

# Ultrasound versus intracavitary electrocardiography for intraprocedural tip location during central venous catheterization in infants and children: A prospective clinical study

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## Abstract

**Background:** Both intracavitary electrocardiography (IC-ECG) and ultrasound (US) have been proven to be safe and accurate for intraprocedural tip location during central venous catheterization, and both are known to be easily applicable and feasible in pediatric patients. Though, no prospective clinical study has directly compared the two methods as regards their applicability, feasibility, and procedural time.

**Methods:** This study prospectively enrolled all children requiring a central venous access device in non-emergency situations, during a period of 1 year. All devices were inserted according to a well-defined insertion bundle including both IC-ECG and US-based tip location. The primary endpoint of the study was to compare the two methods in terms of applicability, feasibility and time required.

**Results:** This study included 100 consecutive central venous catheterizations in children of age ranging from 1 month to 18 years. The applicability of IC-ECG based tip location was 98% and its feasibility 100%; the time required for IC-ECG was  $1.9 \pm 2$  min. The applicability of US-based tip location was 96% and its feasibility was 100%; the maneuver required  $2.2 \pm 3$  min.

**Conclusions:** US is an appropriate alternative method for intraprocedural tip location in children. The combined use of US and IC-ECG (both maneuvers being accurate, inexpensive, cost-effective, non-invasive, and equally fast to perform) should be recommended for tip location in pediatric patients, and it will avoid completely the use of fluoroscopy or of post-procedural x-ray.

## Keywords

Central venous catheterization, pediatrics, tip location, ultrasound, intracavitary ECG

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## Introduction

Central vascular access devices (CVADs) are essential devices in the management of severely ill infants and children. As much as in adults, in this population of patients it is highly important to verify that the catheter tip is properly located in the proximity of the cavo-atrial junction (CAJ): such assessment (so called “tip location”) should be achieved during the maneuver of central venous catheterization, as recommended by current guidelines,<sup>1–3</sup> preferably by non-invasive methods such as intracavitary ECG (IC-ECG)<sup>4,5</sup> or ultrasound (US).<sup>6,7</sup> Assessment of tip

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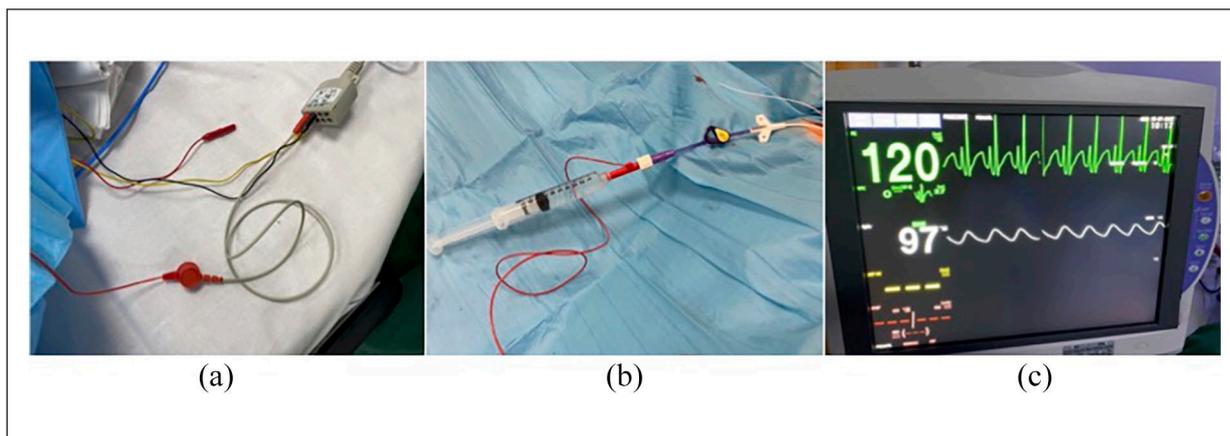
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**Figure 1.** Tip location by intracavitary ECG: (a) connection of one end of the sterile cable with the ECG monitor, (b) connection of the other end of the sterile cable with the catheter, and (c) identification of the maximal amplitude of the P wave on the ECG monitor.

location by chest x-ray is currently discouraged, since it is a post-procedural method, is not accurate, and implies x-ray exposure.<sup>2</sup>

In infants and children, both IC-ECG and US are easy to perform, accurate, and have a high range of applicability and feasibility.<sup>8</sup> In fact, the rhythm disturbances which may limit applicability of IC-ECG in adult patients are extremely rare in the pediatric population.<sup>5</sup> Also, the technique of US-based tip location (as standardized in the so-called ECHOTIP protocol)<sup>9,10</sup> is particularly easy in neonates and infants, due to the presence of good acoustic windows, with minimal interference of bones and soft tissues.

