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Clinical paper

Trends in use of intraosseous and intravenous access in out-of-hospital cardiac arrest across English ambulance services: A registry-based, cohort study

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Abstract

Introduction: The optimum route for drug administration in cardiac arrest is unclear. Recent data suggest that use of the intraosseous route may be increasing. This study aimed to explore changes over time in use of the intraosseous and intravenous drug routes in out-of-hospital cardiac arrest in England.

Methods: We extracted data from the UK Out-of-Hospital Cardiac Arrest Outcomes registry. We included adult out-of-hospital cardiac arrest patients between 2015–2020 who were treated by an English Emergency Medical Service that submitted vascular access route data to the registry. The primary outcome was any use of the intraosseous route during cardiac arrest. We used logistic regression models to describe the association between time (calendar month) and intraosseous use.

Results: We identified 75,343 adults in cardiac arrest treated by seven Emergency Medical Service systems between January 2015 and December 2020. The median age was 72 years, 64% were male and 23% presented in a shockable rhythm. Over the study period, the percentage of patients receiving intraosseous access increased from 22.8% in 2015 to 42.5% in 2020. For each study-month, the odds of receiving any intraosseous access increased by 1.019 (95% confidence interval 1.019 to 1.020, $p < 0.001$). This observed effect was consistent across sensitivity analyses. We observed a corresponding decrease in use of intravenous access.

Conclusion: In England, the use of intraosseous access in out-of-hospital cardiac arrest has progressively increased over time. There is an urgent need for randomised controlled trials to evaluate the clinical effectiveness of the different vascular access routes in cardiac arrest.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Intraosseous infusions, Intravenous infusions, Epinephrine

Introduction

Drug therapy has formed a key part of cardiac arrest management for over fifty years.[1,2] However, the clinical effectiveness of vasopressors in cardiac arrest has only recently been demonstrated in clinical trials.[3,4] The landmark PARAMEDIC-2 randomised controlled trial showed that in 8,014 adult out-of-hospital cardiac arrest (OHCA) patients standard-dose (1 mg) adrenaline, compared with placebo, improved 30-day survival (unadjusted odds ratio 1.39, 95% confidence interval [CI], 1.06 to 1.82).[4]

The optimum route for drug administration in cardiac arrest is uncertain.[5,6] Current resuscitation guidelines recommend the use of the intravenous (IV) route as the primary route for drug administration in cardiac arrest, with the intraosseous (IO) route reserved for cases where IV access cannot be established.[7,8] Research comparing the clinical effectiveness of the IO and IV routes is limited to observational studies, which are at high risk of selection bias, con-

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founding, and resuscitation time bias.[5,6,9,10] A post hoc analysis of the PARAMEDIC-2 trial, which used data from both the adrenaline and placebo arms of the trial to reduce the effect of resuscitation time bias, observed no difference in outcomes between the IV and IO drug administration routes.[11]

Despite a lack of evidence supporting the clinical effectiveness of the IO route and ongoing uncertainty regarding the pharmacokinetics of IO drug administration, successive randomised controlled trials of pharmacological interventions in OHCA seemingly show a gradual increase in IO use over time.[4,12,13] In this study, we aimed to explore whether changes over time had occurred in IO use in adult cardiac arrest using the UK out-of-hospital cardiac arrest registry.

Methods

We conducted a retrospective, registry-based, observational study. The data source was the Out-of-Hospital Cardiac Arrest Outcomes (OHCAO) registry, which has approval to collect and process identifiable patient data without patient consent (South Central—Oxford C Research Ethics Committee- 13/SC/0361; Confidentiality Advisory Group- ECC 8–04(C)/2013). This specific project was approved by the University of Warwick Biomedical and Scientific Research Ethics Committee (BSREC 18/21–22). This report is written in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting checklist.[14]

Setting and dataset

The OHCAO registry currently collects data on OHCA patients treated by all of the 11 National Health Service Emergency Medical Service (EMS) systems in England, covering a total population of around 56 million people. Detailed overviews of the registry have been published previously.[15,16] Cardiac arrest patients are identified both through review of emergency call logs and interrogation of clinical records. Ambulance service personnel upload data to a secure database, hosted at the University of Warwick.

