Intracavitary electrocardiogram guidance for placement of peripherally inserted central catheters in premature infants

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Abstract
This study evaluated the accuracy of intracavitary electrocardiogram (IC-ECG) guidance for placement of peripherally inserted central catheters (PICCs) in premature infants, relative to chest X-ray.

Premature infants (n=173) underwent placement of a PICC monitored by ECG, and a stable heart rhythm was shown. Changes in the P wave of the ECG reflected the position of the catheter tip, and a characterized P wave indicated the correct position. The P wave results were compared with a chest X-ray.

P wave changes were observed in 157 (90.75%) of the premature infants on the ECG. Among them, the catheter tips of 148 (85.55%) patients were in the correct and non-correct position, respectively, which was confirmed by chest X-ray. No characteristic P wave changes were observed in 16 (9.32%) patients on ECG, in which the catheter tips of eight (4.62%) patients each were in the correct and non-correct position, according to the chest X-ray. The accuracy of IC-ECG guidance for placement of the PICC was 90.17%. The PICC tip location results of the IC-ECGs were statistically similar to that of the chest X-rays.

IC-ECG guidance is accurate for placement of PICC in premature infants, and provides an economical assessment without radiation.

Abbreviations: CAJ = cavoatrial junction, IC-ECG = intracavitary electrocardiogram, PICC = peripherally inserted central catheter, SV = subclavian vein, SVC = superior vena cava.

Keywords: chest X-ray, electrocardiogram, intensive care, neonate, peripherally inserted central catheter

1. Introduction
Peripherally inserted central venous catheters (PICCs) have been widely used in neonatal intensive care units. PICCs provide ideal venous access for critically ill newborns and ultra-low birth weight infants. However, the correct position of the PICC tip is crucial, to avoid catheter-related complications. A catheter placement that is too shallow or otherwise malpositioned increases the risk of venous thrombosis or fibrin sheath formation. A catheter that is placed too deeply, in the right atrium or ventricle, risks causing arrhythmia, dysfunction, or erosion of the tricuspid valve, and atrial thrombosis.

After placement of the PICC, a chest X-ray is routinely taken to determine the location of the catheter tip. If the tip is not correct, the sterile area can be re-established and adjusted. However, this increases the risk of infection and the harmful effects of radiation exposure due to repeated chest X-rays.

In recent years, electrocardiography (ECG) has been used to assist the positioning of catheter tips in adults and children. The ECG method is economical, simple, convenient, and highly accurate, and avoids repeated radiation exposure. In neonates, intracavitary electrocardiogram (IC-ECG) has been used to guide PICC placement with higher success rates than the traditional method, with no significant complications.

However, because of the special physiological and structural characteristics of premature infants, it is worthwhile to explore further whether this technology is feasible in such patients. The present study evaluated the accuracy of IC-ECG guidance for placement of PICCs in premature infants, relative to chest X-ray.

2. Methods
2.1. Patients
The Medical Ethics Committee of Bengbu Medical College approved this study, and all legal guardians of the patients signed informed consent prior to inclusion. The study population
comprised 173 preterm infants (104 males), aged 32.55 ± 2.30 weeks (range, 25.14–36.86 weeks), who were treated from January 2018 to January 2019. The average body weight was 1783.80 ± 358.85 g (range, 500–3900 g).

For inclusion in this study, each patient was adjudged premature, and the legal guardian provided signed informed consent. Patients with any of the following were excluded: serious infections before PICC placement, such as sepsis; superior vena cava (SVC) compression syndrome; serious cardiovascular disease with P wave abnormalities such as pulmonary heart disease or atrial fibrillation or atrioventricular block; pacemaker or implantable cardioverter-defibrillator; allergy to the corresponding pipeline; heart disease affecting heart P wave, or unable to cooperate with the chest X-ray.

2.2. ECG stability
After sterilization and volatilization of ethanol, 3 electrode pads were placed on the surface of the body below the left, right subclavian, and lower left abdomen. The real-time ECG was printed during the indexing, and the amplitude of the wave group was measured from the printed ECG. A stable ECG was identified, showing that the real-time ECG baseline was stable, the P-wave and QRS complex waveforms were clearly identifiable, and the amplitude was readable. The same cardiologist determined the stability of the ECG of each subject.