While both IC-ECG and US are considered accurate for tip location of CVAD in pediatric patients,<sup>5,8-10</sup> no prospective study has ever compared the two methods in terms of applicability, feasibility, and procedural time.

## Materials and methods

### Patients and setting

This was designed as a prospective study carried out in the Pediatric Intensive Care Unit (PICU) of a 1300-bed University Hospital. As required by the hospital policies, the study protocol was approved by the local Ethics Committee, and a consent form was prepared, to be submitted to the parents, or tutors.

The primary endpoint of the study was to compare IC-ECG versus US-based tip location (ECHOTIP) in terms of applicability, feasibility and time required. The secondary endpoint was to confirm the accuracy of ECHOTIP for tip location, considering IC-ECG as reference standard.

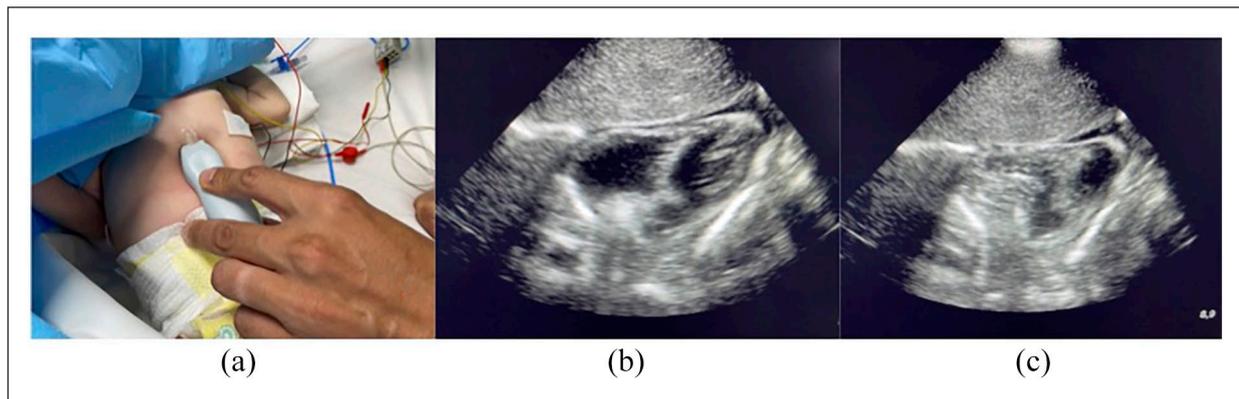
According to the local hospital policies, all elective central venous catheterizations in infants and children are

performed in the procedure room of the PICU, adopting a well-defined insertion bundle which has already been described in a previous study.<sup>8</sup> The study enrolled all central venous catheterizations performed in the PICU during a one-year period. Main exclusion criteria were (a) age less than 1 month or more than 18 years and (b) failure to obtain the informed consent from the parents or tutors. The study included insertions of centrally inserted central catheters (CICCs), peripherally inserted central catheters (PICCs), chest-ports, and PICC-ports. Femorally inserted central catheters (FICC) were included only if the catheter tip was planned to be in the right atrium or at the junction between right atrium and inferior vena cava. Emergency central lines and FICCs with a planned tip location in the midportion of the inferior vena cava were excluded.

All CVADs were placed according to the above mentioned insertion bundle,<sup>8</sup> which includes: pre-operative ultrasound scan of central veins (adopting the RaCeVA, RaPeVA and RaFeVA protocols, already described in the literature),<sup>11,12</sup> appropriate aseptic technique (maximal barrier precautions and skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol), ultrasound-guided venipuncture, intraprocedural assessment of tip location by IC-ECG<sup>4,5</sup> and by ECHOTIP,<sup>9,10</sup> tunneling of the catheter, sutureless securement, and protection of the exit site with cyanoacrylate glue and semipermeable transparent membrane.

### IC-ECG for tip location

The central position of the tip was assessed by intracavitary ECG using a standard ECG monitor and a dedicated sterile ECG cable (Vygoncard, Vygon, Ecoeu, France), considering the maximum amplitude of the P wave in the second lead as a reliable landmark of CAJ<sup>4,13</sup> (Figure 1). Time required to perform IC-ECG was recorded.



**Figure 2.** Ultrasound based tip location according to the ECHOTIP protocol: (a) small sectorial probe placed in the subcostal area, (b) ultrasound visualization of the right heart (four-chamber subcostal view, and (c) appearance of the micro-bubbles in the right heart soon after the injection of saline.

