





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

Antonio La Greca¹, Emanuele Iacobone², Daniele Elisei²,
Daniele Guerino Biasucci³, Vito D'Andrea⁴,
Giovanni Barone⁵, Geremia Zito Marinosci⁶
and Mauro Pittiruti¹

The Journal of Vascular Access
1–10

© The Author(s) 2021

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/11297298211044325

journals.sagepub.com/home/jva



Abstract

Central venous access devices are routinely used in clinical practice for administration of fluids and medications, for drawing blood samples and for hemodynamic monitoring. The adoption of ultrasound guided venipuncture has significantly reduced procedure-related complications, as documented by the recommendations of most recent guidelines. Ultrasound has also an important role also in other aspects of central venous catheterization, such as in the pre-procedural evaluation of the venous patrimony and in the detection of early and late non-infective complications. Recently, bedside ultrasound has been regarded as a promising tool 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 adult patients, and to suggest a structured standardized protocol for clinical practice.

Keywords

Central venous access, ultrasound, tip location, tip navigation, CICC, PICC, femoral catheters, central venous catheters

Date received: 31 July 2021; accepted: 17 August 2021

Introduction

In the past two decades, ultrasound guided venipuncture has dramatically improved the results of central venous access procedures in terms of global and first attempt success and of complications rates.¹ Though, the benefits of ultrasound are not limited to the maneuver of venipuncture, but cover several aspects of the procedure of central venous catheterization:

- the identification of the anatomic characteristics of the vasculature, so to choose the most appropriate vein, using structured protocols of pre-procedural venous examination, such as RaCeVA—Rapid Central Venous Assessment,² RaPeVA—Rapid Peripheral Venous Assessment,³ and RaFeVA—Rapid Femoral Venous Assessment⁴;

¹Department of Surgery, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

²Department of Intensive Care and Anesthesia, Central Hospital, Macerata, Italy

³Department of Emergency, Anesthesiology and Intensive Care Medicine, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

⁴Neonatal Intensive Care Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

⁵Neonatal Intensive Care Unit, Ospedale Infermi di Rimini, Azienda Unità Sanitaria Locale della Romagna, Rimini, Italy

⁶UOC di Rianimazione e Neuroanestesia, Azienda Ospedaliera Santobono-Pausilipon, Naples, Italy

Corresponding author:

Mauro Pittiruti, Department of Surgery, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Largo Agostino Gemelli, 8, Rome 00168, Italy.

Email: mauropittiruti@me.com

- the real-time identification of puncture-related complications (hematomas, pneumothorax, hemothorax, etc.).^{1,5;}
- the early detection of many non-infective complications (venous thrombosis, tip migration, fibroblastic sleeve, etc.).^{1,6}

An additional use of ultrasound during central venous catheterization is the intra-procedural assessment of the correct direction of the guidewire (and/or of the catheter) as it progresses into the vasculature (so called “tip navigation”), as well as the intraprocedural verification of the correct location of the tip of the catheter at the end of the maneuver (so called “tip location”).^{7,8}

Intraprocedural tip navigation—which is not always perceived as necessary by the operator, though it may be very useful in case of difficult progression due to anatomic variations or venous abnormalities—can be performed also by fluoroscopy or by electromagnetic tracking methods. Though, fluoroscopy is inaccurate (since the radiological imaging visualizes the intravascular devices but not the vasculature), expensive and inevitably associated with x-ray exposure.⁹ Electromagnetic methods are inaccurate, expensive, and available only for some central venous access devices.¹⁰ Therefore, ultrasound appears to be the most attractive option for tip navigation.

