Intraosseous Vascular Access Is Associated With Lower Survival and Neurologic Recovery Among Patients With Out-of-Hospital Cardiac Arrest

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Study objective: We seek to determine the effect of intraosseous over intravenous vascular access on outcomes after out-of-hospital cardiac arrest.

Methods: This secondary analysis of the Resuscitation Outcomes Consortium Prehospital Resuscitation Using an Impedance Valve and Early Versus Delayed (PRIMED) study included adult patients with nontraumatic out-of-hospital cardiac arrests treated during 2007 to 2009, excluding those with any unsuccessful attempt or more than one access site. The primary exposure was intraosseous versus intravenous vascular access. The primary outcome was favorable neurologic outcome on hospital discharge (modified Rankin Scale score $\leq$3). We determined the association between vascular access route and out-of-hospital cardiac arrest outcome with multivariable logistic regression, adjusting for age, sex, initial emergency medical services–recorded rhythm (shockable or nonshockable), witness status, bystander cardiopulmonary resuscitation, use of public automated external defibrillator, episode location (public or not), and time from call to paramedic scene arrival. We confirmed the results with multiple imputation, propensity score matching, and generalized estimating equations, with study enrolling region as a clustering variable.

Results: Of 13,155 included out-of-hospital cardiac arrests, 660 (5.0%) received intraosseous vascular access. In the intraosseous group, 10 of 660 patients (1.5%) had favorable neurologic outcome compared with 945 of 12,495 (7.6%) in the intravenous group. On multivariable regression, intraosseous access was associated with poorer out-of-hospital cardiac arrest survival (adjusted odds ratio 0.24; 95% confidence interval 0.12 to 0.46). Sensitivity analyses revealed similar results.

Conclusion: In adult out-of-hospital cardiac arrest patients, intraosseous vascular access was associated with poorer neurologic outcomes than intravenous access. [Ann Emerg Med. 2018;71:588-596.]

Please see page 589 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Intraosseous needle insertion is a quick and safe procedure to obtain vascular access in out-of-hospital cardiac arrest resuscitation, and is used to administer a variety of resuscitative medications and fluids.[1,2] Compared with intravenous access, the intraosseous route has been hypothesized to minimize interruptions in cardiopulmonary resuscitation (CPR), decrease time to vascular access, and potentially improve outcomes.[2]

Importance

Recently published retrospective data, however, have questioned the widely held belief that intraosseous access is equivalent to intravenous access, showing an association between intraosseous vascular access and decreased survival at hospitalization, but no statistical significance in outcomes at hospital discharge.[3] The effect of intraosseous access compared with intravenous access on survival with intact neurologic recovery among patients with out-of-hospital cardiac arrest remains unclear.

Goals of This Investigation

The aim of this study was to assess the association between the vascular access route (intraosseous and intravenous) and outcomes after out-of-hospital cardiac arrest.

Editor's Capsule Summary

What is already known on this topic

In many patients, intraosseous access may provide a faster alternative to intravenous vascular access.

What question this study addressed

Compared with intravenous access, is intraosseous access associated with improved out-of-hospital cardiac arrest survival?

What this study adds to our knowledge

In this analysis of 13,155 out-of-hospital cardiac arrests from the Resuscitation Outcomes Consortium, intraosseous access was associated with poorer neurologically intact survival than intravenous access, even after adjustment for patient severity.

How this is relevant to clinical practice

Intravenous access may be preferable to intraosseous access in out-of-hospital cardiac arrest. A randomized controlled trial is needed to confirm this finding.

MATERIALS AND METHODS

Study Design and Setting

This study was a secondary analysis of the Resuscitation Outcomes Consortium Prehospital Resuscitation Using an Impedance Valve and Early Versus Delayed (PRIMED) publicly available data set, which includes patients from the Trial of an Impedance Threshold Device and the Early vs Later Rhythm Analysis trial.[4-7] Ethics approval for participation in the original study, as well as approval for subsequent secondary analyses, was obtained from the individual local review and ethics boards from each region.[4-7]

The original Resuscitation Outcomes Consortium PRIMED study was conducted in 7 sites in the United States (Pittsburgh, PA; Dallas, TX; Portland, OR [2 sites]; Birmingham, AL; Seattle/King County, WA; and San Diego, CA) and 3 sites in Canada (Toronto Rescu sites, Ontario; Vancouver, British Columbia, and Ottawa/OPALS sites, Ontario). The PRIMED trial compared 2 interventions: strategies for the timing of the first analysis for defibrillation, and application of the impedance threshold device. All study sites prospectively collected data in regard to patient characteristics, out-of-hospital management, and outcomes.

