categorized into four groups: no-access attempt (n=2229), IO access (n=1325), IV access (n=1278), and failed IV (n=261) (Figure 1).

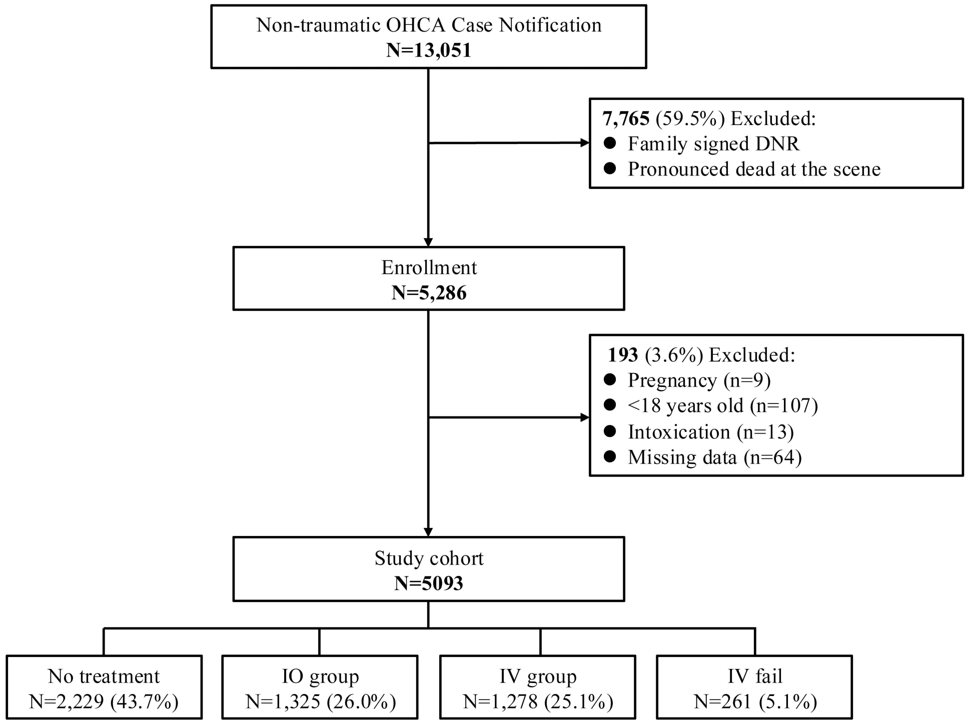

Figure 1 Flow chart of case selection process for the study.

Baseline Characteristics of the Study Population

In the study cohort, the mean age was 68.4 ± 16.3 years, and 64.6% of patients were male. Most cardiac arrests occurred in residential areas (3875 patients, 76.1%). Baseline characteristics varied across prehospital vascular access groups. Witnessed arrests and bystander CPR were most frequent in the IV group (41.7% and 71.4%, respectively). Shockable rhythms were more common in the IO (21.2%) and IV (21.5%) groups compared with the no-access attempt and failed IV groups.

Regarding EMS time intervals, the IO group had the longest scene time (median 17 min, IQR 13–21 min). Epinephrine was administered more frequently in the IO (65.7%). Time to epinephrine administration was longer in the IV group (mean 22.8 min) than in the IO group (mean 19.5 min) (Table 1).

Outcomes by Study Group

The IO group demonstrated higher rates of pre-hospital ROSC (9.6%), 2-hour survival (23.8%), and survival to discharge (10.9%) compared with the no-access attempt group. The IV group showed slightly higher pre-hospital ROSC (10.7%) and favorable neurological outcomes (7.1%) than the IO group, and similar 2-hour survival (24.1%) and survival to discharge (9.9%). In contrast, the failed-IV group had the lowest outcomes across all measures (ROSC 4.6%, 2-hour survival 18.8%, discharge 8.0%, favorable neurological outcomes 3.4%).

Multivariate analysis (Table 2) revealed that, compared with the no-access attempt group, the IO group had significantly higher odds of survival to discharge (aOR 1.44, 95% CI: 1.08–1.91, p=0.012). The IO group also had higher odds of 2-hour survival (aOR 1.24, 95% CI: 1.00–1.53, p=0.046), whereas pre-hospital ROSC (aOR 1.27, 95% CI: 0.93–1.74, p=0.136) and favorable neurological outcomes (aOR 1.06, 95% CI: 0.74–1.53, p=0.740) did not reach statistical significance.

