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# ECHOTIP-Ped: A structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in pediatric patients

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**Abstract**
Central venous access devices are routinely used in pediatric care for administration of fluids and medications and for drawing blood samples. The adoption of ultrasound guided venipuncture, the availability of bedside ultrasound devices and the use of intraprocedural methods for tip location have been shown to reduce procedure-related complications, as documented by the recommendations of most recent guidelines. In pediatric patients, bedside ultrasound is a promising tool not only for optimizing the choice of the vein and guiding the venipuncture, but also for ensuring an accurate and intraprocedural method of tip navigation and tip location. The aim of this paper is to review all the evidence about the accuracy of ultrasound methods for tip navigation and tip location in pediatric patients, and to suggest a structured protocol for clinical practice.

**Keywords**
Pediatric patients, central venous access, ultrasound, tip location, tip navigation, PICC, femoral catheters, central venous catheters, infants—children

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## Introduction

Indwelling central venous access devices (CVADs) are essential tools in pediatric care. They are commonly used for intravenous infusion, blood sampling, hemodynamic monitoring, as well as blood exchange procedures such as hemodialysis and apheresis. Insertion of CVADs is nonetheless associated with risk of potential complications, which may occur during or after the procedure, and even after days or weeks. Complications can be classified as immediate, early (within 48 h) or late (after 48 h); interestingly, late complications are often related to specific maneuvers performed during the procedure.[1]

Ultrasound-based choice of the vein and ultrasound-guided venipuncture have been shown to increase the safety and the success of CVAD insertion as compared to other approaches ("blind" puncture based on surface landmarks; venous cutdown).[2] Furthermore, ultrasound has been shown to be a reliable, fast, and accurate technique to

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diagnose potential life-threatening complications such as pneumothorax, hemothorax, and cardiac tamponade.[3] In this review, we will address another interesting field of application of ultrasound: "tip navigation" (i.e. assessment that the guidewire and/or the catheter are threaded in the right direction inside the vasculature) and "tip location" (verification that the tip of the central venous access device is in the proper final position, that is, in the proximity of the cavo-atrial junction).

In pediatric patients, intracavitary ECG (IC-ECG) should be considered the gold standard for tip location, as it has been shown to be completely safe, applicable in 99% of patients, and accurate in 98.8% of cases, in particular if performed with a dedicated ECG monitor.[4] Widespread clinical application of IC-ECG has made standard radiologic imaging superfluous, considering that chest X-ray is not absolutely safe, since it implies X-ray exposure, and is not really accurate.[5–7]

Furthermore, recent guidelines emphasize the importance of using intra-procedural methods of tip location during CVAD insertion[8] so to optimize the cost-effectiveness of the procedure and to avoid delay in starting infusion therapy. Intraprocedural methods currently include only (a) IC-ECG, (b) fluoroscopy—which is discouraged by recent guidelines, because of the exposure to ionizing radiation[8–11]—and (c) ultrasound-based methods.

We have reviewed the literature in this area, aiming to define a structured approach to the adoption of ultrasound for tip navigation and tip location in pediatric patients, focusing on practical issues such as the choice of the most effective probes and of the most accurate methods of ultrasound visualization. We have focused our attention only on central venous access devices (VADs) in infants and children, since we have addressed ultrasound-based tip navigation and tip location of neonatal central VADs in a previous study.[12]

## Methods

Literature search was performed applying the following criteria querying electronic database searches of PubMed, EMBASE, Google Scholar, and Cochrane Central Register of Controlled Trials. The terms used in the search were "ultrasound," "USG," "point-of-care ultrasound," "POCUS," "infant," "pediatric," "central line," "PICC," "CICC," "FICC," "internal jugular vein," "subclavian vein" "brachiocephalic vein," "Femoral vein"; the search was limited to the last two decades (from 1/1/2000 to 1/1/2021). No language restrictions were applied, and we included all trials, case reports, and case series and filtered the articles by reviewing the abstract. Specificity and sensitivity were first estimated separately for each study, together with their 95% exact confidence interval (CI). A pooled estimate for specificity and sensitivity was obtained and 95% CIs were calculated. Forest plots were made using the calculated 95% Cis. Statistical analysis was performed using Stata/IC 16.0 (StataCorp LLC).