2.3. Characteristic P wave
The ECG reflected the position of the catheter tip, as follows. When the tip is outside the SVC, the P wave is no different from the surface ECG. As the catheter tip enters the SVC, a characteristic P wave (high and sharp) occurs. When the catheter tip enters the lower third of the SVC, the P wave may increase to 50% of the QRS wave and not exceed the QRS amplitude. When the PICC tip enters the cavoatrial junction (CAJ), the P wave exceeds the QRS amplitude. Upon entering the right atrium, the P wave decreases, and a bidirectional P wave or negative P wave can appear in the middle of the right atrium.

2.4. Tip location
With the patient supine, the catheters (Medcomp 1.9-F) were inserted via a peripheral vein by 2 experienced nurses. The expected length was estimated based on the surface landmark (right sternoclavicular joint) and catheterized by venipuncture. The catheter was then flushed using saline and diluted heparin sodium solution (5 U/mL).

Post-insertion chest X-rays were obtained for each patient and reviewed by both a consulting chest physician and a consulting interventional radiologist. The correct position of the PICC was defined as the catheter tip terminating in the lower third of the SVC below the carina or at the CAJ. Malposition was defined as any location other than the lower third of the SVC below the carina, or past the CAJ into the atrium.

The radiological marker of the index SVC is the distance from the right bronchial angle to the right edge of the heart shadow. The radiological marker of the CAJ is 3 cm below the tracheal carina, and the radiology of the lower third of the SVC is tracheal and the distance to the first 3 cm. The catheter tip is in the normal position when in the SVC and CAJ; and the catheter tip in the middle section of the SVC or the lower 1/3 section is the optimal position. The catheter tip was misplaced if in the iliac vein, subclavian vein, brachiocephalic vein, internal jugular vein, or atrium.

After the PICC was successfully placed, a chest X-ray was taken to determine the position of the catheter tip. In accordance with the standard protocol, the ECG was monitored for characteristic P wave changes to determine the accuracy of the PICC head position in the SVC.

2.5. Statistical methods
The data were recorded and analyzed using SPSS 17.0 software (IBM, Armonk, NY). Quantitative variables are described as mean ± standard deviation, and qualitative variables as percentage. The localizations of the catheter tip by ECG and chest X-ray were compared with a chi-squared test. P < .05 was considered statistically significant.

3. Results
The study population comprised 173 patients, including 104 boys (60.12%) and 69 girls (39.88%; Table 1). The gestational age, birth weight, age at the time of catheterization, weight of catheters, ICU stay, and the length of catheters were recorded (Table 1). A ventilator was used in 74 children. There were no significant correlations between clinical data and ECG P wave.

The general clinical data associated with the PICC were noted (Table 2). Five infants had different degrees of phlebitis within 1 week after PICC insertion, and one infant had intraductal blood return.

The catheter tips of 156 patients (90.17%) were in the correct position, as confirmed by chest X-ray. The following misplacements of the catheter occurred: subclavian vein (9 patients, 5.20%); right ventricle (3 patients, 1.73%); brachiocephalic trunk (2 patients, 1.16%); atrium (2 patients, 1.16%); and thoracoepigastric vein (1 patient, 0.58%). There were 157 patients (90.75%) with P waves in the atrial ECG, which characteristically predicted accurately the localization of the catheter tip, as confirmed by chest X-ray (sensitivity 94.26%; specificity 85.55%). Specifically, among these 157 patients, the catheter tips of 148 (94.26%) and 9 (5.73%) were in the correct and wrong positions, respectively. The 9 incorrectly positioned catheter tips included 5 (3.18%), 2 (1.27%), one (0.64%), and one (0.64%) in the contralateral subclavian vein, contralateral

| Table 1 Associations between clinical data of premature infants and P wave amplitude of ECG. |
|---------------------------------|-----------------|-----------------|
| Value                          | Mean ± SD       | P-value P-wave (%) |
| Male, n (%)                    | 104 (60.12)     | 0.635            |
| Gestational age, wk            | 25.14–36.86     | 0.596            |
| Birth weight, g                | 500–3900        | 1783.80 ± 358.85 |
| Ventilator use, %              | 74 (42.77)      | 0.111            |
| Age at the time of catheterization, y | 0.50–36.00 | 3.01 ± 4.01     | 0.353            |
| Weight of catheters, g         | 500–3900        | 1750.00 ± 570.00 |
| ICU stay, d                    | 1–54            | 22.86 ± 11.66    |
| Tube length, cm                | 6–22            | 11.62 ± 3.18     | 0.693            |
| ECG P wave ratio, %            | 30–160          | 69.36 ± 17.56    | 0.584            |

ECG = electrocardiography, P wave ratio = P wave amplitude/QRS wave main wave amplitude.
PICC complications

| PICC Complications | n (%)
|-------------------|--------
| Anhthymia         | 0      |
| Phlebitis         | 5 (2.89)|
| Thrombosis        | 0      |
| Infection         | 0      |
| Intraventricular  | 1 (0.58)|
| Total             | 6 (3.47)|

PICC = peripherally inserted central catheter.