For the IV group, statistically significant improvements were observed across three outcomes compared to the no-access group: pre-hospital ROSC (aOR 1.37, 95% CI: 1.01–1.86, p=0.041), survival over 2 hours (aOR 1.21, 95% CI: 1.05–1.44, p=0.039), and survival to discharge (aOR 1.25, 95% CI: 1.01–1.58, p=0.049). However, there was no significant difference in favorable neurological outcomes (p=0.215). The failed-IV group demonstrated significantly

Table 1 Descriptive Statistics Across Different Study Groups

	All (N=5093)	No Access Attempt (n=2229)	IO (n=1325)	IV (n=1278)	Failed IV (n=261)
Age	68.4±16.29	68.6 ±16.69	68.6 ±15.80	68.1±16.20	67.7 ± 15.76
Sex=M	3291 (64.6)	1386 (62.2)	872 (65.8)	868 (67.9)	165 (63.2)
Witness	1927 (37.8)	832 (37.3)	470 (35.5)	533 (41.7)	92 (35.2)
Bystander CPR	3421 (67.2)	1424 (63.9)	905 (68.3)	913 (71.4)	179 (68.6)
Public AEDs	273 (5.4)	124 (5.6)	82 (6.2)	56 (4.4)	11 (4.2)
Arrest Location					
Residential	3875 (76.1)	1692 (75.9)	1017 (76.8)	960 (75.1)	206 (78.9)
Public	1218 (23.9)	537 (24.1)	308 (23.2)	318 (24.9)	55 (21.1)
Hospital level					
CAC	325 (6.4)	140 (6.3)	91 (6.9)	74 (5.8)	20 (7.7)
Non-CAC	4768 (93.6)	2089 (93.7)	1234 (93.1)	1204 (94.2)	241 (92.3)
Airway					
SGA	265 (5.2)	146 (6.6)	54 (4.1)	51 (4.0)	14 (5.4)
BVM	4828 (94.8)	2083 (93.4)	1271 (95.9)	1227 (96.0)	247 (94.6)
Shockable rhythm	911 (17.9)	318 (14.3)	281 (21.2)	275 (21.5)	37 (14.2)
Numbers of EMT					
3	551 (10.8)	447 (20.1)	39 (2.9)	50 (3.9)	15 (5.7)
4	3538 (69.5)	1521 (68.2)	910 (68.7)	906 (70.9)	201 (77.0)
5+	1004 (19.7)	261 (11.7)	376 (28.4)	322 (25.2)	45 (17.2)
Response time	5 (4–6)	5 (4–7)	5 (4–6)	5 (4–7)	5 (4–6)
Scene time interval	15 (12–19)	14 (11–17)	17 (13–21)	16 (13–20)	14 (11–18)
Transport time (median, IQR)	6 (4–10)	6 (4–9)	6 (4–10)	6 (4–10)	9 (6–13)
Epinephrine used	1594 (31.3)	0 (0.0)	870 (65.7)	724 (56.7)	0 (0.0)
Time to Epinephrine administration (mean ± SD)	N/A	N/A	19.5 ± 7.70	22.8 ± 7.60	N/A

Abbreviations: IV, Intravenous; IO, intraosseous; CPR, Cardiopulmonary resuscitation; AEDs, Automated external defibrillators; CAC, Cardiac arrest center; OHCA, Out-of-hospital cardiac arrest; SGA, Supraglottic airway; BVM, Bag-Valve-Mask; EMT, Emergency medical technician; EMT-P, Emergency medical technician-paramedic; ROSC, Return of spontaneous circulation.

Table 2 Estimated Odds Ratios for the Outcomes

Comparison	Pre-Hospital ROSC[a]		Survival Over 2 Hours[a]		Survival to Discharge[a]		Favorable Neurological Outcomes[a]	
	aOR (95% CI)	*p-value*	aOR (95% CI)	*p-value*	aOR (95% CI)	*p-value*	aOR (95% CI)	*p-value*
IO vs no access attempt	1.27(0.93–1.74)	0.136	1.24(1.00–1.53)	**0.046**	1.44(1.08–1.91)	**0.012**	1.06(0.74–1.53)	0.740
IV vs no access attempt	1.37(1.01–1.86)	**0.041**	1.21(1.05–1.44)	**0.039**	1.25(1.01–1.58)	**0.049**	1.24(0.88–1.75)	0.215
IV fail vs no access attempt	0.67(0.36–1.24)	0.200	0.92(0.66–1.29)	0.631	0.79(0.49–1.28)	0.345	0.48(0.24–0.96)	**0.039**
With vs without epinephrine	1.22(0.92–1.60)	0.163	1.02(0.80–1.18)	0.802	1.26(1.04–1.44)	**0.023**	1.25(1.04–1.54)	**0.046**

Notes: [a]Model adjusted for age, gender, witnessed arrest, bystander cardiopulmonary resuscitation, arrest location, hospital level, airway management, emergency medical services (EMS) time intervals, and initial shockable rhythm. Significance of $p<0.05$ are shown in bold.
Abbreviations: IV, Intravenous; IO, intraosseous; ROSC, Return of spontaneous circulation; CIs, Confidence intervals; aOR, adjusted odds ratio.

lower odds of favorable neurological outcomes (aOR 0.48, 95% CI: 0.24–0.96, p=0.039) compared with the no-access attempt group.

