Intraosseous Vascular Access for In-Hospital Emergency Use

A Systematic Clinical Review of the Literature and Analysis

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Abstract: Intraosseous (IO) vascular access is a viable primary alternative in patients requiring emergent vascular access in the hospital emergency department (ED) (eg, resuscitation, shock/septic shock) but is underutilized.

Objectives: This review has 3 objectives: (1) review the evidence supporting the use of IO access; (2) determine the utilization of IO access as described in the literature; and (3) assess the level of specialty society support.

Methods: Electronic and hand searches were undertaken to identify relevant articles. English-language-only articles were identified. The Cochrane Review methodology along with data forms were used to collect and review data. The evidence evaluation process of the international consensus on emergency cardiovascular care was used to assess the evidence. Studies were combined where meta-analyses could be performed.

Results: In levels 2 to 5 studies, IO access performed better versus alternative access methods on the end points of time to access and successful access. Complications appeared to be comparable to other venous access methods. Randomized controlled trials are lacking. Newer IO access technologies appear to do a better job of gaining successful access more quickly. Intraosseous access is underutilized in the ED because of lack of awareness, lack of guidelines/indications, proper training, and a lack of proper equipment.

Conclusions: Recommendations/guidelines from physician specialty societies involved in the ED setting are also lacking. Underutilization exists despite recommendations for IO access use from a number of important medical associations peripherally involved in the ED such as the American Academy of Pediatrics. To encourage the IO approach, IO product champions (as both supporter and user) in the ED are needed for prioritizing and assigning IO access use when warranted. In addition, specialty societies directly involved in emergent hospital care should develop clinical guidelines for IO use.

Key Words: intraosseous access, resuscitation, systematic review

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Emergent vascular access is of paramount importance in the emergency room (ER) because of such conditions as cardiopulmonary arrest, shock, sepsis, burns, major trauma, and status epilepticus. The criterion standard for vascular access is an intravenous (IV) catheter (peripheral or central venous [CVC] line). However, when IV or CVC access is not possible (eg, because of peripheral vascular collapse or small veins because of patient size) or feasible in a timely manner (eg, CVC access), other vascular access means that provide quick access with high success rates are required.

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Intraosseous (IO) access provides an alternative route of vascular access. The intramedullary space in bones of the tibia or humerus where an IO needle is placed is highly vascular and does not collapse because of the surrounding bone. This intramedullary space provides a direct conduit to the systemic circulation.

Recent advances in device technologies have improved the ability to gain IO access for infusion purposes. These devices penetrate the bone easily. The use of IO access in the prehospital emergency setting is standardized practice and the first vascular access alternative (with specific guidelines) if IV access cannot be obtained.[1,2]

Recent changes in guidelines have also recommended the use of IO access over central access or the endotracheal route for delivery of inotropes in pediatric patients; as few practitioners in the emergency setting are able to establish central venous (CV) access before 2 hours in pediatric patients,[3] in comparative studies on adults (8 [CV] vs 2 minutes [IO] and 15.6 [CV] vs 1.5 minutes [IO][5]), drug delivery in adults versus the endotracheal route,[6] and in infants or children if attempts at establishing IV access are unsuccessful after 1 minute.[6]

Central venous access as an alternative to IV access in patients requiring emergent vascular access is not without its problems. More than 15% of adult patients who receive these types of catheters experience complications including infections, thrombotic complications, and mechanical complications.[7] Furthermore, in studies in children, the complication rates for CVC in the literature may be as high as 22%.[8]

METHODS

Types of Studies/Publications

The levels of evidence of therapeutic interventions in selecting studies to include in the clinical utility analysis according to Morley et al[9] were used. Furthermore, the checklist for meta-analyses of observational studies was used.[10]

As well, published surveys on overall usage of IO access in the ED, policy statements on care in the ED, and technology assessments were identified.

Lastly, recommendations from medical specialty societies were evaluated to determine if guidelines exist for IO access.

Types of Participants

- Patients in whom emergent vascular access is required.
- Nonhuman studies where randomization of the participants was performed in a prospective manner.

Types of Interventions

Types of Interventions used were as follows:

1. Intraosseous access versus peripheral or CV access—prospective randomized trial or prospective studies without true randomization (eg, alternate assignment).
2. One IO access system versus another—prospective randomized trial or prospective studies without true randomization (eg, alternate assignment).

Types of Measures Evaluated

1. Primary Outcome Measures
   - Successful access—percentage of time successful on first try or on subsequent tries until vascular access was obtained.
   - Time to access—insertion time.
2. Secondary Outcome Measures
   - Complications—including technical, infection (adverse events)
   - Pharmacokinetics
   - Cost
3. Clinical Guidelines
   - Clinical guideline support was provided by medical associations involved in ER care.

Search Methods for Identification of Studies

See Appendix 1 for the search methodology used.

Exclusion Criteria

- Level 5: Studies not directly related to the specific patient/population (eg, different patient/population; animal models, mechanical models) that were not randomized controlled trials (RCTs) or; said differently, nonhuman studies except for nonhuman RCTs.
- Studies with less than 10 patients were not included, no matter the level of evidence.
- Duplicates of studies (either in abstract form or published as a manuscript at a later date).
- Review or overview articles on IO access technology and technique.

Data Collection and Analysis

The Cochrane review methodology was used to collect summary data on each of the studies on IO access identified.[11]

Selection of Studies

Studies were selected based on the level of evidence as defined by Morley et al.[9] Prospective randomized trials undertaken on nonhuman subjects were also identified (defined as level 5 by Morley).

Data Extraction and Management

Data extraction forms were used (Appendix 2) for extracting data from studies.

Assessment of Risk of Bias in Included Studies

Assessment of risk of bias was undertaken using Cochrane summary tables[11] for prospective randomized (level 1), quasi-randomized (level 2) trials, and prospective randomized level 5 (nonhuman) trials.

Measures of Treatment Effect (for Levels 1 and 2 Trials Only)

Each study is reported separately. The results of binary outcomes (ie, successful access or not) are descriptively summarized as percentages and treatment comparisons presented with P values and confidence intervals where possible. For continuous data (ie, time to access), we also used P values and confidence intervals where possible.

