Comparison between Intraosseous and Central Venous Access in Adult Trauma Patients in the Emergency Room: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Obtaining an efficient vascular access in a short-time is fundamental for the patient with hypovolemic shock in the emergency room. In case of peripheral venous access failure, the second option is not yet well defined.

Objective: Critically appraise the literature on the use of intraosseous access and central venous access comparing these two interventions with respect to time to complete each of them, rate of success, and complications.

Methods: The electronic databases used were MEDLINE / PubMed, PubMed Central, CAPES Platform, The Cochrane Library, EuroPMC, and Virtual Health Library (VHL). Literature reviews, conference proceedings, case reports, case series, comments, and correspondence were excluded, as were studies with children under 18 and a small sample. For the meta-analysis which estimated success in the first attempt, the odds ratios for success, the Mantel-Haenszel method was used for fixed effects. For the analysis of the execution time between procedures, the inverse variation method for fixed results was used. Meta-analysis calculations were performed using the Reviewer Manager 5.3 software.

Results: A total of 144 studies were found, four of which were selected for the review, totaling 167 patients. There was superiority of intraosseous access in relation to central venous access with respect to the success rate in the first attempt (9.93; 95% CI 5.08–19.40; 0.00,001) and duration of the procedure (1.94; 95% CI 2.02–1.13; 0.00,001). All four studies comparing access found better performance and less time to perform intraosseous access compared to the central venous catheter.

Conclusion: It is possible to determine that intraosseous vascular access is a safe, reliable, and a faster option in trauma patients in shock in the emergency room with inaccessible peripheral veins.

Keywords: Emergency room, Intraosseous infusion, Trauma, Vascular access devices.

RESUMO

Introdução: A obtenção de um acesso vascular eficiente em curto espaço de tempo é fundamental para o paciente em choque hipovolêmico na sala de emergência. Em caso de falha do acesso venoso periférico, a segunda opção ainda não está bem definida.

Objetivo: Avaliar criticamente a literatura sobre o uso de acesso intradossé e acesso venoso central comparando essas 2 intervenções com relação ao tempo para completar cada uma delas, taxa de sucesso e complicações.

Métodos: As bases de dados eletrônicas utilizadas foram MEDLINE / PubMed, Pubmed Central, CAPES Platform, The Cochrane Library, EuroPMC e Virtual Health Library (VHL). Revisões de literatura, anais de conferências, relatos de casos, séries de casos, comentários e correspondência foram excluídos, assim como estudos com crianças menores de 18 anos e uma pequena amostra. Para a metanálise que estimou o sucesso na primeira tentativa, a Odds Ratios (OR) de sucesso, foi utilizado o método de Mantel-Haenszel para efeitos fixos. Para a análise do tempo de execução entre procedimentos, foi utilizado o método da variação inversa para resultados fixos. Os cálculos da meta-análise foram realizados com o software Reviewer Manager 5.3.

Resultados: Foram encontrados 144 estudos, dos quais 4 foram selecionados para a revisão, totalizando 167 pacientes. Houve superioridade do acesso intradossé em relação ao acesso venoso central quanto à taxa de sucesso na primeira tentativa (9.93; IC95% 5.08–19.40; 0.00,001) e duração do procedimento (1.94; IC95% 2.02–1.13; 0.00,001)). Todos os quatro estudos comparando o acesso encontraram melhor desempenho e menos tempo para realizar o acesso intradossé em comparação com o cateter venoso central.

Conclusão: É possível determinar que o acesso vascular intradossé é uma opção segura, confiável e mais rápida em pacientes traumatizados em choque na sala de emergência com veias periféricas inacessíveis.

Palavras-chave: Trauma. Emergência. Infusão intradossé. Dispositivos de acesso vascular.

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Introduction
One of the most common clinical manifestations in the severely injured patient is hypovolemic shock, which is characterized by hemodynamic collapse with impaired perfusion. Hemodynamic shock requires prompt diagnosis and treatment, based on volume replacement, treatment of coagulopathy, and mechanical bleeding control, according to the Advanced Trauma Life Support (ATLS) guidelines. Consequently, obtaining an efficient vascular access in a short time is crucial for the resuscitation of patients in the emergency room.

