

## Clinical paper

## Comparison of intraosseous versus central venous vascular access in adults under resuscitation in the emergency department with inaccessible peripheral veins<sup>☆</sup>

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## ABSTRACT

**Introduction:** Current European Resuscitation Council (ERC) guidelines recommend intraosseous (IO) vascular access, if intravenous (IV) access is not readily available. Because central venous catheterisation (CVC) is an established alternative for in-hospital resuscitation, we compared IO access versus landmark-based CVC in adults with difficult peripheral veins.

**Methods:** In this prospective observational study we investigated success rates on first attempt and procedure times of IO access versus central venous catheterisation (CVC) in adults ( $\geq 18$  years of age) with inaccessible peripheral veins under trauma or medical resuscitation in a level I trauma centre emergency department.

**Results:** Forty consecutive adults under resuscitation were analysed, each receiving IO access and CVC simultaneously. Success rates on first attempt were significantly higher for IO cannulation than CVC (85% versus 60%,  $p = 0.024$ ) and procedure times were significantly lower for IO access compared to CVC (2.0 versus 8.0 min,  $p < 0.001$ ). As for complications, failure of IO access was observed in 6 patients, while 2 or more attempts of CVC were necessary in 16 patients. No other relevant complications like infection, bleeding or pneumothorax were observed.

**Conclusions:** IO vascular access is a reliable bridging method to gain vascular access for in-hospital adult patients under resuscitation with difficult peripheral veins. Moreover, IO access is more efficacious with a higher success rate on first attempt and a lower procedure time compared to landmark-based CVC.

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### 1. Introduction

Current European Resuscitation Council guidelines for resuscitation recommend intraosseous (IO) route for delivery of drugs, if intravenous access cannot be achieved.<sup>1</sup> Peripheral intravenous (IV) access might be difficult, especially in dehydrated patients, those in shock, following chemotherapy, obese, with oedema or IV drug users. Failure rates of IV access in the emergency setting are described around 10–40% and average time needed for peripheral IV catheterisation is reported between 2.5 and 16 min in patients with difficult IV access.<sup>2,3,4,5</sup> Delays in establishing vascular access in the field might be followed by additional delay in the emergency

department, when reattempting vascular access suspend necessary diagnostic and treatment procedures.

Alternative routes of drug and fluid administration are sublingual, endotracheal, subcutaneous and intramuscular. However, these options are not reasonable in most cases of emergencies and controversial due to unpredictable plasma concentrations along with unknown optimal dose of most drugs.<sup>1</sup> Central venous catheterisation (CVC) is an alternative, but it requires the interruption of CPR in the majority of cases and may be associated with risks for the patient, especially in the emergency setting.<sup>1,5–10</sup>

Consequently, a different vascular access technique may be reasonable, at least as a bridging option during ongoing resuscitation efforts. In this context, intraosseous (IO) vascular access of the non-collapsible and highly vascularised intramedullary venous plexus of cancellous bone marrow can provide a rapid, safe and easy vascular access to administer drugs, fluids and blood products.<sup>11</sup> In infants and children IO approach for emergency vascular access has been widespread adopted for decades already.<sup>1</sup> However the role of IO access in adults is much less propagated.<sup>12</sup> Only few studies specifically investigate IO access in adults, and most of them were

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restricted to the prehospital setting or training studies in animal or cadaver models. Own preliminary data of 10 adult patients in the emergency department showed potential benefits of IO access compared to conventional CVC regarding higher success rates and shorter procedure times on first attempt.<sup>7</sup>

Therefore our goal was to compare the time required to establish IO access versus CVC in adult patients undergoing resuscitation who initially had unsuccessful attempts at peripheral IV access, as well as report on their complication rates.

## 2. Methods

### 2.1. Study design and setting

This prospective, clinical trial was conducted between November 2007 and May 2009 at the emergency department of an urban level I trauma centre and teaching hospital with approximately 35,000 presentations a year. Our institutional review committee approved this study.