Registry data are collected in accordance with the Utstein style, such that it comprises both a core and supplementary data set.[17] Both the IV and IO access fields are classified as supplementary variables, such that EMS systems may choose to submit the supplementary data set for all patients or no patients in any specific period. The anatomical site of IV and IO access is not collected by the registry. Patients are followed-up to hospital discharge.

In England, OHCA is managed in accordance with clinical practice guidelines developed by the Joint Royal College Ambulance Liaison Committee, which are based on European Resuscitation Council guidelines.[8,18] Most cardiac arrests are attended by paramedics who are skilled in advanced life support (e.g. manual defibrillation, advanced airway management, IV and IO access) and able to administer key cardiac arrest drugs, including adrenaline and amiodarone.

Participant eligibility

We included adults (≥18 years) who sustained an OHCA between January 2015 and December 2020 and were treated by an EMS system that submitted data on IO vascular access during the month in which the patient was treated. We excluded children and adults with a do not attempt cardiopulmonary resuscitation (DNACPR) decision or equivalent order in place, and those with a return of spontaneous circulation (ROSC) recorded before EMS arrival. We also excluded patients with a recorded age greater than 114 years on the basis of a presumed data transcription error as the oldest living person in England is aged 113 years.

Outcomes

Our primary outcome was the change over time in the use of any IO access during adult cardiac arrest. Our secondary outcome was the change over time in the use of any IV access during adult cardiac arrest.

Statistical analysis

We report continuous variables as mean and standard deviation or median and interquartile range (IQR), depending on normality of data distribution. We report categorical data as number and percentage. For patients where it was not recorded whether they had received either IV or IO access, we assumed that this missingness meant that this type of access was not used. This is consistent with the recommended strategy used in other cardiovascular registries.[19] We did not impute any other data. Data missingness is summarised in the supplementary appendix (table S1). Reported percentages are based on the number of patients for whom data were available.

We initially classified patients in one of four independent groups: 1) received no vascular access; 2) received only IV access; 3) received only IO access; and 4) received both IV and IO access. We compared patient demographics, cardiac arrest characteristics, treatment, and outcomes across these groups using a chi-squared test or Kruskal-Wallis test, as appropriate.

We then classified patients in to one of three non-independent groups: 1) received no vascular access; 2) received IV access; and 3) received IO access. These groups were not independent as patients recorded as receiving both IV and IO access were included in both group two and group three. We plotted the proportion of patients who received IO access and IV access graphically for the whole period from January 2015 to December 2020 across all EMS systems. We used logistic regression models to describe the change in odds per month of patients receiving IO access, and report the odds ratio, 95% confidence interval (CI) and corresponding p-value. Our primary analysis was unadjusted. We undertook the same analysis to explore change in IV access use. We then developed a multivariable logistic regression model that adjusted for EMS system, age, sex, arrest aetiology, cardiac arrest rhythm, bystander cardiopulmonary resuscitation (CPR), and ambulance response time for our primary outcome of receiving IO access. Our variables were chosen a priori based on clinical plausibility and data completeness.

For each individual EMS system, we report change in odds of receiving IO and IV access over time, both graphically and using an unadjusted logistic regression model. Finally, we undertook two sensitivity analyses. Firstly, we explored the change in odds of receiving IO access over time across all EMS systems for patients confirmed as having received adrenaline. Secondly, due to potential changes in clinical practice driven by the COVID-19 pandemic and the need to don additional personal protective equipment which may influence the ability to gain vascular access, we explored the change in odds of receiving IO access over time across all EMS systems up to February 2020.[20,21,22]

All statistical tests were two-sided with a significance level of 0.05. Data were analysed using IBM SPSS Statistics version 28 (IBM, Armonk, NY) and charts were prepared using Microsoft Excel 365 (Microsoft, Redmond, Washington).