Access to the vascular system in trauma patients can be performed in three different ways: the first access option, recommended by both ATLS and Pre-hospital Care Protocols-PHTLS, is peripheral venous access (PVA). If this is not possible, the second option chosen by ATLS for adults is central venous catheterization (CVC) using the Seldinger technique. However, for the Prehospital Care Protocol, regardless of the age of the traumatized subject, after two failed attempts to obtain the PVA, one should move to intraosseous access (IO).

Central venous catheterization is an alternative, although requires interruption during cardiopulmonary resuscitation in most cases and can be associated with risks for the patient, especially in an emergency setting. In this context, IO, through the noncollapsible and highly vascularized intramedullary venous plexus, is a very effective option and has been established in pediatric patients for decades. Its use in adults is less widespread, especially for the in-hospital setting. However, bone marrow can provide quick, safe, and easy vascular access for administering drugs, volume, and blood products to the trauma patient.

In view of high incidence of trauma in the general population, its high potential for evolution to complications such as hemorrhagic shock, as well as the different benefits and complications offered by each vascular access, it is necessary to evaluate the effectiveness of CVC in comparison to IO in adult trauma patients. The aim of this systematic review and meta-analysis is to review the literature comparing IO to CVC accesses with respect to success rate, time to obtain access, and complications. We believe that the results found in this review may contribute to the better therapeutic choice of access during the resuscitation process of trauma patients.

Materials and Methods

Search Strategy
A systematic review with meta-analysis, conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses, was performed by the authors. Literature searches were done in the following electronic databases MEDLINE / PubMed from Jan 1, 1990 to Feb 5, 2019, PubMed Central from Jan 1, 1990 to May 5, 2019, CAPES Platform from Jan 1, 1990 to Feb 5, 2019, The Cochrane Library from Jan 1, 1990 to Feb 5, 2019, EuroPMC from Jan 1, 1990 to Feb 5, 2019 and Virtual Health Library (VHL) from Jan 1, 1990 to Feb 5, 2019, through the combination of descriptors, including terms from Medical Subject Headings (MeSH). Search terms were related to the population of interest and the parameters to be studied: “Central Venous Catheters” OR “central venous vascular access” AND “Infusions Intraosseous” OR “intraosseous vascular access” AND “polytraumatized adult patient” AND “efficiency” AND “comparison.”

Study Selection
We included studies published in English, Spanish, and Portuguese, because would it be difficult to translate from other languages and no other related international studies were found. Studies were included if they were randomized clinical trials, prospective, and retrospective observational cohort studies, comparing efficacy (success rate and time to access) and complications of IO and CVC, during management of adult trauma patients, aged 18 years and over. Literature reviews, conference proceedings, case reports, case series, comments, and correspondence were not considered. In the case of studies that reported results applied to the same population, only the first published study was considered.

Critical Evaluation and Risk of Bias Assessment
Risk of bias in randomized controlled trials was assessed using the Cochrane risk-of-bias tool for randomized trials. Observational cohort studies were evaluated using the STROBE Statement (Strengthening the Reporting of Observational studies in Epidemiology) and the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Those that met quality criteria in this systematic review had at least 15 items fully or partially met. For a structural evaluation of randomized controlled trials, the Guidelines for publication of scientific studies (CONSORT) criteria were used to assign a score of 0 (does not meet) or 1 (meets) for each of the 25 criteria in the checklist. A score of 0 was considered for topics that partially met the criteria, articles with at least 20 fully attended items were included.

Data Extraction
Data extraction was performed by two review authors on a predefined data collection form, with the following studies’ characteristics: title, reference, study design, country, year, and sample size. In addition, we collected: number of participants, age, and reason for the IO or CVC accesses intervention. Furthermore, we collected data on success rate, duration, location of puncture sites (subclavian/femoral/pretibial/humeral/antecubital fossa), equipment and technique, operator category (Nurse, physician, paramedic), and comorbidities were collected. Extracted data were compared, with any discrepancies being resolved through discussion.