As regards tip location, all current guidelines recommend using intraprocedural methods: the old-fashioned strategy of “blind” intraprocedural insertion of the catheter based on approximated length estimation and subsequent chest X-ray is not recommended anymore.⁹ Intraprocedural tip location by fluoroscopy is inaccurate, expensive, and unsafe (due to X-ray exposure). Thus, intracavitary electrocardiography (IC-ECG) is currently regarded as the first-choice method for tip location,⁹ being easy to perform, easy to learn, inexpensive, and very accurate.¹¹ On the other hand, the conventional technique of IC-ECG—as originally described—may be not applicable or not feasible in some clinical conditions when the P wave is not present or not easy to identify (atrial fibrillation, active pacemakers, and several types of arrhythmias); as a result, a significant percentage of patients may not benefit from IC-ECG (up to 10% in selected geriatric or cardiac hospitalized patients). Even though a new modified technique of IC-ECG has been described to be applicable in atrial fibrillation patients,¹² still in a significant percentage of patients IC-ECG may not be applicable (continuously active atrial pacemakers) or not feasible (trembling or uncooperating patients, technical problems due to electric interferences or device failure, emergency). In such conditions, ultrasound-based tip location may be an attractive alternative option.^{1,5,7,9}

Ultrasound-based tip location during placement of central venous access devices has been described since 2012.⁵

Recent guidelines^{1,9} have discussed the pros and cons of ultrasound-based tip location:

- it has certainly a wider range of applicability than IC-ECG, though it may not always be feasible in some adult patients.
- it is as safe as IC-ECG, since both methods do not imply X-ray exposure.
- in adult patients, it is not as accurate as IC-ECG and is less easy to learn.

The latter limitations are probably also secondary to lack of standardization of the technique; the percentage of false positives and false negatives can be minimized by an appropriate definition of the method; on the other hand, an effective training is possible only when the details of the method are clearly defined and standardized.

Though many clinical studies on this topic have been published in the last two decades, standard criteria on how to perform ultrasound-based tip location and navigation in clinical practice are still lacking, in terms of procedural protocols, acoustic windows, tip imaging modalities; moreover, the concept of ultrasound-based “tip navigation” is often not addressed and not clearly distinguished from “tip location.”

The purpose of this paper is (a) to review all the evidence available in the literature about ultrasound-based tip navigation and tip location of central Venous Access Devices (VAD) in adults, and (b) to propose a novel standardized protocol for ultrasound-based tip navigation and tip location based on such evidence. Our protocol (nicknamed “ECHOTIP”) will focus on practical issues such as the choice of the probe and of the acoustic window as well as the definition of the best method for ultrasound visualization of the guidewire and/or catheter and/or tip. The same issue has been already addressed in two recent studies carried out by our group in the context of pediatric¹³ and neonatal¹⁴ populations.

Methods

Literature search was performed on electronic databases 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,” “adult,” “central line,” “PICC,” “CICC,” “FICC,” “internal jugular vein,” axillary 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; we included all trials, case reports, and case series and filtered the articles by reviewing the abstract.

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

In the last two decades, we found 34 observational prospective studies and 1 randomized controlled study that have investigated feasibility and diagnostic accuracy of ultrasound for tip navigation and tip location of central venous access devices. Six of these were conducted in pediatric patients and were thus excluded, as they were discussed in our previous studies on ECHOTIP in children¹³ and ECHOTIP in neonates.¹⁴

Many of the studies have been carried out on centrally inserted central catheters (CICCs),^{15–17} but others on peripherally inserted central catheters (PICCs)¹⁸ and on ports.¹⁹ The differentiation between tip navigation and tip location was not always clear, and most of the studies focused on the latter. For the purposes of this review, we will discuss the literature identifying three main modalities of US-based visualization:

1. Tip navigation: ultrasound-based visualization of the guidewire and/or of the catheter to verify the correct direction into the superior vena cava (SVC) or inferior vena cava (IVC).
2. Tip location by direct visualization of the final position of the tip of the catheter, usually at the junction between right atrium and SVC or between right atrium (RA) and IVC.
3. Tip location by indirect visualization of the final position of the tip of the catheter, using the so-called “bubble test” (visualization of micro-bubbles inside the vasculature after injection of saline or saline/air mixture into the catheter).