Regarding epinephrine, its use was associated with significantly higher odds of survival to discharge (aOR 1.26, 95% CI: 1.04–1.44, p=0.023) and favorable neurological outcomes (aOR 1.25, 95% CI: 1.04–1.54, p=0.046) compared with patients who did not receive epinephrine. Additionally, longer time to epinephrine administration was significantly

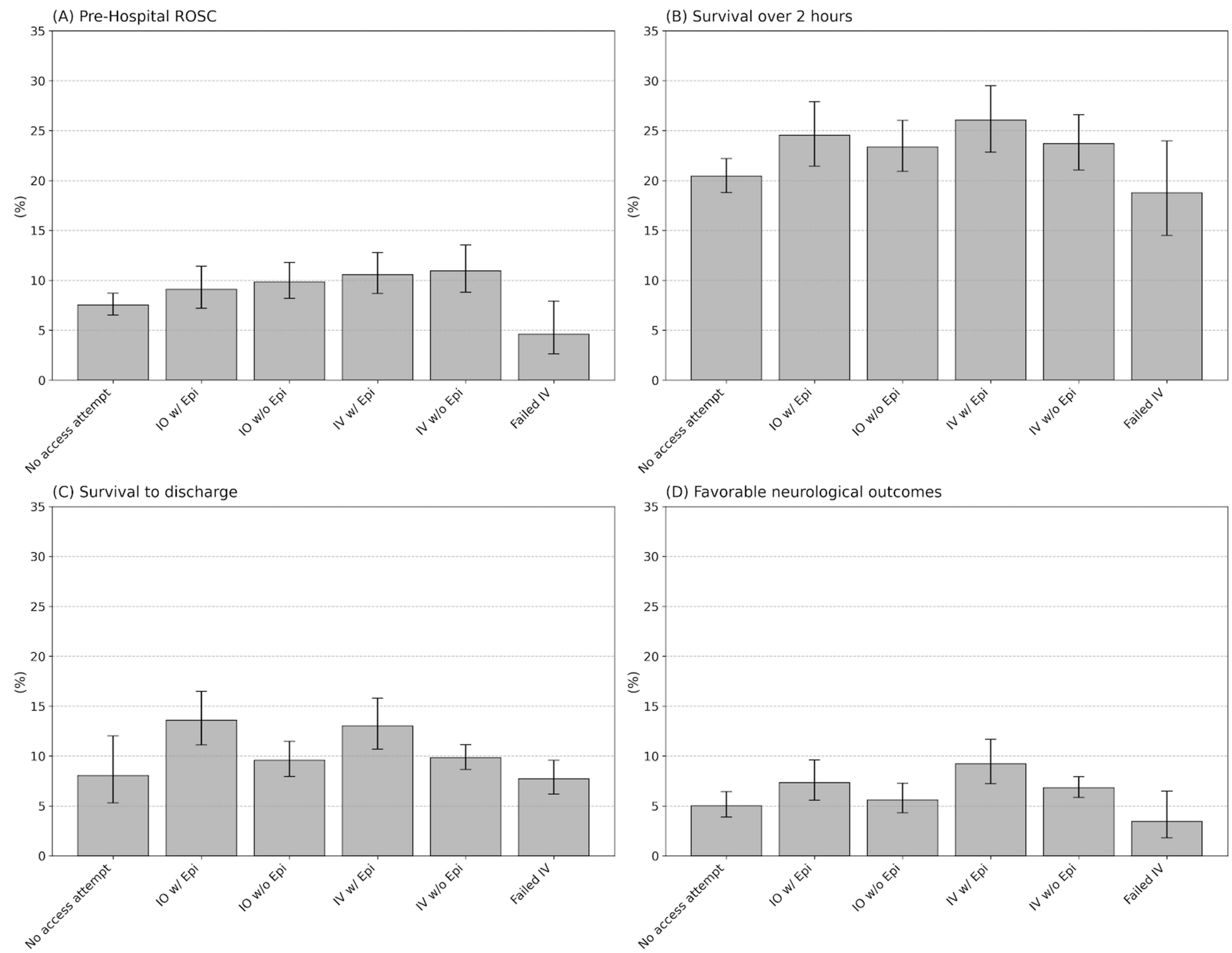

Figure 2 Estimated probabilities for (**A**) pre-hospital ROSC, (**B**) survival over 2 hours, (**C**) survival to discharge and (**D**) favorable neurological outcomes. Adjusted marginal predicted probabilities and 95% confidence intervals were derived from the multivariable logistic regression models.
Abbreviations: IV, Intravenous; IO, intraosseous; Epi, epinephrine.

associated with lower odds for all outcomes (p<0.05). Figure 2 presents the estimated probabilities for different outcomes stratified by vascular access type and epinephrine use.