Results

Between 1st January 2015 and 31st December 2020, 177,462 patients were included in the OHCAO registry (Fig. 1). Of these, we excluded children across all services (n = 17,139, 9.7%), adults with a recorded ROSC or DNACPR before EMS arrival (n = 604, 0.3%), and adults treated by one of four EMS systems that did not submit IO access data (n = 67,120, 37.8%). For the seven EMS systems that submitted any IO data, we excluded 17,252 (9.7%) patients treated in calendar months before the EMS system had started submitting vascular access data to the registry and four patients with a recorded age of 114 years or over.

We included 75,343 patients treated by seven EMS systems. Together, these EMS systems cover approximately 55% of the English population. The number of cases and ambulance services who submitted data increased from 6,789 patients treated by three EMS systems in 2015 to 16,069 patients treated by seven EMS systems in 2019 (supplementary appendix table S2).

The median age of patients was 71.5 years (IQR 58.5–81.3) and 64.1% were male (table one; supplementary table S3). The most common aetiology was cardiac/medical (87.3%) and 22.5% presented in a shockable rhythm. Vascular access was obtained in 67,980 (90.2%) patients, of which 43,660 (57.9%) received only IV access; 18,288 (24.3%) received only IO access; and 6,032 (8.0%) received both IV and IO access. Return of spontaneous circulation at hospital handover was achieved in 29.0% of patients and 8.7% were alive at hospital discharge.

Comparison of patients by vascular access type

In our comparison of patients by vascular access type, we observed statistically significant differences for all comparisons (Table 1). Whilst median age, median response time and OHCA aetiology were numerically similar across groups, we observed marked differences in proportions across groups for all other comparisons. Survival at hospital discharge was 3.7% in the IO only access group, compared with 11.1% in the IV only access group.

Changes in vascular access over time

Over the six-year study period, we observed a progressive increase in IO access use (Fig. 2; Table 2). In 2015, 22.8% patients received IO access, rising to 42.5% in 2020 (supplementary appendix table S4). The odds of receiving IO access increased for each calendar month since January 2015 (unadjusted odds ratio (OR) 1.019, 95% CI 1.019–1.020, $p < 0.001$). The odds ratio was similar after adjustment for baseline characteristics (adjusted OR 1.021, 95% CI 1.020–1.022, $p < 0.01$).

In our first sensitivity analysis comprising only patients confirmed to have received adrenaline, the change in IO access use over time was similar to our primary analysis (unadjusted OR 1.018, 95% CI 1.018–1.019, $p < 0.001$) (supplementary appendix table S5). In our secondary sensitivity analysis that explored only data up to February 2020 to exclude cardiac arrests treated during the COVID-19 pandemic, the change in IO access use over time was also similar to our primary analysis (unadjusted OR 1.020, 95% CI 1.019–1.021, $p < 0.001$) (supplementary appendix table S6).

We observed a corresponding decrease in the use of IV access and no vascular access use over the study period (Fig. 2; supplementary appendix table S4/). In 2015, 68.4% patients received IV access, which decreased to 57.9% in 2020. The odds of receiving IV access reduced for each calendar month since January 2015 (unadjusted OR 0.992, 95% CI 0.991–0.993, $p < 0.001$).

