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Outcomes with Tibial and Humeral Intraosseous Access Compared to Peripheral Intravenous Access in Out-of-Hospital Cardiac Arrest

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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ABSTRACT

Background: The optimal initial vascular access strategy for out-of-hospital cardiac arrest (OHCA) remains unknown. Our objective was to evaluate the association between peripheral intravenous (PIV), tibial intraosseous (TIO), or humeral intraosseous (HIO) as first vascular attempt strategies and outcomes for patients suffering OHCA.

Method: This was a secondary analysis of the Portland Cardiac Arrest Epidemiologic Registry, which included adult patients (≥18 years-old) with EMS-treated, non-traumatic OHCA from 2018-2021. The primary independent variable in our analysis was the initial vascular access strategy, defined as PIV, TIO, or HIO based on the first access attempt. The primary outcome for this study was the return of spontaneous circulation (ROSC) at emergency department (ED) arrival (a palpable pulse on arrival to the hospital). Secondary outcomes included survival to: admission, discharge, and discharge with a favorable outcome (Cerebral Perfusion Category score of ≤2). We conducted multivariable logistic regressions, adjusting for confounding variables and for clustering using a mixed-effects approach, with prespecified subgroup analyses by initial rhythm.

Results: We included 2,993 patients with initial vascular access strategies of PIV (822 [27.5%]), TIO (1,171 [39.1%]), and HIO (1,000 [33.4%]). Multivariable analysis showed lower odds of ROSC at ED arrival (adjusted odds ratio [95% CI]) with TIO (0.79 [0.64-0.98]) or HIO (0.75 [0.60-0.93]) compared to a PIV-first strategy. These associations remained in stratified analyses for those with shockable initial rhythms (0.60 [0.41-0.88] and 0.53 [0.36-0.79]) but not in patients with asystole or pulseless electrical activity for TIO and HIO compared to PIV, respectively. There were no statistically significant differences in adjusted odds for survival to admission, discharge, or discharge with a favorable outcome for TIO or HIO compared to the PIV-first group in the overall analysis. Patients with shockable initial rhythms had lower adjusted odds of survival to discharge (0.63 [0.41-0.96] and 0.64 [0.41-0.99]) and to discharge with a favorable outcome (0.60 [0.39-0.93] and 0.64 [0.40-1.00]) for TIO and HIO compared to PIV, respectively.

Conclusions: TIO or HIO as first access strategies in OHCA were associated with lower odds of ROSC at ED arrival compared to PIV.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a leading cause of morbidity and mortality in the United States, affecting 356,000 individuals annually.[1] Despite gradual improvements in OHCA survival over time, survival remains poor and around 10% nationally.[2,3] Patterns of survival vary significantly across communities and emergency medical services (EMS) systems.[4-6] In addition to differences in bystander defibrillation and cardiopulmonary resuscitation (CPR) rates,[7-9] variation in EMS culture and treatment protocols, as well as system design and quality are thought to account for some of these observed geographic survival differences.[10-13]

An important component of OHCA resuscitation involves the expeditious administration of medications, such as epinephrine and antiarrhythmics, as faster delivery may be associated with improved patient outcomes.[14-20] These medications can be administered via peripheral intravenous (PIV) or intraosseous (IO) vascular access approaches. Although a PIV may be the gold standard for medication delivery, it takes longer to place with a lower rate of success during a resuscitation than an IO,[21] which may explain why IO use continues to increase and is often preferred by EMS providers.[22] While current guidelines recommend initial delivery of Advanced Life Support (ALS) medications via the IV route except where not feasible, IO access is frequently relied upon as a primary or rescue vascular strategy for OHCA by EMS systesm.[23] However, multiple observational studies have suggested that a tibial IO (TIO) may be associated with worse OHCA outcomes compared to an PIV.[24-27] Given the use of IO as both a primary and a rescue vascular access strategy, these observational studies reporting lower survival with TIO use compared to PIV may be biased by an inability to distinguish patients receiving an IO as an initial access strategy from those receiving it later during resuscitation as a rescue procedure after failed attempts at a PIV. Furthermore, most prior studies on IO use evaluated TIO placement, which may be less efficacious in the low-flow state of cardiac arrest than an upper extremity IO, such as a humeral IO (HIO).[28,29]

The objective of this study was to evaluate the association between the first vascular access attempt strategy of PIV, TIO, and HIO and the rate of return of spontaneous circulation (ROSC) at Emergency Department (ED) arrival, defined as a palpable pulse on hospital arrival, in OHCA patients who were still in cardiac arrest at the time of the initial vascular access attempt. Compared to prior investigations, ours is unique in that we evaluate outcomes based on the intended initial strategy of vascular access; this serves to remove potential bias of patients receiving an IO as a rescue route of access after failed PIV attempts.

METHODS

Study Design*:* This was a secondary analysis of the Portland Cardiac Arrest Epidemiologic Registry (PDX Epistry). PDX Epistry is an ongoing observational cohort registry of OHCA patients treated within the Portland, Oregon metropolitan area by participating EMS agencies and hospitals. PDX Epistry is approved by the Institutional Review Board at Oregon Health and Science University (IRB #00001736).

