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Clinical paper

The association of intravenous vs. humeral-intraosseous vascular access with patient outcomes in adult out-of-hospital cardiac arrests

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Abstract

Aim: While intravenous (IV) vascular access for out-of-hospital cardiac arrest (OHCA) resuscitation is standard, humeral-intraosseous (IO) access is commonly used, despite few supporting data. We investigated the association between IV vs. humeral-IO and outcomes.

Methods: We utilized BC Cardiac Arrest Registry data, including adult OHCA where the first-attempted intra-arrest vascular access route performed by advanced life support (ALS)-trained paramedics was IV or humeral-IO. We fit a propensity-score adjusted model with inverse probability treatment weighting to estimate the association between IV vs. humeral-IO routes and favorable neurological outcomes (CPC 1–2) and survival at hospital discharge. We repeated models within subgroups defined by initial cardiac rhythm.

Results: We included 2,112 cases; the first-attempted route was IV (n = 1,575) or humeral-IO (n = 537). Time intervals from ALS-paramedic on-scene arrival to vascular access (6.6 vs. 6.9 min) and epinephrine administration (9.0 vs. 9.3 min) were similar between IV and IO groups, respectively. Among IV and humeral-IO groups, 98 (6.2%) and 20 (3.7%) had favorable neurological outcomes. Compared to humeral-IO, an IV-first approach was associated with improved hospital-discharge favorable neurological outcomes (AOR 1.7; 95% CI 1.1–2.7) and survival (AOR 1.5; 95% CI 1.0–2.3). Among shockable rhythm cases, an IV-first approach was associated with improved favorable neurological outcomes (AOR 4.2; 95% CI 2.1–8.2), but not among non-shockable rhythm cases (AOR 0.73; 95% CI 0.39–1.4).

Conclusion: An IV-first approach, compared to humeral-IO, for intra-arrest resuscitation was associated with an improved odds of favorable neurological outcomes and survival to hospital discharge. This association was seen among an initial shockable rhythm, but not non-shockable rhythm, subgroups.

Keywords: Heart arrest, Out-of-hospital cardiac arrest, Intravenous, Intraosseous

Introduction

Out-of-hospital cardiac arrest (OHCA) is major source of mortality, with an incidence of approximately 60 emergency medical services (EMS)-treated cases per 100,000 persons annually in North America, and survival at hospital discharge of ranging from 9.4% to 12%.[1] Recommended OHCA resuscitation includes high-quality cardiopulmonary resuscitation (CPR), early defibrillation, and advanced life support (ALS) interventions, namely, the administration of intravascular epinephrine.[2] For vascular access, international guidelines recommend the intravenous (IV) route as the first-line strategy, with intraosseous (IO) access recommended if IV attempts are (or are likely to be) unsuccessful.[2] Interestingly, IO usage appears to be increasing over time: a recent study reported that the proportion of OHCA receiving IO access increased approximately 2-fold from 2015 to 2020, with the odds of patients receiving IO access increasing each month.[3]

Published studies comparing clinical outcomes of adult OHCAs treated with IO vs. IV have been observational, reporting that that IO is associated with worse neurological outcomes,[4–8] survival,[4–8] and return of spontaneous circulation (ROSC).[4–10] In adults, IO

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access is typically tibial or humeral,[11] and while several of these studies did not specify the IO location, it is likely that the majority were tibial sites.[7,9,12] The association of worse outcomes with IO may be explained by the inferior delivery of medications through tibial-IO vascular access: swine models have demonstrated that drugs administered via IV access, in comparison to tibial-IO access, result in higher maximum concentration[13–16] and lower time to maximum drug concentration.[13,15,17,18]

In contrast, the pharmacokinetic profiles of humeral-IOs, in comparison to IV, appear similar in cardiac arrest swine models.[15–17,19–22] Operational metrics have also demonstrated similar time intervals from paramedic arrival to initial successful vascular access, and from paramedic arrival to drug administration delivery.[23] There are few data comparing IV vs. humeral-IO vascular access with regards to clinically relevant outcomes. A single study reported that humeral-IO, compared to IV, was associated with a lower odds of ROSC at emergency department arrival, but not survival or neurological outcomes at hospital discharge.[24]

Further research is needed comparing clinical outcomes of patients treated with IV vs. humeral-IO strategies. We investigated whether a strategy of IV vs. humeral-IO as the first-attempted intra-arrest vascular route access was associated with clinical outcomes.

