Original Article

Comparison of intraosseous access and central venous catheterization in Chinese adult emergency patients: A prospective, multicenter, and randomized study

Yan-yan Liu[1], Yu-peng Wang[1], Ling-yun Zu[1], Kang Zheng[2], Qing-bian Ma[2], Ya-an Zheng[2], Wei Gao[1]

[1] *Department of Cardiology and Institute of Vascular Medicine, Peking University Third Hospital; NHC Key Laboratory of Cardiovascular Molecular Biology and Regulatory Peptides; Key Laboratory of Molecular Cardiovascular Sciences, Ministry of Education; Beijing Key Laboratory of Cardiovascular Receptors Research, Beijing 100191, China*

[2] *Department of Emergency Medicine, Peking University Third Hospital, Beijing 100191, China*

Corresponding Author: *Ling-yun Zu, Email: dr_zly@126.com*

BACKGROUND: It is challenging to establish peripheral intravenous access in adult critically patients. This study aims to compare the success rate of the first attempt, procedure time, operator satisfaction with the used devices, pain score, and complications between intraosseous (IO) access and central venous catheterization (CVC) in critically ill Chinese patients.

METHODS: In this prospective clustered randomized controlled trial, eight hospitals were randomly divided into either the IO group or the CVC group. Patients who needed emergency vascular access were included. From April 1, 2017 to December 31, 2018, each center included 12 patients. We recorded the data mentioned above.

RESULTS: A total of 96 patients were enrolled in the study. There were no statistically significant differences between the two groups regarding sex, age, body mass index, or operator satisfaction with the used devices. The success rates of the first attempt and the procedure time were statistically significant between the IO group and the CVC group (91.7% vs. 50.0%, $P<0.001$; 52.0 seconds vs. 900.0 seconds, $P<0.001$). During the study, 32 patients were conscious. There was no statistically significant difference between the two groups regarding the pain score associated with insertion. There were statistically significant differences between the two groups regarding the pain score associated with IO or CVC infusion (1.5 vs. 0.0, $P=0.044$). Complications were not observed in the two groups.

CONCLUSIONS: IO access is a safe, rapid, and effective technique for gaining vascular access in critically ill adults with inaccessible peripheral veins in the emergency departments.

KEYWORDS: Intraosseous access; Central venous catheterization; Success rates; Procedure time; Pain score

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INTRODUCTION

The success rate and the time needed to achieve vascular access are crucial in emergency patients. The traditional method for vascular access is an intravenous (IV) catheter. In emergency situations, the placement of an IV catheter is not feasible. For instance, it may be challenging to establish IV access in dehydrated or hemodynamically unstable patients. The failure rates of IV access reported in the emergency setting range from 10% to 40%.[1-3] The procedure time of peripheral intravenous (PIV) catheterization is reported to be 2.5–13.0 minutes, and sometimes even up to 30 minutes for patients in whom establishing peripheral veins is difficult.[1-4] This additional time can lead to treatment delay.

Intraosseous (IO) access is an alternative method. The current guidelines recommend IO access in adults if peripheral venous access is unavailable under emergency circumstances. In 1986, the American Heart Association

formally approved IO infusion in pediatric emergency resuscitation procedures. The European Resuscitation Council recommends that IO access can be established in pediatric and adult emergency patients if it is difficult or impossible to establish peripheral venous access for cardiopulmonary resuscitation (CPR).[5,6] Since 2009, the Chinese guidelines for CPR recommend that IO access could be established if it is impossible to establish PIV access for CPR.[7] Furthermore, several guidelines recommend the use of IO access.

However, most medical staff in China are not aware of IO access, and will choose central venous catheterization (CVC) if it is difficult or impossible to establish PIV access. A survey on a professional medical rescue team showed that only 19.8% of medical staff knew about IO access.[8] In another study, when the medical staff failed to achieve peripheral venous access twice, 22.1% (93/420) of them would try the peripheral venous puncture again, 70.7% (297/420) would consider CVC, and only 4.1% (17/420) would try IO access.[9]

In order to obtain data on IO access in China, we conducted a single-center study. The study showed that the success rate of the first attempt of the IO access was higher than that of the CVC (91.7% vs. 66.7%, P=0.158).[10] However, because of the small sample size, there was no statistical difference in the success rate of the first attempt between the two groups. We also found that the main reason for conscious patients to refuse participation was the worry about the pain associated with IO insertion. Therefore, this multicenter randomized controlled study was conducted to compare the success rate of the first attempt and the pain score in establishing IO access and CVC in Chinese critically ill patients.