Sub-group analyses and post-hoc analyses

Across all seven EMS systems, we observed an increase in the odds of receiving IO access for each calendar month over time. The point estimate for the odds ratio for all EMS systems ranged from 1.012 to 1.038 (supplementary appendix table S7/figure S1). There was nev-

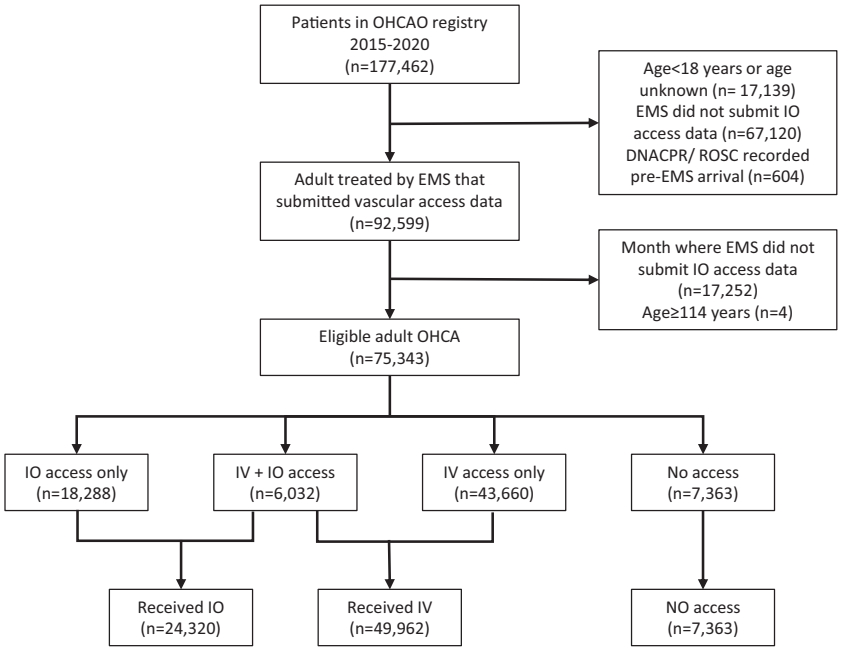

Fig. 1 – Flowchart of participant selection. Footer: DNACPR- Do not attempt cardiopulmonary resuscitation; EMS- Emergency Medical Service; IO- Intraosseous; IV- Intravenous; OHCAO- Out-of-hospital cardiac arrest outcomes; ROSC- Return of spontaneous circulation.

Table 1 – Comparison of patients by type of vascular access during cardiac arrest.