Tip navigation

Some studies have demonstrated the possibility of achieving a good visualization of the guidewire and of the catheter inside the SVC, using either a micro-convex or a sectorial probe (“phased array probe”). By placing the probe on the supraclavicular fossa, the SVC can be followed down to the intersection with the right pulmonary artery.^{20,21} This technique should be regarded as a method of tip navigation, since the guidewire (or catheter) can be tracked into SVC, but the final position of the tip cannot be properly assessed. The method has been used for both supraclavicular access (puncture of the internal jugular vein) and infraclavicular access (puncture of the axillary vein). The overall feasibility of the method was 96% and its specificity 100% (no false positives). Still, the limit of the method is that—while the wire can be easily visualized inside the IVC—the catheter is not easily identified, unless it still has the guidewire inside.

In other studies, tip navigation has been carried out placing a linear probe on the supraclavicular fossa. The linear probe allows a proper visualization of all central veins of the supraclavicular area (internal jugular vein, external jugular vein, subclavian vein, and brachio-cephalic vein), so to ascertain that the guidewire (or catheter) has entered the brachio-cephalic vein. In these studies, tip navigation by linear probe was coupled with tip location by direct visualization of the tip,^{15–19,22} or by indirect visualization with “bubble test.”^{23–26} The specificity of the method appears to be close to 100% (no false positives) in all studies.^{15,17–19,23–27} The sensitivity is quite variable from 55% to 80% depending on the study^{17,18,24,25,27}; false negatives have been described when attempting to visualize the CICC in the subclavian vein,^{24,26} brachio-cephalic vein,^{17,18} and internal mammary vein.²⁴ In clinical studies on tip navigation of PICCs,^{18,22} many false negatives have been reported: in 3 cases out of 7¹⁸ and in 15 cases out of 95²² ultrasound could not detect the wrong direction of the catheter into the ipsilateral internal jugular vein.

Tip location by direct visualization of the final position of the tip of the catheter

Most clinical studies addressing ultrasound-based tip location of central venous access in adult patients have adopted 2.5–3.5 MHz sectorial probes (phased array).^{15,24,28–34} The subcostal four-chamber (longitudinal) view has been considered as the first choice in most studies^{15,24,28,29,31–34}; this view can be easily applied in patients with respiratory problems (mechanical ventilation, lung emphysema) but it may be difficult in some cases of previous surgery of the upper abdomen.^{27,34} An alternative option is the four-chamber transthoracic apical view, which—on the other hand—may be difficult in obese patients^{27,34} and in patients with acute or chronic lung disease.

In adult patients, with either the subcostal view or the apical view, sensitivity is quite low: if the tip of the catheter is inside the SVC or at the junction between SVC and RA, false negatives may occur.²⁹ The tip may be easier to visualize in the RA,^{15–19,27} as demonstrated in clinical studies on CICCs,^{15–17} on PICCs,¹⁸ and on ports.¹⁹ The double maneuver of ultrasound-guide venipuncture and ultrasound-based tip location has been described as performed by one operator¹⁶ or by two operators.^{27,34} In the study on tip navigation/location during PICC insertion, one operator performed the venipuncture, and a second operator performed the ultrasound-based verification of the direction of the catheter and of the final position of the tip.²² The method of direct visualization of the tip by ultrasound had high feasibility (94.1%) and high specificity (98.9%)^{15–19,22,27}; its sensitivity was evaluated only in six studies^{15–19,22} and estimated to be 78.4%, though quite variable from study to study.

One critical issue is the training of the operators. In some studies,^{16,19,22} the experience of the operators was not

addressed. In one study, the operators were defined as experts, even if no formal training was mentioned.¹⁵ In another study, a one-day training course is mentioned.¹⁸ In another study, the authors compared the performance of two formally trained operators with two operators with minimal training,²⁷ the former being more successful than the latter in the visualization of the catheter (95% vs 83%). Other authors¹⁷ have defined the level of experience of the operators adopting the criteria suggested by the American College of Emergency Physicians.³⁵

Tip location by indirect visualization of the final position of the tip of the catheter