METHODS

Study design and setting

A clustered randomized controlled trial was carried out in eight hospitals in Beijing, China. The eight hospitals were Peking University Third Hospital, Peking University People's Hospital, China-Japan Friendship Hospital, Beijing Friendship Hospital, Beijing Jishuitan Hospital, Beijing Haidian Hospital, Beijing Chaoyang Integrative Medicine Emergency Medical Center, Beijing Luhe Hospital (Beijing Jingmei Group Hospital). The eight hospitals were randomly divided into the IO group or the CVC group. From April 1, 2017 to December 31, 2018, each center consecutively included 12 patients who needed emergency vascular access according to the inclusion criteria. After informing the patient or his/her family about the risks and obtaining signed informed consent forms, we established IO access or CVC according to the measures allocated by the patient's center. Drugs or fluids were administered through the established pathway. The center grouping was implemented by SAS 9.0 software, and the randomized grouping scheme was entrusted to the Clinical Epidemiology Research Center of Peking University Third Hospital. We obtained written informed consent for all enrolled patients. The treatment protocols were carried out in accordance with the principles of the *Helsinki Declaration*.

Participant selection

Inclusion criteria were: (1) older than 18 years old; (2) need to establish vascular access immediately; (3) unsuccessful attempts (two times) to establish peripheral venous access.

Exclusion criteria were: (1) unwillingness to participate in clinical trials; (2) fracture of the puncture site; (3) arthroplasty of the punctured joints; (4) infection of the puncture site.

Operators of IO access and CVC

Operators worked in the emergency departments. Operators were trained specialists and well-experienced in resuscitation. Before the commencement of the study, operators were trained in a 2-hour education program outlining the use of the IO device with instructional videos and subsequent hands-on training. Each operator practised using IO devices on the adult intraosseous bone models as much as he or she felt needed. When each operator felt sufficiently adept and confident in using the IO device, the sessions ended. All operators had more than one year of experience with CVC.

Instruments for IO access and CVC

IO access was performed with a spring-loaded driven device named Adult Bone Injection Gun (BIG, PerSys Medical, WaisMed Ltd., Lod, Israel). This single-use device weighs approximately 83 g with a "pull-out" safety latch and a safety stopper mechanism. For an adult patient, the device contains a 15G (1.8 mm) stainless cannula that is 25 mm in length with an adjustable insertion depth depending on the anatomic site. This device is suitable for the adult tibia, iliac bone, and femur, but not for the sternum. According to our protocol, the insertion site was the proximal tibia for IO access, and IO access was removed within 24 hours. After the time needed for emergency rescue, venous

access should be established as soon as possible.

CVC was performed with a standard double- or triple-lumen 7-French catheter (Arrow International Inc., Limerick, USA), depending on the patients' condition. The insertion site was determined by the operators according to the clinical situation, and CVC was removed within one month.

Primary and secondary outcomes

The primary outcomes were the success rate of the first attempt and procedure time of IO access or CVC. The success rate of the first attempt was defined as the successful administration of drugs or fluids via the newly established vascular IO access or CVC on the first attempt. Failure of IO access was defined as extravasation or unsuccessful (first) attempt of IO insertion. Failure of CVC was defined as an incomplete insertion or no possible advancement of the guide wire. However, more than one attempt to puncture a central vein was not considered as failure. The procedure time was defined as the duration of opening the packaging of the IO device or CVC set, preparation of the access set and patients' insertion sites (including disinfection and draping), insertion procedure of the IO device or CVC cannula itself, assembling the access set, and the first successful administration of the drugs or fluids through the newly established vascular access. An independent observer with a stopwatch recorded the time of the procedure time.

Secondary outcomes included complications and operator satisfaction with devices used. All patients were followed up for two weeks. During the two-week observation period, possible complications were recorded, including malposition, dislodgment, bleeding, compartment syndrome, arterial puncture, haemothorax, pneumothorax, venous thrombosis, and vascular access-related infection. The operator satisfaction with devices used was rated using visual analogue scale (VAS) in which 0 implied that the device was not user-friendly, and 10 implied the highest user-friendliness. If the patient was conscious, the pain score associated with IO or CVC insertion or infusion would be recorded. The pain score was recorded using VAS in which 0 implied that the patient did not feel pain and 10 implied that the patient felt the worst pain. Baseline data, including age, sex, height, weight, and diagnosis, were recorded subsequently if they were not available on admission.