*Within 7 days.

Table 2
General clinical data associated with PICC parameters in preterm infants.

| Puncture Vein Site | Unadjusted | Adjusted |
|--------------------|------------|----------|
| Cephalic           | 13 (7.51)  | 17 (10.5) |
| Basilic            | 36 (21.97) | 38 (25.9) |
| Medial cubital     | 58 (33.53) | 46 (28.5) |
| Axillary           | 46 (26.59) | 25 (14.9) |
| Superficial temporal | 18 (10.40)| 20 (11.9) |

| Punctures, n ≥ 1  | Unadjusted | Adjusted |
|-------------------|------------|----------|
| 1                 | 96 (55.49) | 58 (34.6) |
| 2                 | 47 (27.17) | 25 (15.4) |
| ≥3                | 30 (17.34) | 17 (10.5) |

| Success Rate      | Unadjusted | Adjusted |
|-------------------|------------|----------|
| Correct           | 148 (85.55%) | 156 (90.17%) |
| Non-correct       | 9 (5.20%)  | 17 (9.83%) |

| Total             | 157 (90.75%) | 173 (100%) |
|-------------------|-------------|----------|
| χ²                | 0.473       |
| P value           | >0.05       |

Table 3
ECG and chest X-rays to determine the position of the PICC catheter tip.

| Catheter Tip | ECG P Wave |
|--------------|------------|
|              | Characteristic | Non-characteristic | Total |
| Chest X-ray  | Correct      | Non-correct       |       |
| Correct      | 148 (85.55%) | 8 (4.62%)         | 156 (90.17%) |
| Non-correct  | 9 (5.20%)    | 8 (4.62%)         | 17 (9.83%)  |
| Total        | 157 (90.75%) | 16 (9.25%)        | 173 (100%)  |

ECG = electrocardiography, PICC = peripherally inserted central catheter.

4. Discussion

Hellerstein et al.[29] found that P waves can change significantly when the catheter tip goes through the sinus node to the right atrium. Intracavitary electrocardiogram converts the ECG in the atrium into a surface ECG through an intracardiac connection transducer and directly displays the changes of the P wave under the ECG. When the catheter tip is located outside the SVC, the P wave is no different from that of the surface ECG. When the catheter tip enters the SVC, a characteristic P wave (high P wave) occurs. When entering the lower third of the SVC, the P wave can be as much as 50% of the main wave amplitude. When the catheter tip enters the junction of the SVC and the right atrium, the P wave peaks and even exceeds the main wave amplitude. When the catheter enters the right atrium, the amplitude of the P wave subsides, and a bidirectional P wave or a negative wave can occur in the middle of the right atrium. This change in the P wave thus helps guide the positioning of the PICC tip.[19,29,30]

An Italian multicenter study on long-term central venous access, GAVeCeLT, showed that IC-ECG technology is safe, feasible, and accurate for central venous catheter positioning in adults.[19] Another multicenter study applied IC-ECG technology to children younger than 4 years (except newborns) and showed a coincidence rate with a chest X-ray of 96.2%.[30] The present study evaluated the utility of IC-ECG for localizing 173 PICC tips based on specific P waves, and the coincidence rate with chest X-rays was 90.17%. This confirms that IC-ECG technology is viable for guiding the tip position of PICCs in preterm infants.

After insertion of a PICC, a chest X-ray is important to corroborate that the tip is correctly positioned in the SVC.[31] Fricke et al.[32] found that in pediatric patients, the rate of correct initial PICC placement at the center of the vein was only 14.2%. Thus, readjustment of the PICC tip is needed in the majority of cases, and the child is exposed repeatedly to radiation. However, compared with chest X-ray, locating the tip by monitoring the ECG is easy, fast, and accurate, and the catheter can be placed and adjusted at any time.[21]

In the present study, among 173 patients, the PICC placement determined by the characteristic P wave was successful in 156 (90.17%), with reference to the X-ray. In 8 patients, the P wave was not detectable, and the catheter position was readjusted until the characteristic P wave was seen on the ECG monitor. Finally, the chest X-ray film confirmed that the catheter tip was in the SVC. There was no significant disagreement between the location of the catheter tip as indicated by the ECG or by the X-ray. Thus, the atrial ECG can clearly and reliably reflect the position of the PICC catheter tip.