	All patients (n = 75343)	No vascular access (n = 7363)	IV only (n = 43660)	IO only (n = 18288)	IV and IO (n = 6032)	p-value*
Year of OHCA- n(%)						
2015	6789 (9.0%)	1033 (14.0%)	4211 (9.6%)	1110 (6.1%)	435 (7.2%)	<0.001
2016	11,041 (14.7%)	1471 (20.0%)	7222 (16.5%)	1832 (10.0%)	516 (8.6%)	
2017	12,565 (16.7%)	1536 (20.9%)	7723 (17.7%)	2409 (13.2%)	897 (14.9%)	
2018	14,437 (19.2%)	1115 (15.1%)	8577 (19.6%)	3575 (19.5%)	1170 (19.4%)	
2019	16,069 (21.3%)	909 (12.3%)	8927 (20.4%)	4588 (25.1%)	1645 (27.3%)	
2020	14,442 (19.2%)	1299 (17.6%)	7000 (16.0%)	4774 (26.1%)	1369 (22.7%)	
Age- median (IQR)	71.5 (58.5–81.3)	73.7 (59.9–83.8)	72.6 (60.3–82.0)	68.9 (54.8–79.0)	68.7 (54.8–79.1)	<0.001
Sex- male- n(%)	48,187 (64.1%)	4376 (59.8%)	28,657 (65.8%)	11,270 (61.8%)	3884 (64.7%)	<0.001
OHCA aetiology- n(%)						
Cardiac/medical	60,050 (87.3%)	3958 (87.4%)	36,365 (88.2%)	14,892 (84.6%)	4835 (89.2%)	<0.001
Trauma	1433 (2.1%)	109 (2.4%)	596 (1.4%)	515 (2.9%)	213 (3.9%)	
Overdose	1195 (1.7%)	72 (1.6%)	560 (1.4%)	470 (2.7%)	93 (1.7%)	
Asphyxia	1707 (2.5%)	118 (2.6%)	945 (2.3%)	476 (2.7%)	168 (3.1%)	
Other†	4402 (6.4%)	270 (6.0%)	2760 (6.7%)	1260 (7.2%)	112 (2.1%)	
OHCA witnessed- n(%)	44,788 (62.7%)	2807 (53.8%)	27,520 (64.7%)	10,831 (60.4%)	3630 (62.9%)	<0.001
Bystander CPR- n(%)	43,996 (58.4%)	2617 (48.2%)	26,446 (61.3%)	11,200 (61.9%)	3703 (62.8%)	<0.001
Ambulance response time (minutes)- median (IQR)	7.5 (5.0–11.6)	7.2 (4.8–12.0)	7.8 (5.0–11.8)	7.2 (5.0–11.0)	7.4 (5.0–11.4)	<0.001
Initial rhythm						
Asystole	39,242 (54.1%)	5044 (71.7%)	20,379 (48.6%)	10,669 (60.2%)	3150 (54.3%)	<0.001
Shockable- VF/VT	16,315 (22.5%)	1030 (14.6%)	11,125 (26.5%)	2853 (16.1%)	1307 (22.5%)	
PEA	16,639 (22.9%)	945 (13.4%)	10,263 (24.5%)	4104 (23.2%)	1327 (22.9%)	
AED- non-shockable	323 (0.4%)	16 (0.2%)	200 (0.5%)	93 (0.5%)	14 (0.2%)	
Tracheal tube- n(%)	17,670 (23.5%)	597 (16.3%)	10,516 (30.6%)	4478 (29.8%)	2079 (41.6%)	<0.001
Supraglottic airway- n(%)	36,615 (48.6%)	1173 (34.4%)	21,233 (63.4%)	10,780 (74.1%)	3429 (75.2%)	<0.001
Adrenaline administered- n(%)	60,718 (87.6%)	953 (25.1%)	37,179 (89.0%)	17,149 (95.6%)	5437 (93.2%)	<0.001
Amiodarone administered- n (%)	8897 (15.8%)	162 (5.0%)	5892 (17.7%)	2007 (13.3%)	836 (17.5%)	<0.001
ROSC at any time- n(%)	27,952 (37.1%)	1204 (23.3%)	19,035 (44.4%)	5495 (30.7%)	2218 (38.4%)	<0.001
ROSC at hospital handover- n (%)	20,847 (29.0%)	1059 (20.2%)	14,687 (34.2%)	3624 (20.2%)	1477 (25.7%)	<0.001
Survival at hospital discharge- n(%)	6148 (8.7%)	587 (9.7%)	4592 (11.1%)	654 (3.7%)	315 (5.7%)	<0.001

Key- AED- automated external defibrillator; IO- Intraosseous; IV- Intravenous; OHCA- out-of-hospital cardiac arrest; PEA- pulseless electrical activity; ROSC- return of spontaneous circulation; VF/VT- ventricular fibrillation/ventricular tachycardia.

†- other includes submersion, exsanguination, electrocution, and other category.

*- The p-value shows the comparison across the No vascular access; IV only; IO only; and IV and IO groups.

Reported percentages are based on the number of patients for whom data were available- a summary of data missingness by variable is included in the electronic supplement.

ertheless marked variation in practice across EMS systems, such that in 2020, use of IO access across ambulance services ranged from 32.0% to 51.4% (supplementary appendix table S4).

There was a corresponding decrease in IV access use across six of the seven EMS systems (supplementary appendix table S7/figure S1). In one EMS system, we observed an increase in use of both IO access and IV access over time.