Statistical Analysis
Fixed effect model was used for studies that showed the same interest effect. For the meta-analysis which estimated success on the first attempt, the odds ratios (OR) for success were combined using the Mantel-Haenszel method for fixed effects. The meta-analysis for the execution time between exams determined the standard mean difference by the inverse variation method for fixed results. The heterogeneity of the both analyses was accessed statistically using the Chi-square test, the I² value and the random effects model instead. Analyses were performed using the Software Review Manager 5.3 (Review Manager (RevMan) (Computer program). Version 5.3. Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014).

Results

Characteristics of the Included Studies
The search strategy identified 139 studies. After removing duplicates, we examined 121 medical records and 94 articles were excluded. Thus, 27 full-text documents were reviewed and finally included four papers (prospective, randomized, observational, and clinical trials). Later, we searched documents that cited any
of the initially included studies as well as the references of the initially included studies. However, no extra articles that fulfilled inclusion criteria were found in these searches. We excluded 23 studies from our study, and we listed reasons for exclusion in the Figure 1. Characteristics of excluded studies tables. We excluded studies because they not shown the success rate of the access, only the time to do the access or use different access techniques and equipment. The characteristics of the included studies are shown in Table 1.

STROBE and CONSORT Assessments
A randomized clinical trial and three observational analytical cohort studies were included. In the critical evaluation procedure, the clinical trial conducted by Leidel et al. performed well, fulfilling 23 of the items fully proposed by CONSORT and 2 items partially fulfilled by the article (Supplement 2). Another study described by Chreiman, et al., performed better, fulfilling all the items proposed by STROBE: 22 items fulfilled in full (Supplement 3). Leidel et al., fulfilled 21 items, with nineteen fulfilled entirely and two partially. Lee et al., fulfilled eighteen items in full and four items partially (Supplement 3).

Risk of Bias Assessment
The quality of the clinical trial study is shown in Supplement 1, using the Cochrane collaboration tool. The randomization methods were adequate and sufficiently described in the study. As for the blinding of outcome evaluators, the risk of bias is uncertain, as the authors did not report who was responsible for assessing the outcome, they were only cited as experienced professionals. Follow-up was possible for all patients, there were no frictions or exclusions.

The methodological quality of the cohort studies was assessed using the New castle Ottawa Scale (NOS), presented in Supplement 4. Two of them were a high-quality source reaching 90% and 70% of the methodological criteria. Only one article was evaluated with moderate quality, reaching 60% of the criteria, not evaluating in the Outcome, the adequacy of monitoring of cohorts result and if the follow-up was long enough for the results to occur.

Table 1: General features of selected studies, sorted by publication year

| Author            | Country/Year     | Study profile                      | Success rate                                      | IO site              | CVC site              |
|-------------------|------------------|------------------------------------|---------------------------------------------------|----------------------|-----------------------|
| Leidel BA et al.  | Berlim, 2009     | Observational analytical cohort study | First successful placement attempt and insertion time | Proximal humerus     | Subclavian vein       |
| Leidel BA et al.  | Ireland, 2012    | Randomized Clinical Trial           | Successful administration of drugs or fluids through vascular IO or CVC was established in first effort. | Proximal humerus     | Subclavian vein       |
| Lee PMJ et al.    | United States, 2015 | Observational analytical cohort study | First successful placement attempt and insertion time | Proximal tibial      | Femoral vein          |
| Chreiman KM et al.| United States, 2018 | Observational analytical cohort study | Visualization of liquid flow through device placed on first attempt | Proximal tibial and proximal humerus and subclavian vein | Femoral vein and subclavian vein |

CVC, central venous catheter; IO, intraosseous access

Fig. 1: Flowchart of article selection
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Supplement 1: Cochrane tool adapted to evaluate bias risk

| Topic                        | Leidel et al., 2013 |
|------------------------------|---------------------|
| Random sequence generation   | •                   |
| Allocation concealment       | •                   |
| Professionals and participants blinding | • |
| Outcome evaluators blinding  | •                   |
| Incomplete outcomes          | •                   |
| Selective outcomes           | •                   |
| Intention to treat analysis  | •                   |