## Ultrasound for tip navigation and tip location for central venous access in children: Evidence from the literature

The success rate of central line placement in pediatric patients has increased since the introduction of ultrasound guidance into clinical practice, with a parallel reduction in complications.[13] Different other strategies have been investigated, so to provide the best safety profile of the maneuver and reduce the procedure-related risks. One of this strategy—strongly recommended by current guidelines is the adoption of an accurate methodology of intraprocedural tip location.[3,8] In the first decade of our century, the standard for tip location—in adults as in children—was a two-step strategy of[1] length estimation based on anthropometric measurements during the procedure[14–19] followed by[2] a post-procedural radiological control (chest X-ray) for final confirmation.[20] Another option—though expensive and invasive—was the use of intraprocedural tip location using fluoroscopy.

Radiological methods of tip location (chest X-ray and fluoroscopy) have two limitations: they are not safe, implying an X-ray exposure, and they are rather inaccurate, since the CAJ cannot be identified but its location can only be indirectly suggested by radiological landmarks (tracheal carina, main right bronchus, vertebral bodies, etc.).[5,19,21] Such landmarks are largely unreliable, since MR studies have shown a high degree of variability in the length of the lower third of the superior vena cava and in its relationship with the surrounding structures.[7] Therefore, more recently, IC-ECG has been introduced in clinical practice as a safe, inexpensive, and accurate method of intraprocedural tip location.[4,22]

Though, IC-ECG may not always be available or applicable or feasible; in such conditions, as an alternative option, correct placement of the central catheter can be assessed using ultrasound.[3] In the last two decades, 34 observational prospective studies and 1 randomized controlled study have investigated the feasibility and the accuracy of ultrasound for tip navigation and tip location of CVADs.[3,23,24] Among these 34 studies, 6 observational prospective trials were conducted in pediatric patients (a total of 451 children, aged from 1 week of birth up to 14 years-old) (Table 1).

These observational pediatric studies have shown that the incidence of primary malposition of the CVAD may be reduced by visualizing the direction of the guidewire during the procedure.[3,23,24] This technique, which consists in the real-time sonographic visualization of wires and catheters as they are threaded toward the superior or inferior vena cava, has been named "tip navigation." Evidence have shown that ultrasound-based tip navigation coupled

**Table 1.** Summary of the six studies on ultrasound-based tip location in children (2000–2020).

| Study | Sample size | Protocol | Probe | Windows |
|---|---|---|---|---|
| Lanza et al.[25] | 107 | Tip navigation | Linear | Short axis of neck veins |
| | | | Convex | Coronal view of SVC |
| | | Tip location + ”bubble” test | Convex | Subcostal four-chambers view |
| Park et al.[26] | 106 | Tip location, no “bubble” | Small sectorial | Right parasternal in long and short axis |
| Alonso-Quintela et al.[27] | 40 | Tip navigation | Linear | Short and long axis view of IJV, SV, BCV, and FV |
| | | | Small sectorial | Coronal view of SVC (for CICC) |
| | | | | Subcostal longitudinal view of IVC (for FICC) |
| | | Tip location | Small sectorial | Subcostal bi-caval or right parasternal (as alternative) |
| Yesilbas et al.[28] | 77 | Tip location + “bubble” test | Small sectorial | Subcostal four-chambers or apical four-chambers (as alternative) |
| Korsten et al.[29] | 100 | Tip location + “bubble” test | Small sectorial | Subcostal four-chambers or apical four-chambers (as alternative) |
| Oliveira et al.[30] | 21 | Tip location + “bubble” test | Convex | Apical four-chambers |

SVC: superior vena cava; IJV: internal jugular vein; SV: subclavian vein; BCV: brachiocephalic vein; FV: femoral vein; IVC: inferior vena cava; CICC: centrally inserted central catheter; FICC: femoral inserted central catheter.

together with an intra-procedural tip location may virtually cancel the occurrence of primary malposition.[3,23]

To our knowledge, the first study investigating the accuracy and the feasibility of transthoracic ultrasound to determine the correct position of catheter tip in pediatric patients was published in 2006. In this study, conducted on a cohort of 107 patients aged from 1 day of birth up to 7 years-old, using a subcostal four-chambers view and a saline flush, Lanza et al.[25] found that ultrasound-based tip location had 84.6% sensitivity and 100% specificity, with a 98.1% concordance with chest radiography. In this study, 12 primary malpositions occurred, but 10 of them were correctly identified by ultrasound, using a subcostal four-chambers view with a “bubble test” by agitated saline flush.