Sensitivity and Stratified Analyses

Sensitivity and stratified analyses are presented in Table 3. Regarding treatment timing, among patients with a time to epinephrine administration within 15 minutes, IO access was significantly associated with higher odds of survival over 2-hours (adjusted odds ratio [aOR], 1.44; 95% CI, 1.10–1.87; P=0.008) and survival to discharge (aOR, 2.03; 95% CI, 1.45–2.85; P<0.001) compared with no access attempts. IV access in this cohort was also associated with improved survival to discharge (aOR, 1.25; 95% CI, 1.11–1.49; P=0.042). In the subgroup analysis of EMT-P providers, IV access demonstrated significant benefits for survival to discharge (aOR, 3.65; 95% CI, 1.16–11.49; P=0.027) and favorable neurological outcomes (aOR, 6.36; 95% CI, 1.23–32.73; P=0.027). Notably, IO access in the EMT-P group was also significantly associated with survival to discharge (aOR, 2.29; 95% CI, 1.28–7.24; P=0.008), although its association with pre-hospital ROSC and favorable neurological outcomes did not reach statistical significance. Outcomes varied significantly based on the administration of epinephrine and the site of access. Among patients receiving epinephrine, humeral IO access was associated with slightly higher odds of survival to discharge (aOR, 1.29; 95% CI, 1.02–1.59; P=0.043) and favorable neurological outcomes (aOR, 1.19; 95% CI, 1.04–1.43; P=0.045) compared with IV access. Conversely, tibia IO access was associated with significantly lower odds of pre-hospital ROSC (aOR, 0.64; 95% CI,

 https://doi.org/10.2147/IJGM.S579765

https://doi.org/10.2147/IJGM.S579765

Table 3 Sensitivity and Stratified Analysis

Condition/Comparison	Pre-Hospital ROSC[a]		Survival Over 2 hours[a]		Survival to Discharge[a]		Favorable Neurological Outcomes[a]	
	aOR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**
Time to Epinephrine administration <=15 min								
IO vs no access attempt	1.19(0.79–1.79)	0.403	1.44(1.10–1.87)	**0.008**	2.03(1.45–2.85)	**<0.001**	1.23(0.79–1.91)	0.367
IV vs no access attempt	1.09(0.74–1.61)	0.676	1.29(1.16–1.38)	**0.017**	1.25(1.11–1.49)	**0.042**	1.11(0.59–1.43)	0.693
With vs without epinephrine	2.09(1.31–3.34)	**0.002**	1.25(0.88–1.78)	0.204	1.66(1.21–2.01)	**0.003**	1.74(1.37–2.05)	**0.002**
EMTP level								
IO vs no access attempt	2.31(0.74–7.20)	0.148	1.02(0.44–2.40)	0.955	2.29(1.28–7.24)	**0.008**	3.42(0.66–17.74)	0.144
IV vs no access attempt	2.98(0.96–9.27)	0.059	1.23(0.53–2.89)	0.627	3.65(1.16–11.49)	**0.027**	6.36(1.23–32.73)	**0.027**
With vs without epinephrine	1.53(1.11–1.75)	**0.021**	1.18(0.56–1.54)	0.509	1.86(1.31–2.49)	**0.002**	1.45(1.24–1.76)	**0.008**
With Epinephrine treatment								
Humeral IO vs IV	1.13(0.71–1.42)	0.476	1.25(1.00–1.44)	0.054	1.29(1.02–1.59)	**0.043**	1.19(1.04–1.43)	**0.045**
Tibia IO vs IV	0.64(0.42–0.97)	**0.036**	0.87(0.65–1.17)	0.364	0.61(0.39–0.96)	**0.032**	0.44(0.23–0.84)	**0.012**
Time to Epinephrine administration (per minute delay)	0.95(0.93–0.98)	**<0.001**	0.97(0.96–0.99)	**0.003**	0.96(0.94–0.98)	**0.005**	0.96(0.93–0.99)	**0.017**
Without Epinephrine treatment								
Humeral IO vs no access attempt	1.49(1.28–1.62)	**<0.001**	1.60(1.09–2.33)	**0.016**	1.75(1.34–1.82)	**0.002**	1.49(1.24–1.76)	**0.007**
Tibia IO vs no access attempt	0.53(0.24–1.17)	0.116	0.59(0.25–1.37)	0.218	0.88(0.58–1.35)	0.566	0.34(0.10–1.16)	0.084
IV vs no access attempt	2.04(1.25–3.33)	**0.004**	2.34(1.64–3.12)	**<0.001**	2.53(1.77–3.61)	**<0.001**	2.74(1.62–4.63)	**<0.001**
IV fail vs no access attempt	0.59(0.30–1.17)	0.133	0.90(0.71–1.56)	0.220	0.97(0.66–1.43)	0.883	0.65(0.29–0.95)	**0.026**

Notes: Significance of $p<0.05$ are shown in bold. [a]Model adjusted for age, gender, witnessed arrest, bystander cardiopulmonary resuscitation, arrest location, hospital level, airway management, emergency medical services (EMS) time intervals, and initial shockable rhythm.
Abbreviations: IV, Intravenous; IO, intraosseous; ROSC, Return of spontaneous circulation; CIs, Confidence intervals; aOR, adjusted odds ratio.