While the metallic guidewire is usually easy to visualize by ultrasound, the direct visualization of the catheter, and in particular of the tip of the catheter, may be difficult in adult patients. Therefore, a new technique of indirect ultrasound visualization of the catheter using a saline flush (so-called “bubble test”) has been introduced in the clinical practice.^{20,23} The rapid infusion of normal saline or of a 9:1 mixture of saline + air creates microbubbles inside the vasculature: such microbubbles act as contrast medium, and their appearance in the RA facilitates the visualization of the tip. If the tip is not in the RA but in the lower part of the SVC, the immediate appearance of the bubbles in the RA will confirm the proximity of the tip; if the bubbles do not appear or appear with a significant delay, the tip is not in the SVC.

The technique is simple and absolutely safe for the patient^{36,37}; it has been tested in many clinical studies.^{17,31–34,38–43} As in the technique of direct ultrasound visualization, a sector probe is used, and the preferred views are the four-chamber subcostal view and the apical view.

As contrast, different solutions have been used^{31,32,34,38,43}: 10 ml normal saline, 5 ml “shaken” saline, 5 or 10 ml of 9:1 mixture of saline + air.

When the tip cannot be visualized directly inside the RA, the delay of appearance of the microbubbles is of critical importance. According to some authors,²⁹ if the delay is <2 s, the tip of the catheter is in the SVC. If the bubbles do not appear, some authors^{28,43} recommend a second saline injection: if the bubbles still do not appear or if they appear with a delay >2 s, the tip of the catheter is not in the correct position. When the bubbles appear immediately (delay <2 s) inside the RA, a laminar flow is suggestive of a tip inside the SVC, while a turbulent flow suggests an intra-atrial position of the tip.^{28,32}

More recently, several authors have questioned the cut-off of 2 s, originally proposed by Vezzani et al.²³ Weekes et al.³¹ found that when the tip of a CICC is in the lower third of the SVC, the mean time of appearance of the bubbles in the RA was 1.1 ± 0.3 s. Meggiolaro et al.²⁴ have demonstrated that when the tip of the CICC is in the final tract of the SVC or at the junction between SVC and RA, the time of appearance must be less than 500 ms; if the tip

is inside the RA, the expected delay is 150 ms. Iacobone et al.⁴³ have shown that when the tip is at the junction between SVC and RA, the appearance time of the microbubbles is different comparing CICC versus PICC (0.89 ± 0.33 vs 1.1 ± 0.20 s).

The “bubble test” has been proven to be applicable not only to CICCs and PICCs, but also to dialysis catheters.^{39,42}

The overall feasibility of the “bubble test” method is 98%; its specificity is 99.5% and its sensitivity 64.9%, but with a wide variability among the studies (33.3%–100%).^{28,31–33,38–41}

There is wide variability in the experience and training of the operators who have carried out the clinical studies with the bubble test. In two studies^{28,33} the operators met the criteria suggested by the American College of Emergency Physicians³⁵; in other studies, it was stated that the operators had many years of clinical experience with ultrasound,^{34,39} or that they had rapid training courses.⁴¹ In most studies, the level of competence of the operators is not specifically mentioned.^{31,32,38,40}

In a few studies, the indirect method of ultrasound-based tip location by bubble test was coupled with ultrasound-based tip navigation.^{23–26} A linear probe is used for both ultrasound-guided venipuncture and ultrasound-based tip navigation (probe in the supraclavicular area). Tip location is then performed using a sectorial probe or—in one study²⁵—a convex probe. The overall feasibility was 96.3%, the specificity 97.5%, and the sensitivity 50.5%.^{23–26} No detail is offered about the level of competence and training of the operators.

Recently, two reviews have evaluated the applicability and feasibility of ultrasound-based tip location.^{36,37} In summary, both reviews concluded that the overall feasibility of the method is very high (96.8%) and that the current limitations for an extensive clinical use are (a) the lack of standardization in technical terms (probe, acoustic window, procedure), (b) the lack of studies evaluating the accuracy of the technique using as reference accurate methods of tip location (intracavitary ECG or trans-esophageal echocardiography) rather than relatively inaccurate radiological methods, and (c) the lack of information about the minimal training required for a proper performance of the method.