Supplement 2: Quality evaluation of study, based on CONSORT essential items

| Topic                          | Leidel et al., 2012 |
|--------------------------------|---------------------|
| Title and summary              | 1                   |
| Introduction                   | •                   |
| Foundation and objectives      | 2                   |
| Methods                        | •                   |
| Study profile                  | 3                   |
| Participants                   | 4                   |
| Interventions                  | 5                   |
| Outcomes                      | 6                   |
| Sample size                    | 7                   |
| Randomization generation       | 8                   |
| Allocation                     | 9                   |
| Implementation                 | 10                  |
| Blinding                       | 11                  |
| Statistical methods            | 12                  |
| Results                        | 13                  |
| Participants flow              | 14                  |
| Recruiting                     | 15                  |
| Base Data                      | 16                  |
| Analyzed numbers               | 17                  |
| Outcomes and estimation        | 18                  |
| Auxiliary analyses             | 19                  |
| Damage                         | 20                  |
| Discussion                     | 21                  |
| Limitations                    | 22                  |
| Generalization                 | 23                  |
| Interpretation                 | 24                  |
| Other information              | 25                  |

Supplement 3: Quality evaluation of selected studies, based on STROBE initiative items

| Topic                          | Leidel et al., 2009 | Lee et al., 2015 | Chreiman et al., 2018 |
|--------------------------------|---------------------|------------------|------------------------|
| Title and summary              | 1                   | •                | •                      |
| Introduction                   | •                   | •                | •                      |
| Foundation and objectives      | 2                   | •                | •                      |
| Objectives                     | 3                   | •                | •                      |
| Methods                        | •                   | •                | •                      |
| Study profile                  | 4                   | •                | •                      |
| Context                        | 5                   | •                | •                      |
| Part                           | 6                   | •                | •                      |
| Variables                      | 7                   | •                | •                      |
| Data sources/ measurement      | 8                   | •                | •                      |
| Bias                           | 9                   | •                | •                      |
| Study size                     | 10                  | •                | •                      |
| Quantitative variables         | 11                  | •                | •                      |
| Statistical methods            | 12                  | •                | •                      |
| Results                        | 13                  | •                | •                      |
| Participants                   | 14                  | •                | •                      |
| Descriptive data               | 15                  | •                | •                      |
| Outcome data                   | 16                  | •                | •                      |
| Main results                   | 17                  | •                | •                      |
| Other analyses                 | 18                  | •                | •                      |
| Discussion                     | 19                  | •                | •                      |
| Main results                   | 20                  | •                | •                      |
| Limitations                    | 21                  | •                | •                      |
| Generalization                 | 22                  | •                | •                      |
| Other information              | 23                  | •                | •                      |
| Financing                      | 24                  | •                | •                      |

Outcome Assessments

Success Rate IO vs CVC

Lee et al.,\textsuperscript{15} found the biggest difference between procedure success rates in the first attempt, presenting a difference of 52.8. Leidel et al.,\textsuperscript{14} and Leidel et al.,\textsuperscript{13} also found a higher success rate for IO compared to CVC, (90%; 85% IO–60%; 60 % CVC). C Chreiman et al.,\textsuperscript{16} presented the second biggest difference in the success rate between accesses, with 44% of success when trying IO.

All studies evaluated the success rate of both vascular accesses in the emergency department. The average success rates for each study can be seen in Table 2, in percentage points. The researches’ combined effect shows that the IO has an odds ratio of 9.93 [95% CI 5.08–19.40; \( p < 0.0001 \)] in relation to CVC for success in first attempt (Fig. 2 Meta-analysis of the relationship between IO and CVC success rates).