0.42–0.97; P=0.036), survival to discharge (aOR, 0.61; 95% CI, 0.39–0.96; P=0.032), and favorable neurological outcomes (aOR, 0.44; 95% CI, 0.23–0.84; P=0.012) compared with IV access. In patients not receiving epinephrine, IV access showed the strongest association with survival over 2 hours (aOR, 2.34; 95% CI, 1.64–3.12; P<0.001) and favorable neurological outcomes (aOR, 2.74; 95% CI, 1.62–4.63; P<0.001) compared with no access attempts. Humeral IO access without epinephrine also showed significant benefits across all outcomes, whereas tibia IO access showed no statistically significant associations. Overall, these sensitivity and stratified analyses confirmed the robustness of the main findings, with treatment timing, provider level, and epinephrine administration modifying the magnitude of effect.

Discussion

Establishing peripheral vascular access before hospital arrival was associated with higher survival than no prehospital access, whereas failed IV attempts were linked to worse neurological outcomes. We also observed an association between shorter time to epinephrine delivery and improved outcomes, which is consistent with established resuscitation guidelines When IV attempts are prolonged or unsuccessful, considering earlier transition to IO access to minimize delay appears reasonable; however, this interpretation is hypothesis-generating because our analysis classified patients by final access route and did not evaluate within-case transitions. In adjusted analyses within this cohort, epinephrine administration was associated with higher odds of survival to discharge and favorable neurologic outcome and should be interpreted cautiously given our observational design and the neurologic findings reported in randomized evidence (eg, PARAMEDIC-2).[19] Our findings that IO access is associated with improved survival compared to no access must be interpreted in the context of recent randomized evidence. The PARAMEDIC-3 and IVIO trials found no survival benefit for an IO-first strategy compared to IV-first. The apparent advantage of IO in our observational cohort likely reflects "resuscitation time bias". In our study, the IO group had a shorter time to epinephrine compared to the IV group (19.5 vs 22.8 min). Nevertheless, in real-world settings, the high success rate of IO avoids the "failed IV" scenario, which we found to be associated with the poorest neurological outcomes.[16,17] In particular, OHCA patients who experienced failed IV attempts and received no further intervention had the worst prognosis. Prioritize rapid vascular access and early IO when IV attempts are prolonged or unsuccessful.

According to our study, establishing peripheral vascular access before hospital arrival is associated with improved outcomes compared with no-access attempts group, particularly in the stratified analysis of patients who did not receive epinephrine. When peripheral IV access cannot be established promptly in the field, IO access provides a reliable alternative. An IO line placed prehospital remains usable on emergency department arrival, allowing immediate administration of medications and fluids without waiting for IV cannulation.[20] This positions IO as a bridge until definitive peripheral access is secured, consistent with our finding that minimizing delays to drug delivery is reasonable. In our cohort, IV epinephrine was associated with worse outcomes than humeral IO after adjustment. Consistent with previous physiological studies, our sensitivity analysis showed that tibial IO was associated with worse outcomes compared to IV access, whereas humeral IO showed comparable or superior results.[15] This aligns with evidence suggesting that flow rates and drug delivery times from the humerus to the central circulation are faster than from the tibia, approaching those of central venous access. Therefore, when IO is indicated, the humeral site should be prioritized if feasible. However, two contemporary randomized trials (IO-first vs IV-first) reported no survival advantage for either approach,[16,17] highlighting that route-level efficacy remains uncertain and may be sensitive to system-level factors such as time-to-epinephrine. Furthermore, a recent systematic review and meta-analysis by the International Liaison Committee on Resuscitation (ILCOR) indicated that IO access was associated with lower odds of ROSC compared with IV access.[21] These findings underscore that while IO serves as a critical rescue bridge to minimize time-to-drug, it may not be physiologically equivalent to IV access. This aligns with our sensitivity analysis where tibial IO was associated with inferior outcomes compared to IV access, supporting the recommendation that IV remains the preferred route when feasible. Unlike those trials, epinephrine via IO was administered earlier in our system (19.5 vs 22.8 minutes for IV), supporting prior evidence that delays in epinephrine administration are associated with decreased survival rates.[15] Notably, in the subgroup of patients treated by EMT-Ps, IV access was associated with significantly higher odds of survival than IO access. This suggests that in the hands of advanced providers who can establish IV access proficiently,

 https://doi.org/10.2147/IJGM.S579765

the intravenous route remains the gold standard, likely due to more predictable pharmacokinetics. IO access serves as a crucial safety net for difficult cases or less experienced providers.