In a very recent clinical study,⁴⁴ the bubble test has been used as a rapid bedside maneuver for verifying the intravascular position of totally implanted venous devices with persistent withdrawal occlusion.

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

The techniques described in the abovementioned clinical studies are quite heterogeneous, especially in terms of

probes and views. The methodology for an optimal ultrasound-based tip navigation and tip location has not been standardized by any author, and little attention has been given to the competence and training of the operators. Furthermore, most authors have used an imperfect reference standard for tip location, that is, chest X-ray, which is known to be quite inaccurate⁹ if compared to intracavitary ECG or transesophageal echocardiography.

After our systematic review, we have tried to develop a novel standardized protocol for ultrasound-based tip navigation and tip location of central venous VADs in adult patients. We have developed three different protocols, dealing with the three different central VADs that are inserted in adult patients:

- (a) centrally inserted central catheters (CICC), inserted by venipuncture of veins of the supra/intra-clavicular area (internal jugular, external jugular, subclavian, brachio-cephalic, axillary vein)
- (b) peripherally inserted central catheters (PICC), inserted by venipuncture of the deep veins of the upper arm (basilic, brachial, axillary)
- (c) femorally inserted central catheters (FICC), inserted by venipuncture of deep veins of the lower limb (common femoral, superficial femoral, saphenous).

The definition of 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.

All three protocols can be adopted also during insertion of totally implantable vascular access devices (ports), considering that the issues of tip navigation and tip location are not affected by the subsequent connection of the catheter with a reservoir.

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 insertion²; RaPeVA (Rapid Peripheral Venous Assessment) before PICC insertion³; RaFeVA (Rapid Femoral Venous Assessment) before FICC insertion.⁴ Also, we assume that all central VAD insertions (either CICC, or FICC or PICC) must be always performed adopting real time ultrasound guided venipuncture.^{1,5,9}

ECHOTIP-adults for CICC insertion

Tip navigation protocol:

Probe: first option, 7–12 MHz linear probe (same probe used for venipuncture).

Acoustic window: same windows as described in RaCeVA²

Procedure: Soon after venipuncture, the guidewire is threaded into the vein and observed sequentially in the RaCeVA windows to ensure its intravascular placement and its direction. Guidewires are echogenic and usually easy to identify; though, 0.018" wires might be harder to visualize than 0.035" wires. Both a negative assessment (absence of the wire in an undesired vessel) and a positive assessment (presence of the wire in the desired vessel) should be obtained. The same RaCeVA-based procedure is repeated when the catheter progresses into the vasculature; as the catheter is less echogenic than the guidewire, its visualization may be enhanced by using a saline flush (the turbulence at the catheter tip will help to identify the direction of the catheter). With this method, the operator can rule out any wrong direction of the guidewire and/or of the catheter (e.g. into the internal jugular vein after axillary venipuncture) and confirm that the guidewire and/or the catheter are directed toward the SVC.

Tip location Protocol:

Probe: 2–6 MHz sectorial probe; as alternative option, 3–8 MHz convex probe.

Acoustic window: a subcostal four-chamber view (Figure 1) or a subcostal bi-caval view (Figure 2) are recommended, since these views are easy to obtain and require minimal training; a trans-thoracic apical four-chamber view (Figure 3) may be an alternative option, when the subcostal scans are not feasible due to local acoustic interferences (gastric meteorism, large surgical scars, etc.).

Procedure: as the catheter has entered the SVC and is in the proximity of the junction between SVC and RA, a quick flush of "shaken" saline (5–10 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 (less than 1 s) proves that the tip is in the proximity of the RA (Figures 1–3)

ECHOTIP-adults for PICC insertion

Tip navigation protocol:

Probe: 7–12 MHz linear probe (same probe used for venipuncture).