Eight years later, Park et al.[26] proposed the use of the right parasternal view—both in long and short axis—to identify the correct location of the catheter tip in pediatric patients. In fact, the right parasternal view allows optimal sonographic visualization of the crista terminalis, the sonographic landmark of the junction between superior vena cava (SVC) and right atrium (RA). In a cohort of 106 pediatric patients with a mean age of 4.1 ± 3.1 months-old (ranging from 1 week of birth up to 12 months), using the right parasternal view, Park et al.[26] were able to identify the crista terminalis and place the catheter tip at the CAJ in 102 patients. However, this view has some disadvantages: it may be difficult in critically ill, ventilated patients; also, it requires a specific echocardiographic training and a significantly longer learning curve if compared with the subcostal view.

In 2015, Alonso-Quintela et al.[27] were the first to propose an ultrasound-based protocol that included both tip navigation and tip location. In this study including 51 centrally or femorally inserted central VADs placed in a cohort of 40 critical pediatric patients aged from 1 week of birth up to 14 years-old, the catheter tip was identified as located at the CAJ or in the RA, using a subcostal bi-caval view.[24] When the tip was not identifiable with the subcostal view, the authors used a right parasternal view. Ultrasound-based tip navigation was also investigated in this study: CICCs were visualized in the ipsilateral internal jugular, subclavian, and brachiocephalic veins, using a suprasternal view; FICCs were visualized in the inferior vena cava using a long axis approach. In summary, the authors reported that ultrasound-based tip location—when performed by appropriately trained physicians—had a 100% sensitivity and a 93.8 specificity, as well as a good concordance (94%) ) with chest X-ray.[27]

In a cohort of 77 pediatric patients with a median age of 7 months, Yesilbas et al. found that the subcostal or the apical four chambers views—using with the “bubble test”—allow to identify those catheters which were too short. In this study, the disappearance time instead of the appearance time of the bubbles after the injection of the agitated saline was significatively correlated with primary malposition of short catheters. These authors have found a cut-off of 3 s for disappearance time of bubbles from the right atrium to identify short catheters, with an 85.7% sensitivity and a 77.9% specificity.[28]

Korsten et al., in a cohort of 100 pediatric patients, reported that ultrasound-based tip location—using the four-chambers subcostal or apical views with bubble test—had a 95% sensitivity and 100% specificity. Furthermore, these authors found that this technique was characterized by a good inter-rater agreement, as proved by a Cohen’s kappa of 0.726. Moreover, data from this study have also shown that the training to achieve proficiency in performing a four-chambers apical or subcostal view for tip location in children has a rather steep learning curve.[29]