Statistical analysis

Data were analyzed using the SPSS software package version 22.00 (SPSS Inc., Chicago, USA). All quantitative data were tested for a normal distribution using the Kolmogorov-Smirnov test. Normal distribution data were expressed as mean±standard deviation. Non-normal distribution data were expressed as the median and 25% to 75% interquartile range. Normal distribution data were analyzed using independent sample *t*-test. Abnormal distribution data were analyzed using non-parametric tests. Qualitative data were expressed as frequencies and percentages. Qualitative data were analyzed using the Chi-square test or Fisher's exact test. A P-value <0.05 was considered significant.

The sample size was calculated using PASS 11 (NCSS, LLC, Kaysville, Utah, USA). Based on the preliminary experimental results, the success rates of the first attempt were 92% for the IO group and 66% for the CVC group. To detect a difference between the two groups with 80% power, we used two-sided testing at the 5% level and an intraclass correlation coefficient of 0.001 with four clusters per group, and nine patients per cluster were needed. Considering a 20% design effect, 12 patients were needed per cluster.

RESULTS

A total of 96 adult patients who received IO access or CVC from eight hospitals were enrolled in the study, with 48 patients in each intervention group. Follow-up was possible for all 96 patients.

Characteristics of patients

A total of 63 men and 33 women, aged 20 to 95 (on average 65.6±17.1) years, were included. The IO insertion site was the proximal tibia. CVC was achieved in 29 internal jugular veins, 15 subclavian veins, and 4 femoral veins. There were no statistically significant differences between the two groups regarding gender, age, or body mass index. The main injury mechanism was shock, including cardiogenic shock, hypovolemic shock, and septic shock. Other injury mechanisms were poisoning and gastrointestinal bleeding. Isolated cases of cerebrovascular diseases, severe burn, and aortic dissection were reported in this study.

Success rates of the first attempt, procedure time, and operator satisfaction with the devices used

The overall success rate of the first attempt was 70.8% (68/96) for all patients. The success rate of the first attempt was 91.7% for IO access and 50.0% for CVC (P<0.001). Four IO procedures failed at the first attempt,

and 24 CVC procedures failed at the first attempt, requiring at least one more attempt. The procedure time was statistically significant between IO access and CVC (52.0 seconds vs. 900.0 seconds, $P<0.001$). There was no statistically significant difference between the two groups regarding operator satisfaction with the instruments used (8.0 vs. 8.0, $P=0.064$).

Pain score

During this study, 32 patients were conscious, including 12 in the IO group and 20 in the CVC group. There was no statistically significant difference between the two groups regarding the pain score associated with IO or CVC insertion (5.5 vs. 3.0, $P=0.091$). Moreover, there were statistically significant differences between the two groups regarding the pain scores associated with IO or CVC infusion (1.5 vs. 0.0, $P=0.044$).

Complications

Other than the above-mentioned unsuccessful access procedures on the first attempt following IO or CVC, no further complications were detected. In particular, no malposition, dislodgment, bleeding, compartment syndrome, arterial puncture, haemothorax, pneumothorax, venous thrombosis, or vascular access-related infection was observed.

DISCUSSION

IO access has a long history and can be traced back to 1922.[11] IO access is established with different devices, including the First Access for Shock and Trauma, EZ-IO, and BIG. In China, BIG and EZ-IO have been approved by the National Medical Products Administration. BIG is compact, easy to carry, and widely used. Since 2013, performing IO access has been included as a standardized resident training in the USA. However, there is no relevant content covering IO infusion in Chinese medical textbooks and standardized resident training. In China, although the guidelines for CPR (preliminary draft) in 2009 recommended that IO access was suitable for all age groups, IO access should only be established if it is impossible to establish peripheral venous access for CPR.[7] The guidelines do not include a clear operation process, which is inconvenient to promote the use of IO. At present, there is no government quotation for IO devices in Beijing, which makes the purchase of IO devices difficult. All these reasons limit the development of IO access in China.

This prospective randomized multicenter study was the first to compare IO access and CVC in adult Chinese emergency patients. In this clustered randomized controlled trial, our results showed that the IO group had a significantly higher success rate of the first attempt than the CVC group (91.7% vs. 50.0%, $P<0.001$), and the mean procedure time was significantly shorter for the IO group than for the CVC group. Our results were in line with previous findings and demonstrated that IO access could be an alternative procedure to establish vascular access in emergency situations. Moreover, the adult BIG and CVC devices were user-friendly.