Selection of Participants

We analyzed patients included in the PRIMED data set, which enrolled consecutive emergency medical services (EMS)–treated patients aged 18 years or older with nontraumatic out-of-hospital cardiac arrest, excluding those incarcerated or pregnant, those with do-not-resuscitate orders, and those with arrests presumed to be the result of exsanguination or severe burns.[6] We classified patients by initial route of vascular access: intraosseous versus intravenous. To obtain a cohort whose access route was the intended primary choice of the treating paramedic, we excluded individuals who had any failed attempts at either route of vascular access, those who had both intraosseous and intravenous access, and those without vascular access.

Methods of Measurement

Information about patient characteristics, out-of-hospital management, and outcomes was prospectively collected from dispatch, EMS, and hospital records onto a standardized report form consistent with Utstein standards.[4,6] Trained Resuscitation Outcomes Consortium research assistants, unaware of this post hoc study hypothesis, reviewed neurologic outcomes at hospital discharge from hospital records.[4,6]

The systematically collected data were as follows: patient demographics, initial EMS-recorded rhythm (shockable [ventricular fibrillation or pulseless ventricular tachycardia] or nonshockable [asystole, pulseless electrical activity, automated external defibrillator–advised "no shock" and unclassified]), witness status (none, bystander, or EMS), bystander CPR, use of public automated external defibrillator, episode location (public or nonpublic), time from 911 call to paramedic scene arrival, time from call to advanced life support (ALS) paramedics scene arrival, out-of-hospital treatments (medications administered, electric defibrillation, and advanced airway placement [intubation and supraglottic airway]), CPR quality metrics for the first 5 minutes of EMS resuscitation (chest compression fraction rate and chest compression rate), inhospital treatments (therapeutic hypothermia, fibrinolytics, and diagnostic or interventional catheterization), return of spontaneous circulation (at any time), and survival and neurologic outcome to hospital discharge. Data specific to vascular access were likewise prospectively collected, recording all attempts at intravenous and intraosseous lines, in addition to all successful placements.

Chest compression fraction was defined as the proportion of time spent delivering chest compression during CPR.[8,9] Chest compressions were defined as any attempts to compress the chest, detected by monitoring devices. The target chest compression fraction was 0.85, and the chest compression rate was 100 per minute. For fluid administration, flow rate was obtained by total amount of fluid administered per 1 minute during

out-of-hospital treatment, defined as the time from EMS CPR to time of termination of resuscitation at the scene or time of EMS destination arrival.

Outcome Measures

The primary outcome was favorable neurologic outcome at hospital discharge, defined as patients' having a modified Rankin Scale score of 0 to 3.[10] Secondary outcomes included return of spontaneous circulation and survival to hospital discharge.

Primary Data Analysis

We conducted univariate and multivariate logistic regression models in the complete data set (individuals who had no missing data), examining the association between the outcomes and intraosseous or intravenous access. We adjusted for age, sex, initial EMS-recorded rhythm (shockable or nonshockable), witness status, bystander CPR, use of public automated external defibrillator, episode location (public or not), and time from call to paramedic scene arrival, based on previously published standards.[11,12] We used the Hosmer-Lemeshow goodness-of-fit test to assess overall model performance for favorable neurologic outcome, and calculated area under the receiver operating characteristic curve to test the discrimination in this model for the same outcome. Multicollinearity was checked by variance inflation factor.

We conducted a series of sensitivity analyses to test the robustness of the results. Because out-of-hospital vascular access was not randomly assigned across this cohort, we applied propensity score analysis to mitigate the potential effects of selection bias and unmeasured confounders. The probability of EMS vascular access (intraosseous or intravenous) was determined by a multivariate logistic regression analysis; a full nonparsimonious model was fit with intraosseous as the dependent variable, which included the same confounders in previous multivariable regression model. After adaptation of the match algorithm by Leuven, a subgroup of patients with intraosseous access was identified and matched with unique control patients with intravenous access, according to a propensity score. Standardized difference was calculated to detect imbalance in baseline covariates before and after matching. An absolute standardized difference within 10% is considered a negligible imbalance between 2 groups.[13] We conducted logistic regression models (unadjusted and adjusted for the same confounders as previous models) for each of the outcomes as a dependent variable.