Study Setting: The study included patients treated by combinations of 16 different fire-based and transport-based ALS capable EMS agencies transporting to 14 hospitals in a geographic area spanning three counties in Oregon covering a total population of approximately 1.75 million. All patients in PDX Epistry are served by a dual-ALS response EMS system. Fire-based EMS agencies provide ALS first response and transport is provided by both fire and private ALS ambulances in the region. Participating agencies follow similar cardiac arrest treatment guidelines in the region and only paramedics or emergency medical technician intermediates (EMT-I) can place vascular access (IV or IO). In the PDX Epistry region, due to the dual-ALS response structure it is exceedingly rare for non-paramedics to attempt vascular access during OHCA. Following national guidelines, regional protocols recommend IV placement unless this is determined to not be feasible or is unsuccessful by the treatment team. The ultimate decision of first vascular access attempt is determined by the paramedics on-scene. Patients in this study period were treated from January 1, 2018, through December 31, 2021.

Patient Population: Adult patients (age ≥18 years-old) with non-traumatic OHCA with EMS resuscitation attempted (cases eligible for inclusion if EMS CPR or any defibrillation performed) by participating agencies. The PDX Epistry database is maintained using REDCap and analysis of the research dataset was conducted using STATA 17.0 (College Station, TX). Patients were excluded if they had achieved ROSC prior to the initial vascular access attempt. We further excluded cases with missing information regarding initial vascular access strategy (PIV, TIO, or

HIO) or missing timing of vascular access or initial ROSC (if ROSC was obtained), as the goal was to evaluate the differences in outcome by vascular access strategy in OHCA. Prespecified subgroup analyses included stratifying patients by the first EMS recorded rhythm, shockable or non-shockable, and subgroups of non-shockable rhythms including pulseless electrical activity (PEA) and asystole.

Variables*:* The primary independent variable in our analysis was the initial vascular access strategy, defined as PIV, TIO, or HIO. The additional variables used to adjust for potential confounding included age, sex, witness status (bystander or EMS), bystander CPR, bystander AED application, arrest location (home, assisted living, healthcare facility or clinic, public location), 911 call to EMS arrival time, year, and county of arrest. These variables were chosen as they are felt to be associated with the outcome (ROSC or pulses present at ED arrival) but not on the causal pathway using a direct acyclic graph approach. In addition, adjustment for year accounts for the increasing use over time of HIO from 2018 to 2021 that could be confounded by the COVID-19 pandemic's impact during the latter years of the cohort (2020-2021). The dual-ALS response structure of our study region, which sometimes includes mutual aid response, often results in multiple fire agencies being on-scene at one time. Each county is primarily served by a unique private ground transport-EMS agency, accordingly the county where the arrest occurred was used to consider any clustering effects. Data abstraction was performed by trained research assistants using standardized forms for collecting information for the Epistry database.

Outcomes*:* The primary outcome for this study was ROSC at ED arrival, defined as a palpable pulse as documented by EMS. ROSC at ED arrival reflects the most distal prehospital care outcome and helps to eliminate the potential for differences in care by treating hospital that could further confound outcomes. The secondary outcomes included survival to hospital admission, survival to hospital discharge, and survival with good neurological recovery (determined as a Cerebral Performance Category [CPC] of 1 or 2). Process outcomes included the number of vascular access attempts, successfully obtaining the primary vascular access strategy, first-attempt success of the primary access strategy, and timing of care elements including time from EMS arrival on-scene to first successful vascular access, first defibrillation (if performed), first epinephrine dose (if given), and first amiodarone dose (if given).

Statistical Analysis*:* We used descriptive statistics to characterize the sample stratified by the first vascular access strategy. Unadjusted outcomes are reported as means and 95% confidence intervals (CIs) with statistical testing against the reference (PIV) made separately for TIO and HIO groups using t-tests with unequal variance for continuous variables and chi-squared tests for binary outcomes. We conducted multivariable logistic regressions, adjusting for confounding variables and for clustering by county of arrest using a mixed-effects approach. Continuous variables were checked for normality visually prior to conducting regressions. Logistic regression models were evaluated for evidence of specification error, goodness of fit testing, and collinearity. We report adjusted odds ratios and results stratified by initial rhythm, given evidence that antiarrhythmic medications in shockable arrest may differ in efficacy by route of administration.[25] We collapsed the categorical variable for arrest location to only private (home or assisted living) or public (health care facility or clinic or public location) due to small numbers of events in health care facilities or clinics. We performed multiple sensitivity analyses including excluding cases where arrests were witnessed by EMS, where the primary access strategy was not ultimately successful, and data during the early transition to HIO use categorized by a county using an HIO as a first attempt on less than 25% of cases in a given year. Our study was 80% powered to detect an unadjusted absolute difference in ROSC or sustained pulse at ED arrival of 6% in the separate comparisons of TIO to IV and HIO to IV. All comparisons were two-tailed with significance determined at an alpha of 0.05 without corrections for multiple comparisons.

RESULTS

There were 3,900 non-traumatic EMS-treated adults (age ≥18 years old) OHCA cases enrolled in PDX Epistry from 2018-2021, and the initial vascular access attempt site of PIV, TIO, or HIO as well as covariates and outcomes were known for 2,993 cases who did not have ROSC prior to the first vascular access attempt (Figure 1). The initial vascular access strategies in the study cohort were PIV (822 [27.5%]), TIO (1,171 [39.1%]), and HIO (1,000 [33.4%]). Compared to patients with either IO-first strategy, PIV-first patients tended to be more male with EMS-witnessed arrests with shockable initial rhythms (Table 1). The proportion of cases by vascular access strategy, specifically HIO compared to TIO use, varied by year from 2018-2021.