Methods

Study setting, data source and design

This observational study analysed cases from the British Columbia (BC) Cardiac Arrest registry, approved by the University of British Columbia-affiliated Providence Health Care Research Ethics Board (H15-03059). We included cases as of January 1, 2019 (the date the registry footprint expanded to include the entire province), and up to June 30, 2023 (the closest half-year to the date the data was downloaded). The BC Cardiac Arrest Registry prospectively includes consecutive non-traumatic EMS-assessed OHCA cases throughout the province of BC, defined as any case identified by EMS to be pulseless.

EMS medical care

EMS medical care for OHCAs in BC is initiated by a 9-1-1 call to a centralized dispatch centre, with a coordinated response from the provincial BC Emergency Health Services (BCEHS) and municipal fire-rescue departments. Fire-rescue units are trained in basic life support (BLS), including automated external defibrillation (AED) application.[2] BCEHS personnel are trained in basic life support (BLS) (some of whom are trained to insert IVs), with some also trained in advanced life support (ALS).[2] Only ALS-trained paramedics are licenced to insert IO vascular access devices.

Data collection

Trained BC Cardiac Arrest Registry staff review Utstein-based templated prehospital patient care records and abstract data into a RedCap data base (Vanderbilt, Nashville), which contains standard Utstein variables,[25] including location type, witnessed status, patient and cardiac arrest characteristics, bystander interventions, EMS response data (including the arrival times and service levels of EMS vehicles), and time-stamped EMS-performed treatments. The registry also collects data on non-prescription drug use. Staff ascertain hospital discharge outcomes from hospital clinical records.

Selection of participants

We reviewed all cases from the BC Cardiac Arrest Registry for inclusion. We excluded cases that: (1) were not treated by EMS; (2) the first-attempted vascular access site was not an IV or humeral-IO; (3) an ALS-trained unit was not the first BCEHS unit to arrive at the scene (given that both BLS and ALS-trained paramedics place IV's, but only ALS-trained paramedics place IO's; thus, including only cases with ALS unit first on-scene achieves comparability between the two groups with regards to the level of training of the provider leading the resuscitation and the vascular access attempt); (4) return of spontaneous circulation (ROSC) was achieved prior to the first vascular access attempt or there was missing data to determine the sequence of ROSC and the first vascular access attempt; (5) the first vascular access attempt preceded an EMS-witnessed arrest or there was missing data to determine the sequence of the EMS-witnessed arrest and the first vascular access attempt; and (6) age < 18 years. In summary, the study cohort included adult OHCA cases that received intra-arrest IV or humeral-IO as the first vascular access attempt led by ALS-trained paramedics (regardless of whether the attempt was successful).

Outcome and exposure variables

Cases were dichotomized based on the variable of interest: IV or humeral-IO as the first-attempted vascular access route. The primary outcome was favorable neurological outcome at hospital discharge, defined as a cerebral performance category (CPC) of 1 or 2.[26] Secondary outcomes included: (1) survival to hospital discharge; (2) ROSC (defined as a palpable pulse for any duration of time); and (3) ROSC at time of emergency department (ED) arrival (defined as a palpable pulse present at the time of ED arrival).

Data analysis

Data was exported from RedCap[27] and analyzed using R version 4.1.2[28] and SAS version 9.4.[29] We described patient characteristics according to the first-attempted vascular access route (IV vs. humeral-IO), using counts (with percentages) for categorical variables and median (with interquartile range [IQR]) for continuous variables.