We undertook a post-hoc analysis, as shown in supplementary table S8, in which we observed a decrease in the proportion of odds of receiving no vascular access for each calendar month over time (unadjusted OR 0.985, 95% CI 0.983–0.986, p < 0.001). Supplementary table S8 also shows changes over time in IO, IV, and no vascular use for other time periods.

Discussion

In this large registry-based cohort study that included 75,343 adults in cardiac arrest from seven EMS systems across England over five-years, we observed sustained increases in the use of IO access. This observation was consistent across each individual ambulance service and when limited to the cohort of patients who were confirmed to have received adrenaline. We observed corresponding decreases in the use of IV access.

Since 2005, European resuscitation guidelines, on which English EMS clinical practice is based, have supported the use of IO access only when IV access cannot be rapidly established.[23] In practice, this has meant that UK paramedics will typically make two attempts at IV access before attempting IO access. Despite there being no changes to clinical guidelines, it is clear from our study findings that there have been changes in clinical practice, although it is unclear what has driven these changes. There is a need for further research to explore precisely how practice has changed and what factors may have driven this change.

The clinical rationale for a potential progressive shift to an IO-first strategy is unclear. Early drug treatment of OHCA with non-shockable rhythms is associated with better outcomes.[24] A randomised controlled trial and several observational studies provide

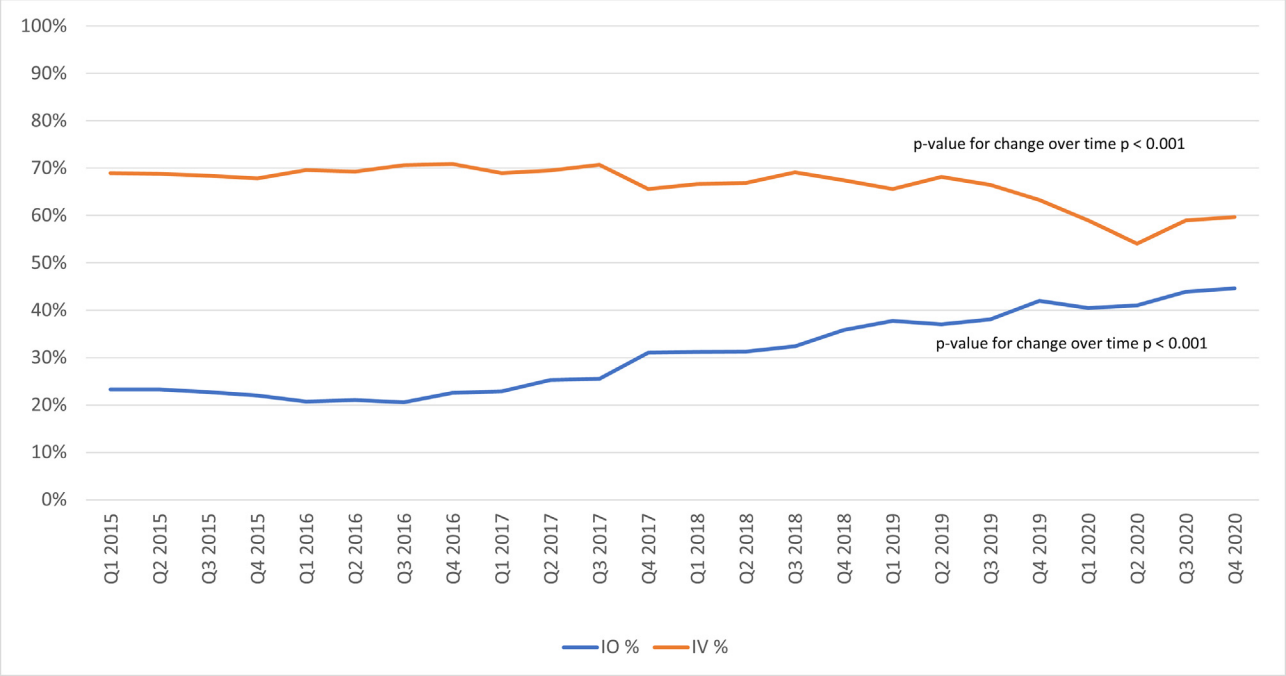

Fig. 2 – Changes over time in intravenous and intraosseous use across all EMS systems. Footer: Data presented by year and quarter. Reported p-values are based on logistic regression models, summarised in the supplementary appendix table S7.