Assessment of Heterogeneity

If trials could be combined, assessment of statistical heterogeneity was made using the I^2 statistic to determine appropriateness for meta-analysis. If the I^2 statistic was at or below 60%, the heterogeneity was considered moderate, and meta-analysis was appropriate. If the value was greater than 60%, reasons were explored as to why this heterogeneity existed.

RESULTS

Results of the Search

Levels 1 and 2 Evidence

The PubMed search identified 3 studies that appeared to meet the criteria for high-quality evidence (levels 1 and 2).[12–14]

The Cochrane Central Register of Controlled Trials identified 13 studies of which 1 study was selected for inclusion based on the quality of the evidence.[15] Correspondence with an author of an excluded study identified an updated level 2 study that included a larger number of patients.[16] The characteristics of the levels 1 and 2 studies appear in Appendix 3.

Level 3 Evidence

A search of company Web sites identified 6 level 3 studies (studies using retrospective controls).[5,16–20] One trial was eliminated because of it being a duplication of a prior trial.[20]

Level 4 Evidence

Searches of company Web sites, PubMed, relevant journals, reference sections of levels 1 and 2 trials, and the Internet identified 22 level 4 studies (studies without a control group, eg, case series).[21–42] One trial was eliminated because of it being a duplication of a prior trial.[42]

Level 5 Evidence (Prospective Randomized Trials on Nonhuman Subjects)

The PubMed search identified 6 studies that appeared to meet this criteria.[43–48] Two trials were excluded based on nonrelevant outcomes.[49,50] Searching the reference sections of levels 1 and 2 articles and of review articles identified 2 additional nonhuman studies.[51,52] The characteristics of the level 5 studies appear in Appendix 3.

Medical Society Recommendations

Medical society Web site searches identified for clinical guidelines on use of IO access identified 11 such recommendations.[1–3,6,53–59]

Technology Assessments on IO Access

Searching technology assessment Web sites using the search term *intraosseous access* identified 2 assessments.[60,61]

Clinical Use/Nonuse of IO Access Within the Hospital Environment

Using an Internet search (first 8 pages), searching journal Web sites (specifically *Emergency Medicine Journal*, *Annals Emergency Medicine*, *Canadian Journal Emergency Medicine*), reviewing the bibliographies of product-specific Web sites (Vidacare, San Antonio, Tex), and reviewing clinical guidelines for use of IO access, 7 articles were identified on clinical use/nonuse of IO access in the hospital setting.[31,52,62–66]

Description of Studies

Level 1 Studies

Three prospective randomized trials (level 1) on IO access using human subjects were identified.[12–14] The Hartholt and

Leidel studies[12,13] evaluated one IO access device versus another. As it relates to the primary end points of successful access, the following were observed:

- Hartholt: Successful access was achieved in 80% to 86.5% of adult and pediatric patients, respectively, with all devices tested.
- Leidel: Success rates on first attempt were 90% with EZ-IO (Vidacare) and 80% with BIG (Bone Injection Gun; Waismed Ltd, New York, NY).

As it relates to the secondary end point of pharmacokinetics, Von Hoff et al[14,15] examined the morphine concentrations infused either via the IO or IV routes. There was no difference in the pharmacokinetic parameters between the 2 groups.

Level 2 Studies

Two prospective nonrandomized trials (level 2) on IO access in human subjects were identified[15,16] The following end points were observed:

- significantly faster and more reliable access with IO versus IV (Banerjee et al[15])
- significantly faster and more reliable access with IO versus CVC (Leidel et al[4])

Level 3 Studies

Prospective studies using a historical control were mainly supportive of the use of IO access[16,18,19] except for one[16] (Appendix 4). Specifically, as it relates to the primary end points of successful access (also, see meta-analysis, Fig. 1):

- The overall success rate at gaining access with IO access with newer devices was improved (Pointer et al[18]; Frascone et al[19]).

In examining the levels 1, 2, and 3 studies (studies using a comparator), only 2 studies could be combined for meta-analysis purposes. These studies, Frascone et al[19] and Pointer et al,[18] analyzed the success rates of gaining access with the EZ-IO (Vidacare) versus FAST1 (Pyng Medical, Vancouver, British Columbia, Canada) devices. It was found that with the EZ-IO device, success at gaining vascular access was significantly higher versus the FAST1 device (relative risk [RR], 1.18; 95% confidence interval [CI], 1.09–1.27; $P < 0.0001$; $I^2 = 0\%$) (Mantel-Haenszel random-effects model) (Fig. 1).

Level 4 Studies

Studies without a control group (prospective observational and retrospective reviews) were all supportive of the use of IO access as an alternative to gaining vascular access. They demonstrate a high success rate in either first time or overall vascular access. Furthermore, the success rates of gaining vascular access, with IO access, was higher with the newer IO access designs (Appendix 5).

Level 5 Studies

Nine prospective randomized trials using IO access on nonhuman models were examined.[43–48,51,52] Overall, they demonstrated the following:

- faster time with IO access versus alternative access methods (Abe et al[43]; Hubble and Trigg[46]).
- faster time to first access with newer IO access technologies (Brenner et al[44]; Jun et al[47]; Shavit et al[48]).

Adverse Event Analysis

A meta-analysis of adverse events is provided in Figure 2. This analysis demonstrated no difference in the occurrence of adverse events between IO and Peripheral intravenous (PIV)/CV access, although there was a trend toward less adverse events with IO access (RR, 0.58; 95% CI, 0.30–1.12; $P = 0.11$) (M-H random-effects model). Furthermore, an analysis where adverse events were reported for both IO and peripheral or CV access demonstrated no real difference (Appendix 6).

Cost Analysis

Costs were not reported in any of the studies identified.