### 2.2. Selection of participants

Based on physiological criteria we approached consecutively all severely injured or critically ill adult patients under resuscitation admitted to our emergency department without at least 1 efficient 18-gauge peripheral IV access. A senior attending physician, consultant in surgery directed resuscitative efforts as team leader following protocols of advanced trauma life support for severely injured and advanced cardiac life support for critically ill patients. Indications for vascular access included blood drawing for serum analysis, delivery of drugs, antibiotics, fluids or blood products when no other access was available. Exclusion criteria were age under 18 years, pregnancy and prisoners. Informed consent was obtained delayed from each patient when returning to full consciousness or from legal representative as surrogate after enrolment. Each patient received both, IO access and CVC to compare success rate on first attempt and necessary procedure time. To compare 2 different IO access devices we prospectively randomised and assigned them to patients prior to the beginning of this trial. Patients were randomised to one of two IO access devices by computer-generated block randomisation. Allocation assignments were concealed in serially numbered opaque sealed envelopes. The operator and patient became aware of the access device only after enrolment.

### 2.3. Interventions

During initial resuscitation in accordance with present standards of care, peripheral IV access was attempted for a maximum of 3 efforts or a maximum of 2 min. If unsuccessful, IO access and CVC were performed in a standardised course of action by 2 independent operators.

### 2.4. Operators of IO and CVC

Operators were trained specialists and well experienced in resuscitation. Anaesthesiologists experienced of at least 25 successful traditional landmark CVC procedures without supervision performed CVC while surgeons provided the IO access. Before commencement of the study, surgeons participated in a 2-h education program outlining the use of the IO device with instructional videos and consecutive hands-on training.

### 2.5. Central venous catheterisation

CVC was performed in a standardised procedure using traditional landmark orientated Seldinger technique.<sup>13,14</sup> For haemodynamic monitoring option, internal jugular or subclavian vein was preferred to femoral access. According to our protocol, insertion site was primarily subclavian vein for CVC, but a different insertion site was chosen appropriate to injury pattern or disease. For CVC a standard triple- or quad-lumen 7-French (2.3 mm), 20 cm in length catheter (Arrow International Inc., 155 South Limerick Road, Limerick, PA 19468-1699, USA) was used, depending on patients' need. A chest radiograph was obtained in each patient following CVC to confirm placement and assess for complications.

### 2.6. Intraosseous vascular access

IO access was performed in a standardised course of action. According to our protocol, insertion site was primarily the proximal humerus. Different insertion sites were chosen appropriate to injury pattern or patients' condition. For example, if there was an obvious or suspected injury of both upper limbs, the tibial insertion site was used. Lower limbs were also preferred if anatomical landmarks of proximal humerus insertion site were unable to identify due to excessive soft tissue. After IO cannulation the prepared extension tubing was attached before drug and fluid administration. Each IO cannula was used only once and removed within 24 h of insertion according to manufacturers' recommendations. IO access was established with 2 different FDA-approved devices: the battery driven EZ-IO system (Vidacare Corporation, 722 Isom Road, San Antonio, TX, USA) and the spring load driven Adult BIG Bone Injection Gun (WaisMed Ltd., 2 Hamada Street, Yokneam, Israel). Technical specifications and procedure details of both devices have been published elsewhere.<sup>15</sup>

### 2.7. Methods of measurement, data collection and processing

Success rate of the procedure on first attempt was defined as successful administration of drugs or fluids via the newly established vascular IO access or CVC on first effort. Failure in CVC was defined as impossible insertion or advancing the guide wire. However, more than one (the first) attempt to puncture a central vein was not distinct as failure. The measured time of each procedure was defined as the duration of picking up the prepared set of IO access device or CVC set from the shelf, preparation of the access set and patients' insertion site including sterilisation and draping, insertion procedure of IO access or CVC itself, assembling of the access set and first successful administration of drugs or fluids through the newly established vascular access. An independent observer with 2 stopwatches took the time of each procedure. The patient's baseline characteristics such as age, gender, injury or cause of vital organ disorder were retrieved subsequently from the hospital record, if not available on admission. All treatment data and variables were collected prospectively in a structured form for each patient.