Because excluding missing data cases can cause bias in this analysis and lose study power to detect a statistical significance, we repeated the primary analysis after using multiple imputation to address missing data, performed with the ice and mim commands developed for Stata (version 13.1; StataCorp, College Station, TX). Multiple imputation is a valid and effective method to minimize bias resulting from missing data.[14-16] Data missing was assumed to occur at random. The variables included in the multiple imputation model were the outcomes, the same covariates in previous logistic regressions. Fifty imputed data sets were created though imputation, and their estimates and standard errors were combined by Robin's rule.

Because EMS protocols and other treatment characteristics may have varied with the treatment location, possibly affecting outcomes, we conducted a multivariable analysis using generalized estimating equations to account for clustering by study region.[17,18] We adjusted this model with the same covariates as in the primary analysis, within complete data and multiply imputed data sets (methods as above but also included imputed data for study enrolling region). In addition, we repeated the main analysis in a subgroup limited to the study enrolling regions that used intraosseous access at least once.

To evaluate interactions in this model, we repeated the main analysis stratified by the following: sex (male or female), initial recorded rhythm (shockable or nonshockable), and witness status (bystander witness or nonbystander witness). We used Microsoft Excel 2008 (Microsoft, Redmond, WA) and Stata (version 13.1; StataCorp, College Station, TX) for data analysis.

RESULTS

From June 2007 to November 2009, there were 17,445 nontraumatic out-of-hospital cardiac arrests treated by 115 EMS agencies. We included 13,155 (75.4%) in these

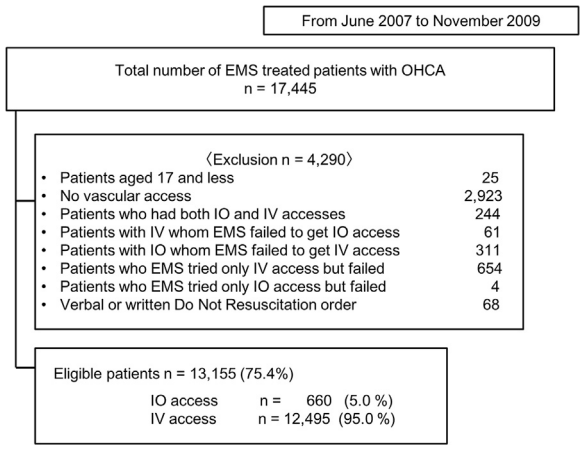

Figure 1. Study flow diagram. *OCHA*, Out-of-hospital cardiac arrest; *IO*, intraosseous vascular access; *IV*, intravascular access.

Table 1. Patient demographics and outcomes for those with intraosseous or intravenous access and out-of-hospital cardiac arrest.