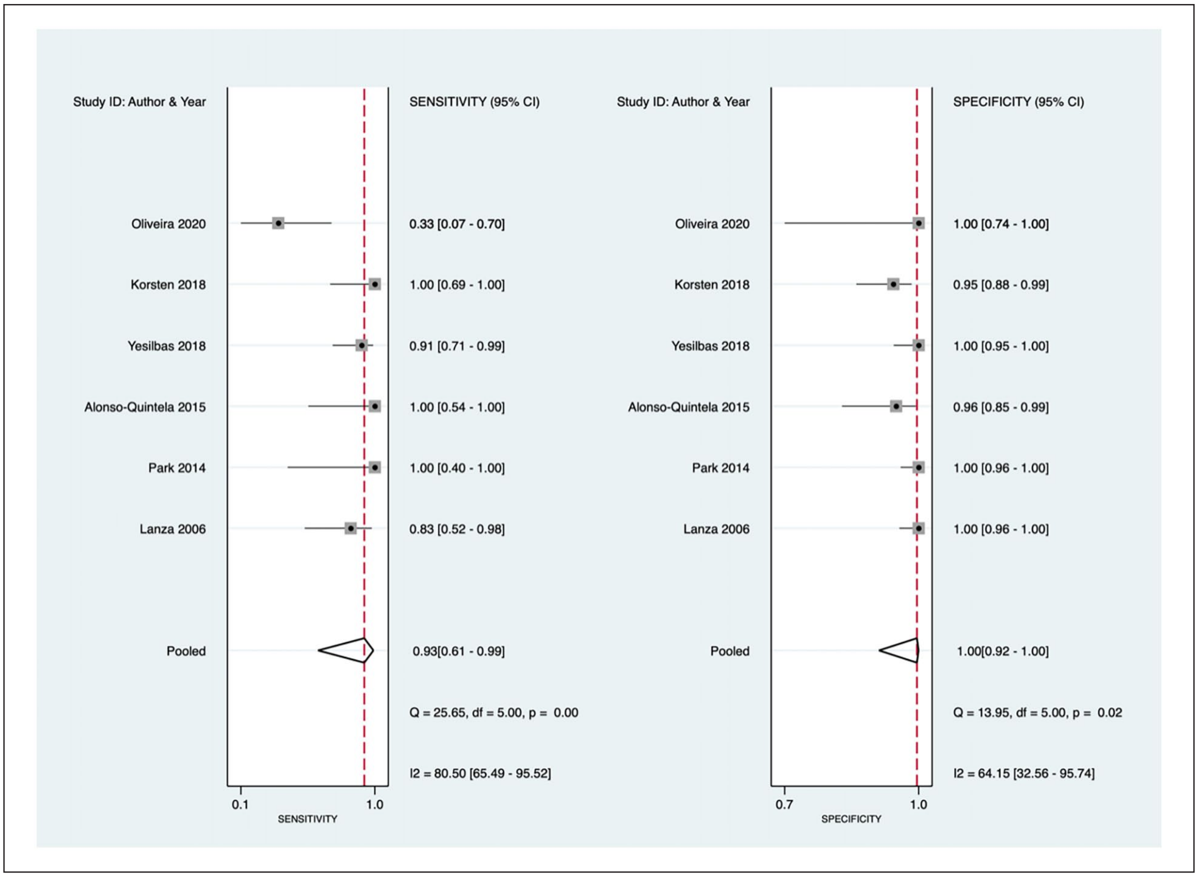


**Figure 1.** Forest-plot showing pooled estimate for specificity and sensitivity obtained along calculated 95% CIs. Studies showed significant statistical heterogeneity; for specificity, $I^2 = 64.15$ (95% CI: 32.56–95.74) and, for sensitivity, $I^2 = 80.5$ (95% CI: 65.49–95.52).

In a further small observational prospective study on 21 pediatric patients, transthoracic ultrasound—using exclusively a four-chambers apical view—was found to have a low sensitivity (33%) but high specificity (100%), when the identification of the catheter tip was facilitated by a rapid infusion of 10 ml saline. The authors concluded that further research was needed, possibly investigating other acoustic windows, such as the subcostal view.[30]

In a small cohort of 28 pediatric patients, ultrasound confirmation of PICC placement had a positive predictive value of 43% for identification of malpositioned lines if compared to chest X-ray.[31]

We performed a meta-analysis of the six above mentioned observational studies,[25–30] which overall included 451 pediatric patients and 480 procedures: pooled sensitivity was 93% (95% CI: 61–99, Heterogeneity $I^2$: 80,5%, $p < 0.001$) and pooled specificity was 100% (95% CI: 92–100, heterogeneity $I^2$: 64,15%, $p = 0.02$) (Figure 1).

The techniques described in the abovementioned studies are quite heterogeneous, especially in terms of echocardiographic views. The technique for ultrasound-based tip navigation and tip location was not standardized, and there was little information about the training of the operators. Furthermore, all authors used an imperfect reference standard, the chest X-ray, which is known to be inaccurate if compared to intracavitary ECG or transesophageal echocardiography.