In unadjusted analyses, patients with a PIV-first access strategy had a higher proportion of palpable pulses at ED arrival (ROSC at ED arrival of 32.5%) relative to those with a TIO (25.0%, risk difference [95% CI]: 7.5% [3.5%-11.5%]) or HIO (23.5%, risk difference [95% CI]: 9.0% [4.9%-13.1%]) first strategy. Compared to the PIV-first group, patients with TIO or HIO as the first attempt had lower survival to hospital admission (PIV 35.4%; TIO 30.5% risk difference [95% CI]: 4.9% [0.7%-9.1%]; HIO 27.8% risk difference [95% CI]: 7.6% [3.3%-11.9%]), survival to hospital discharge (PIV 14.4%; TIO 8.8% risk difference [95% CI]: 5.6% [2.8%-8.4%]; HIO 7.9% risk difference [95% CI]: 6.5% [3.6%-9.3%]), and good neurologic outcome at discharge (PIV 13.9%; TIO 8.0% risk difference [95% CI]: 5.8% [3.1%-8.6%]; HIO 6.9% risk difference [95% CI]: 7.0% [4.2%-9.7%]). Stratifying outcomes by the initial rhythm at time of EMS arrival demonstrated that patients with shockable rhythms who received IO access had a lower proportion of ROSC at ED arrival relative to those with a PIV first strategy (TIO risk difference [95% CI]: 12.6% [4.0%-21.1%], HIO risk difference [95% CI]: 16.2% [7.6%-24.9%]) (Figure 2). Compared to patients with shockable initial rhythms who received a PIV as first attempt, those with TIO and HIO attempts had lower unadjusted survival to discharge (TIO risk difference [95% CI]: 8.4% [0.5%-16.3%], HIO risk difference [95% CI]: 12.0% [4.0%-19.9%]) and survival with a good neurologic outcome (TIO risk difference [95% CI]: 9.2% [1.4%-16.9%], HIO risk difference [95% CI]: 12.1% [4.2%-19.9%]), respectively

(Figure 2). Secondary outcomes among IO patients relative to PIV patients were not significantly different in those presenting with non-shockable initial rhythms. There were no differences in unadjusted outcomes between TIO and HIO (p-values>0.2). Results for additional prehospital outcomes, including ROSC at any time (regardless of rearrest) and sustained initial ROSC to ED arrival without any episodes of prehospital re-arrest, were similar to ROSC at ED arrival and are listed in Supplemental Table 1.

Multivariable logistic regression analysis shows that, compared to the group with a PIV-first strategy, the adjusted odds of ROSC at ED arrival were significantly lower for TIO (OR 0.79 [0.64-0.98]) or HIO (OR 0.75 [0.60 – 0.93]) in all patients. Evaluating only those with shockable initial rhythms revealed significantly lower odds of ROSC at ED arrival for TIO (OR 0.60 [0.41-0.88]) and HIO (OR 0.53 [0.36-0.79]) compared to PIV (Table 2). This significance was not present when evaluating those with PEA or asystole as an initial rhythm (Table 2).

Secondary outcomes were not significantly different in all patients for TIO or HIO compared to the PIV-first group for survival to admission, survival to discharge, or survival with a good neurologic outcome (Table 2). Patients with shockable initial rhythms showed lower adjusted odds of survival to admission for HIO (OR 0.63 [0.43-0.92]), survival to discharge for both TIO (OR 0.63 [0.41-0.96]) and HIO (OR 0.64 [0.41-0.99]), and good neurologic outcome at discharge for TIO (OR 0.60 [0.39-0.93]) relative to the PIV-first group (Table 2). There were no significant differences when evaluating secondary outcomes by initial rhythms of PEA or asystole (Table 2). There were no differences comparing HIO to TIO on adjusted analyses across all rhythms and outcomes (Table 2). Results for additional prehospital outcomes, including ROSC at any time (regardless of rearrest) and sustained initial ROSC to ED arrival (without any re-arrest), were generally similar to ROSC at ED arrival and are listed in Supplemental Table 2.

Among patients with arrests not witnessed by EMS, time from EMS arrival to first successful vascular access was fastest for TIO (6.40 minutes) compared to PIV (7.02 minutes, p<0.001) or HIO (7.11 minutes, p<0.001) with no significant differences between PIV and HIO (p=0.603). These results were similar when using time of 911 call as the reference, rather than time of EMS arrival on-scene (Table 3). For patients with initial shockable rhythms, there were no significant differences across vascular access strategies for time from EMS arrival to initial shock, first epinephrine dose, or first amiodarone dose (Table 3). For patients with PEA arrests not witnessed by EMS, time from EMS arrival to initial epinephrine was similar for TIO compared to PIV (p=0.775), but significantly slower for HIO than PIV (p=0.030) or TIO (p=0.013) (Table 3). Among non-EMS witnessed arrests where patients presented with an initial rhythm of asystole, TIO was significantly faster than PIV (p<0.001) or HIO (p<0.001) (Table 3), and there was no difference between HIO and PIV (p=0.78).