We calculated operational metrics of the vascular access routes including: (1) successful placement of the first-chosen vascular access route (either on the initial or subsequent attempts); (2) time interval from ALS-trained paramedic on-scene arrival to successful vascular access; (3) time interval from ALS-trained paramedic on-scene arrival to first epinephrine administration; and (4) receipt of intravascular medications (epinephrine, amiodarone, or lidocaine) through any route.

Our primary analysis was a propensity-score adjusted model with inverse probability treatment weighting. Since paramedics may have preferentially attempted IV or IO access depending on patient characteristics, we first calculated propensity scores using binary logistic regression models to determine the probability of receiving either treatment modality. We included the following covariates: (1) age; (2) sex; (3) witness status (unwitnessed, bystander witnessed, vs. EMS witnessed); (4) bystander CPR; (5) time interval from call received at dispatch to first ALS-trained paramedic vehicle arrival; (6) location type (public location [street, public building, place of recreation, airport, casino, outpatient medical facility, nursing home, industrial site, other public locations] vs. private location [house, apartment, condominium, other private location]); (7) initial cardiac rhythm (shockable vs. non-shockable); (8) history of non-prescription drug use (defined as either a past medical history of non-prescription drug use or evidence of non-prescription drug use preceding the OHCA, based on paraphernalia present at the scene or bystander reports); and (9) calendar year. We included "history of non-prescription drug use" in the model as this may affect a paramedic's first choice of vascular access, given that IV access may be expected to be challenging.

We created a pseudopopulation (the "weighted cohort") through inverse probability treatment weighting (IPTW),[30] calculated as the inverse of the estimated propensity scores, to ensure that confounding variables were equally distributed across the IV and humeral-IO groups. The balance of this weighted cohort was assessed using Absolute Standardized Mean Difference (ASMD; where an ASMD < 0.1 indicates the groups are well balanced).[30,31] Using the weighted cohort, we performed a multivariable analysis to assess the association between IV (with reference to humeral-IO) and the outcomes measures, to calculate adjusted odds ratios (AOR) and corresponding 95% confidence intervals (95% CI). As a secondary analysis, we fit a simple logistic regression model, with the same outcomes and adjustment covariates, on the full study cohort.

In addition, we investigated the hypothesis that the association between vascular access route and outcomes may differ between strata defined by initial cardiac rhythm, through two different sensitivity analyses. First, we repeated the primary and secondary analyses (for the primary outcome), incorporating an interaction term including IV vascular access and initial shockable cardiac rhythm, to determine if the term was statistically significant. Second, we repeated the primary and secondary analyses within subgroups of shockable and non-shockable initial cardiac rhythms.

Results

Study population

The BC Cardiac Arrest Registry enrolled 34,787 OHCA cases during the study period (Fig. 1). After exclusions, the full study cohort included 2,112 cases, of which the first-attempted vascular access route was IV (n = 1,575) or humeral-IO (n = 537).

Patient characteristics and outcomes

Table 1 shows patient characteristics dichotomized by first-attempted vascular access route. For the full cohort, the IV and humeral-IO groups had a median age of 66 (IQR 51–78) and 63 (IQR 49–75) years, and 428 (27%) and 158 (29%) were female, respectively. The time intervals from call received at dispatch to first EMS vehicle (either fire-rescue or ALS-trained paramedic) on scene were 6.9 (IQR 5.4–8.7) and 7.1 (IQR 5.6–8.9) minutes for the IV and humeral-IO groups, respectively.

Table 2 shows patient outcomes. Among the full IV and humeral-IO groups, 98 (6.2%) and 20 (3.7%) cases had favorable neurological outcomes at hospital discharge, and 107 (6.8%) and 25 (4.7%) cases survived to hospital discharge, respectively (Table 2).

Operational metrics

Table 3 shows operational metrics. For IV group cases, 1458 (93%) had successful placement of the first-chosen vascular access route, in comparison to 529 (98%) of the humeral-IO group cases. The time intervals from ALS-paramedic arrival to successful vascular access and to epinephrine administration were similar between the IV and humeral-IO groups.