Applicability of IC-ECG was defined as the visualization of the P wave on the surface ECG. Feasibility of IC-ECG was defined as the appearance of variations of the height of the P wave, enabling the operator to establish the maximal amplitude of the P wave.

### *ECHOTIP for tip location*

Soon after assessment of tip location by IC-ECG, ultrasound-based tip location was performed according to the pediatric ECHOTIP protocol.<sup>10</sup> The ultrasound device used for tip location was the same adopted for ultrasound guided venipuncture (Edge II, FujiFilm-Sonosite, Bothell, WA, USA), but utilizing a small sectorial probe 3 to 7 MHz and not a linear probe. As a first option, a subcostal view (bi-caval or four-chamber) was adopted, since this view is the easiest and fastest; an apical four-chamber view was chosen as an alternative option, when subcostal visualization of the right heart could not be obtained.

As described in the pediatric ECHOTIP protocol,<sup>10</sup> a small amount of “shaken” normal saline (5 or 10 ml) was rapidly injected through the catheter: the immediate appearance of ‘micro-bubbles’ in the right atrium (less than 1 s after injection) was considered a confirmation of the proper position of the catheter tip at the CAJ (Figure 2). A longer delay (>1 s) was considered as suggestive of an inappropriate position of the tip. The amount of saline solution was weight based (5 mL in children <10 kg and 10 mL in children  $\geq$  10 kg). In case of failed or uncertain visualization of the micro-bubbles, the saline injection was repeated. Time needed to assess tip location by US was recorded. The time delay of bubble appearance was measured with a chronometer and recorded. Applicability of ECHOTIP was defined as the possibility of obtaining a satisfactory acoustic window (either subcostal or apical) with visualization of the right atrium. Feasibility was

defined as the visualization of the appearance of “micro-bubbles” in the right atrium. When both IC-ECG and ECHOTIP were feasible, the accuracy of ECHOTIP was defined as the immediate appearance of bubbles (<1 s) after saline injection, after that the correct tip location had been established by IC-ECG.

### *Statistical analysis*

Statistical analysis was carried out with a commercially available statistical software (STATA, 2020, College Station, TX, USA). Continuous data were expressed as mean ( $\pm$  standard deviation) or median (interquartile range) according to the distribution of data. Categorical data were expressed as relative frequencies. Continuous data were compared using Student’s *t* test or Mann–Whitney U test, whereas categorical data were compared using the Fisher exact test. Logistic regression was performed to recognize variables that might influence the feasibility of ultrasound-based tip location.

### **Results**

Between May 2021 and July 2021, 100 children required CVAD insertion in the procedure room of the PICU. The mean age of children was  $85 \pm 68$  months (range 1–216), and their mean weight was  $31 \pm 25$  kg (range 1.8–110) with BSA  $0.98 \pm 0.58$  (range 0.15–2.64). The underlying diseases most frequently requiring a CVAD were brain tumor (19%), severe burns (10%), and leukemia (5%). Some children were already hospitalized in our PICU when the CVAD was required (27%), but most children were hospitalized in other wards of our hospital (pediatric oncology 31%, pediatric surgery 13%, general pediatrics 13%, pediatric neurosurgery 8%, etc.) and moved to the PICU specifically for CVAD insertion.

A total of 100 CVADs were inserted (65 PICCs, 27 CICC, 4 FICC and 4 ports). No immediate or early insertion-related complication was recorded.

IC-ECG was found to be applicable in 98% of cases (98 out of 100), since in two cases the P wave could not be identified properly on the surface ECG; in these two children, tip location was performed by ECHOTIP only. The feasibility of IC-ECG – when applicable – was 100% (98 out of 98). The mean time required for performing IC-ECG was  $1.9 \pm 2$  min (range 1–20).

Applicability of ultrasound-based tip location (ECHOTIP) was 96% (96 out of 100 cases): in four cases, both the subcostal window and the apical window were not satisfactory, due to burns and/or presence of open surgical wounds. In these four children, tip location was assessed by IC-ECG only. The feasibility of ECHOTIP was 100% (96 out of 96 cases). In all 96 patients where the ECHOTIP maneuver was performed, the micro-bubbles appeared in the right atrium immediately (within 1 s), confirming the proper location of the tip at the CAJ. The amount of “shaken” saline injected during the ECHOTIP maneuver was 10 ml in 65%, and 5 ml in 35% of cases.