A PIV-first strategy required 1.19 (95% C.I. 1.16 – 1.22) attempts on average before access was achieved – more than either the HIO or TIO approach, where average number of attempts before vascular access success was 1.05 (95% C.I. 1.03 – 1.06, p<0.001) and 1.05 (95% C.I. 1.04 – 1.07, p<0.001), respectively. Accordingly, vascular access was more likely to be successful on the first attempt at both IO locations compared to PIV (Table 3, p-values <0.001). A PIV was eventually successful in 79% of patients with a PIV-first strategy, significantly lower than the eventual success rates of both HIO (95%, p<0.001) and TIO (98%, p<0.001).

We performed multiple sensitivity analyses to assess the robustness of our results related to our primary outcome of ROSC at ED arrival. Excluding EMS-witnessed cases did not significantly change the results, with retained significantly reduced adjusted odds (95% CI) of ROSC at ED arrival for TIO and HIO relative to PIV in the overall analysis (TIO OR 0.75 [0.60-0.95] and HIO OR 0.73 [0.58-0.93]) and in patients with shockable rhythms (TIO OR 0.59 [0.40-0.89] and HIO OR 0.52 [0.35-0.79]) without significant differences for patients with PEA or asystole. Excluding patients that did not achieve success (regardless of number of attempts) at their primary access strategy did not change the results, with similar significantly reduced adjusted odds of ROSC at ED arrival overall (TIO OR 0.74 [0.59-0.93] and HIO OR 0.71 [0.56-0.89]) and in subgroups of patients with shockable rhythms (TIO OR 0.58 [0.39-0.87] and HIO OR 0.53 [0.35-0.80]) without significant differences for patients with PEA or asystole. Next, we excluded data from years when HIO use was under 25% of all vascular access attempts for a given county to account for any confounding during years when HIO use was rarely being used. In this subset, there were no differences in the overall adjusted odds ratios of ROSC at ED arrival (HIO OR 0.73 [0.57-0.93]) or in the subgroup of shockable rhythms (HIO OR 0.51

[0.33-0.79]) without significance for patients with PEA or asystole. Finally, we included airway management choice (bag-valve-mask only, endotracheal intubation, supraglottic airway) in the multivariable models, though this was excluded in the primary analysis as it may be on the casual pathway between more rapid access and drug delivery and earlier field ROSC. This analysis had similar results, with significantly reduced adjusted odds of ROSC at ED arrival overall (TIO OR 0.78 [0.63-0.97] and HIO OR 0.75 [0.60-0.94]) and in subgroups of patients with shockable rhythms (TIO OR 0.65 [0.44-0.97] and HIO OR 0.63 [0.42-0.95]) without significant differences for patients with PEA or asystole.

DISCUSSION

In this study we report that TIO or HIO access as a first attempt is associated with lower odds of ROSC at ED arrival when compared to patients where PIV was used as the initial attempt, particularly among patients with shockable initial rhythms. These associations remained after adjustment for multiple potential confounders, though given this is a retrospective and non-randomized study, additional unmeasured confounders may remain. Notably, ROSC at ED arrival did not appear to differ by anatomic site of IO placement (TIO or HIO). Our study adds to the growing body of evidence suggesting that IO as a first access strategy in OHCA is associated with lower odds of ROSC by the time of hospital arrival and, for those with shockable initial rhythms, may be associated with worse survival outcomes.

Few studies exist evaluating outcomes among patients using the initial strategy for vascular access, including different sites of IO placement. A recent meta-analysis by Hsieh et al. identified nine retrospective studies totaling 111,746 adults experiencing OHCA evaluating vascular access strategy and patient outcomes.[30] This study showed pooled effect estimates demonstrating no association between IO and favorable neurologic outcome or survival at hospital discharge. However, in the same meta-analysis, pooled effects for ROSC at ED arrival across studies favored the IV route (OR 0.71 [0.59 - 0.85]). Feinstein et al.,[24] and more recently Mody et al.,[25] demonstrated decreased rates of ROSC in association with attempted IO access compared to attempted PIV. Mody et al. assessed outcomes by attempted access (PIV or TIO) in 19,731 patients with OHCA and showed that IO access attempts were associated with lower rates of sustained ROSC independent of differences in timing of key interventions. However, they did not investigate how anatomic location of the IO or initial rhythm contributed to these differences in outcomes.

Mechanisms exist that may explain why IO access appears comparatively worse in patients with shockable rhythms, as compared to a PIV. Unlike those with non-shockable rhythms, patients with VF or pulseless VT often receive antiarrhythmics, such as amiodarone or lidocaine, to treat refractory or recurrent VF/VT. Recent evidence suggests antiarrhythmics, particularly amiodarone, may be effective only when given via PIV with no difference compared to placebo when given via an IO.[28] A proposed explanation is that this may be in part due to the lipophilic nature of amiodarone and lidocaine and the higher lipid content in bone marrow.[31] Porcine models have shown important differences in absorption of both antiarrhythmic and vasoactive agents,[31-34] across access routes, with studies tending to favor greater absorption (as measured by point estimates for maximum concentration and time to maximum concentration) for both therapies via the PIV route – particularly when compared to TIO.[35] Any role that interactions between lipophilic antiarrhythmic medications administered via the IO route plays in driving outcomes may be minimized among non-shockable patients, where multiple high doses epinephrine – with a highly hydrophilic catechol moiety – may lead to less sequestration in the fatty bone marrow and more equivalent efficacy between routes.[23,36]

The anatomic site of IO access has been suggested as an additional, important mediator in clinical studies evaluating vascular access approaches. Physical proximity to the heart, faster flow rates and lack of SVC venous valves in minimizing regurgitant flow – have all been proposed as mechanisms suggesting that humeral or other upper extremity access could be a superior access site to TIO.[28,31,37,38] Our study showed no association between IO site (TIO vs. HIO) and ROSC compared to PIV.