evidence that, compared with the IV route, IO route success rates may be higher and facilitate more rapid drug delivery.[25–27] These potential advantages are most marked when the proximal tibia site is used. However, animal studies highlight important ongoing uncertainties regarding the pharmacokinetics of drug delivered by the IO route in cardiac arrest.[10] As such, any reduction in time to drug delivery may be off-set by a longer time for cardiac arrest drugs to reach the central circulation.

We found that use of the IO route increased over time across all EMS systems. Nevertheless, despite use of a common set of clinical guidelines, we did observe important variations in practice across EMS systems in use of the IO route. Data from the North American randomised controlled trial of amiodarone, lidocaine and placebo in shock-refractory cardiac arrest showed even greater variability in practice, such that across study sites use of the IO route ranged from 1% to 53% patients.[12,28] Nevertheless, use of the IO route in England lags behind some systems. In the recent randomised controlled trial of calcium in adult cardiac arrest, 60% patients received the study drug via the IO route.[13].

Our study showed changes in clinical practice over time. Similar changes in clinical practice over time have been reported for airway management and drug use at in-hospital cardiac arrest.[29,30] In some cases, these changes in practice may provide no benefit or may even be harmful. In a cohort of 126,031 adults with in-hospital cardiac arrest included in the North American Get with the Guidelines registry, there was a sustained increase in the use of calcium over time.[29] Subsequently, a randomised controlled trial showed that for OHCA, routine calcium was not clinically effective and might even be associated with harm.[13]

Our study has important limitations. First, in line with the Utstein style, collection of vascular access data in our dataset was voluntary for EMS systems. As such, our data may be subject to selection bias. Nevertheless, study data were based on practice across seven EMS services that cover the majority of the English population. Second, approximately 9% of patients who received vascular access were reported to have received both IO and IV access. The registry does not collect information on why two routes were attempted, which route was attempted first, and which of these routes was used for drug administration. Third, we assumed in this study that individuals with missing vascular access route data did not receive vascular access. Patients that do not receive vascular access during cardiac arrest are likely those that had an early ROSC or there was an early decision to discontinue resuscitation attempts. Unfortunately, we did not have a reliable way to test this assumption. Fourth, we are cognisant that there may be inconsistencies across EMS systems in whether an unsuccessful attempt at vascular access is recorded in the registry. Fifth, our study included only English EMS systems which may limit the generalizability of study findings to other international systems.

Conclusion

In this large registry-based observational study, we observed a marked increase over time in the use of IO vascular access in adult cardiac arrest and a corresponding decrease in the use of IV vascular access. This change in practice highlights the urgent need for the ongoing randomised controlled trials in UK, China, Taiwan and Denmark that are evaluating the clinical effectiveness of the IV and IO route in cardiac arrest.[10].

Table 2 – Regression models showing association between baseline characteristics and odds of receiving intraosseous access.