Logistic regression models

Results of the primary analysis (using the weighted cohort), demonstrated that an IV-first approach, compared to a humeral-IO-first approach, was associated with improved favorable neurological outcomes at hospital discharge (AOR 1.7; 95% CI 1.1–2.7), survival at hospital discharge (AOR 1.5; 95% CI 1.0–2.3), and ROSC at time of ED arrival (AOR 1.3; 95% CI 1.1–1.6; Table 2). Model results using the full cohort are shown in Table 2.

Sensitivity analyses

The interaction term including IV vascular access and initial shockable cardiac rhythm was statistically significant for both the weighted and full cohort models examining the primary outcome. Results of the sensitivity analyses performed on the weighted and full cohorts are displayed in Table 4. Among those with a shockable initial cardiac rhythm, an IV-first approach, compared to a humeral-IO-first approach, was associated with greater odds of a favorable neurological outcome at hospital discharge, when analyzing both the weighted (AOR 4.2; 95% CI 2.1–8.2) and full cohorts (AOR 4.9; 95% CI 1.8–13). Analyses of secondary outcomes were consistent. Among those with a non-shockable initial cardiac rhythm, we did not detect an association between first-attempted vascular access route and any outcome measure.

Discussion

We examined 2,112 adult OHCA cases that received either an IV or humeral-IO as the first-attempted vascular access route. Despite similar operational metrics including time to placement and drug delivery, when compared to a humeral-IO-first approach, an IV-first approach was associated with improved favorable neurological outcomes and survival at hospital discharge. Our sensitivity analyses suggest that these findings are primarily due to those with shockable initial cardiac rhythms. Our data support current recommendations endorsing IV as the primary vascular access for OHCA resuscitations, especially for those with shockable initial cardiac rhythms.

International OHCA guidelines recommending IV as the preferential vascular access strategy[2] are based on previous observational studies demonstrating that IO access, in comparison to IV, is associated with lower survival.[4–8] However, given that the majority of IO access in these studies were likely tibial location,[7,9] we investigated whether a humeral-IO-first approach might yield better or similar outcomes as an IV-first approach. While our study shows that humeral-IO tended to have marginally improved placement success, clinically relevant endpoints including neurological outcomes and survival at hospital discharge favoured an IV strategy.

Several previous cardiac arrest swine models have demonstrated similar pharmacokinetics of medications delivered through IV and humeral-IO routes, reporting no differences in maximum drug serum concentration and time to maximum serum concentration,[15–17,19–22] and both appearing superior to a tibial-IO route.[15–17] One study in 10 humans investigating intra-arrest delivery of contrast dye reported faster enhancement of the right ventricle with humeral-IO administration (5.60 ± 1.71 s), compared to IV (15.40 ± 3.24 s; P < 0.001).[32]

Only two previous studies have examined clinical outcomes of humeral-IO-treated OHCAs. One study compared adult OHCA cases