Utilization of IO Access as Reported in the Literature

Surveys of emergency medicine departments on the use of IO access revealed the following:

- Lack of the proper equipment (48%).[59] Emergency department did not have guidelines on the use of IO access (42%).[60]
- Prior training or lack of knowledge on the use of IO devices had not been provided (32.6%–47%).[60] Indications for use of IO access were not clearly defined.[60]
- Real-life experience in use of IO access, even when it is clearly recommended for resuscitation, significantly increases the likelihood of use.[61]
- For unstable patients in which a peripheral IV is unobtainable, the majority of ED programs in US academic EDs use a central line as the second- and third-line options for vascular access. Central lines were reported to be used 62% of the time for second attempts as vascular access and 45% for third attempts. Intraosseous use became more frequent if a fourth attempt was required being used 24% of the time. Results from this US survey confirmed that IO access is underutilized.[62] Median time from initiation of resuscitation to successful IO placement was 8 minutes (interquartile range, 4–25 minutes).[30] This was the result of multiple (>3 times and/or 90 seconds as recommended by the American Heart Association; American Academy of Pediatrics[53] attempts at IV access before IO placement).

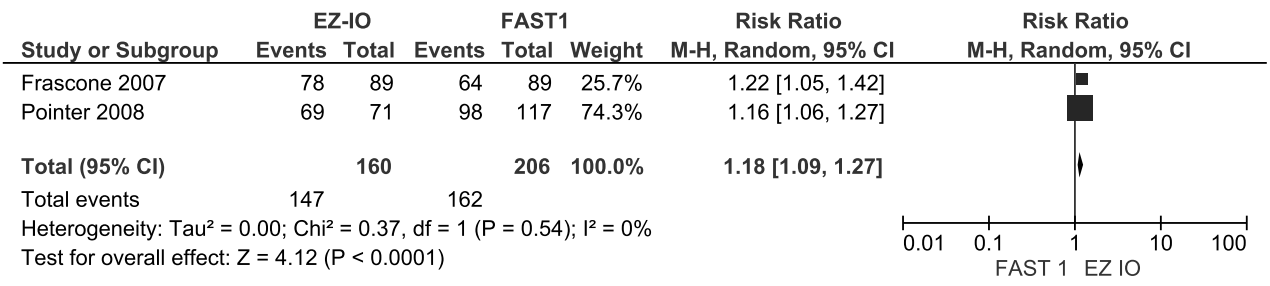

FIGURE 1. Success at gaining IO access—FAST1 versus EZ IO.

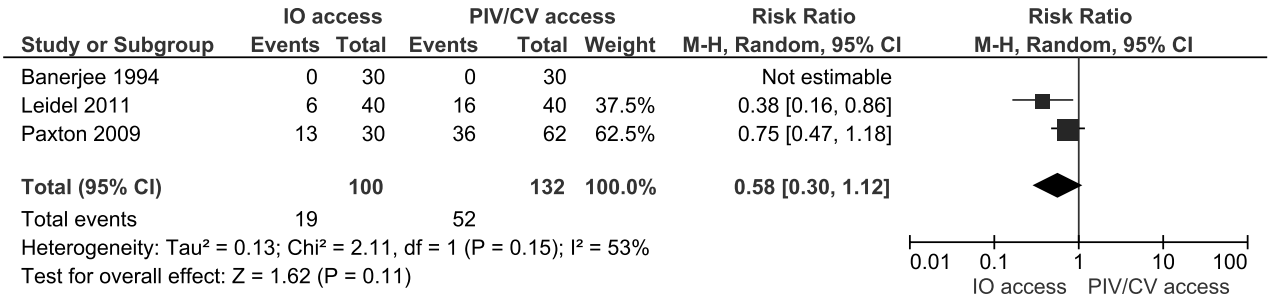

FIGURE 2. Adverse events—IO versus PIV/CV access.

Whereas 74% of ED survey respondents were aware of IO access, only 7% used the technique in practice.[63] Furthermore, it was stated that IO access is infrequently taught and used in ER departments.

Medical Society Guidelines or Technology Assessments on Use of IO Access

There are a number of recent recommendations made in guidelines by specialty societies and tech assessment Web sites on the use IO access for emergency use in the and outside the hospital.[53,55–59,67] These guidelines were developed by the following specialty societies/associations: American Academy of Pediatrics (Committee on Pediatric Emergency Care), American College of Emergency Physicians (Pediatric Committee), Emergency Nurses Association (Pediatric Committee), American College Critical Care Medicine (pediatric advance life support with relevance to the emergency care clinician), National Association of EMS Physicians, American Heart Association, Infusion Nurses Society, European Resuscitation Council, and the Canadian Agency for Drugs and Technologies in Health (technology assessment). These guidelines focus on ensuring there are vascular access supplies and equipment available in the ED[2,56]; the need for adequate training and clinical competency[2,56]; the fact that IO access should be established if vascular access is not achieved in a rapid fashion,[6,55,57,58] that is, should be the first alternative to failed IV access[1,57] that qualified registered nurses should insert, maintain, and remove IO access devices[54]; and that medical protocols that include specific criteria for the appropriate clinical application and reasonability for IO access should be made available in emergency situations.[2,68,69] Further guidelines stress the importance of administering inotropes as soon as possible (eg, via IO routes if peripheral access is not possible) in pediatric and neonatal septic shock, as delays in doing so are associated with a 20-fold increased mortality risk,[3] and the need for hemodynamic support of pediatric and newborn patients with septic shock—emphasizing the importance of time-sensitive stepwise use of fluid resuscitation and the need for rapid vascular access to reduce mortality.[68,69]

Risk of Bias in Included Studies (for Levels 1, 2, and 5 Prospective Randomized Studies Only)

In total, the levels 1, 2, and 5 studies identified for inclusion in this review were of lower quality. The overall quality of the studies was deemed to be fair to poor based on the risk-of-bias summary and graphs shown in Figures 3 and 4.

Measures of Treatment Effect and Examination of Heterogeneity

Two of the above trials could be combined for meta-analysis purposes in examining success at IO vascular access.[18,19] Heterogeneity was low when combining these 2 trials. In another meta-analysis examining adverse events, 3 trials[4,5,15] were combined, and it was found that heterogeneity was found to be moderate (I^2 = 53%) (Figs. 1 and 2).

DISCUSSION

What are apparent from the results when examining the best evidence (levels 1 and 2) are the following:

- All IO access devices when compared with each other were similarly fast (<1 minute) in gaining vascular access[12,13] (level 1 evidence).