Timely administration of epinephrine is critical in cardiac arrest resuscitation. Current resuscitation guidelines recommend early epinephrine administration in patients with non-shockable rhythms to improve ROSC and neurological outcomes.[22] Several studies have demonstrated that epinephrine given within five minutes of collapse is associated with higher survival to hospital discharge in both shockable and non-shockable OHCA patients.[23] In traumatic OHCA, prehospital epinephrine use has also been linked to increased rates of sustained ROSC.[24] However, this finding should be interpreted as an association within the context of comprehensive ALS care, and does not account for the post-resuscitation neuro-prognostic concerns raised in recent randomized trials.[19] In our study, prehospital administration of epinephrine was associated with significantly higher rates of survival to discharge and favorable neurological outcomes compared to no epinephrine use. Prior research has reported a 4% decrease in survival for every one-minute delay in epinephrine administration.[8] Consistent with this, our findings showed that epinephrine was administered a median of three minutes earlier in the IO group compared to the IV group. In prehospital settings, IV access failure rates may be as high as 50%,[10] which could lead to delaying drug delivery. The high first-attempt success rate and rapid placement of IO access may reduce interruptions in chest compressions and delays in defibrillation analysis or the administration of medication, thereby contributing to a more efficient and uninterrupted resuscitation process. Beyond earlier epinephrine administration, several system- and patient-level features may account for the IO cohort's higher survival: greater procedural efficiency with fewer CPR interruptions; a workflow characterized by longer on-scene time despite shorter response time, suggesting more complete resuscitation before transport; larger and more advanced crews (≥5 providers; higher EMT-P ratio); and a patient mix skewed younger with more shockable rhythms. Although age and rhythm were included in the multivariable models, residual confounding remains possible. Crossover events were rare in our cohort (IV failure → IO: n=20, 0.45%; IO failure → IV: n=14, 0.32%) and were analyzed per protocol by the final attempted prehospital route before ED arrival. Given their very low frequency, any misclassification or bias from crossover is unlikely to materially affect our effect estimates, although the small numbers precluded a dedicated outcome comparison of crossover subgroups.

The poor neurological outcomes in the Failed IV group are likely multifactorial. First, prolonged attempts delay transport and medication. Second, IV access failure itself may serve as a marker of physiological severity; collapsed peripheral vasculature due to severe hypoperfusion makes visual identification and palpation of veins difficult.[25] Thus, failed IV access often reflects a more critical underlying condition rather than merely a procedural complication. In such circumstances, IO access provides a critical and reliable alternative, serving as an immediate "bridge" to in-hospital management. Our findings suggest that in scenarios where IV access is difficult, strategies that facilitate earlier transition to IO access may be a reasonable approach to minimize delays in medication administration.

Limitations

This study has several limitations. First, as a retrospective cohort study, it is inherently subject to bias and unmeasured confounders. To minimize this, we adjusted for multiple variables in the multivariable logistic regression model and conducted stratified analyses based on epinephrine administration. Second, the choice between IV and IO access was determined by EMS personnel in real time based on clinical judgment, including anticipated cannulation difficulty, patient condition, and crew composition. Such provider-driven decisions may introduce confounding by indication and selection bias, potentially influencing the observed associations. To mitigate this, we classified patients according to the final successful vascular access route, compared baseline characteristics between groups, and applied multivariable adjustment; however, residual confounding from unmeasured factors may still remain. Third, detailed data on CPR quality—such as compression depth, rate, and hands-off time—were not available in our dataset. Nevertheless, we incorporated key EMS performance metrics, including response time and on-scene time, as indirect indicators of resuscitation process efficiency. Fourth, patients were classified based on the final successful vascular access rather than the initially attempted access. Although this approach is commonly used in retrospective EMS studies and allows for objective classification, it does not fully reflect real-world clinical decision-making, in which treatment decisions precede knowledge of procedural success. Moreover, classifying patients based on successful access (IV vs IO) rather than an

 https://doi.org/10.2147/IJGM.S579765

intention-to-treat framework may introduce selection bias, as patients in whom IV access fails likely represent a physiologically distinct and more severely ill population with collapsed vasculature, which may be a marker of disease severity rather than procedural failure alone. Finally, this study was conducted within a single urban EMS system in Taiwan, which may limit the generalizability of the findings to other EMS settings. Nonetheless, the large OHCA cohort, standardized data collection based on the Utstein guidelines, and consistency with prior studies enhance the internal validity of our results and support the importance of prompt IO access when IV attempts are unsuccessful. Future prospective, multicenter studies are warranted to validate these findings across diverse EMS systems.