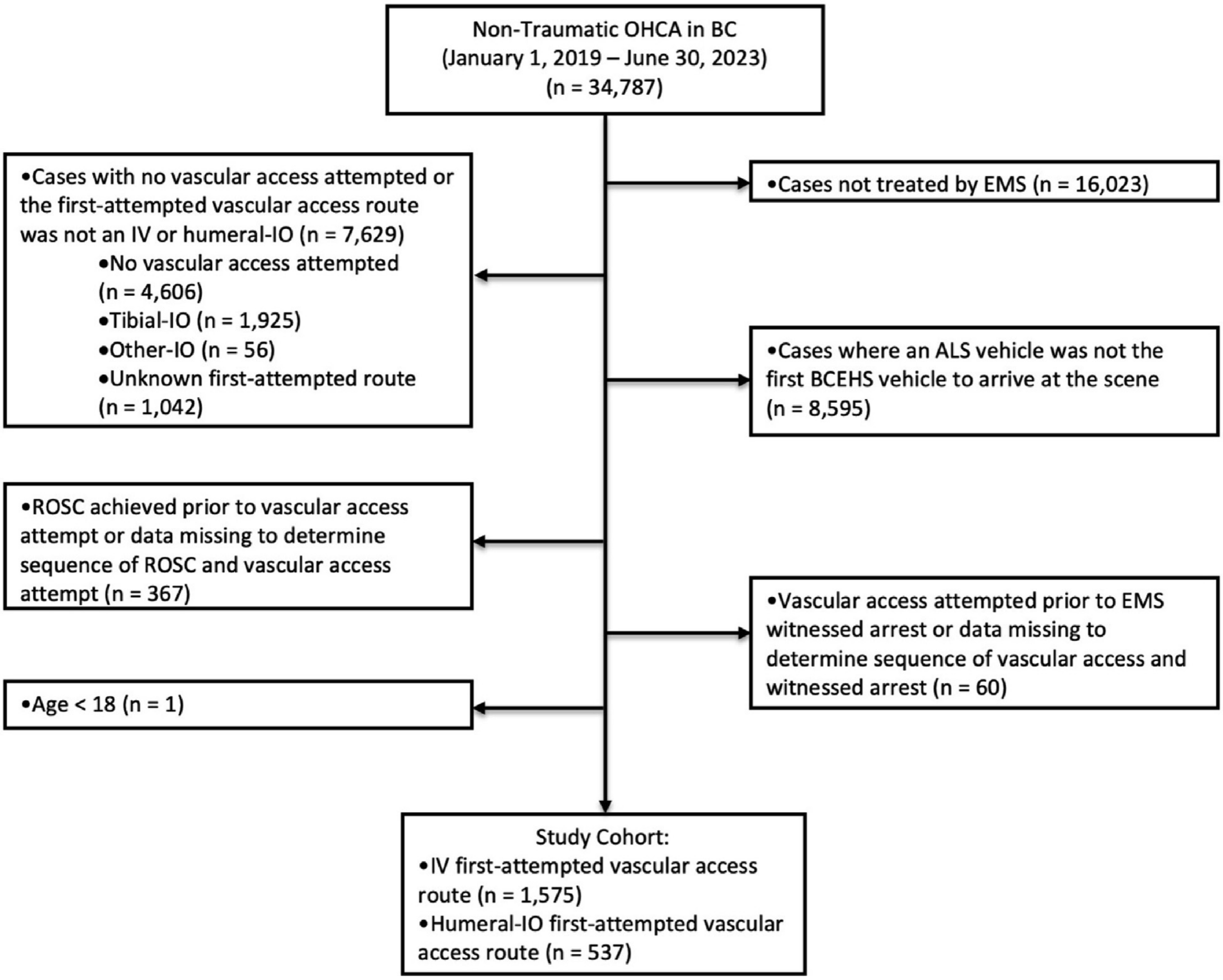

Fig. 1 – Study Flow. "Other-IO" refers to an IO site other than the proximal humerus or proximal tibia. OHCA, out-of-hospital cardiac arrest; BC, the Province of British Columbia; n, number; EMS, emergency medical services; IV, intravenous; IO, intraosseus; ALS, advanced life support; BCEHS, BC Emergency Health Services; ROSC, return of spontaneous circulation.

treated with a tibial-IO-first vs. humeral-IO-first approach, and reported no differences in favorable neurological outcomes or survival at hospital discharge.[33] The second study, conducted by Benner and colleagues, reported that both tibial-IO and humeral-IO, each in comparison to IV, were associated with similarly decreased odds of having a pulse at hospital arrival (the primary outcome).[24] In contrast with our data, humeral-IO use was not associated with the study's secondary outcomes of survival or good neurological outcomes at hospital discharge; however, point estimates were consistently under 1 and were very close to statistical significance. Outcomes of those treated with tibial vs. humeral-IO's were very similar. Authors performed subgroup analyses based on initial cardiac rhythm, and reported that among those with shockable rhythms, an IV-first approach (in comparison to both humeral-IO and tibial-IO groups) was positively associated with the study's secondary outcomes of hospital-discharge survival and good neurological outcomes; this association was not seen among those with non-shockable rhythms. These initial cardiac rhythm-specific findings in both the Benner and current study are suggestive that an IV approach may be preferential among those with shockable initial cardiac rhythms, whereas this signal is not apparent among non-shockable cases.