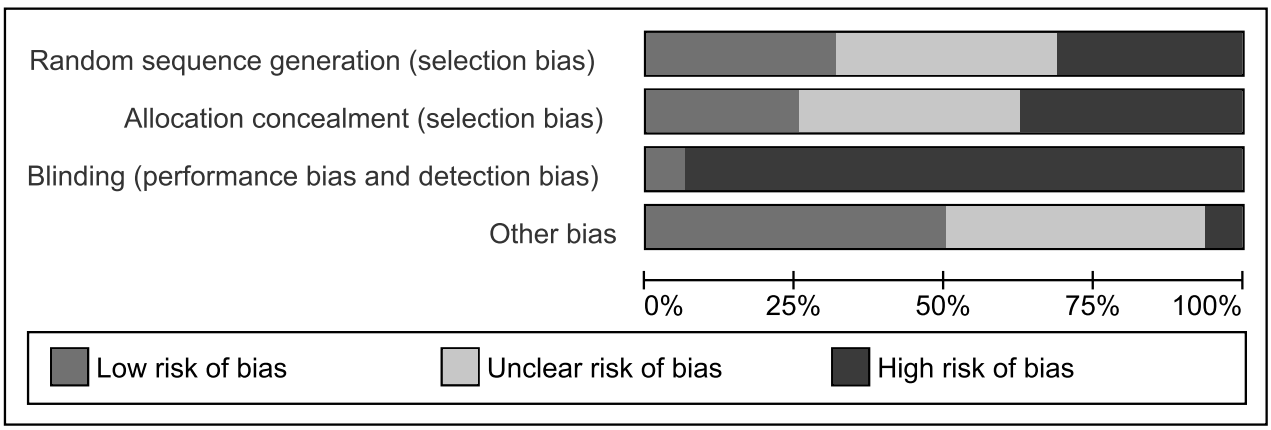

FIGURE 3. Risk-of-bias summary all articles included in analysis.

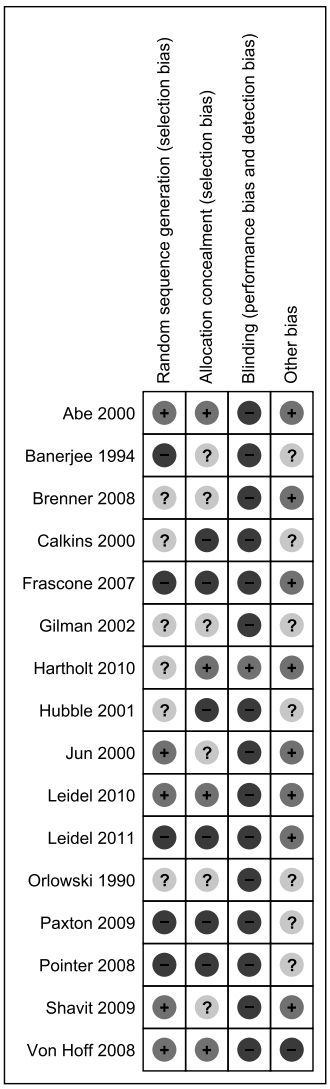

FIGURE 4. Risk-of-bias table—all studies.

- Pharmacokinetics were equivalent between IO and IV access methods[4,15] (level 1 evidence).
- In patients with emergent access needs where IV access was difficult, the IO alternative was significantly faster[15,16] (level 2 evidence).

It may be extremely difficult to perform well-executed RCTs on IO versus IV access because of issues associated with institutional review board (IRB) approval, the methodology required for a well-run randomized trial, and the emergent condition of these patients, where immediate intervention is required and fast thinking is needed. Institutional review board approval may be further compounded by the fact that other vascular access methods have such high complication rates and lengthy time to access (ie, CVC access) such that using them as one of the treatment arms may not be ethical. Consent of a patient in an emergency situation is also likely problematic (because of their condition and/or family). The time required in developing adequate concealment and in controlling for other biases, such as blinding (clinician performing procedure, patient), versus the emergent need to care for these patients in an ER setting would also result in a questionable quality (ie, biases) of the results.

It was found when performing a meta-analysis of adverse events between IO and PIV/CV access that heterogeneity was very high, calling in to question the ability to combine these studies. This heterogeneity was likely due to the methodologies used in collecting the data and the fact that none of the combined trials were RCTs. It should be noted, however, that all vascular access methods are not without complications and that training in both IO and PIV/CV is necessary.

It appears based on what is stated in the literature that IO access is underutilized within the hospital ED setting. Furthermore, IO access appears not even to be a second-line option to peripheral vascular access, when peripheral access cannot be obtained. These factors translate into a longer time to gain appropriate access, in excess of the current Pediatric Advance Life Support recommendations of 90 seconds or 3 IV attempts.[53]

In relation to guidelines for the use of IO access within the hospital setting, what were not found in the searches were specific guidelines for ED clinicians as to when IO access should be attempted if vascular access fails. As well, in searching via the Internet (Google—first 8 pages; search terms: hospital, vascular access policies and procedures, IO access; search performed on December 28, 2010) for hospital-specific ED protocols for patients with emergent need for vascular access, there was only one hospital IO access protocol identified.[67] If these sorts of guidelines were developed, specific hospital protocols, competency training, and oversight could in turn be developed; as suggested by O'Connor.[2] Furthermore, it appears that nursing associations have taken an active role in "owning" this activity within the ED.[56,68,69] The possibility may exist for ED nurses to become more proactive within hospital ED departments in driving appropriate use of this technology. Whether this translates into protocol development, training, and appropriate care remains to be seen.

What has been recommended in the literature is that more widespread teaching of the IO access technique be undertaken.[64] The 2 main reasons why survey respondents did not teach adult IO access in the article of Lavis et al[66] were that it was not in guidelines/accepted practice and that they felt that it was not needed/not necessary or other techniques were preferable. A possible impediment to teaching thus appears to be lack of widespread support by clinicians who work within the ED setting. This lack of widespread support may in part be manifested in lack of clear clinical guidelines for its use by the primary clinical decision makers in the ED as described below.

What were also not found in the searches were specific guidelines from the physician specialty societies dealing with in-hospital emergency situations and IO access. These societies included the American College of Emergency Physicians, American Academy of Emergency Medicine, Society for Academic Emergency Medicine, and the American College of Surgeons committee on trauma (position paper on emergency vascular access in children but not for adults). Perhaps, if these types of guidelines were developed, the appropriate utilization of IO access could be achieved.