		Univariable		Multivariable	
		Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Time (per calendar month since January 2015)		1.019 (1.019–1.020)	<0.001	1.021 (1.020–1.022)	<0.01
EMS system					
	EMS 7 (i)				
	EMS 1	1.363 (1.087–1.709)	<0.01	0.839 (0.659–1.069)	0.16
	EMS 2	1.368 (1.277–1.466)	<0.001	1.128 (1.037–1.228)	<0.01
	EMS 3	0.723 (0.684–0.763)	<0.001	0.588 (0.548–0.631)	<0.001
	EMS 4	0.774 (0.732–0.818)	<0.001	0.660 (0.614–0.710)	<0.001
	EMS 5	1.546 (1.472–1.625)	<0.001	1.497 (1.399–1.602)	<0.001
	EMS 6	1.56 (1.46–1.660)	<0.001	0.973 (0.899–1.052)	0.490
Age (per 1-year increase)		0.985 (0.984–0.986)	<0.001	0.985 (0.984–0.986)	<0.001
Sex					
	Female (i)				
	Male	0.899 (0.871–0.928)	<0.001	0.886 (0.854–0.918)	<0.001
Arrest aetiology					
	Cardiac/medical (i)				
	Trauma	2.111 (1.900–2.344)	<0.001	1.404 (1.249–1.578)	<0.001
	Overdose	1.821 (1.623–2.043)	<0.001	1.126 (0.990–1.281)	0.07
	Asphyxia	1.238 (1.121–1.368)	<0.001	0.753 (0.675–0.840)	<0.001
	Other	0.926 (0.866–0.989)	0.02	1.113 (1.035–1.196)	<0.01
Rhythm					
	Asystole (i)				
	Shockable- VF/VT)	0.630 (0.604–0.656)	<0.001	0.558 (0.533–0.583)	<0.001
	PEA	0.891 (0.858–0.926)	<0.001	0.872 (0.835–0.909)	<0.001
	AED- non-shockable	0.911 (0.722–1.150)	0.43	0.746 (0.585–0.949)	0.02
Bystander CPR					
	No (i)				
	Yes	1.102 (1.068–1.138)	<0.001	1.111 (1.072–1.152)	<0.001
Ambulance response time (per 1-minute increase)		0.997 (0.995–0.998)	<0.001	1.000 (0.999–1.002)	0.60

(i)- indicates index category.

Key- AED- automated external defibrillator; EMS- Emergency Medical Service; OHCA- out-of-hospital cardiac arrest; PEA- pulseless electrical activity; VF/VT- ventricular fibrillation/ventricular tachycardia.

Number (%) of cases in each unadjusted analysis: Time- 75,343 (100%); EMS system- 75,343 (100%); Age- 75,343 (100%); Sex- 75,123 (99.7%); Aetiology- 68,787 (91.3%); Rhythm- 72,519 (96.3%); Bystander CPR- 72,577 (96.3%); Response time- 73,787 (97.9%).

Number (%) of cases in the adjusted analysis: 64,567 (85.7%).

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CRediT authorship contribution statement

Sharvari Vadeyar: Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Alexandra Buckle:** Writing – review & editing, Methodology, Conceptualization. **Amy Hooper:** Writing – review & editing, Methodology, Conceptualization. **Scott Booth:** Writing – review & editing, Methodology, Investigation, Data curation. **Charles D. Deakin:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Rachael Fothergill:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Chen Ji:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Jerry P Nolan:** Writing – review & editing, Methodology, Conceptualization. **Martina Brown:** Writing – review & editing, Investigation, Data curation. **Alan Cowley:** Writing – review & editing, Investigation, Data curation. **Emma Harris:** Writing – review & editing, Investigation, Data curation. **Maureen Ince:** Writing – review & editing, Investigation, Data curation. **Robert Marriott:** Writing – review & editing, Investigation, Data curation. **John Pike:** Writing – review & editing, Investigation, Data curation. **Robert Spaight:** Writing – review & editing, Investigation, Data curation. **Gavin D Perkins:** Supervision, Methodology, Investigation, Conceptualization, Writing – review & editing. **Keith Couper:** .

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: CDD, RF, CJ, JPN, GDP and KC are co-investigators of the PARAMEDIC-3 trial (a randomised controlled trial of the IV versus IO route for vascular access in out-of-hospital cardiac arrest). JPN is Editor in Chief and GDP is an editor of Resuscitation. CDD and KC are editorial board members of Resuscitation.

Appendix A. Supplementary data

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