The mean time required for assessing tip location by the ECHOTIP method was  $2.2 \pm 3$  min (range 1–20 min). In all cases where both IC-ECG and ECHOTIP were applicable and feasible (94 cases), the micro-bubbles appeared immediately, confirming the accuracy of ECHOTIP.

There was no significant difference between IC-ECG and ECHOTIP in terms of applicability (98% vs 96%) ( $p=0.68$ ), feasibility (100% vs 100%) ( $p=0.68$ ), or procedural time (1.9 vs 2.2 min) ( $p=0.79$ ). There was no correlation between feasibility of ECHOTIP and weight ( $p=0.33$ ) or feasibility of ECHOTIP and BSA ( $p=0.13$ ). Even considering the sub-population of infants and small children (i.e. weight < 40 kg), IC-ECG and ECHOTIP had similar feasibility (97% vs 98%).

## Discussion

The correct position of the tip of the CVAD is of crucial importance and should be verified before starting any intravenous infusion. Such assessment of tip location should be done using an intraprocedural method.<sup>2,3</sup>

The use of intraprocedural fluoroscopy and/or post-procedural chest x-ray is not recommended, especially in the pediatric population, considering the risks associated with x-ray exposure. Apart from being less safe than other methods of tip location, the radiological methods are also known to be less accurate and less cost effective.<sup>2,3</sup> Therefore, current guidelines<sup>2,3</sup> recommend that intraprocedural methods such as IC-ECG and ECHOTIP should be adopted, especially in children.

While both methods have been demonstrated to be accurate and cost-effective for tip location in neonates and

children,<sup>5,9,10,14,15</sup> no prospective study has ever compared them in practical terms of applicability, feasibility and time required.

This prospective study shows that in the pediatric population ultrasound-based tip location – performed according to the pediatric ECHOTIP protocol<sup>10</sup> – has the same rate of applicability and feasibility as the IC-ECG method, which is currently considered the gold standard for intraprocedural tip location.<sup>2–4,13</sup>

Considering IC-ECG as the reference method for tip location, the study confirmed the accuracy of ECHOTIP, since in all cases ( $n=94$ ) where IC-ECG and ECHOTIP were simultaneously feasible, the micro-bubbles appeared immediately (within 1 s).

As described in the literature,<sup>5</sup> the applicability and feasibility of IC-ECG cannot be expected to be 100% in children; unidentified disturbances of the cardiac rhythm or technical failures of the ECG monitor may account for 1%–2% cases where tip location cannot be satisfactorily obtained by IC-ECG.

On the other hand, the applicability and feasibility of ECHOTIP cannot be expected to be 100% in children: ultrasound-based tip location implies (a) the possibility of a proper acoustic window (subcostal or apical), which may be sometimes difficult or impossible to obtain, depending on the anatomy of the child and the underlying disease, (b) an ultrasound probe of adequate quality so to detect the appearance of micro-bubbles, and (c) appropriate training of the operator. This accounts for 1%–2% of cases where the ECHOTIP cannot be successfully performed.

In this prospective study on infants and children, both IC-ECG and ECHOTIP were equally effective and clinically useful for tip location. Both were easy and fast to perform, without significant differences in practical terms. Considering that both methods are inexpensive and non-invasive, and that neither method has 100% applicability, it seems wise to adopt the two methods simultaneously, allowing a double intraprocedural control of tip location, thus avoiding completely the need of a post-procedural chest x-ray.

## Limitation of the study

This study is limited by its small sample size. Also, its results refer mainly to patients with medical/surgical conditions, which precludes the extrapolation of these findings to specific populations of children where IC-ECG may be not applicable/feasible (e.g. severe cardiac abnormalities with complex rhythm disturbances) or where ECHOTIP may be not applicable/feasible (e.g. cardiothoracic surgery, where scars and chest drainage tubes may interfere with the ultrasound maneuver). Last, the staff performing the procedures was appropriately trained both in the IC-ECG method and in the ECHOTIP method: thus,

these results cannot be automatically extended to units where the clinical staff may be not familiar either with IC-ECG or with ECHOTIP.

## Conclusions

In this prospective study, ultrasound-based tip location with “bubble test” (the ECHOTIP protocol) had the same applicability and feasibility of tip location by IC-ECG in pediatric patients requiring central venous access. ECHOTIP was not time consuming, as it required the same procedural time as IC-ECG.

In conclusion, the ECHOTIP protocol is an alternative method for intraprocedural tip location in children; also, the combined use of ECHOTIP and IC-ECG (both maneuvers being accurate, inexpensive, cost-effective, non-invasive) should be recommended since it will avoid completely the use of fluoroscopy or of post-procedural x-ray.

## Declaration of conflicting interests

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