There are 3 main advantages in localizing the PICC catheter tip by the P wave observed on ECG. First, the required equipment is simple; an ordinary ECG monitor is sufficient. Second, the operation is simple and easy to learn and can be performed independently by a PICC specialist nurse. Francesca Rossetti et al.[19] reported that the success rate using an atrial ECG of the positioning catheter was 96.2%. In the present study, the success rate of catheterization was 85.55%, which was consistent with previous reports. A misplaced PICC catheter can be determined relatively quickly during surgery and corrected, avoiding the drawbacks of the traditional X-ray positioning method. Finally, the method is noninvasive and without exposure to radiation.

During the catheterization, the shape and amplitude of the P wave in the atrium also changes. For patients in whom the SVC is accessed via the upper extremity vein, jugular vein, or by superficial venous puncture, when the tip of the catheter is in the peripheral vein the ECG in the atrium is the same as the surface ECG. When the SVC is reached, the amplitude of the P wave will increase. As the catheter is inserted deeper and higher, there is a high-point P wave. When the junction of the SVC and the right atrium is reached, closest to the sinus node, the amplitude of the P wave is the highest and the characteristic P wave for the correct position appears. As the catheter continues deep into the right atrium, the amplitude of the P wave decreases or a negative P wave occurs. In the present study, 157 catheters were initially fixed at the location of the characteristic P waves. Katheria et al.[33] considered that the best position of the catheter tip was the SVC and right atrium junction, or slightly lower than the inferior vena cava and right atrium junction. The characteristic P wave is mainly at T5–9.

brachiocephalic trunk, right ventricle, and right atrium, respectively. Thus the prediction by ECG guidance was statistically comparable with the X-ray localization (Table 3).
Considering the extremely low birth weight of premature infants, their body mass and body length will grow rapidly during hospitalization. As the body grows, the tip of the catheter will shift away from the heart. In addition, the location of the characteristic P waves varies from person to person. The P wave will not be specific to the location, but can help determine whether the catheter is running correctly. Therefore, the P wave has clinical significance and prospects for application. In infants with very low or ultra-low birth weight, the atrial ECG method can be used to monitor changes in the position of the catheter tip, to reduce the radiation damage caused by frequent X-ray positioning.

The neonatal PICC catheter has a specification of 1.9F. It is thinner than the adult PICC catheter and contains no guidewire. Therefore, how to apply this technique in neonatal PICC catheterization is the focus of the present study. Nowlen et al.\(^\text{28,34}\) reported that a 10% sodium chloride injection is electrically conductive. When 10% sodium chloride can be directly injected into the right atrium through the PICC catheter, a change in the P wave of the atrial ECG can be detected, and used to determine the position of the catheter tip. Because neonatal kidney function is relatively immature and the ability to excrete sodium is low, a 10% sodium chloride injection is not suitable for newborns. The present study used the conductivity of 0.9% sodium chloride as a detection electrode to assist in the positioning of neonatal PICC catheters. Of the 173 patients, 157 had characteristic changes in the P wave. The chest X-ray confirmed that in 148 patients, the infant PICC catheter head position was in place. This indicates that 0.9% sodium chloride injection is feasible as a probe electrode.

There are two main reasons for catheter placement failures. First, no P wave may appear, although the tip of the catheter is in the right place. Of the 16 patients in the present study for whom catheter placement by ECG failed, this was the cause in 8 of them. This may be because the patient moved during the positioning, or the use of ventilators and other unpredictable electromagnetic waves affected the appearance of the characteristic P waves. Catheter placement by ECG monitor may also fail if the catheter is misplaced, which was the case in 9 patients in this study. Among these, the catheters in 5 patients were too deep, and the P wave reflected that they were not in the best position. In 4 patients, the catheter placement was affected by a manual bulus of saline and limb position, which resulted in an uncharacteristic P wave.

This was a preliminary observation study, and its statistical power is limited. A random control study is necessary to confirm the accuracy of IC-ECG-guided PICC placement compared with X-rays in premature infants. In addition, we only detected the changes in P wave on ECG, and changes in f amplitude and waveform remain to be investigated.

5. Conclusion
Our study indicated that IC-ECG can be used to guide placement of the PICC tip in premature infants with high accuracy. This assessment method based on changes in P waves on IC-ECG is economical, easy, and does not involve exposure to radiation.

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