### 2.8. Outcome measures

Main outcome measures were success rate and procedure time of IO cannulation and CVC on first attempt. Secondary outcome measures included the prior determined possible complications according to literature, including failure of vascular access, malposition, dislodgment, bleeding, compartment syndrome, arterial puncture, haemothorax, pneumothorax and vascular access

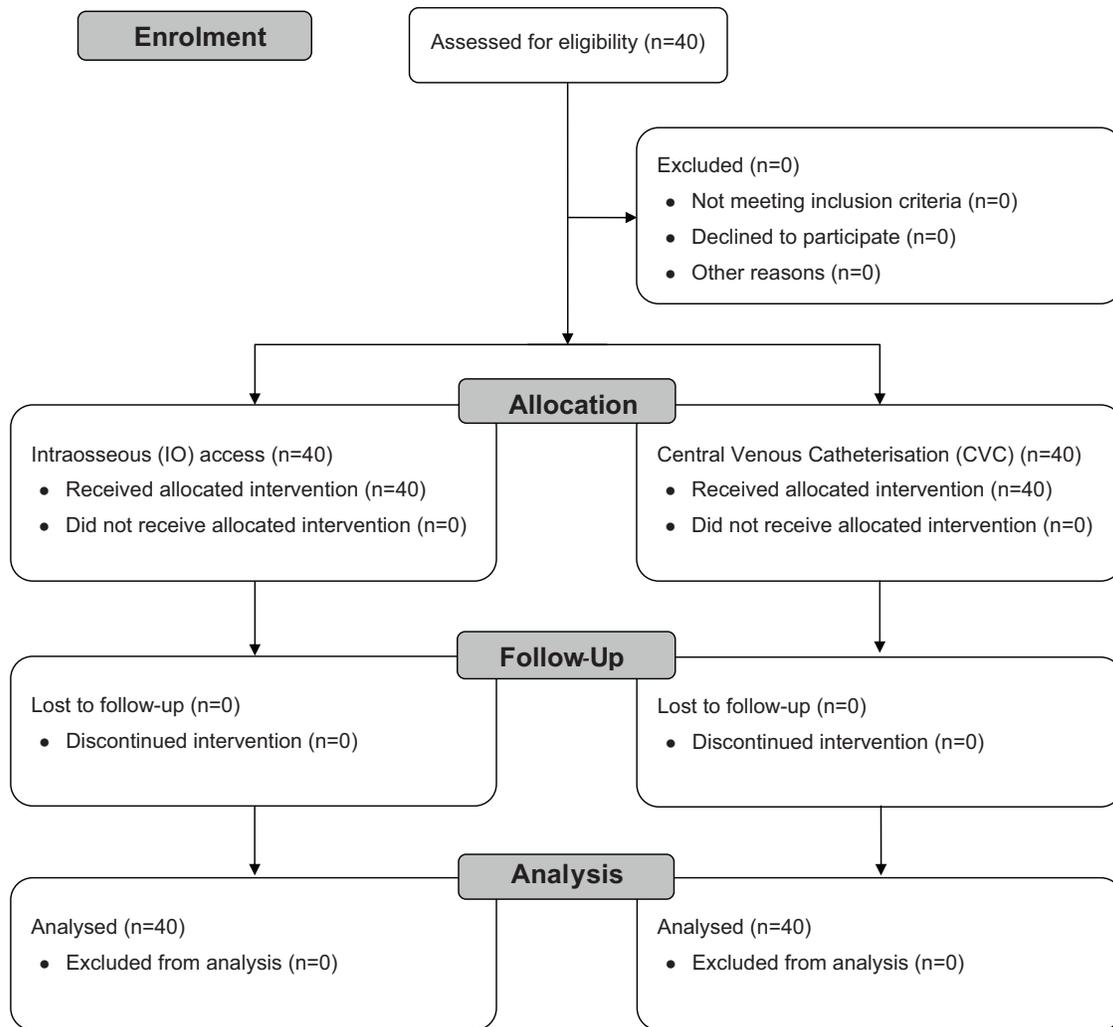


Fig. 1. CONSORT flowchart of enrolment, intervention allocation, follow-up, and data analysis. All 40 patients enrolled were allocated, followed-up and analysed.

related infection.<sup>5,10,13,14,16,17</sup> For instance to assess for complications following CVC, each patient obtained a chest radiograph. To determine vascular access related infection, insertion sites were inspected and documented 3 times daily. Additionally, every IO cannula was cultured after removal. All complications were recorded standardised for each access attempt in all patients. A patient follow-up was performed until hospital discharge. If patients were discharged within 14 days of admission, a standardised telephone interview 2 weeks after admission was conducted.