Variable	IO Group (n=660)		IV Group (n=12,495)		Standardized Difference (%)
	n or Median	Missing (%)	n or Median	Missing (%)	
Age (IQR), y	64 (52–77)	0.2	68 (55–80)	0.1	−19.4
Female sex, No. (%)	309 (46.8)	—*	4,211 (33.7)	<0.1	26.8
Initial rhythm, No. (%)		1.1		0.6	−28.6
Shockable	91 (13.9)	—	3,258 (26.2)	—	
Nonshockable	562 (86.1)	—	9,156 (73.8)	—	
Bystander witness, No. (%)	202 (34.9)	12.3	5,015 (41.1)	2.4	−11.7
EMS witness, No. (%)	67 (10.2)		1,378 (11.1)		−1.6
Bystander CPR (1/0), No. (%)	260 (39.4)	—	4,728 (37.8)	—	3.4
Bystander AED (1/0), No. (%)	16 (2.4)	—	272 (2.2)	—	1.9
Location, No. (%)		—		—	−16.5
Public	65 (9.9)		2,016 (16.1)		
Nonpublic	595 (90.2)		10,479 (83.9)		
Time from call to paramedic scene (IQR), min	4.6 (3.3–5.9)	1.8	5.6 (4.4–7.0)	3.3	−35.1
Time from call to ALS scene (IQR), min	5.0 (4.0–6.6)	0.6	8.0 (5.9–11.3)	0.7	−70.1
Out-of-hospital treatment					
Total doses of epinephrine (IQR), mg	3.0 (2.0–4.0)	—	3.0 (2.0–4.0)	0.3	
Amiodarone, No. (%)	55 (8.3)	—	1,183 (9.5)	0.2	
Sodium bicarbonate, No. (%)	153 (23.2)	—	2,750 (22.0)	0.2	
Lidocaine, No. (%)	29 (4.4)	—	1,630 (13.1)	0.2	
Fluid delivered, No. (%)	489 (74.1)	—	8,500 (68.0)	—	
Volume of fluid among receivers (IQR), mL	255 (200–500)	44.4	500 (300–1,000)	65.7	
Flow rate (IQR), mL/min	11.1 (6.3–17.6)	46.4	18.4 (10.9–29.6)	66.7	
Electric defibrillation (1/0), No. (%)	166 (25.2)	—	5,256 (42.2)	—	
Advanced airway, No. (%)	611 (92.6)	—	11,472 (91.9)	0.1	
Quality of CPR during the first 5 min					
CCF rate (IQR), No. (%)	75.2 (59.5–86.4)	31.5	71.8 (60.5–81.8)	34.2	
Chest compression rate (IQR), min	113 (99.1–129)	31.5	108 (98.2–120)	34.3	
Inhospital treatment, No. (%)†					
Therapeutic hypothermia	34 (45.3)	41.4	1,503 (58.9)	29.4	
Fibrinolytics	1 (1.3)	41.4	146 (5.7)	29.5	
Diagnostic catheterization	25 (33.3)	41.4	802 (31.5)	29.5	
Interventional catheterization	9 (12.0)	41.4	621 (24.4)	29.5	
Outcomes, No. (%)					
Return of spontaneous circulation	158 (23.9)	—	4,783 (38.3)	<0.1	
Survival at hospital discharge	25 (3.8)	—	1,287 (10.3)	0.1	
Favorable neurologic outcome	10 (1.5)	—	945 (7.6)	0.3	

IQR, Interquartile range; *shockable*, ventricular fibrillation or pulseless ventricular tachycardia; *nonshockable*, asystole, pulseless electrical activities, no shock delivered by an AED, and unclassifiable rhythm; *AED*, automated external defibrillator; *CCF*, chest compression fraction; *favorable neurologic outcome*, patients with a modified Rankin Scale score of 0 to 3.

*Dashes indicate that there is no missing data.

†Denominator includes all who survived until admission to a hospital ward.

analyses. Vascular access used on these cases included 660 intraosseous (5.0%) and 12,495 intravenous (95.0%) (Figure 1). Table 1 describes patient characteristics, out-of-hospital treatment, CPR quality, and outcomes of intraosseous and intravenous groups. Patients with intraosseous access had a higher proportion of nonshockable initial rhythms, fewer public location and witnessed arrests, and shorter times from call to first paramedic and ALS paramedics arrival. Although a higher proportion of patients in the intraosseous group had fluid delivery than those in the intravenous group, the volume of fluid per minute was lower in intraosseous group. In the intraosseous group, 158 of 660 patients (23.9%) achieved return of spontaneous circulation, and 25 of 660 (3.8%) survived to hospital discharge; in the intravenous group, 4,783 of 12,491 (38.3%) achieved return of spontaneous circulation and 1,287 of 12,484 (10.3%) survived. The proportion of patients with a favorable neurologic outcome among those with intraosseous and intravenous access was 10 of 660 (1.5%) and 945 of 12,462 (7.6%), respectively.

The estimates of the main analysis including 12,162 complete cases are described in Figure 2. The result of the Hosmer-Lemeshow goodness-of-fit test was not significant. The area under the receiver operating characteristic curve in this model was 0.86 (95% confidence interval [CI] 0.85 to 0.88). All variance inflation factor values were less than 10, and the mean variance inflation factor of this model was 1.3. The multivariable regression models showed that compared