Considering the evidence from our systematic review and meta-analysis, we have tried to develop a novel standardized protocol for ultrasound-based tip navigation and tip location of central venous VADs in children.

## Proposal of a structured approach for the use of ultrasound for tip navigation/location of central venous access in children: The ECHOTIP-Ped protocol

We have developed three different protocols, considering the three main central VADs that are inserted in children, that is, according to the WoCoVA nomenclature (WoCoVA = World Conference of Vascular Access): (a) centrally inserted central catheters (CICC), inserted by venipuncture of veins of the supra/infra-clavicular area (internal jugular, external jugular, subclavian, brachio-cephalic, axillary); (b) peripherally inserted central catheters (PICC), inserted by venipuncture of the veins of the upper arm (basilica, brachial, axillary); (c) femorally inserted central catheters (FICC), inserted by venipuncture of veins of the lower limb (common femoral, superficial femoral, saphenous). The need for three different protocols is justified by the different ultrasound techniques required by the different approaches to the vasculature of the superior and inferior vena cava.

The protocol we described for PICC insertion can be adopted obviously also during implantation of PICC-ports, as much as the protocol for CICC insertion can be adopted during implantation of chest-ports, considering that the issues of tip navigation and tip location are not affected by the subsequent connection of the catheter with a reservoir.

Of course, we assume that ultrasound must be consistently used also for choosing the best vein via a systematic ultrasound scan of the vein of the area, according to standardized protocols previously described: RaCeVA (Rapid Central Venous Assessment) before CICC insertion[32]; RaPeVA (Rapid Peripheral Venous Assessment) before PICC insertion[33]; RaFeVA (Rapid Femoral Venous Assessment) before FICC insertion.[34] Also, we assume that all CVAD insertions in pediatric patients (either CICC, or FICC or PICC) must be always performed by ultrasound guided real time venipuncture, as recommended by current guidelines.[8,13]

## ECHOTIP-Ped protocol for CICC insertion

1. Tip Navigation Protocol:

- *Probe*: Linear "hockey-stick" probe, preferably 10–14 MHz; micro-convex probe 4–8 MHz (optional).
- *Acoustic windows*: Using the same linear probe used for ultrasound-guided puncture, the supraclavicular view provides a proper visualization of the internal jugular, subclavian, and brachiocephalic veins, as described in the RaCeVA protocol[32]: with this approach, the operator can rule out any wrong direction of the guidewire and/or of the catheter (i.e. in the internal jugular vein after axillary venipuncture) and confirm that the guidewire and/or the catheter are directed toward the SVC. Visualization of the guidewire and/or the catheter inside the SVC is also possible using a coronal view of the SVC with a micro-convex probe 4–8 MHz (optional).
- *Procedure*: After visualization of the needle inside the vein during ultrasound-guided venipuncture, the guidewire is visualized as it passes and progresses into the brachio-cephalic vein (please note that 0.018" wires might be more difficult to visualize than 0.035" wires); the micro-introducer can also be visualized inside the vasculature; the catheter can also be easily visualized inside the brachiocephalic vein and—in small infants—even inside the SVC.

2. Tip location Protocol:

- *Probe*: Micro-convex probe 4–8 MHz or small sectorial probe 3–7 MHz
- *Acoustic windows*: A subcostal bi-caval or four-chambers view is recommended as first option, since this view is easy to obtain and requires minimal training; an apical four-chambers view may be an alternative option, when subcostal visualization of the heart is not obtained.
- *Procedure*: As the catheter has entered the SVC and is in the proximity of the CAJ, a quick flush of saline (2 or 5 ml) is injected, so to confirm the location of the tip: the flush of saline arriving in the RA is visualized as a sudden cloud of "bubbles," coming from the tip of the catheter; even if the tip of the catheter is not directly visualized, the immediate appearance of the bubbles soon after injection proves that the tip is in the proximity of the CAJ (Figure 2).