### 2.9. Primary data analysis

The outcome measures of success rate on first attempt were analysed using the  $\chi^2$  test with 1 degree of freedom and the z-test. For the outcome measures of procedure time, a 2-sided Mann–Whitney rank sum test was performed according to the distribution and sample size. A value of  $p < 0.05$  was considered statistically significant. For statistical testing SPSS version 13.0 software (SPSS, Chigaco IL, USA) was employed. Based on previous literature, a sample size of 38 evaluable subjects was expected to yield 80% power to demonstrate a 30% absolute difference in success rate on first attempt and a sample size of 5 subjects to demonstrate a difference in mean procedure time of 4 min, assuming  $p = 0.05$ . Therefore we enrolled 40 subjects.

## 3. Results

Forty consecutive adult patients under resuscitation receiving simultaneously IO access and CVC were enrolled into the study, 40 subjects in each intervention group. The follow-up was possible for all 40 patients (Fig. 1).

### 3.1. Characteristics of study subjects

Altogether 40 adult patients, 13 women and 27 men, ranging in age from 18 to 87 (on average  $48 \pm 21$ ) years were included. Obesity with a body mass index  $> 30 \text{ kg/m}^2$  was observed in 7 subjects, trauma was causative for resuscitation in 29 subjects. The IO insertion site was humeral in 22 and proximal tibial in 18 patients. The majority of CVC was achieved in 33 subclavian veins (Table 1).

### 3.2. Success rates on first attempt and procedure times

Our study found a significant difference of 25% in successful IO vascular access compared to CVC ( $\chi^2 = 5.078$ ,  $df = 1$ ,  $p = 0.024$ ). The success rate on first attempt was 85% (34/40) for IO access versus 60% (24/40) for CVC (Table 2). We demonstrated also a highly significant difference of 6.0 min in faster IO route compared to CVC ( $p < 0.001$ , 95% confidence interval [CI] 5.0–7.0 min). The median

**Table 1**  
Baseline characteristics.

	Overall (n = 40)
Gender male (%)	27/40 (68)
Mean age ± SD, years	48 ± 21
Min–max, years	18–87
Obesity, BMI > 30 kg/m <sup>2</sup> (%)	7/40 (18)
Trauma (%)	29/40 (73)
IO access insertion site humeral (%)	22/40 (55)
CVC insertion site subclavian vein (%)	33/40 (83)

BMI: body mass index, IO: intraosseous, CVC: central venous catheterisation.

**Table 2**  
Success rate and procedure time.

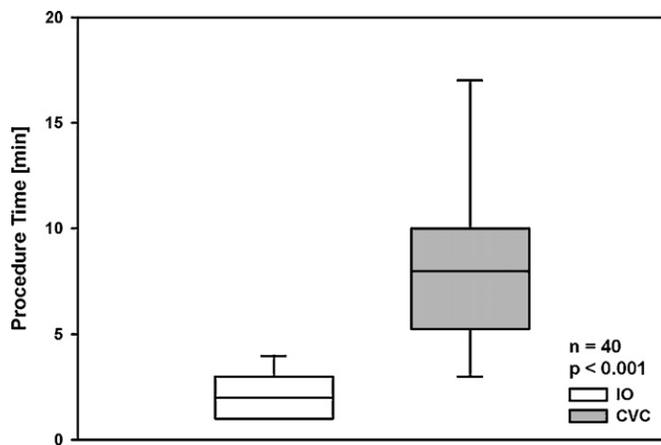
	IO (n = 40)	CVC (n = 40)	p
Success rate on first attempt (%)	34/40 (85)	24/40 (60)	0.024
95% CI, percentage	74–96	45–75	
Procedure time median, min	2.0	8.0	<0.001
Procedure time Q <sub>0.25</sub> –Q <sub>0.75</sub> , min	1.0–3.0	5.5–10.0	
Procedure time IQR, min	2.0	4.5	
Procedure time, min–max, min	1.0–4.0	3.0–17.0	
95% CI, min	1.0–3.0	4.0–13.0	

IO: intraosseous, CVC: central venous catheterisation; Q<sub>0.25</sub>: lower quartile, 25%, Q<sub>0.75</sub>: upper quartile, 75%, IQR: inter quartile range.

procedure time was 2.0 (inter quartile range [IQR] 2.0) min for IO access versus 8.0 (IQR 4.5) min for CVC (Fig. 2, Table 2).