Conclusions

Establishing prehospital vascular access, whether IV or IO, is associated with improved survival outcomes compared to no access attempt. In our cohort, failed IV attempts were associated with the poorest prognosis, suggesting that the time costs associated with unsuccessful procedures may be detrimental. Our data suggests that prioritizing early transition to IO serves as a reasonable rescue strategy to minimize time to drug administration when IV access is challenging. However, considering the inferior outcomes observed with tibial IO in our sensitivity analysis, humeral IO or successful IV remains the preferred route when feasible. While IV access remains associated with excellent outcomes in the hands of advanced providers (EMT-P), minimizing the time to epinephrine administration through rapid vascular access appears to be a pragmatic strategy for the broader OHCA population.

AI Statement

No AI program was utilized in the construction of this manuscript.

Abbreviations

OHCA, Out-of-hospital cardiac arrest; IV, Intravenous; IO, Intraosseous; CAC, Cardiac arrest center; EMS, Emergency Medical Services; ED, Emergency department; CPR, Cardiopulmonary resuscitation; ROSC, Return of spontaneous circulation; CPC, Cerebral performance category; DNR, Do-not-resuscitate; AEDs, Automated external defibrillators; IQR, Interquartile range; CIs, Confidence intervals; SGA, Supraglottic airway; BVM, Bag-Valve-Mask; EMT, Emergency medical technician; QA, Quality assurance; TYFD, Taoyuan Fire Department; AHA, American Heart Association; ACLS, Advanced Cardiovascular Life Support.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the first author on reasonable request.

Ethics Approval and Informed Consent

The study protocol was reviewed and approved by the Hospital Ethics Committee on Human Research of Taiwan's Chang Gung Medical Foundation (permit number: 202400158B0). Given the retrospective nature of the study, the requirement for informed consent was waived. All data were anonymized and analyzed in de-identified form. Only authorized study personnel had access to the dataset, and confidentiality was maintained in accordance with IRB and institutional privacy regulations. All methods were carried out in accordance with guidelines and regulations as stated in the Hospital Ethics Committee on Human Research of Taiwan's Chang Gung Medical Foundation to Support Research Integrity, which are both consistent with the Declaration of Helsinki.

Acknowledgments

The authors thank the staff and participants of the study for their important contributions. This paper has been uploaded to medRxiv as a preprint: https://www.medrxiv.org/content/10.1101/2025.06.19.25329959v1.This paper has been uploaded to Research Square as a preprint: https://www.researchsquare.com/article/rs-7080822/v1.

Author Contributions

The first draft of the manuscript was written by S.M.L. and C.Y.C. and all authors revised each version of the manuscript. SML, K.C.F. and CYC: Conceptualization, Methodology, Writing – Review & Editing. CJN, K.C.F. and LTC: Formal analysis, Writing – Original Draft. K.C.F. and HTY: Data curation, Validation. PTH and MFW: Data curation. HJT: Validation. SML, K.C.F., CJN and CYC: Software, Formal analysis. CYC and CHH take responsibility for the paper as a whole. 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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors declare that they have no competing interests in this work.