In this study, we utilized the first-attempted access strategy to mitigate potential confounding by the ‘IO as a rescue strategy’ paradigm that likely undermines studies demonstrating inverse associations between IO use and ROSC at ED arrival. Cases where the patient has been down for considerable time in a ‘no flow’ state represent a challenging scenario for intravenous access due to collapsed vasculature and these patients are overall much less likely to have a favorable outcome. If these factors motivate providers towards an IO first initial strategy it can appear as if IO as an initial strategy correlates with worse outcomes simply because these patients are comparatively ‘sicker’. We attempted to account for this by adjusting for arrest characteristics and the time from 911 call time to EMS arrival in all models. We did not adjust for time to medication administration as we considered time to be on the causal pathway of drug administration and outcome, with the hypothesis that an IO route would result in faster drug delivery than a PIV and have a theoretical benefit as a result.

Limitations

Our study has multiple limitations. Most importantly among these, as this was an observational study, it is likely there remain unmeasured confounding, risk of selection bias, and confounding by indication despite extensive efforts to control for these. Specifically, first vascular access attempt was up to paramedic discretion, though per guidelines PIV was recommended as a first attempt. As a result, there may be unmeasured confounders in those where a PIV was not chosen that are associated with worse outcomes. There may additionally be charting errors, regarding initial access attempt location, though without reason to suspect these would not occur at random across all comparison groups. We used several strategies to minimize potential biases. First, we focused on the first strategy of vascular access to eliminate instances where an IO was used as a rescue after a failed PIV attempt. Patients with failed PIV-first attempt and a successful rescue IO would be included in the PIV-first strategy group. Second, we excluded patients who achieved ROSC prior to the access attempt, which required detailed timing measurements including the time of access attempt and time of initial ROSC (even if this was brief and not sustained). This would help eliminate bias where a PIV might be chosen by EMS for patients rapidly achieving ROSC whereas an IO was chosen for those still pulseless. Third, we present an analysis excluding EMS witnessed cases to reduce the bias that may occur for patients with PIV placed or nearly placed by EMS prior to arrest. Fourth, we adjusted our analyses by county of care to account for potential differences in protocols, training, and experience with PIV, TIO, and HIO placement. Finally, we include a variable for year of treatment in our adjusted analysis in the event that the COVID-19 pandemic impacted outcomes in 2020 and 2021, since use of an HIO was more common in these years than in 2018 and 2019. Nevertheless, as other investigators have noted, it is difficult to control for all potential confounders in observational cardiac arrest research.[39] Overall, these limitations and our findings support the need for a large, multisite randomized controlled trial studying initial vascular access strategy in the EMS systems in the United States.

CONCLUSIONS

We found that IO access as an initial vascular access strategy in patients experiencing OHCA, particularly those with a shockable initial rhythm, is associated with lower odds of ROSC at ED arrival, regardless of anatomic site (TIO or HIO), when compared to a PIV-first strategy. For patients with shockable initial rhythms, there were also significantly lower adjusted odds of survival to discharge for both TIO and HIO relative to PIV. Randomized controlled trials are needed to determine the optimal initial vascular access strategy in OHCA and if this strategy should differ based on whether the initial rhythm is shockable or non-shockable.

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Table 1. Patient characteristics by 1st access strategy in out-of-hospital cardiac arrest

	Peripheral IV (n = 822)	**Tibial IO** (n = 1171)	**Humeral IO** (n = 1000)
Age, years (median [interquartile range])	67 (53-77)	62 (50-72)	64 (52-74)
Male sex, n (%)	589 (71.7)	739 (63.1)	666 (66.6)
Bystander witnessed, n (%)	288 (35.0)	452 (38.6)	357 (35.7)
EMS witnessed, n (%)	182 (22.1)	103 (8.8)	78 (7.8)
Bystander CPR, n (%)	438 (53.3)	634 (54.1)	596 (59.6)
Bystander AED shock, n (%)	25 (3.0)	20 (1.7)	20 (2.0)
911 call to 1st EMS arrival, - minutes (median [interquartile range])	5.3 (4.1-6.8)	5.4 (4.1-7.0)	5.2 (3.8-6.6)
Arrest Location, n (%)			
Home	611 (74.3)	856 (73.1)	728 (72.8)
Assisted Living	67 (8.2)	97 (8.3)	91 (9.1)
Health care Facility or Clinic	10 (1.21)	18 (1.5)	12 (1.2)
Public Location	134 (16.3)	200 (17.1)	169 (16.9)
Initial rhythm, n (%)			
VF/VT	253 (30.8)	258 (22.0)	231 (23.1)
Asystole	324 (39.4)	661 (56.5)	553 (55.3)
PEA	221 (26.9)	246 (21.0)	208 (20.8)
Unknown non-shockable	24 (2.9)	6 (0.5)	8 (0.8)
Year of Arrest, n (%)			
2018	181 (22.0)	323 (27.6)	91 (9.1)
2019	164 (20.0)	322 (27.5)	199 (19.9)
2020	224 (27.3)	294 (25.1)	270 (27.0)
2021	253 (30.8)	232 (19.8)	440 (44.0)

Abbreviations: SD = Standard Deviation, EMS = Emergency Medical Services, AED = Automated external defibrillator, CPR = Cardiopulmonary Resuscitation, VF = Ventricular fibrillation, VT = Ventricular Tachycardia, PEA = Pulseless Electrical Rhythm. Means with Standard Deviations are presented for continuous variables.