### 3.3. Unsuccessful attempts and complications

In all 6 unsuccessful IO attempts the cannula did not penetrate the bone cortex due to incorrect tibial insertion site in 4 (BIG Bone Injection Gun), and excessive humeral overlying soft tissue in 2 subjects (EZ-IO). Details have been already published previously.<sup>15</sup> Sixteen CVC procedures failed at first attempt with inability to insert or advance the guide wire into the vessel probably due to incorrect insertion site or technique. Other relevant complications, like infection, extravasation, compartment syndrome, cannula dislodgment, bleeding, arterial puncture, haematothorax, pneumothorax, venous thrombosis or vascular access related infection were not observed.



**Fig. 2.** Procedure time of intraosseous (IO) cannulation was significantly shorter than central venous catheterisation (CVC) for vascular access in adult emergency patients under resuscitation. The box plots show median values (central line), 25th and 75th percentile, respectively (margins of box) and range (outer lines).

## 4. Discussion

In this trial, we compared success rate on first attempt and necessary procedure time to perform IO vascular access versus CVC in adults under resuscitation in the emergency department lacking peripheral IV access. To our knowledge, this prospectively observational study is the first to compare IO access versus CVC in a real scenario in-hospital setting. We observed that IO cannulation was significantly more successful and faster to gain vascular access when compared to landmark-based CVC, without relevant complications.

There are no randomised clinical trials in literature comparing in-hospital IO approach versus CVC in adults, but at least some case series and observational studies<sup>5,16–21</sup> (Table 3). In line with these findings, our results showed also a high success rate of 85% and a low mean procedure time of 2.0 min.

Alternative vascular access techniques in the adult patient under resuscitation with difficult peripheral veins include CVC, ultrasound-guided peripheral IV cannulation and saphenous vein cutdown. Central venous catheterisation provides vascular access for fluid resuscitation, drugs, antibiotics, allows haemodynamic monitoring and cardiac pacing. Central line placement enables higher peak drug concentrations and shorter circulations times compared to peripheral venous administration. However, CVC is relatively time-consuming and associated with complications especially in the emergency setting.<sup>5,8,22,23</sup> Complication rates for traditional landmark-based CVC are reported around 15–20%, including malposition, arterial puncture, haematoma, pneumothorax, venous thrombosis and catheter related infections.<sup>8–10,14,22</sup> The average rate of CVC-associated bloodstream infections is 5.3 and can add up to calculated 33 per 1000 catheter-days for emergency department-placed lines.<sup>23,24</sup> An estimated 250,000 cases of CVC-associated bloodstream infections occur per year in the USA. Attributable mortality is an estimated 12–25% for each infection and marginal cost of USD 25,000 per case.<sup>24</sup> Because compliance with infection control procedures is low in the emergency setting, a bridging procedure to perform vascular access may gain additional time for subsequent central line placement in a less busy environment under a maximum of barrier precautions to lower infection risk. Ultrasound-guided CVC increases success rates and reduces the number of attempts and complications associated with CVC. However, the initial time demand to power, set up the ultrasound machine and to cover the probe with a sterile sheath may delay urgent patient management compared to traditional landmark CVC, especially in experienced CVC operators. Data from literature regarding necessary procedure times of ultrasound-guided CVC are conflicting due to lack of uniformity in study methodology where most investigators report “skin to blood” time and neglect time taken for the positioning and preparation of the ultrasound machine, assembling the related equipment and locating the central vein.<sup>6,8,9,22,25,26</sup> The evidence currently available supports ultrasound guidance in general. However, it is less clear whether the advantages mostly described in intensive care unit populations apply to the emergency department setting as well.<sup>8,22,25,26</sup> Further randomised controlled trials are needed, to evaluate especially patient-centred outcomes (e.g. mortality, quality of life or length of stay) in the emergency setting regarding the routine application of ultrasound guidance in CVC. Peripheral IV cannulation with ultrasound guidance is an option worth considering, but it is described less successful and slower than IO access. Ultrasound-guided peripheral IV access enabled success rates of 46–84% on first attempt and 73–100% following several attempts with analogous delays.<sup>2,3,27–29</sup> Procedure times are reported 6.5–20 min in most studies, not including the time for set up of the ultrasound machine and preparation of the probe.<sup>2,3,27,28,30</sup> Taken into account this additional time need, delay