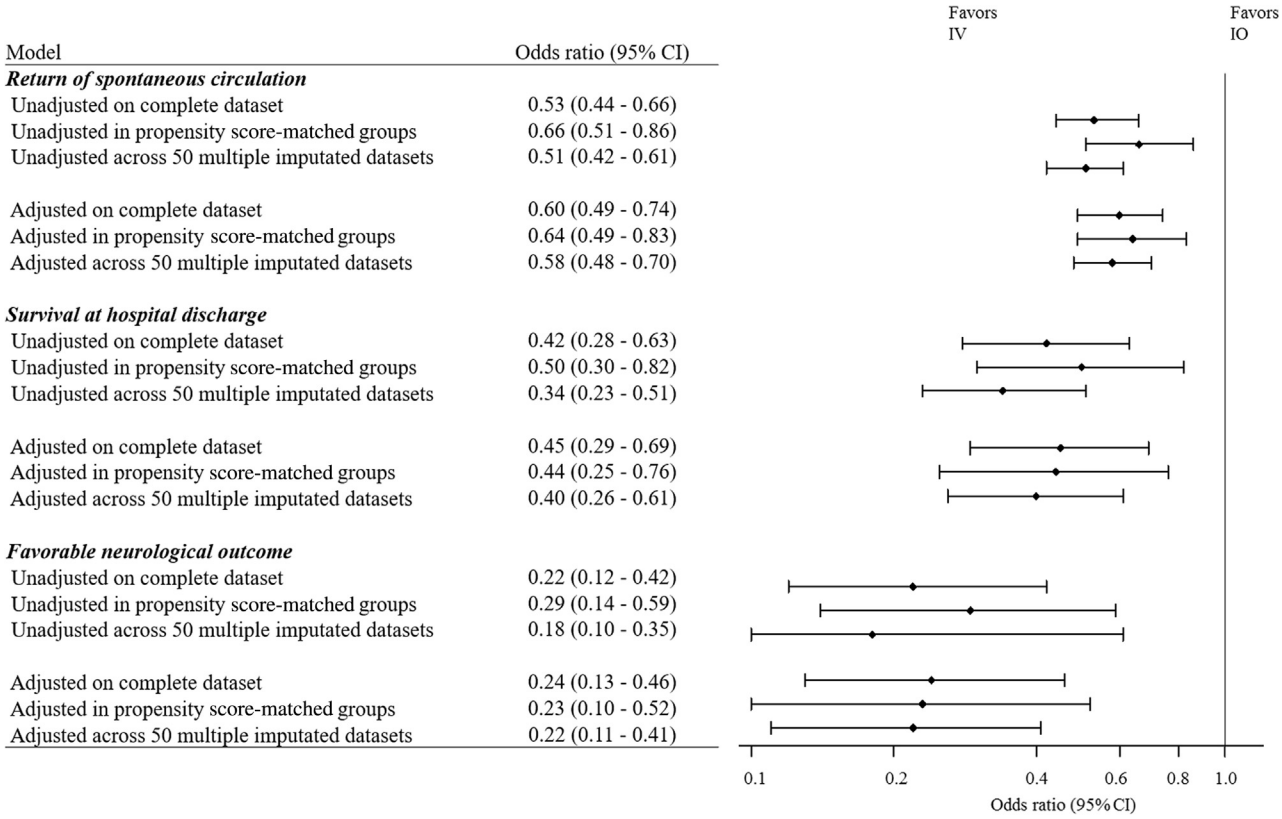

Figure 2. Results of logistic regression models used to assess the association of intraosseous access on the rate of survival or favorable neurologic outcome at hospital discharge compared with intravenous access in complete, propensity score–matched, and multiply imputed data sets.

with intravenous access, intraosseous access was associated with a decreased probability of return of spontaneous circulation (odds ratio [OR] 0.60; 95% CI 0.49 to 0.74), survival (OR 0.44; 95% CI 0.35 to 0.76), and favorable neurologic outcome (OR 0.24; 95% CI 0.13 to 0.46).

Demographics for the 1,116 patients identified by propensity score matching method are shown in Table 2. Absolute standardized difference in each variable was below 10%. In the unadjusted model, intraosseous access was associated with a decreased probability of return of spontaneous circulation, survival, and favorable neurologic outcome to hospital discharge (OR for return of spontaneous circulation 0.66, 95% CI 0.51 to 0.86; OR for survival 0.50, 95% CI 0.30 to 0.82; OR for neurologic outcome 0.29, 95% CI 0.14 to 0.59) (Figure 2). In the adjusted model, this association was consistent (adjusted OR for return of spontaneous circulation 0.64, 95% CI 0.49 to 0.83; adjusted OR for survival 0.44, 95% CI 0.25 to 0.76; adjusted OR for neurologic outcome 0.23, 95% CI 0.10 to 0.52).

The analysis across 50 multiply imputed data sets including 13,155 out-of-hospital cardiac arrest patients resulted in a similar negative association between intraosseous vascular access and outcomes (adjusted OR for survival 0.40, 95% CI 0.26 to 0.61; adjusted OR for neurologic outcome 0.22, 95% CI 0.11 to 0.41) (Figure 2).