Agreements and Disagreements With Other Studies or Reviews

This evaluation is consistent from a clinical utility standpoint with the findings of a number of the evidence-based guidelines and assessments for pediatric patients in the ER[3,54,57,58] and for adults.[1,59,60]

CONCLUSIONS

Implications for Practice

Despite recommendations from a number of specialty societies on the use of IO access when IV access has failed in emergent patients, IO access appears to be an underutilized access tool in the hospital ED. Based on the above analysis, the following recommendations are made: that IO access be the priority as an alternative, definitions be developed on what point IO access should be attempted and on what types of patients, that continuing education and in-servicing programs be developed for further and reminder training, that physician ED specialty societies develop clinical guidelines for its use (as none exists), and ED nursing be designated product champions (user and supporter) for IO access in the ED.

Implications for Research

There are a small number of patients evaluated in higher-quality studies (level 2) that compare different vascular access methods (eg, peripheral vs IO).[13,15] Studies involving a larger number of patients would add to the body of evidence supporting the use of IO access as a next best alternative to IV access. Although higher-quality studies are needed, it may be extremely difficult to perform well-executed RCTs on IO versus IV access based on the emergent condition of these patients—where immediate intervention is required, fast thinking is needed, and performing time consuming unbiased allocation may be problematic because of life-threatening patient conditions.

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APPENDIX 1: Search Methodology Used

Electronic Searches

Searches were undertaken using the PubMed Web site and using the following MESH search terms:
- Intraosseous infusion (explode all trees) and RCTs (explode all trees) (searched on December 12, 2010).
- Intraosseous infusion (explode all trees) and prospective studies (explode all trees) (searched on February 16, 2011).
- Intraosseous infusion (explode all trees) and longitudinal studies (explode all trees) (searched on February 16, 2010).
- Intraosseous infusion (explode all trees) and retrospective studies (explode all trees) (searched on February 21, 2011).

The Cochrane Central Register of Controlled Trials—The Cochrane Library Issue 42, 2010, was searched using the term *intraosseous access* (search undertaken on December 12, 2010).

The following clinical/technology assessment Web sites were searched on February 18, 2011, for IO access:
- National Institute of Health and Clinical Excellence
- Agency for Healthcare Research and Quality
- Canadian Agency for Drugs and Technologies in Health
- California Technology Assessment Forum
- BCBS Technology Assessment

The following medical specialty society Web sites were searched for clinical guidelines on the use of IO access (search undertaken on February 18, 2011):
- American College of Emergency Physicians
- American Academy Emergency Medicine
- Society for Academic Emergency Medicine
- American Heart Association
- American College Cardiology
- Society of Critical Care Medicine
- American Academy of Pediatrics
- American College Surgeons (Committees on Trauma and Perioperative Care)
- European Society of Intensive Care Medicine
- American Society of Anesthesiologists
- American Burn Association
- National Association of EMS Physicians
- Emergency Nurses Association
- Infusion Nurses Society

The following journal Web sites related to emergency care were searched on February 16 and 17, 2011, for the term *intraosseous access*:
- *American Journal Emergency Medicine*
- *Annals Emergency Medicine*
- *Clinical Pediatric Emergency Medicine*
- *Pediatric Emergency Journal*
- *Circulation*
- *Emergency Medicine Journal*
- *Journal Emergency Medical Services*
- *Canadian Journal Emergency Medicine*

The following clinical guideline Web site was searched on December 28, 2010, for the term *intraosseous access*:
- Institute for Clinical Systems Improvement

The Web sites of the following companies involved in IO technologies were searched to identify bibliographies and articles relating to IO access: Vidacare(EZ-IO), PYNG Medical (FAST1), and Waismed (BIG).

Searching Other Resources

The reference sections of position papers on clinical guidelines from specialty societies were searched to identify levels 1 and 2 evidence as outlined above and, for prospective randomized trials on different patient populations/nonhuman, simulation models.

The reference sections of published articles qualifying as levels 1 and 2 evidence were also searched for additional levels 1 and 2 evidence. As well, reference sections of review articles on IO access were searched for levels 1 and 2 studies.

An Internet search was undertaken on December 28, 2010, using the search terms: hospital protocol—indications for IO access and IO access, clinical use, hospital ED. The first 8 pages of each search were used to identify articles.

Only English-language publications were evaluated.

APPENDIX 2: Data Collection Form

Name of person/reviewer extracting data:			
Author of article:			
Title:			
Source (eg, journal title):			
Date of study:			
Study location (geographical):			
Care setting (eg, hospital):			
Inclusion/exclusion criteria (list of patient inclusion and exclusion criteria)			
Inclusion:			
Exclusion:			
Sample size:			
Number in each arm of trial			
A priori power calculation?	Yes	No	Not stated
Trial powered adequately?			
Patient baseline characteristics:			
Age range:			
Sex:			
Medical condition(s):			
Trial design details:			
Single-center/multicenter trial?			
Study type			
RCT/matched control/unmatched concurrent control/historic control:			
Allocation			
Was it random?	Yes	No	Not stated
Method of randomization:			
Was it concealed?	Yes	No	Not stated
Intervention details			
Care setting:			
Treatment group(s):			
Control(s):			
Cointerventions:			
Duration of intervention:			
Who delivered the intervention?			
Was the provider performing the procedure blinded?	Yes	No	Not stated
Was the patient blinded?	Yes	No	Not stated
Outcome measures			
What were they?			
Methods of assessing outcome measures:			
Blind assessment?	Yes	No	Not stated
When were they measured?			
Validity of assessment:			
Length of follow-up:			
Costs			
Considered?	Yes	No	Not stated
Cost-effectiveness details:			
Results:			
Analysis:			
Description of analysis used:			
Statistical methods:			
Comparisons made:			
Intention-to-treat analysis?			
Adjustment for confounding?			
Subgroups considered?			
Exploration of heterogeneity?			
Results:			
Missing data:			
Length of follow-up:			