Acoustic window: same windows as described in RaPeVA³ and RaCeVA²: the deep veins of the arm up to

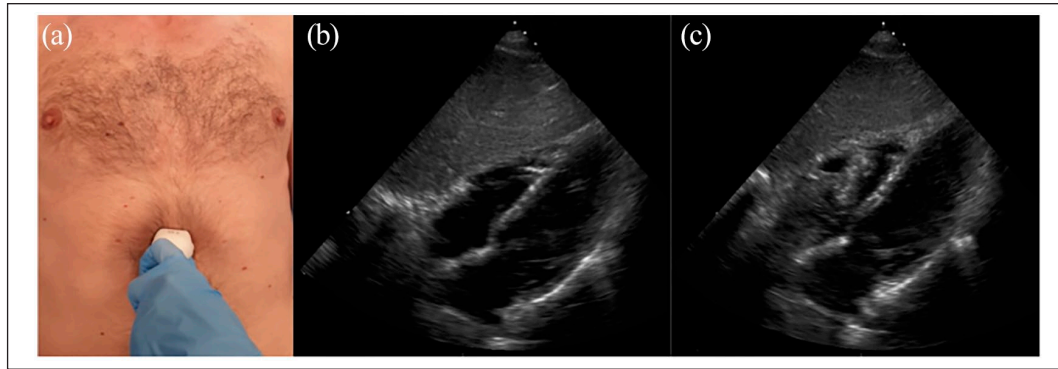


Figure 1. Subcostal (longitudinal) four-chamber view: placement of the probe (a), visualization of the heart chambers (b), and visualization of the microbubbles in the right atrium (c).

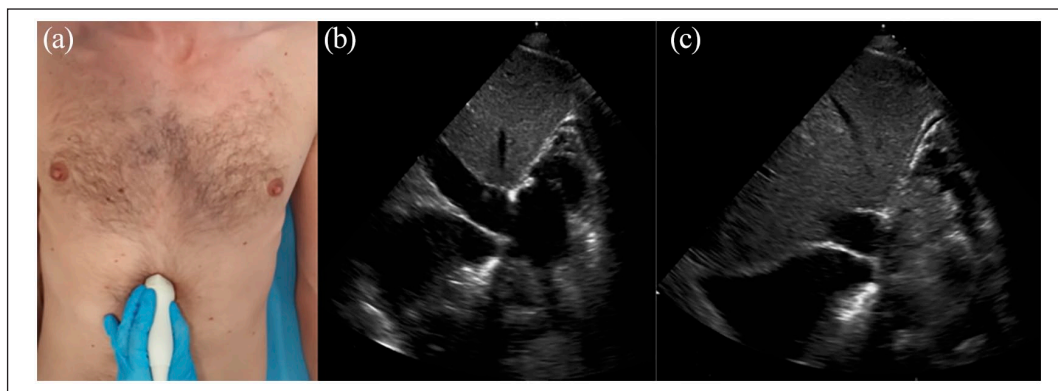


Figure 2. Subcostal (oblique) bi-caval view: placement of the probe (a), visualization of the superior vena cava, inferior vena cava, and right atrium (b), and visualization of the microbubbles in the right atrium (c).