It has been theorized that the poorer outcomes associated with IOs, in comparison to IVs, may be a result of drug trapping of lipophilic medications within the medullary cavity.[24,34] As one ages, the medullary cavity accumulates fatty marrow;[35] this fatty marrow may attract lipophilic drugs administered through IOs, thus preventing or slowing the medication from reaching central circulation. Given the lipophilic properties of amiodarone,[36,37] which was administered to approximately half of cases with shockable initial cardiac rhythms (in both the IV and humeral-IO groups), this drug trapping effect may explain the differential outcomes of patients treated with IV vs. humeral-IOs—results that were not apparent in the non-shockable groups. This may be supported by a secondary analysis of the ALPS trial (a randomized trial which compared amiodarone vs. lidocaine vs. placebo), which demonstrated improved survival in patients receiving amiodarone by IV, but not by IO.[34] However, the drug trapping effect on lipophilic medications has not been consistently supported through swine models;[20,38,39] a study of 28 Yorkshire swine found no difference in serum amiodarone availability when administered through the humeral-IO or IV routes.[20]

Epinephrine, a non-lipophilic drug indicated for OHCAs of all rhythms,[2] has been shown to be of particular benefit to those with

Table 1 – Full and weighted cohort characteristics.

	Full Cohort			Weighted Cohort		
	Humeral-IO (*n* = 537)	IV (*n* = 1,575)	ASMD	Humeral-IO	IV	ASMD
	n (%) or median (IQR)	*n* (%) or median (IQR)		% or median	% or median	
Patient age	63 (49–75)	66 (51–78)	0.098	63	63	0.013
Female sex	158 (29)	428 (27)	0.050	28	28	0.013
Witnessed Status			0.102			0.016
Unwitnessed	308 (57)	911 (58)		57	57	
Bystander witnessed	198 (37)	603 (38)		39	38	
EMS witnessed	31 (5.8)	57 (3.6)		4.0	4.0	
Bystander CPR	304 (57)	989 (63)	0.150	62	62	0.006
Calendar year			0.206			0.029
2019	74 (14)	287 (18)		17	17	
2020	112 (21)	359 (23)		22	23	
2021	98 (18)	340 (22)		20	21	
2022	175 (33)	405 (26)		27	27	
2023	78 (15)	184 (12)		13	13	
Dispatch call received-to-ALS arrival interval, minutes	9.1 (6.8–12)	9.1 (7.0–12)	0.037	9.0	9.0	0.043
Public location[1]	124 (23)	335 (21)	0.044	22	22	0.004
Shockable initial cardiac rhythm	67 (13)	310 (20)	0.197	18	18	<0.001
History of non-prescription drug use[2]	21 (3.9)	47 (3.0)	0.051	3.0	3.0	0.002

IO: intraosseous; IV: intravenous; *n*: number; IQR: Interquartile Range; BCEHS: British Columbia Emergency Health Services; CPR: cardiopulmonary resuscitation; SD: Standard Deviation; ASMD: Absolute Standardized Mean Difference; ASMD < 0.1 indicates that the IV and humeral-IO groups was well balance (there is no difference between groups).

[1] "Public Location" includes: street, public building, place of recreation, airport, casino, other public location, outpatient medical facility, nursing home, and industrial site.

[2] "History of non-prescription drug use" is defined as either a past medical history of non-prescription drug use or evidence of non-prescription drug use preceding the OHCA, based on paraphernalia present at the scene or bystander reports.

Table 2 – Primary and secondary outcomes for the full and weighted cohorts.