There were 9,936 of 13,155 patients (75.5%) with data on study enrolling region. Intraosseous access was used in 73 of 192 regions (38.0%) in a median of 7.6% of cases (interquartile range 3.2% to 21.9%). The analysis accounting for clustering in both complete data capture (9,284 cases) and 50 multiply imputed data sets (9,883 cases) resulted in a negative association between intraosseous vascular access and all outcomes (Figure 3). When the subgroup of 3,211 patients within the 73 study enrolling regions that used intraosseous access was analyzed separately, results similarly showed an association between intraosseous use and outcomes compared with intravenous use (adjusted OR for return of spontaneous circulation 0.67, 95% CI 0.52 to 0.89; adjusted OR for survival 0.47, 95% CI 0.24 to 0.88; adjusted OR for favorable neurologic outcome 0.27, 95% CI 0.11 to 0.70).

The estimates of the stratified analyses within the 12,162 patients with complete data capture are described in Table 3. All analyses demonstrated a negative association between intraosseous vascular access and all 3 outcomes.

Table 2. Patient demographics and outcomes of 1,116 propensity score matched intraosseous or intravenous patients with out-of-hospital cardiac arrest.

Variable	n or Median		
	IO Group (n=558)	IV Group (n=558)	SD (%)
Age (IQR), y	64 (53–77)	64 (50–77)	5.6
Female sex, No. (%)	261 (46.8)	263 (47.1)	−0.7
Initial rhythm, No. (%)			4.5
Shockable	83 (14.9)	73 (13.1)	
Nonshockable	478 (85.2)	485 (86.5)	
Bystander witness, No. (%)	200 (35.8)	198 (35.5)	−0.7
EMS witness, No. (%)	61 (10.9)	64 (11.4)	1.1
Bystander CPR (1/0), No. (%)	221 (39.4)	200 (35.7)	−0.7
Bystander AED (1/0), No. (%)	13 (2.3)	16 (2.9)	−3.7
Location, No. (%)			2.1
Public	58 (10.4)	54 (9.7)	
Nonpublic	500 (89.6)	504 (90.3)	
Time from call to paramedic scene (IQR), min	4.6 (3.4–6.0)	4.5 (3.6–5.9)	1.3
Time from call to ALS scene (IQR), min	5.0 (4.0–6.6)	5.1 (4.0–6.7)	−1.6
Inhospital treatment, No. (%)*			
Therapeutic hypothermia	31 (47.7)†	70 (61.4)‡	
Fibrinolytics	1 (1.5)†	8 (7.0)‡	
Diagnostic catheterization	22 (33.9)†	27 (23.7)‡	
Interventional catheterization	6 (9.2)†	21 (18.4)‡	
Outcomes, No. (%)§			
Return of spontaneous circulation	141 (25.3)	189 (33.9)	
Survival at hospital discharge	25 (4.5)	48 (8.6)	
Favorable neurologic outcome	10 (1.8)	33 (5.9)	

*Denominator includes all patients who survived until admission to a hospital ward in the propensity-matched cohort.
†These data were unavailable for 48 of the 113 IO patients who were admitted to a hospital ward in the propensity-matched cohort.
‡These data were unavailable for 40 of the 114 IV patients who were admitted to a hospital ward in the propensity-matched cohort.
§Denominator includes all patients in the propensity-matched cohort.

LIMITATIONS

First, although our study was conducted at 10 diverse North American sites with a combined catchment area of approximately 24 million citizens,[4,6] our observations might not be generalizable in other settings, especially where patient characteristics and out-of-hospital medical management are different.

Second, although we adjusted the association between intraosseous access use and outcomes for clustering, regional practices, policies, and respective outcomes may have affected the selection of vascular access and our estimates. Although we excluded patients with failed vascular access attempts, it is possible that they were chosen for initial intraosseous access because of the characteristics predictive of difficult intravenous access, which may also be predictive of poor outcomes.

Third, we were unable to identify intraosseous infusion devices, the specific location of intraosseous access, and whether intraosseous access had a fluid bolus of 20 mL or pressure bags, which are known to affect drug distribution.[19,20]

Fourth, this was a secondary analysis of data from 2 clinical trials, which may introduce bias; however, because neither of the original studies demonstrated a statistically significant difference between treatment arms,[5,7] this risk of bias is likely low.