**Table 3**  
Studies of in-hospital IO vascular access in adults.

Study	n	Outcome	Comments
Cooper et al. <sup>18</sup>	22	Success 97%	No complications
Iserson <sup>19</sup>	22	Time <1 min	No complications
Iwama and Katsumi <sup>20</sup>	31	Success 94% Time <1 min	No complications, IO flow rates similar to CVC
Ong et al. <sup>16,17</sup>	24	Success 97% Time ≤ 20 s	No complications
Paxton et al. <sup>5</sup>	30	Success 81% Time, 1.5 min	11 secondary dislodgments of IO within on average 6.9 h after placement, no further complications
Valdes <sup>21</sup>	15	Success 87%	No complications with an average use of 5.4 days

IO: intraosseous, CVC: central venous catheterisation; n: number of patients; Success: success rate; Time: application time, min: Minute; s: seconds.

end up to 39 min.<sup>29</sup> Furthermore, besides the ultrasound machine an experienced operator is required. Saphenous vein cutdown is also slower, less successful and associated with higher risks than IO access. The reported time need was shown between 2 and 8 min with a success rate around 69–94% when performed by experienced operators. Trauma to the lower extremities might preclude saphenous vein cutdown. Time effect of administered drugs and fluids to the saphenous vein may be delayed due to long distance between vein cutdown and the heart, especially in shock conditions with impaired circulation.<sup>31,32</sup>

There were several potential limitations to our study. Assembly bias due to differences in subjects' was limited by our study design. All subjects were enrolled consecutively and each subject received both, IO cannulation and CVC simultaneously. The sample size of this study is quite small, reflecting the rare incidence of adults under resuscitation with inaccessible peripheral veins. We are aware, that only larger sample sizes comparing a single IO device to CVC might have answered the question more clearly. However, this would have been impossible to achieve in a 2-year period taking into account the rare IO infusions in the emergency department. On the other side, the results regarding success rate and procedure time between the 2 different applied IO devices did not show statistically significant differences. Potential bias of the investigators favouring towards IO access was limited by performing IO access and CVC simultaneously by two independent operators. Potential bias of one particular IO device was limited by randomisation.<sup>15</sup> With regard to operator experience, our definition was arbitrary and may not truly reflect the familiarity with the procedure. Although more than 25 successful traditional landmark CVC procedures without supervision should enable sufficient knowledge, skill and practice to be classified as experienced operator. The effective use of diverse IO access devices following an instruction course of a maximum of 2 h have been demonstrated by different studies, revealing success rates of 93–100% within 2 min.<sup>33,34</sup> Therefore the 2-h education program with hands-on training of each IO device before commencement of this study should enable experienced operators. Furthermore all operators were experienced consultants with at least 6 years expertise in resuscitating patients in the emergency department following standardised protocols.

As a result of the present study, we continued the IO vascular access protocol in adult patients under resuscitation with impossible peripheral IV access in the emergency department.

## 5. Conclusions

We found IO vascular access a safe, reliable and rapid option in adults under resuscitation in the emergency department with inaccessible peripheral veins. Compared to landmark-based CVC, IO cannulation was significantly more successful on first attempt and required significantly less time. However, IO access is not a surrogate for CVC and cannot replace it. Complications following IO access are rare, providing correct indication and appropriate handling. Therefore, IO access is worth to be considering a valuable

bridging technique in the emergency department, if peripheral IV access was attempted unsuccessful 3 times for a maximum duration of 2 min. These findings are in accordance with current guidelines of the European Resuscitation Council.<sup>1</sup>

## Conflicts of interest

The authors declare that they have no conflict of interest regarding any financial or personal relationships with the manufacturers or with any other people or organisations that could inappropriately influence or bias their work.

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