Table 2. Adjusted odds for patient outcomes by initial prehospital vascular access strategy in out-of-hospital cardiac arrest

aOR (95% CI) for Tibial Intraosseous versus Peripheral Intravenous Access (reference)				
	Overall	**VF/VT**	**PEA**	**Asystole**
ROSC at ED Arrival	**0.79 (0.64-0.98)**	**0.60 (0.41-0.88)**	0.92 (0.61-1.39)	0.89 (0.60-1.32)
Survival to Admission	0.85 (0.68-1.07)	0.87 (0.60-1.27)	1.04 (0.69-1.56)	0.89 (0.59-1.26)
Survival to Discharge	0.76 (0.53-1.09)	**0.63 (0.41-0.96)**	0.57 (0.28-1.15)	2.33 (0.74-7.37)
Good Neurologic Outcome	0.72 (0.51-1.01)	**0.60 (0.39-0.93)**	0.59 (0.29-1.21)	1.83 (0.56-6.04)
aOR (95% CI) for Humeral Intraosseous versus Peripheral Intravenous Access (reference)				
	Overall	**VF/VT**	**PEA**	**Asystole**
ROSC at ED Arrival	**0.75 (0.60-0.93)**	**0.53 (0.36-0.79)**	0.78 (0.51-1.21)	0.92 (0.63-1.37)
Survival to Admission	0.83 (0.66-1.04)	**0.63 (0.43-0.92)**	1.13 (0.73-1.73)	0.91 (0.62-1.34)
Survival to Discharge	0.78 (0.55-1.10)	**0.64 (0.41-0.99)**	0.79 (0.39-1.60)	1.92 (0.55-6.75)
Good Neurologic Outcome	0.71 (0.50-1.02)	**0.64 (0.40-1.00)**	0.61 (0.28-1.31)	1.50 (0.40-5.67)
aOR (95% CI) for Tibial Intraosseous versus Humeral Intraosseous Access (reference)				
	Overall	**VF/VT**	**PEA**	**Asystole**
ROSC at ED Arrival	1.06 (0.85-1.31)	0.89 (0.59-1.33)	0.85 (0.55-1.30)	1.04 (0.75-1.44)
Survival to Admission	1.03 (0.83-1.27	0.72 (0.49-1.06)	1.09 (0.64-1.45)	1.05 (0.77-1.45)
Survival to Discharge	0.98 (0.68-1.40)	1.01 (0.63-1.62)	1.38 (0.65-2.96)	0.83 (0.34-1.98)
Good Neurologic Outcome	1.01 (0.70-1.47)	1.06 (0.66-1.72)	1.03 (0.46-2.31)	0.82 (0.31-2.19)

Abbreviations: ROSC = Return of spontaneous circulation; aOR = Adjusted Odds Ratios; 95% CI = 95% Confidence Intervals; ED = Emergency Department; Survival to Admission = Survival to Hospital Admission; Survival to Discharge = Survival to Hospital Discharge; Good Neurologic Outcome = Survival to Hospital Discharge with a Cerebral Perfusion Category Score of 1 or 2; VF/VT = ventricular fibrillation or ventricular tachycardia (pulseless); PEA = Pulseless Electrical Activity. **Multivariable analyses:** Overall group includes all adjusting variables and categorical variable for initial patient rhythm. **Bolded values** indicate those with $p<0.05$.

Table 3. Process Outcomes by 1st Attempt Strategy and Initial Rhythm

		VF/VT			PEA			Asystole		
		PIV	**TIO**	**HIO**	**PIV**	**TIO**	**HIO**	**PIV**	**TIO**	**HIO**
Process Metrics (mean [95% CI])	**Attempts before successful placement**	**1.19** (1.13-1.25)	**1.06** (1.03-1.10)	**1.06** (1.02-1.09)	**1.20** (1.14-1.26)	**1.05** (1.02-1.08)	**1.06** (1.02-1.09)	**1.18** (1.13-1.23)	**1.04** (1.02-1.05)	**1.05** (1.03-1.07)
	1st attempt success	**0.77** (0.72-0.83)	**0.95** (0.92-0.98)	**0.95** (0.92-0.97)	**0.68** (0.61-0.74)	**0.95** (0.92-0.97)	**0.97** (0.95-0.99)	**0.70** (0.65-0.75)	**0.96** (0.95-0.98)	**0.96** (0.94-0.98)
	Successful placement (regardless of attempts)	**0.86** (0.82-0.90)	**0.97** (0.95-0.99)	**0.95** (0.92-0.98)	**0.77** (0.72-0.83)	**0.96** (0.94-0.99)	**0.95** (0.92-0.98)	**0.77** (0.72-0.81)	**0.98** (0.97-0.99)	**0.95** (0.94-0.97)
Key Intervals for non EMS-witnessed Arrests - minutes (mean [95% CI])	**Time from <u>911 Call</u> to successful 1st access**	**11.75** (11.21-12.28)	**11.76** (11.34-12.17)	**12.11** (11.62-12.59)	**12.37** (11.77-12.97)	**11.84** (11.36-12.31)	**12.55** (11.98-13.11)	**13.18** (12.69-13.67)	**12.41** (12.06-12.76)	**12.73** (12.37-13.08)
	Time from <u>EMS arrival</u> to successful 1st access	**6.33** (5.88-6.78)	**6.05** (5.69-6.41)	**6.66** (6.25-7.07)	**6.83** (6.28-7.37)	**6.42** (5.99-6.84)	**7.32** (6.80-7.83)	**7.51** (7.08-7.93)	**6.54** (6.26-6.83)	**7.23** (6.95-7.52)
	Time from <u>EMS arrival</u>	**8.04** (7.50-8.57)	**7.70** (7.28-8.12)	**8.30** (7.86-8.73)	**8.20** (7.65-8.75)	**8.09** (7.59-8.59)	**9.24** (8.48-9.99)	**9.07** (8.61-9.52)	**8.04** (7.76-8.33)	**8.99** (8.66-9.31)