	Full Cohort			Weighted Cohort		
	Humeral-IO (*n* = 537)	IV (*n* = 1,575)	Adjusted Odds Ratio[1]	Humeral-IO	IV	Adjusted Odds Ratio[1]
	n (%)	*n* (%)	(95% CI)	(%)	(%)	(95% CI)
Favorable Neurological Outcome[2]	20 (3.7)	98 (6.2)	1.5 (0.90–2.7)	4.0	6.0	1.7 (1.1–2.7)
Survival to Hospital Discharge	25 (4.7)	107 (6.8)	1.4 (0.84–2.3)	5.0	7.0	1.5 (1.0–2.3)
ROSC	191 (36)	593 (38)	1.1 (0.87–1.4)	35	38	1.1 (0.93–1.4)
ROSC at Time of ED Arrival	136 (25)	468 (30)	1.3 (1.0–1.7)	25	30	1.3 (1.1–1.6)

IO: intraosseous; IV: intravenous; *n*: number; CI: Confidence Interval; ROSC: Return of Spontaneous Circulation; ED, emergency department.

[1] Reference Group: Humeral-IO.

[2] "Favorable Neurological Outcome" is defined as a Cerebral Performance Category score of 1–2, measured at hospital discharge..

non-shockable initial cardiac rhythms.[40] An initial cardiac rhythm-based secondary analysis of the PARAMEDIC2 trial, which randomized OHCAs to epinephrine vs. placebo, found that epinephrine was associated with improved outcomes among those with non-shockable initial cardiac rhythms (AOR 2.15; 95% CI 1.13–4.09), but not those with shockable initial rhythms (AOR 1.32; 95% CI 0.95–1.86).[40] A secondary analysis of the same clinical trial data compared IV vs. IO-treated cases, and found no difference in epinephrine treatment effect between vascular access routes.[41] As epinephrine is the primary (and seemingly beneficial) pharmacological therapy for non-shockable cardiac rhythms, with efficacy not appearing to be dependent on vascular access routes,[41] this may explain our subgroup analysis of non-shockable cases showing similar outcomes between vascular access routes. Overall, it is possible that initial cardiac rhythm should influence the decision of whether to place an IV or IO, however clinical trial data is required to support or refute this hypothesis.

There is currently no available clinical trial evidence to inform clinicians of the optimal vascular access site for OHCA. One recently-completed clinical trial in Taiwan randomized adult OHCAs to either IV or humeral-IO, evaluating survival at hospital discharge, the results of with are forthcoming.[42] Two additional clinical trials are

Table 3 – Operational characteristics according to the first-attempted vascular access route.

	Full Cohort	
	Humeral-IO (*n* = 537) *n* (%) or median (IQR)	IV (*n* = 1,575) *n* (%) or median (IQR)
Successful access of first-chosen route[1]	529 (98)	1458 (93)
ALS arrival-to-successful vascular access interval, minutes[2]	6.9 (4.8–10)	6.6 (4.5–9.5)
ALS arrival-to-epinephrine administration interval, minutes	9.3 (7.1–12)	9.0 (6.8–12)
Epinephrine administered through any route	519 (97)	1457 (93)
Antiarrhythmic administered through any route	69 (13)	258 (16)
Amiodarone	68 (13)	252 (16)
Lidocaine	0	3 (0.19)

IO: intraosseous; IV: intravenous; *n*: number; IQR: Interquartile Range.

Note: Among those with shockable initial cardiac rhythms, 168/310 (54%) and 35/67 (52%) cases in the IV and humeral-IO groups, respectively, received antiarrhythmic drug administration; 167/168 (99%) and 35/35 (100%) of these IV and humeral-IO cases, respectively, received amiodarone.

[1] "Successful access of first chosen route" defined as the successful placement of the first-chosen route (IV vs humeral-IO) either on the initial attempt or subsequent attempts.

[2] Successful vascular access is of any route, either IO or IV. For example, a case first with a humeral IO attempted first would be classified as "humeral IO", however if this attempted failed, and an IV was then successfully placed, the time of the IV access would be represented as the time of successful vascular access.