Execution Time IO vs CVC

Lee et al.,\textsuperscript{15} portrayed better performance in IO as well as better execution time, as well as Chreiman et al.,\textsuperscript{16} which showed a shorter time to perform the procedure, with a minimum of 0.13 minute and a maximum of 0.65 minute. Leidel et al.,\textsuperscript{14} and Leidel et al.,\textsuperscript{13} portrayed better performance in IO as well as better runtime. Similarly, Leidel et al.,\textsuperscript{14} and Leidel et al.,\textsuperscript{13} also found the best time to perform the IO, 2 minutes for the IO, in addition to having the longest procedure duration in the performance of CVC, with an average of 8 min for CVC.
The relationship between times when CVC and IO were performed were also considered in all studies. However, the paper published by Lee et al.,\(^1\) provides only the average time to perform the procedure and does not show the standard deviation. It was therefore excluded from the time analysis. Statistical evaluation of the three other studies with time standard deviation, showed that on average the IO is done 1.94 minutes [95% CI 2.02–1.13; \(P < 0.00001\)] before CVC (Fig. 3 Meta–analysis of the relationship between the IO and the CVC performance time).

**Complications**

In all articles, complications of the two techniques were assessed as a secondary outcome. Relevant complications, such as infection, hemothorax, pneumothorax, venous thrombosis, or infection related to vascular access were not observed in any of the analyzed studies. In their work, Chreiman et al.,\(^1\) reported that, because of short follow-up time of the study and data evaluation through videos, it was not possible to report incidence of these complications in the study, but mentioned the main possible risks such as compartment syndrome, osteomyelitis, and displacement of accesses (Table 2).

**Other Analysis IO vs CVC**

The variables of success and access time in question were investigated in the Chreiman et al.,\(^1\) study, by comparing them with PVA and showing that attempts of this access and CVC attempts had similar success rates (43% and 44%, respectively). In addition, there was no difference between PVA duration attempts and IO
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| Study or Subgroup | Intraosseous Mean | SD | Total | Central Venous Mean | SD | Total | Std. Mean Difference IV, Random, 95% CI | Std. Mean Difference IV, Random, 95% CI |
|------------------|------------------|----|-------|---------------------|----|-------|----------------------------------------|----------------------------------------|
| Leidel 2009      | 2.3              | 0.8 | 10    | 9.9                 | 3.7 | 10    | -2.72 [-4.00, -1.43]                  | -2.39 [-2.97, -1.81]                   |
| Leidel 2012      | 2.06             | 1.11 | 40    | 8.09                | 3.35 | 40    | -1.68 [-2.02, -1.33]                  | -1.58 [-2.02, -1.13]                  |
| Chreiman 2018    | 0.39             | 0.39 | 52    | 3.39                | 2.67 | 50    | -2.10 [-2.80, -1.41]                  | -2.00 [-2.69, -1.30]                  |
| Total (95% CI)   | 102              |     |       | 100                 |     |       |                                        |                                        |

Heterogeneity: Tau² = 0.24; Chi² = 6.31, df = 2 (P = 0.04); I² = 68%

Test for overall effect: Z = 5.90 (P < 0.00001)

Fig. 3: Meta-analysis of the relationship between the IO and the CVC performance time

D I S C U S S I O N

This systematic review and meta-analysis aimed at evaluating the effectiveness of IO and CVC in adult trauma patients in the emergency room. Two of the studies presented the biggest differences between access success rates in the first attempt (90.3% IO - 37, 5% CVC and 92% AIO- 44% CVC). Other authors found a higher success rate for IO in comparison with CVC, despite having lower values than the other studies. Like the present review, Engels et al., found that IO had a 81% success rate in patients with hemorrhagic shock, with no possibility of PVA. In another prospective randomized study, examining the use of IO access in trauma patients, Fulkerson et al., also reported an average time to insertion of the IO of 3 minutes, obtained in the first attempt in 72% of cases.