References

1. Gräsner J-T, Wnent J, Herlitz J, et al. Survival after out-of-hospital cardiac arrest in Europe: results of the EuReCa TWO study. *Resuscitation*. 2020;148:218–226.
2. Wang C-Y, Wang J-Y, Teng N-C, et al. The secular trends in the incidence rate and outcomes of out-of-hospital cardiac arrest in Taiwan: a nationwide population-based study. *PLoS One*. 2015;10(4):e0122675. doi:10.1371/journal.pone.0122675
3. Ong M-E, Shin S-D, De Souza -N-N, et al. PAROS Clinical Research Network. Outcomes for out-of-hospital cardiac arrests across 7 countries in Asia: the Pan Asian Resuscitation Outcomes Study (PAROS). *Resuscitation*. 2015;96:100–108. doi:10.1016/j.resuscitation.2015.07.026
4. Yan S, Gan Y, Jiang N, et al. The global survival rate among adult out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation: a systematic review and meta-analysis. *Crit Care*. 2020;24:61. doi:10.1186/s13054-020-2773-2
5. Merchant RM, Topjian AA, Panchal AR, et al. Part 1: executive summary: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(16_suppl_2). doi:10.1161/cir.0000000000000918
6. Chi C-Y, Chen Y-P, Yang C-W, et al. Characteristics, prognostic factors, and chronological trends of out-of-hospital cardiac arrests with shockable rhythms in Taiwan – a 7-year observational study. *J Formos Med Assoc*. 2022;121(10):1972–1980.
7. Holmberg MJ, Issa MS, Moskowitz A, et al. Vasopressors during adult cardiac arrest: a systematic review and meta-analysis. *Resuscitation*. 2019;139:106–121.
8. Hansen M, Schmicker RH, Newgard CD, et al. Resuscitation Outcomes Consortium Investigators. Time to epinephrine administration and survival from nonshockable out-of-hospital cardiac arrest among children and adults. *Circulation*. 2018;137(19):2032–2040. doi:10.1161/CIRCULATIONAHA.117.033067
9. Park SY, Choi B, Kim SH. Impact of intravenous accessibility and prehospital epinephrine use on survival outcomes of adult nontraumatic out-of-hospital cardiac arrest patients. *BMC Emerg Med*. 2024;24:79. doi:10.1186/s12873-024-00998-9
10. Reades R, Studnek JR, Vandeventer S, Garrett J. Intraosseous versus intravenous vascular access during out-of-hospital cardiac arrest: a randomized controlled trial. *Ann Emerg Med*. 2011;58(6):509–516.
11. Brebner C, Asamoah-Boaheng M, Zaidel B, et al. The association of tibial vs. humeral intraosseous vascular access with patient outcomes in adult out-of-hospital cardiac arrests. *Resuscitation*. 2023;193:110031. doi:10.1016/j.resuscitation.2023.110031
12. Yang SC, Hsu YH, Chang YH, Chien LT, Chen IC, Chiang WC. Epinephrine administration in adults with out-of-hospital cardiac arrest: a comparison between intraosseous and intravenous route. *Am J Emerg Med*. 2023;67:63–69. doi:10.1016/j.ajem.2023.02.003
13. Lee AF, Chang YH, Chien LT, Yang SC, Chiang WC. A comparison between intraosseous and intravenous access in patients with out-of-hospital cardiac arrest: a retrospective cohort study. *Am J Emerg Med*. 2024;80:162–167. doi:10.1016/j.ajem.2024.04.009
14. Benner C, Jui J, Neth MR, et al. Outcomes with tibial and humeral intraosseous access compared to peripheral intravenous access in out-of-hospital cardiac arrest. *Prehosp Emerg Care*. 2024;28(6):761–770. doi:10.1080/10903127.2023.2286621
15. Yang C-H, Ng C-J, Huang H-L, et al. Intraosseous and intravenous epinephrine administration routes in out-of-hospital cardiac arrest: survival and neurologic outcomes. *J Am Heart Assoc*. 2024;13(21). doi:10.1161/JAHA.124.036739
16. Couper K, Ji C, Deakin CD, et al. A randomized trial of drug route in out-of-hospital cardiac arrest. *N Engl J Med*. 2025;392(4):336–348. doi:10.1056/NEJMoa2407780
17. Vallentin MF, Granfeldt A, Klitgaard TL, et al. Intraosseous or intravenous vascular access for out-of-hospital cardiac arrest. *N Engl J Med*. 2025;392(4):349–360. doi:10.1056/NEJMoa2407616
18. Lin SM, Chien CY, Ng CJ, et al. Comparison of prehospital vascular access strategies and their impact on survival in out-of-hospital cardiac arrest. *medRxiv*. 2025. doi:10.1101/2025.06.19.25329959
19. Perkins GD, Ji C, Deakin CD, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. *N Engl J Med*. 2018;379(8):711–721. doi:10.1056/NEJMoa1806842
20. Dornhofer P, Kellar JZ. Intraosseous vascular access. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing; June 5, 2023. PMID: 32119260.

21. Couper K, Andersen LW, Drennan IR, et al. Intraosseous and intravenous vascular access during adult cardiac arrest: a systematic review and meta-analysis. *Resuscitation*. 2025;207:110481. doi:10.1016/j.resuscitation.2024.110481
22. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(16 suppl 2). doi:10.1161/cir.0000000000000916
23. Okubo M, Komukai S, Callaway CW, Izawa J. Association of timing of epinephrine administration with outcomes in adults with out-of-hospital cardiac arrest. *JAMA Network Open*. 2021;4(8):e2120176. doi:10.1001/jamanetworkopen.2021.20176
24. Streams JR, Wallace MW, Nordness MF, Smith M, Guillamondegui OD. The role of epinephrine in the resuscitation of pre-hospital traumatic cardiac arrest. *J Am Coll Surg*. 2021;233(5 Suppl 2):e225. doi:10.1016/j.jamcollsurg.2021.08.609
25. Loon FHJV, Puijn LAPM, Houterman S, Bouwman ARA. Development of the A-DIVA scale: a clinical predictive scale to identify difficult intravenous access in adult patients based on clinical observations. *Medicine*. 2016;95(16):e3428. doi:10.1097/MD.0000000000003428