## ECHOTIP-Ped protocol for PICC insertion

1. Tip Navigation Protocol:

- *Probe*: Linear hockey-stick probe 10–14 MHz; micro-convex probe 4–8 MHz (optional).
- *Acoustic windows*: Same windows as described in RaPeVA[33] and RaCeVA[32]: the deep veins of the arm up to the axilla, the axillary vein in the infraclavicular area, as well as the subclavian, the internal jugular, and the brachiocephalic veins in the supraclavicular area are all easily visualized, with the same linear probe used for venipuncture: this will confirm the proper direction of wires and catheters, ruling out any wrong direction, for example into the ipsilateral internal jugular vein. The confluence between the two brachiocephalic veins and the SVC can also be visualized with a suprasternal/supraclavicular coronal view using a micro-convex probe 4–8 MHz (optional).
- *Procedure* (Figure 3): After venipuncture, the presence of the guide wire inside the brachial tract of the axillary vein can be assessed with the linear probe; with this same probe, the operator can visualize the trajectory of the catheter into the thoracic tract of the axillary vein (infraclavicular view), and then into the subclavian vein and the ipsilateral brachiocephalic vein (supraclavicular view), ruling out

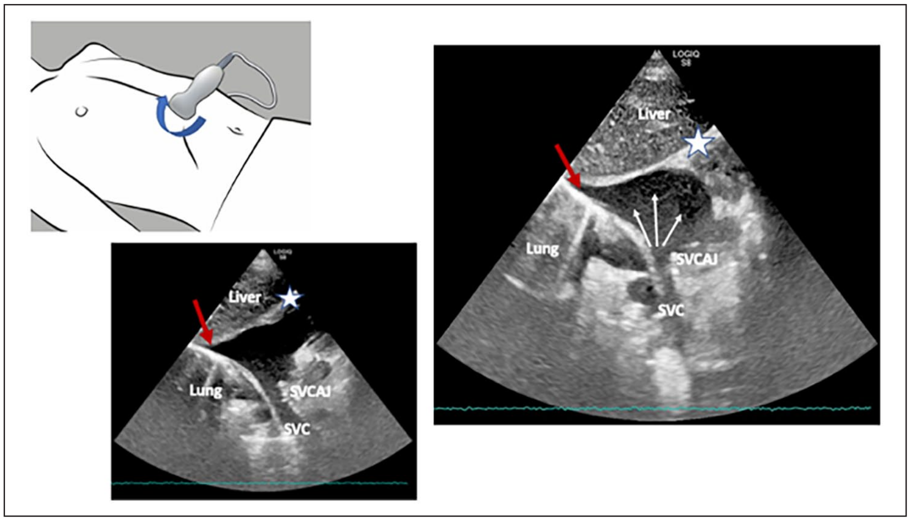


**Figure 2.** Subcostal bi-caval view for tip location of a CICC. The figure shows the early swirling (white arrows) after a bubble test when the catheter tip lies at the superior cavo-atrial junction (SVCAJ). SVC: superior vena cava; red arrow: inferior vena cava; white star: diaphragm.