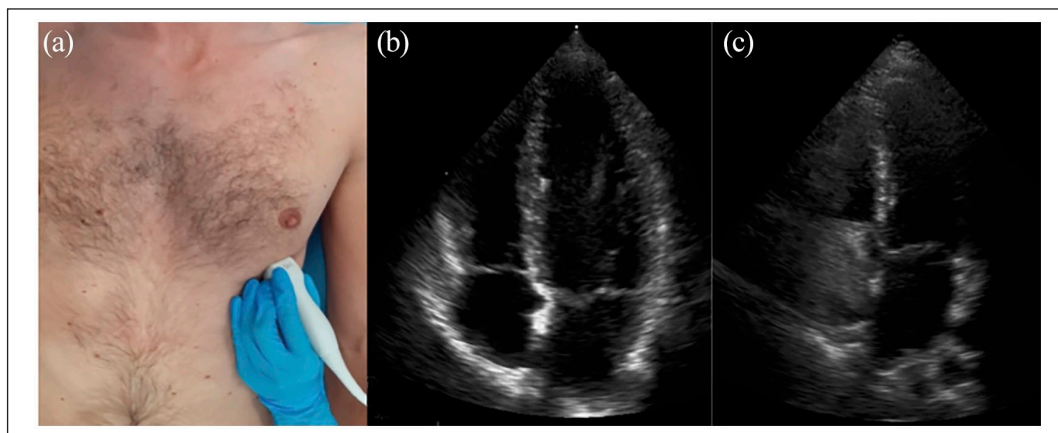


Figure 3. Transthoracic apical four-chamber view: placement of the probe (a), visualization of the heart chambers (b), and visualization of the microbubbles in the right atrium (c).

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

the catheter into the brachio-cephalic vein, ruling out any wrong direction (e.g. into the ipsilateral internal jugular vein).

Procedure: 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 misdirection to the ipsilateral internal jugular vein.

Tip location Protocol:

Probe: 2–6 MHz sectorial probe; as alternative option, 3–8 MHz convex probe.

Acoustic windows: a subcostal four-chamber view (Figure 1) or a subcostal bi-caval view (Figure 2) are recommended, since these views are easy to obtain and require minimal training; a trans-thoracic apical four-chamber view may be an alternative option, when the subcostal scans are not feasible due to local acoustic interferences.

Procedure: as the catheter has entered the SVC and is in the proximity of the junction between SVC and RA, a quick flush of “shaken” saline (5–10 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 (less than 2 s) proves that the tip is in the proximity of the RA. This cut-off limit of 2 s is higher than what suggested for CICC (1 s), since we must consider that PICCs are longer than CICCs, as demonstrated in the clinical study by Iacobone et al.⁴³

ECHOTIP-adults for FICC insertion

Tip navigation protocol:

Probe: 7–12 MHz linear probe; 3–8 MHz convex probe.

Acoustic window: short and long axis view of the common femoral vein (linear probe); short and long axis view of the external iliac vein (linear probe); short axis view of the common iliac vein (linear or convex probe) lateral to the psoas muscle; short axis view of the IVC beneath and behind the liver (convex probe). As an optional maneuver, a long axis view of the inferior vena cava can be obtained by a “right flank” window (i.e. probe placed on the mid-axillary line and sliding in between the last intercostal spaces and the subcostal area). The latter view may not be easy in the obese patient.

Procedure: After venipuncture, the guide wire is visualized inside the common femoral vein and inside the

external iliac vein, using combined short and long axis views. The progression of the catheter from the common femoral vein toward the external iliac vein can be assessed with the linear probe; the visualization of the catheter in the common iliac vein often requires a convex probe. The trajectory of the catheter inside the IVC can also be assessed with a convex probe, visualizing the IVC in short and long axis views at the level of the umbilicus and/or in its pararenal and retro-hepatic tract, using a “right flank” window (see above).

Tip location Protocol (flush/bubble test):

Probe: 2–6 MHz sectorial probe; as alternative option, 3–8 MHz convex 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 may be useful; a subcostal bi-caval view is recommended to visualize the junction between IVC and the RA, above the confluence of the hepatic veins; a four-chamber subcostal view may also be effective for performing the “bubble test.”

Procedure: a rapid flush of “shaken” saline (5–10 ml) is injected: the immediate appearance of the bubbles inside the IVC confirms that the tip is inside this vein; a delayed appearance of the bubbles inside the IVC indicates that the tip is in the iliac veins or in collateral veins; the immediate appearance of the bubbles in the RA confirms that the tip is at the junction between IVC and RA. If the tip of the catheter is inside the RA, it can be directly visualized by a subcostal view, and the bubble test may facilitate the visualization of the tip.