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APPENDIX 2: *(Continued).*

Withdrawals/dropouts—are proportion and characteristics of participants lost to follow-up comparable for the study groups at the end of the trial?
Reasons for withdrawal:
Loss to follow-up:
Percent of successful access (primary outcome):
  Intervention arm (1):
  Intervention (or control) arm (2):
  Intervention arm (if >2 intervention arms are included in the trial):
  Intervention are (if >2 intervention arms are included in the trial):
Time to access (primary outcome):
  Intervention arm (1):
  Intervention (or control) arm (2):
  Intervention arm (if >2 intervention arms are included in the trial):
  Intervention are (if >2 intervention arms are included in the trial):
Pharmacokinetic data (primary outcome):
  Intervention arm (1):
  Intervention (or control) arm (2):
  Intervention arm (if >2 intervention arms are included in the trial):
  Intervention are (if >2 intervention arms are included in the trial):
No. adverse events:
  Intervention arm (1):
  Intervention (or control) arm (2):
  Intervention arm (if >2 intervention arms are included in the trial):
  Intervention are (if >2 intervention arms are included in the trial):
Cost data included?
Conclusions:
Implications (eg, for practice):
Other comments:
Methodological quality of study:
Comparability of intervention:
Baseline comparability:

APPENDIX 3: Characteristics of Studies

Characteristics of Included Levels 1, 2, and Level 5 (Prospective Randomized) Studies

Abe et al[43] (2000)	
Methods	RCT—coin flip.
Participants	First- and second-year medical students training and evaluating 2 vascular access routes in newborns.
Interventions	IO access using turkey bone/plastic infant leg/turkey bone model (n = 22)—inexperienced and experienced (after training) evaluations (2 access attempts for each participant; for a total of 42 attempts).
	Peripheral access (umbilical vein catheterization) using a infant formula bottle model (N = 22)—inexperienced and experienced (after training) evaluations (2 each attempts for each participant for a total of 42 attempts).
Outcomes	Placement times for IO access or peripheral access.
	Visual analog scale (VAS) for 0 (easy) to 10 (difficult) recorded for each.
Notes	Study performed in the US.
	Pretraining and posttraining evaluation of both access techniques.
Banerjee et al[15] (1994)	
Methods	Prospective nonrandomized trial.
Participants	Children (3 months to 2 y of age) with severe dehydration.
Interventions	Intraosseous access (n = 30)—18-gauge spinal needle with stylet (Vygon) or 16- to 18-gauge hypodermic needle with stylet used.
	Intravenous access (n = 30)—22- or 24-gauge Teflon catheter (Viggo).
Outcomes	Ability to start fluid infusion within 5 min of attempt at cannulation.
	Time from skin puncture to starting infusion.
Notes	Study performed in India.
	Pediatric resident physicians performed either the IV or IO access.

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APPENDIX 3: *(Continued).*

Brenner et al[44] (2008)	
Methods	Prospective randomized trial—human cadaver model.
Participants	Clinicians involved in gaining IO access.
Interventions	Manual IO access (n = 39) (Cook Medical Inc, Bloomington, Ind).
	EZ-IO access (n = 45) (Vidacare).
Outcomes	Time to access—time to insertion of needle.
	Percent successful on first attempt.
	No. attempts required to obtain access.
	Technical complications including needle breakage, bent needle, defective battery.
Notes	Study performed in Heidelberg, Germany.
	Participants were trained for 1 h before using IO access—had never used this type of access before—study undertaken at the sixth Invasive Emergency Techniques seminar.
	Written consent obtained by participants and approved by local ethical committee.
Calkins et al[45] (2000)	
Methods	Prospective randomized trial—testing of units on cadavers in random order of placement.
Participants	Adult cadavers.
Interventions	First access for shock and trauma (FAST; Pyng Medical) (n = 31).
	BIG (Wais Medical, Kress, USA) (n = 31).
	SurFast (Cook Critical Care, Bloomington, Ind) (n = 31).
	Jamshidi needle (Baxter, McGaw Park, Ill) (n = 31).
Outcomes	Time to access success—determined via aspiration of bone marrow, flow of fluid with flushing of syringe used for aspiration, flow of crystalloid under pressure, and security of needle after placement.
	No. attempts.
Notes	Study performed in a cadaver lab in the US with special forces medics.
	IRB approval.
	Training on devices (60-min lecture with hands on practice) before use in study.
Gilman et al[51] (2002)	
Methods	Prospective randomized cross over design using a pediatric pig model and placed in the tibial plateau of the pig.
Participants	25 ER residents evaluated 2 IO needles.
Interventions	Jamshidi 15-gauge (Baxter Healthcare Corp).
	SLN needle 15-gauge (BIG; Wais Medical Ltd).
Outcomes	Time to access.
	Success rates in placement.
Notes	Study origin: US.
Hartholt et al[12] (2010)	
Methods	Prospective randomized trial of use of IO access prehospital in emergency trauma situations.
Participants	Pediatric patients (1–13 y of age) (n = 23) and adult patients (n = 69).
Interventions	Intraosseous access systems which included:
	For pediatric use:
	• Jamshidi 15-gauge (Cardinal Health, Dublin, Ohio) (n = 12).
	• BIG 18-gauge (n = 11).
	For adult use:
	• Jamshidi 15-gauge (Cardinal Health) (n = 25).
	• BIG 18-gauge (Waismed Ltd) (n = 22).
	• First access for shock and trauma (FAST1) (Pyng Medical Corp) (n = 22).
Outcomes	Time to access.
	Success rate for first time access.
	Adverse events (complications including: extravasation, blood loss, trocar stuck in bone, needle bending, malpositioning of needle).
	User satisfaction as scored via a VAS: 0 implied device is not user-friendly, and 10 implied highest user-friendliness.
Notes	Study performed in Rotterdam, the Netherlands: Erasmus Medical Center (level I trauma center).
	Local ethics committee approval obtained.
	All helicopter emergency medical service personnel trained on use of IO access.
	Study was powered to detect a difference in insertion time of 30 s between the IO needles (80% power, $P = 0.05$).
	Nurses placed needles.