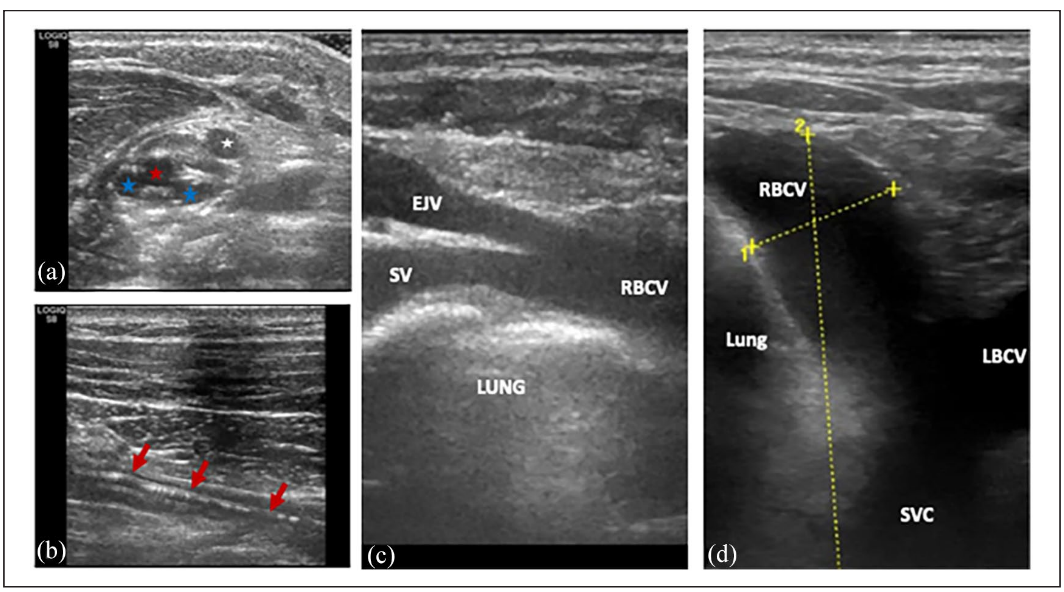


**Figure 3.** Tip navigation for PICC placement. Blue stars: brachial veins; red star: brachial artery; white star: basilic vein (a). The PICC can be visualized in the axillary vein, using a long axis view (b). Visualizing the confluence of the right external jugular vein (EJV) and the right subclavian vein (SV) into the right brachiocephalic vein (RBCV) (c), it is possible to follow the catheter in its direction toward the RBCV. Visualizing the confluence between the two brachiocephalic veins (left: LBCV and right: RBCV) into the superior vena cava (SVC) (d), it is possible to follow the catheter as it enters the SVC.

misdirection to the ipsilateral internal jugular vein. A coronal view of the SVC—using the micro-convex probe—may allow to visualize the catheter inside the SVC, ruling out its misdirection into the contralateral brachiocephalic vein (optional).

2. Tip location Protocol:

- *Probe*: Micro-convex probe 4–8 MHz, or small sectorial probe 3–7 MHz.
- *Acoustic windows*: A subcostal bi-caval or four-chambers view is recommended as first option, since this view is easy to obtain and requires minimal training; an apical four-chambers view may be a secondary option, when subcostal visualization of the heart is not obtained.
- *Procedure*: As the catheter has entered the SVC and is in the proximity of the CAJ, a quick flush of saline (2 or 5 ml) is injected, so to confirm the

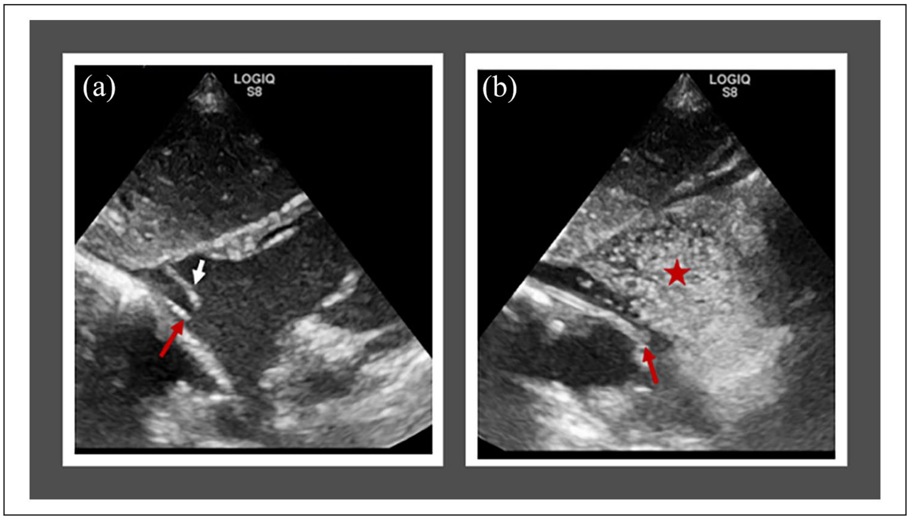


**Figure 4.** Subcostal bi-caval view for tip location of a FICC. The tip of the FICC (red arrow) enters the right atrium coming from the inferior vena cava (a), close to the Eustachio valve (white arrow). After bubble test, a swirling (red star) is visible in the right atrium (b).

location of the tip: the flush of saline arriving in the RA is visualized as a sudden cloud of "bubbles," coming from the tip of the catheter; even if the tip of the catheter is not directly visualized, the immediate appearance of the bubbles soon after injection proves that the tip is in the proximity of the CAJ.