The result of the meta-analysis confirmed what had been identified by the systematic review, a significant primacy of IO over CVC in patients suffering from severe trauma, relative to success in the first attempt. Engels et al., as well as the present study, reported a period of 20 minutes to successfully obtain the CVC in patients with hemorrhagic shock, while the IO was performed in just one 90-second attempt. This may be related to a more difficult insertion technique for CVC, since catheter placement is performed through reference techniques based on knowledge of the structures and palpation of the arteries close to the veins, which requires training and experience of the professionals, in addition to IO the spinal cord has the anatomical advantage of functioning as a rigid vein, which does not collapse during the hypovolemic state. More than 15% of patients will have a complication related to catheter. Most of the failures in CVC attempts without guided ultrasound reported in the studies resulted from errors in the insertion technique, as well as the use of incorrect anatomical references for access, while the IO presents greater facility in locating the puncture sites and is simpler to perform technique. 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.

CVC is relatively time-consuming and associated with several complications, especially in emergency situations. Complication rates for traditional CVC based on reference points are reported to be around 15 to 20%, including malposition, arterial puncture, hematoma, pneumothorax, venous thrombosis, and catheter-related infections.

There were also complications linked to the incorrect passage of the CVC catheter, guide wire advancement at the CVC and incorrect puncture sites. It was reported that 40% of CVC procedures failed on the first attempt, requiring at least one more attempt and that this 40% failure on the first attempt was due to the inability to insert or advance the guidewire into the venes.

In IO, different types of complications are described in cases including failure in placement, poor flow, catheter displacement, iatrogenic bone fracture, growth plate rupture, fat embolism, hematoma formation, osteomyelitis, compartment syndrome, neurovascular injury, and tissue necrosis, which are uncommon. Other related complications are pain, reported during fluid administration and intraosseous needle displacement during transport. In addition to these, there was first attempt failure due to an error in the anatomical puncture reference, which made it impossible for the cannula to penetrate the bone cortex, especially in the tibial and humeral insertion site. More serious complications including osteomyelitis, cellulitis and skin abscesses are more related to prolonged use of IO and not to the procedure itself and the most serious complication, tissue necrosis, usually happens due to the infusion leakage to the subdermal space. All these complications are uncommon, less than 1%.

Limitations

The moderate success rate heterogeneity (I² = 46%), coupled with the high execution time heterogeneity (I² = 68%) found in meta-analyses and the absence of time standard deviation in the article by Lee et al., are limitations of the present study.

All articles covered relatively small populations, which explains the presence of large confidence intervals between the results, the over-all population size is way too small to make any strong conclusions. Only four articles were selected for this review, which demonstrates the main finding: that there are no high-quality studies done comparing the two IV access methods. Only one of the articles was randomized controlled blinding; the other three are prospective observational studies that are more likely to increase the risk of bias that weakens rejection of the null hypothesis. Furthermore, there is an inconsistency in the population character of the studies, the study by Leidel et al., includes cardiac arrests in the outcome and the study by Chreiman et al., used videos for evaluation in the nonemergency context.

In the absence of PVA, IO should be increasingly considered as an emergency tool to gain access to systemic circulation in critically ill patients. Studies show that, despite being more used, CVCs may not be a fast and effective vascular access for reestablishing unadjusted hemodynamic balance that results from the state
of shock.\textsuperscript{30} However, more clinical trials are needed to test the hypothesis of IO insertion as the second safest option.

**Conclusion**

IO is a safe, reliable, and fast option in adult trauma patients in the emergency department with inaccessible peripheral veins. It can become the preferred route of fluid replacement, but more high-quality clinical trials with larger and better defined populations are needed to test the hypothesis of IO insertion as the second safest option.

**Article Summary**

- **Why is this topic important?**
  In view of the high severity of hypovolemic shock, obtaining an efficient vascular access in a short time is fundamental for the resuscitation of trauma patients in the emergency room.

- **What does this review attempt to show?**
  IO can be a quick, safe, and easy vascular access for the administration of medications, volume, and blood products to the traumatized patient, in comparison with CVC in cases of PVA failure.

- **What are the key findings?**
  In general, the IO is faster and has a much higher rate of success in the first attempt in relation to CVC, being a safe option in the emergency department with inaccessible peripheral veins.

- **How is patient care impacted?**
  The results found in the present study may contribute to the better choice of therapeutic approach for polytrauma patients, restoring hemostasis, and avoiding worse outcomes. The conclusions of this systematic review will serve as a basis for future research on the topic.

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