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APPENDIX 3: *(Continued).*

Hubble and Trigg[46] (2001)	
Methods	Prospective randomized crossover trial on a cadaver model comparing one access method (saphenous vein cut down) to IO access.
Participants	Students in a paramedic program (n = 13).
Interventions	Saphenous vein cut down (n = 13).
	IO access (n = 13) with BIG.
Outcomes	Success rate.
	Time to access.
	Complications.
Notes	Study origin: US.
	IRB approval.
	Before initiation of study, students were trained for 8 h on both techniques—including hands on training.
Jun et al[47] (2000)	
Methods	Prospective randomized trial—use of coin flip to randomize students to one IO access device or the other.
Participants	Medical students training and evaluating 2 IO access needles in turkey femur bone model and pork rib bone.
Interventions	• Sur-Fast IO access needle (Cook Medical, Cook Critical Care) (n = 42).
	• Standard bone marrow needle (n = 42).
Outcomes	Time to placement of needle.
	Success rate.
	Difficulty of insertion as measured by VAS (10 = easy vs 0 = difficult).
Notes	Study origin: US.
	Experienced operators (defined as trained with practice sessions) were significantly more successful in placing Sur-Fast vs SBNM (95% vs 79%; $P < 0.05$); viewed Sur-Fast to be significantly easier to place [VAS] (5.0 ± 1.7 vs 2.5 ± 1.7; $P < 0.001$) and experienced no statistical difference in time to placement (27 ± 31 vs 32 ± 47), respectively.
Leidel et al[4] (2011)	
Methods	Prospective observational pilot study—1 access method vs another used at the same time on the same patient.
Participants	Patients ≥18 y of age under trauma and medical resuscitation admitted to the ER.
Interventions	Central venous access (n = 40).
	EZ-IO access (Vidacare) (n = 40).
Outcomes	Procedure time until first drug or infusion solution administered.
	Success rate on first attempt for either humeral or tibial IO access.
	Complications associated with each successful access method. Complications included failure of vascular access, malposition, dislodgment, bleeding, compartment syndrome, arterial puncture, hemothorax, pneumothorax, venous thrombosis, and vascular access related infection.
Notes	Study performed in Berlin, Germany, at Charite Hospital, level I trauma center.
	Local ethics committee approval and written informed consent obtained from patient when returning to full consciousness or from the next of kin or a legal representative.
	Peripheral IV access attempted first and tried 3 times for a maximum of 2 min. If unsuccessful, IO access and central venous access were performed simultaneously by 2 independent participants. A third independent observer with 2 stopwatches took the time of each procedure.
	Clinicians performing access procedures were trained in both techniques. Clinicians trained in IO access received a 60-min lecture on the use of the IO device and self-performed insertion on an IO model.
Leidel et al[13] (2010)	
Methods	Prospective randomized trial comparing the use of 2 IO access devices in patients under trauma or medical resuscitation and with impossible vascular access.
Participants	Severely injured or critically ill patients (≥18 y of age) under resuscitation.
	Excluded patients:
	• <18 y.
	• Pregnant patients.
	• Prisoners.
Interventions	BIG 18G (Waismed Ltd) (n = 20).
	EZ-IO (Vidacare) (n = 20).
Outcomes	Time to access.
	Success rate on first attempt.
	Complications including: dislodgment of needle, bleeding (extravasation), compartment syndrome, and vascular access related complications.

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APPENDIX 3: *(Continued).*

Notes	Study performed in Berlin, Germany, Charite Hospital, level I trauma center.
	Clinicians performing IO access were trained via a 2-h workshop with instructional video and hands-on sessions with each IO device.
	Complications with the devices included: 2 cases of extravasation with the EZ-IO at the humeral head insertion site.
Orlowski et al[52] (1990)	
Methods	Prospective randomized trial on infusion of emergency drugs in an animal model.
Participants	Twenty one dogs weighing 18.4–26.8 kg.
Interventions	Intraosseous 14-gauge needle (n = 21).
	CV 16-gauge, 2-in catheter (n = 21).
	peripheral IV 16G—2 inch catheter (n = 21).
Outcomes	Pharmacokinetics of emergency drugs and solutions (epinephrine hydrochloride, sodium bicarbonate, calcium chloride, hydroxyethyl starch, and dextrose) administered via IO, CV, and peripheral venous routes.
	Time required to place an IO needle.
Notes	Study performed in the US
	Approved by animal care and research projects committee of the Cleveland Clinic Foundation.
Shavit et al[48] (2009)	
Methods	RCT—turkey model.
Participants	Paramedic students trained on 2 types of IO devices.
Interventions	Use of BIG (Waismed Ltd) on a turkey model (pediatric model).
	Use of EZ-IO (Vidacare) on a turkey model (pediatric model).
Outcomes	Success based on first attempt access.
	Ease of use of device—questionnaire.
Notes	Origin of study: Israel.
	Paramedics trained first then evaluated on performance.
	Crossover design so participants were randomized to first treatment group and then crossed over to use other treatment.
Von Hoff et al[14] (2008)	
Methods	Prospective randomized crossover trial.
Participants	Cancer patients (>18 y of age) with both IO and IV access who required additional vascular access due to venous insufficiency and who required pain medications.
Interventions	Administration of morphine via IO route (IO device implanted in iliac crest) (n = 22).
	Administration of morphine via IV route (n = 22).
	Exclusion criteria included patients who exhibited any condition that rendered iliac crest unsuitable for implantation, infection, body weight in excess of 125% of their ideal weight, life expectancy of <12 wk or if they had a performance status ≥2 according to Southwest Group criteria for oncology patients.
Outcomes	Blood concentrations of morphine concentration as measured via radioimmunoassay.
	Time to maximum plasma concentration.
	Area under the concentration-time curve.
Notes	Study performed in the US at 8 clinical sites across the country.
	Study protocol approved by each IRB and written informed consent.
Characteristics of excluded studies	
Ben-Abraham et al[49] (2003)	
Reason for exclusion	Study was an evaluation of the time it took a clinician to gain IO access with and without protective gear and was thus not clearly related to ER use of IO access.
Strausbaugh et al[50] (1995)	
Reason for exclusion	Randomized trial on a dog model to determine if circumferential pressure applied around the IO needle site is a useful method in assessing IO placement.