### ECHOTIP-Ped for FICC insertion

1. Tip Navigation Protocol:

- *Probe*: Linear hockey-stick probe 10–14 MHz; micro-convex probe 4–8 MHz (optional).
- *Acoustic windows*: Short and long axis view of the common femoral vein; long axis view of the external iliac vein.
- *Procedure*: After venipuncture, the guide wire is visualized inside the common femoral vein and inside the external iliac vein, using a long axis view. The progression of the catheter from the common femoral vein toward the external iliac vein can be assessed with the linear probe. In small children, the trajectory of the catheter inside the inferior vena cava (IVC) can also be assessed using the micro-convex probe, visualizing the IVC in transverse and longitudinal view at the level of the umbilicus.

2. Tip location Protocol:

- *Probe*: micro-convex 4–8 MHz probe.
- *Acoustic windows*: Short and long axis view of the IVC above the confluence of the common iliac veins, below the confluence of the hepatic veins; a subcostal bi-caval view is recommended to visualize the junction between IVC and the RA, above the confluence of the hepatic veins.
- *Procedure*: A quick flush of saline (2 or 5 ml) is injected, so to confirm the position of the tip: the immediate appearance of the bubbles of injected saline in the IVC allows to confirm that the tip is inside this vein, while a delayed appearance of the bubbles indicates that the tip is still far from the confluence of the iliac veins. The appearance of the bubbles in the RA immediately after injection confirms that the catheter tip is at the junction between IVC and right atrium, above the confluence of the hepatic veins (Figure 4).
- Please note that the tip FICCs is not necessarily located in the RA or at junction between IVC and RA: if the FICC is not to be used for hemodynamic monitoring, the tip can be left in the mid-portion of the IVC, above the confluence of the iliac veins and below the renal veins. In this latter case, the catheter can be located with the tip the IVC/RA junction as described above and then withdrawn.

## Conclusions

In this proposal of the "ECHOTIP-Ped" protocol—summarized in Table 2—we have tried to develop a stepwise and standardized procedure, potentially useful to perform ultrasound-based tip navigation and tip location during the insertion of all central venous access devices currently used in children.

Some of these maneuvers are easy and require only a minimal training, while some others imply a well-trained

**Table 2.** Summary of ECHOTIP-Ped.

| CVC | Protocol | Probe | Windows |
|---|---|---|---|
| CICC | Tip navigation | Linear "hockey stick" probe, 10–14 MHz | Same acoustic windows as RaCeVA |
| | Tip location | Micro-convex probe, 4–8 MHz, or small sectorial probe, 3–7 MHz | Subcostal bi-caval view (recommended) or four-chambers apical view (as alternative option) |
| PICC | Tip navigation | Linear "hockey stick" probe, 10–14 MHz | Same acoustic windows as RaPeVA and RaCeVA |
| | Tip location | Micro-convex probe, 4–8 MHz, or small sectorial probe, 3–7 MHz | Subcostal bi-caval view (recommended) or four-chambers apical view (as alternative option) |
| FICC | Tip navigation | Linear "hockey stick" probe, 10–14 MHz, or micro-convex probe, 4–8 MHz | Short + long axis views of the femoral vein and external iliac vein; and short + long axis views of IVC |
| | Tip location | Micro-convex probe, 4–8 MHz | Subcostal longitudinal view of the IVC |

PICC: peripherally inserted central catheter; RaCeVA: rapid central vein assessment; RaPeVA: rapid peripheral vein assessment; CICC: centrally inserted central catheter; FICC: femoral inserted central catheter; IVC: inferior vena cava.

operator with more than basic knowledge in the field of vascular ultrasound and echocardiography. Thus, training is the main open question, and we suggest that more evidence should be published about the proper training required for achieving appropriate skills of real-time ultrasound for CVAD insertion in children.

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