Fifth, there was an imbalance in inhospital treatments between patients with either intraosseous or intravenous access, which may represent differences in care provided between groups. However, in this retrospective analysis it is unlikely that there was a systematic difference in the care provided based on out-of-hospital vascular access route; rather, care was likely based on the clinical status and characteristics of individual patients (which may have been affected by preceding medical decisions). Furthermore, this imbalance may be due to the large proportion of missing data.

Sixth, the type of vascular access was not randomly selected in our data; paramedics may have selected patients with certain characteristics for intraosseous access: although we excluded those with unsuccessful attempts at either route and applied propensity score-matching techniques to adjust for this selection bias, residual confounders may have affected our estimates. Furthermore, data on the time of vascular access and the time of first epinephrine use were not recorded, and thus it is unclear whether there were differences in the time of vascular access or epinephrine administration and whether these differences may have affected outcomes.

DISCUSSION

We examined 13,115 consecutive EMS-treated adult patients with nontraumatic out-of-hospital cardiac arrest across North America, of whom 5% received intraosseous access as the first and only attempted access route. Intraosseous access was negatively associated with the probability of return of spontaneous circulation, survival, and favorable neurologic outcome at hospital discharge. This relationship was consistent after adjustment for baseline characteristics and for selection bias and unmeasured confounders by propensity score-matching techniques. These data have raised concerns about intraosseous vascular access in the resuscitation of out-of-hospital cardiac arrest. Further work is needed to evaluate the effect of intraosseous vascular access on out-of-hospital cardiac arrest outcomes, ideally in randomized controlled trials.

In a recent similar retrospective single-region study involving 1,800 out-of-hospital cardiac arrests, although there was no statistically significant association between