	to 1st epinephrine									
	Time from <u>EMS arrival</u> to 1st shock	**4.81** (4.27-5.35)	**4.55** (4.08-5.03)	**4.98** (4.52-5.45)	-	-	-	-	-	-
	Time from <u>EMS arrival</u> to 1st amiodarone	**12.93** (11.91-13.95)	**13.20** (12.23-14.17)	**13.97** (12.88-15.05	-	-	-	-	-	-

Abbreviations: PIV = Peripheral intravenous IV, TIO = Tibial intraosseous, Humeral intraosseous, ROSC = return of spontaneous circulation, VF = ventricular fibrillation, VT = ventricular tachycardia, PEA = pulseless electrical activity, ED = emergency department, EMS = Emergency Medical Services

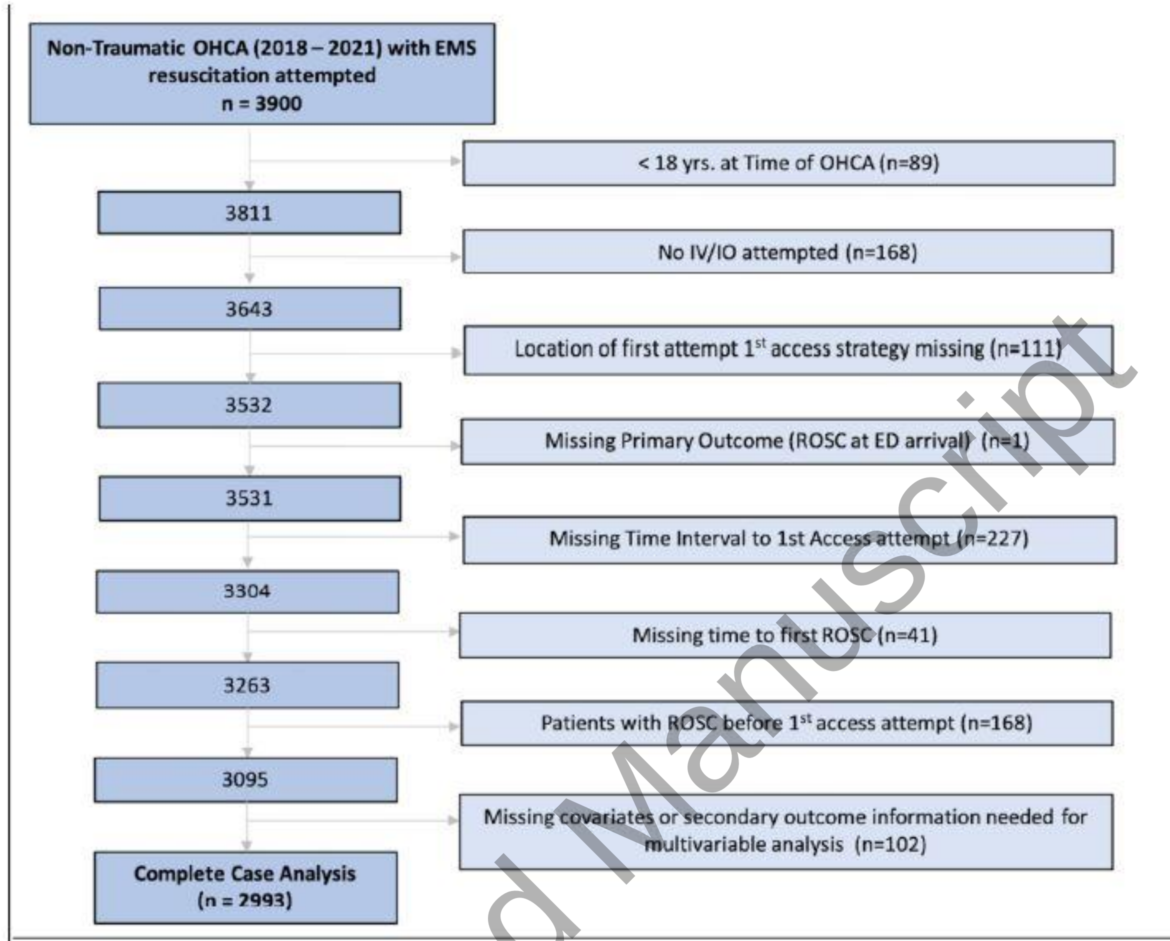

Figure 1. Flow of included subjects. Abbreviations: ROSC = return of spontaneous circulation, VF = ventriclar fibrillation, VT = ventricular tachycardia, PEA = pulseless electrical activity, ED = emergency department.