Table 4 – Sensitivity regression analyses of subgroups defined by initial cardiac rhythm.

	Full Cohort Adjusted Odds Ratio[1] (95% CI)	Weighted Cohort Adjusted Odds Ratio[1] (95% CI)
Shockable initial cardiac rhythm subgroup		
Favorable neurological outcome[2]	4.9 (1.8–13)	4.2 (2.1–8.2)
Survival to hospital discharge	2.8 (1.1–6.5)	2.7 (1.4–4.9)
ROSC	1.7 (0.95–3.0)	1.8 (1.1–2.8)
ROSC at time of ED arrival	1.9 (1.1–3.6)	2.1 (1.3–3.3)
Non-shockable initial cardiac rhythm subgroup		
Favorable neurological outcome[2]	0.73 (0.37–1.4)	0.73 (0.39–1.4)
Survival to hospital discharge	0.86 (0.46–1.6)	0.86 (0.48–1.5)
ROSC	1.0 (0.79–1.3)	1.0 (0.82–1.3)
ROSC at time of ED arrival	1.2 (0.90–1.6)	1.2 (0.93–1.5)

IO: intraosseous; IV: intravenous; *n*: number; OR: Odds Ratio (calculated using IO humerus as the reference); CI: Confidence Interval; ROSC: Return of Spontaneous Circulation

[1] Reference Group: Humeral-IO.

[2] "Favorable Neurological Outcome" is defined as a Cerebral Performance Category score of 1–2, as measured at hospital discharge.

ongoing. The IVIO trial randomizes patients to IV vs. IO, with the IO group further randomized to humeral or tibial sites.[43] The PARAMEDIC3 trial randomizes patients to IV and IO, allowing for paramedics to chose the IO placement site (humeral vs. tibia).[44]

Limitations

Our study had several limitations. First, we excluded cases for which an ALS-trained paramedic was not the first BCEHS unit at the scene, and thus our results may not apply to IVs and/or humeral-IOs attempted by differently-trained personnel or in different regions, and may not be generalizable to systems where all paramedics are ALS-trained. Secondly, although our model balanced covariates between the exposure groups, there may have been other unmeasured covariates important to these relationships, including other factors that may have influenced a paramedic's decision to attempt one vascular access route over another. For example, cases with elevated body mass index or with medical conditions that lead to vasculopathy may have been perceived by paramedics to be more technically difficult for IV access, and thus may have preferentially chosen IO for these cases. Thus, the IO group in our study may have included cases with less comorbidities (who may have been more likely to be resuscitated), which may have biased our results. Lastly, missing data is a limitation; for example, paramedics may not have documented missed vascular access attempts, which may have impacted the analyses.

Conclusion

In adult OHCA's, an IV-first approach was associated with an improved odds of a favorable neurological outcome, survival to hospital discharge, and ROSC at ED arrival, compared to a humeral-IO-first approach. In subgroup analyses, an IV-first approach (compared to a humeral-IO-first approach) was associated with improved outcomes among those with shockable initial cardiac rhythms, but this association was not detected among those with non-shockable rhythms.

CRediT authorship contribution statement

Callahan Brebner: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Michael Asamoah-Boaheng:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Bianca Zaidel:** Writing – review & editing, Methodology, Investigation, Data curation. **Justin Yap:** Writing – review & editing, Methodology, Investigation, Data curation. **Frank Scheuermeyer:** Writing – review & editing, Methodology, Investigation. **Valerie Mok:** Writing – review & editing, Methodology, Investigation. **Jacob Hutton:** Writing – review & editing, Methodology, Investigation. **Garth Meckler:** Writing – review & editing, Methodology, Investigation. **Robert Schlamp:** Writing – review & editing, Methodology, Investigation. **Jim Christenson:** Writing – review & editing, Resources, Methodology, Investigation, Funding acquisition. **Brian Grunau:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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