APPENDIX 4: Level 3 Evidence (Studies Using Retrospective Controls)

Search Source	Study	Evidence	Outcomes	Adult/Pediatric
Vidacare IO access bibliography	Schutt et al[16] (2009)	Opposing	IO placement vs IV was not associated with improved survival in patients with out-of-hospital cardiac arrest.	Adult
Vidacare IO access bibliography	Ong et al[17] (2009)	Supportive	EZ-IO placement in 24 tibial and 11 humeral insertions. Success rate of 97% on first attempt and 100% on second attempt. Flow rates no different between tibial and humeral access.	Adult
Vidacare IO access bibliography	Paxton et al[5] (2009)	Supportive	Proximal humerus IO infusion significantly faster than either IV or CVC during emergency resuscitation.	Adult
Vidacare IO access bibliography	Pointer et al[18] (2008)	Supportive	Success rates significantly higher with EZ-IO vs FAST1 device in gaining IO access in prehospital setting.	Adult
Vidacare IO access bibliography	Frascone et al[19] (2007)	Supportive	Success rates significantly higher with EZ-IO vs FAST1 device in gaining IO access in prehospital setting.	Adult

APPENDIX 5: Evaluation of the Primary Outcome for Each Level 4 IO Access Study

Study	Design and No. Patients	Primary Outcome
Resuscitation 2010 (Gazin et al[21])	Prospective observational study (n = 39)	Success for first insertion (84%); overall success at access (97%).
Pediatr Anesth 2010 (Neuhaus et al[22])	Observational study (n = 14)	Success on first attempt (100%).
Scand J Trauma Resusc Emerg Med 2010 (Sunde et al[23])	Pediatric patients (n = 70)	First attempt success = (EZ-IO = 96%; BIG = 56%; manual = 40%); Overall success (EZ-IO = 96%; BIG = 56%; manual = 50%).
J Emerg Med Serv 2009 (Davidoff et al[33])	Case series n = 250	Overall success rate 242/250 = 92%.
Pediatr Emerg Care 2009 (Frascone et al[24])	User experience (n = 19)	Successful insertion 18/19 (95%).
J Trauma 2009 (Gerritse et al[25])	Prospective series on children (n = 14) and adults (n = 26)	Success rate (irrespective of no. attempts) (BIG at 73%).
Ann Emerg Med 2008 (Fowler et al[27])	Case series (n = 1199)	Success defined as good flow irrespective of no. tries (92%); also successful insertion on first attempt measured (84%).
Pediatr Emerg Care 2008 (Horton and Beamer[28])	Pediatric Patients (n = 95)	Success defined as good flow irrespective of no. tries (94%); also successful insertion on first attempt measured (77%).
Ann Emerg Med 2007 (Harrington et al[29])	Retrospective chart review (n = 50)	Success defined as good flow irrespective of no. tries (92%); also successful insertion on first attempt measured (89.6%).
Prehosp Emerg Care 2007 (Mathew et al[30])	Consecutive series (n = 245)	Success rate (irrespective of no. attempts) (EZ-IO at 80%).
J Trauma Inj Infect 2008 (Schwartz et al[26])	Consecutive series (n = 189)	Success defined as good flow irrespective of no. tries (91%); also successful insertion on first attempt measured using BIG device (91%).
J Emerg Med Serv 2007 (Stouffer et al[32])	Case series over a period of 24 mo (n = 280)	Success rate (irrespective of no. attempts); 260/280 = 94.6%.
Prehosp Emerg Care 2007 (Vu et al[31])	Retrospective review (n = 17)	Success rate (irrespective of no. attempts) (FAST1 at 88.2%).

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APPENDIX 3: *(Continued).*

Pediatr Crit Care Med 2005 (Fiorito et al[34])	Consecutive series (n = 47)	Success rate—first attempt (78%).
Pediatr Emerg Care 2003 (Claudet et al[36])	Case series (n = 23)	Tibial growth post–IO insertion.
J Emerg Med Serv 2005 (Gillum and Kovar[35])	Case series (n = 125)	Success rate (irrespective of no. attempts); 118/125 = 94%.
Can J Emerg Med 2000 (Nijssen-Jordan[37])	Retrospective chart review of pediatric patients (n = 42)	Overall success rate (86%).
Pediatr Emerg Care 1997 (Fiser et al[38])	Prospective case series (n = 10); blinded clinical assessor	Tibial length post–IO insertion.
Ann Emerg Med 1993 (Glaeser et al[39])	Prospective case series (n = 152)	Success defined as good flow irrespective of no. tries (76%); also successful insertion on first attempt measured (70%).
Pediatrics 1989 (Seigler et al[41])	Case series (n = 17)	Success defined as good flow irrespective of no. tries (16/17 = 94%); also successful insertion on first attempt measured (13/17 = 76.5%).

APPENDIX 6: Adverse Event Reporting (Human Trials Only)

The Table Identifies the Adverse Events in the Studies Where They Were Reported for Both IO and Peripheral or CV Access

	IO Access					Peripheral IV or
Study	**BIG 15- and/or 18-Gauge**	**FAST1**	**Jamshidi 15-Gauge**	**EZ-IO**	**16- to 18-Gauge**	**CV access (PIV/CV)**
Banerjee et al[15] (1994)					0/30	0/30
Frascone et al[19] (2007)		23/64		8/87		N/A
Leidel et al[4] (2011)				6/40		16/40
Paxton et al[5] (2009)				13/30		36/62
Hartholt et al[12] (2009)	7/33	5/22	3/37			N/A
Leidel et al[13] (2010)	4/20			2/20		N/A

Adverse events were defined as malposition, dislodgement/dislocation, bleeding (extravasation), osteomyelitis, compartment syndrome, gas or fat embolism, tibial fracture, effects on tibial growth, device failure (eg, breakage), and/or device failure to infuse upon placement, arterial puncture, and vascular related infection. These definitions of adverse events were consistent with those reported on in the literature.[9] In those studies that compared IO access to peripheral or CV access (Banerjee et al,[15] Leidel et al,[16] and Paxton et al[5]), a meta-analysis of adverse events is provided in Figure 2. This analysis demonstrated no difference in the occurrence of adverse events between IO and PIV/CV access (RR, 0.58; 95% CI, 0.30–1.12; $P = 0.11$), although there was a trend toward less adverse events with IO access (M-H random-effects model).