The success rate and the time needed for achieving vascular access are vital in an emergency setting. Multiple previous observational studies, which were not randomized controlled studies, demonstrated that IO access outperformed PIV access and CVC in the success rate of the first attempt and procedure time in emergency situations.[12-17] Ross et al[12] described 2,601 patients who received IO access and 55 patients who received PIV access in the setting of out-of-hospital cardiac arrest. The mean time from arrival at the patient's side to the administration of the first dose of epinephrine was 5.0 minutes for the IO group and 8.8 minutes for the PIV group ($P<0.001$). The first IO success rate was 95.6%. Paxton et al[13] published their experience of 29 IO access cases, 57 PIV access, and 5 CVC during emergency room resuscitation. The mean time to access with good flow in the IO group was 1.5±1.1 minutes, which was significantly shorter than those in the PIV access (3.6±3.7 minutes, $P<0.001$) and CVC (15.6±6.7 minutes, $P=0.006$) groups. The success rate of the first attempt in the IO group was 80.6%, which was higher than those in the PIV access (73.3%) and CVC (20.0%) groups. Leidel et al[14] published a study of 50 patients with impossible PIV. IO access and CVC were performed simultaneously in each patient. The success rate of the first attempt was significantly higher for the IO group than for the CVC group (85% vs. 60%, $P=0.024$), and procedure time was significantly shorter for the IO group than for the CVC group (2.0 minutes vs. 8.0 minutes, $P<0.001$). In our study, the success rate of the first attempt and procedure time for the IO group were similar to those of Paxton et al[13] and Leidel et al.[14] In our study, the procedure time of CVC group was close to that reported by Paxton et al, while the success rate of the first attempt was higher than that recorded by Paxton et al,[13] which may be related to the small number of patients in the CVC group. In addition, the procedure time for the CVC group in our study was different from the results of Leidel et al,[14]

which may be related to the operators' experience and the severity of the patients' disease. Although differences were noted in the results of these studies, they suggest that the IO access may be more suitable for critically ill patients needing vascular access than the CVC.

Besides the success rate and the mean procedure time, we also recorded the pain score. Our results showed that pain scores associated with infusion were significantly higher in the IO group than in the CVC group. However, there was no statistically significant difference between the two groups regarding the pain score associated with IO or CVC insertion. Paxton et al[13] investigated pain scores associated with insertion and infusion, and found that VAS pain scores were higher in the IO group, with a mean pain score from insertion of 4.5±4.2 and a mean pain score from fluid or medication infusion after lidocaine administration of 3.8±4.1. The VAS pain scores averaged 0.9±1.4 with PIV insertion and 1.0±1.7 with CVC insertion in patients with a Glasgow Coma Scale (GCS) score of 15. These results indicated that pain management during IO access in conscious patients was important. In addition, 2% IV preservative-free lidocaine was effective in limiting or alleviating IO infusion pain. The duration of the anesthetic effect varied between patients. Repeat doses of lidocaine may be necessary to maintain the anesthetic effect.

Regarding complications following IO access, the rate of adverse events was low.[18-20] Some prospective studies of IO access that included 553 adults did not describe any complications.[21-23] Early literature reported an infection rate of 0.6% in 4,270 cases of IO access to the sternum or tibia in children.[24] The complication rate for CVC was 15%–20%, and complications included malposition, arterial puncture, hematoma, pneumothorax, venous thrombosis, and catheter-related infections.[25-29] In our study, no IO- or CVC-related complications were detected.

Limitations of the study

There were several limitations in this study. Our study focused on the success rate of the first attempt of IO access or CVC. The sample size was too small to show the difference in the incidence rate of complications between the two groups. Whether IO access can improve the prognosis of patients is unclear. Further clinical trials with larger sample size and a longer follow-up period are recommended to answer these questions.

CONCLUSIONS

IO access is a safe, rapid, and effective technique for gaining vascular access in critically ill adults with inaccessible peripheral veins in the emergency departments. IO access is more successful on the first attempt and requires significantly less time than CVC. However, pain scores were significantly higher in the IO group than in the CVC group. Thus, it is necessary to give adequate doses of lidocaine before IO infusion if the patients are conscious. IO access can be used as an alternative method to quickly establish vascular access in emergency situations.

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