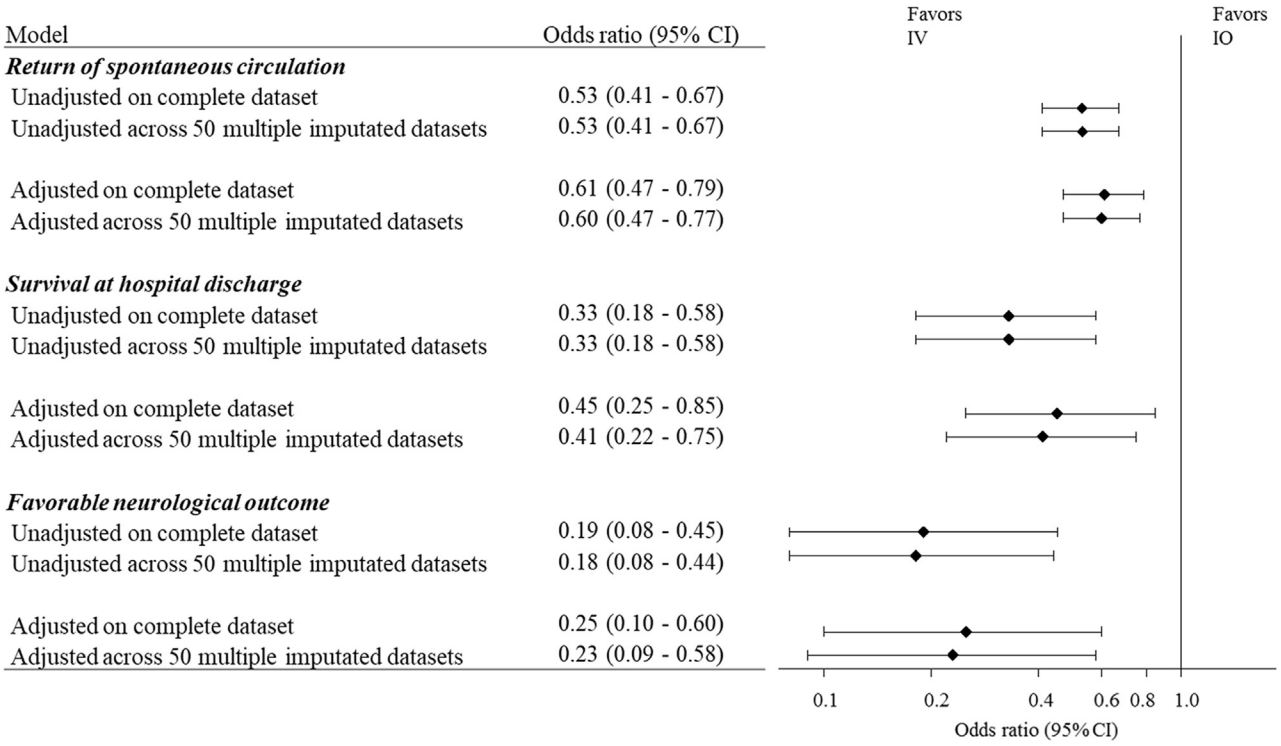

Figure 3. Results of generalized estimating equations logistic regression models used to assess the association of intraosseous access on the rate of survival or favorable neurologic outcome at hospital discharge compared with intravenous access in complete and multiply imputed data sets.

access route and survival at discharge, there was a negative association between intraosseous access and both return of spontaneous circulation and survival at hospitalization.[21] Our large cohort study from 10 North American sites supports these important findings, demonstrating a statistically significant association between intraosseous access and a decreased likelihood of neurologically intact survival. Furthermore, the multicenter nature of our data enhances the generalizability of the results. Whereas in the previous study protocols dictated that intraosseous access be performed only after initial intravenous attempts were unsuccessful, which may interrupt resuscitative maneuvers or be representative of refractory efforts or large body habitus, our study included only patients with intraosseous or intravenous access as a first and only route selection.

A wide variety of medications used for cardiac resuscitation can be administered though intraosseous access[22]; however, their actual effectiveness by this route is unclear; drugs may remain stagnant in bone marrow, especially without a fluid bolus of 20 mL or pressure bags.[23] During hemorrhagic shock, bone marrow blood

Table 3. The analysis stratified by important predictors within 12,162 patients with complete data capture.

			IO Vascular Access vs IV Vascular Access, OR (95% CI)		
Stratified Analysis	**IO, n**	**IV, n**	**ROSC**	**Survival**	**Favorable Neurologic Outcome**
Stratified by sex					
Male	297	7,678	0.52 (0.39–0.69)	0.50 (0.28–0.87)	0.17 (0.59–0.46)
Female	262	3,925	0.70 (0.53–0.93)	0.38 (0.19–0.76)	0.34 (0.14–0.81)
Stratified by initial rhythm					
Shockable	83	3,049	0.50 (0.32–0.79)	0.40 (0.21–0.75)	0.25 (0.11–0.57)
Nonshockable	476	8,554	0.62 (0.50–0.78)	0.49 (0.27–0.90)	0.22 (0.07–0.69)
Stratified by witness status					
Bystander	199	6,814	0.56 (0.41–0.76)	0.52 (0.30–0.90)	0.24 (0.10–0.56)
Nonbystander	360	4,789	0.62 (0.47–0.81)	0.34 (0.16–0.71)	0.24 (0.09–0.67)

ROSC, Return of spontaneous circulation.

flow decreases by 70% to 80%,[23] and it is likely that bone blood flow during CPR might be equally or more reduced because cardiac output generated by chest compression is only 20% to 30% of its normal output.[24,25] In addition, epinephrine is known to both reduce bone marrow flow rate and increase bone vascular resistance.[23] In a swine model of ventricular fibrillation, peak coronary perfusion pressure after epinephrine injection was achieved a median 17 seconds slower with tibial intraosseous administration compared with intravenous (60 versus 43 seconds).[26] Another animal study demonstrated that the mean atrial concentration of drugs through the tibial intraosseous route was 53% of the drug concentration as delivered though the central venous route.[19] In our study, flow rate through intraosseous access (11.1 mL/min) was significantly slower than through intravenous access (18.4 mL/min). Because this may be a proxy for vascular resistance, it is possible that resuscitative drugs are distributed slower through the intraosseous route than the intravenous route, and some may be trapped in bone marrow.

Because equipment for intraosseous access was relatively new in the time frame of our 2007 to 2009 data, intraosseous access use may be more prevalent currently; in a recent study, intraosseous access was used in 22% of patients.[27] This trend for an increased use of intraosseous access without evidence of benefit or equivalence with intravenous access could result in reduction of potential survival.

In conclusion, in this prospective observational study of patients with nontraumatic out-of-hospital cardiac arrest, intraosseous access was associated with lower survival and poor neurologic recovery compared with intravenous access. Further research is required to determine the effectiveness of the intraosseous vascular access route in out-of-hospital cardiac arrest resuscitations.

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