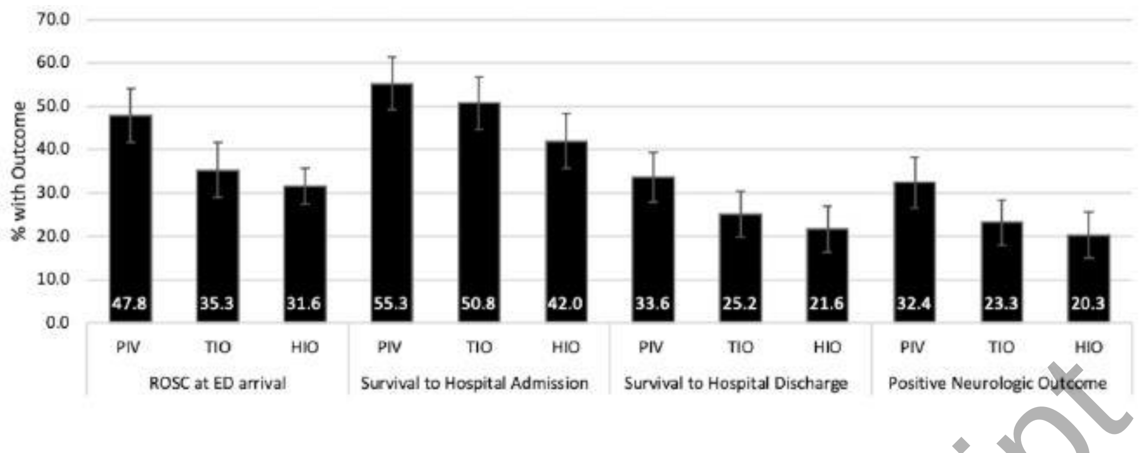

Figure 2A. Patients with VF/VT initial Rhythm

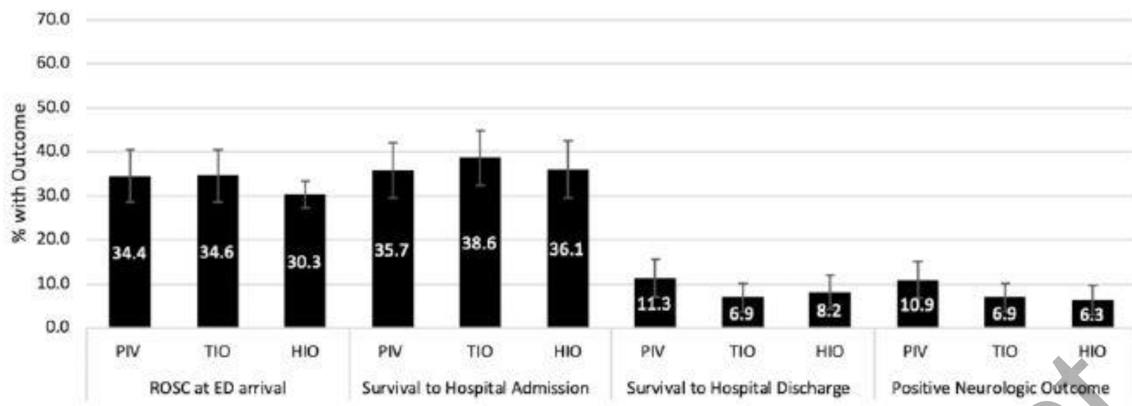

Figure 2B. Patients with PEA initial Rhythm

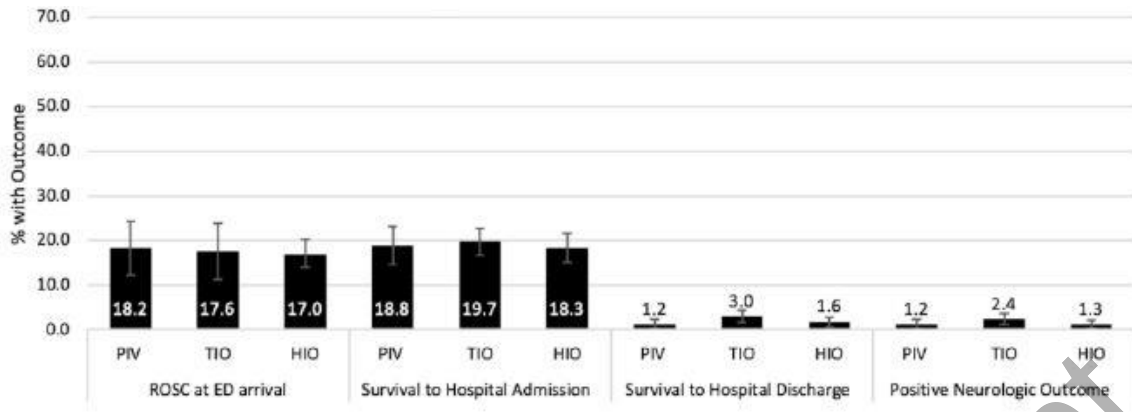

Figure 2C. Patients with Asystole initial Rhythm