Please note that the maneuvers of tip navigation are not strictly necessary in most FICC insertions. On the contrary, ultrasound-based tip location for FICC is highly useful, since the other methods of tip location (intracavitary ECG and X-ray) are not accurate and not properly standardized for FICC. As regards tip location, please also note the tip of a FICC is not necessarily located in the RA or at the junction between IVC and RA: if the FICC is not to be used for hemodynamic monitoring, the tip is usually left in the mid-portion of the IVC, above the confluence of the iliac veins and below the renal veins.⁴⁵ In this latter case, it is easy to locate the catheter tip in the RA by the bubble test (as described above) and then withdraw it.

A summary of the ECHOTIP protocol is shown in Table 1.

Conclusions

We have tried to develop a stepwise and standardized procedure (the ECHOTIP protocol), potentially useful to

Table 1. (a) ECHOTIP protocol for CICCs.

	Probe	Technique
Tip navigation	7–12 MHz linear probe	Visualization of the cannulated vessel (wire/catheter inside the vein)
Tip location	2–6 MHz sectorial probe As alternative option: 3–8 MHz convex probe	Visualization of the deep vessels of neck and chest according to RaCeVA Immediate visualization (<1 s) of bubbles in RA after flushing First option: subcostal views (four-chamber or bi-caval) Second option: four-chamber apical view

(b) ECHOTIP protocol for PICCs.

	Probe	Technique
Tip navigation	7–12 MHz linear probe	Visualization of the deep veins of the arm and of the infra/supraclavicular area according to RaPeVA and RaCeVA
Tip location	2–6 MHz sectorial probe As alternative option: 3–8 MHz convex probe	Immediate visualization (<2 s) of bubbles in RA after flushing First option: subcostal views (four-chamber or bi-caval) Second option: four-chamber apical view

(c) ECHOTIP protocol for FICCs.

	Probe	Technique
Tip navigation	7–12 MHz linear probe (femoral vein and external iliac vein)	Visualization of the deep vessels of the lower limb according to RaFeVA
Tip location	3–8 MHz convex probe (common iliac vein and IVC) 2–6 MHz sectorial probe As alternative option: 3–8 MHz convex probe	Visualization of IVC in short and long axis views Visualization of bubbles after flushing Tip in IVC: immediate visualization of bubbles in IVC Tip in RA or at the junction RA/IVC: immediate visualization of bubbles in RA

perform ultrasound-based tip navigation and tip location during the insertion of all central venous access devices currently used in adults.

Some of these maneuvers are easy and require only a minimal training, while some others imply a well-trained 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 central venous catheterization in adult patients.

Tip location by subcostal or trans-thoracic ultrasound is almost always applicable and feasible, but certainly less accurate than tip location by intracavitary ECG or trans-esophageal echocardiography. Though, clinical studies show that it is as accurate as radiological methods, so that it may play an important role when intracavitary ECG is not applicable (due to specific cardiac rhythm abnormalities) or not feasible (in emergency, or because of logistic or technical issues).

The combined use of intracavitary ECG and ultrasound-based tip location may completely avoid the need for intraprocedural fluoroscopy and/or post-procedural chest

X-ray in adult patients requiring central venous catheterization.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Emanuele Iacobone  <https://orcid.org/0000-0002-1508-0651>
 Daniele Guerino Biasucci  <https://orcid.org/0000-0001-6839-2416>
 Vito D'Andrea  <https://orcid.org/0000-0002-0980-799X>
 Mauro Pittiruti  <https://orcid.org/0000-0002-2225-7654>

References

1. Lamperti M, Biasucci DG, Disma N, et al. European Society of Anaesthesiology guidelines on peri-operative use of ultrasound-guided for vascular access (PERSEUS vascular access). *Eur J Anaesthesiol* 2020; 37(5): 344–376.

2. Spencer TR and Pittiruti M. Rapid Central Vein Assessment (RaCeVA): a systematic, standardized approach for ultrasound assessment before central venous catheterization. *J Vasc Access* 2019; 20(3): 239–249.
3. Emoli A, Cappuccio S, Marche B, et al.; Aperto di Studio sugli Accessi Venosi Centrali a Lungo Termine Gruppo. Il protocollo 'ISP' (Inserzione Sicura dei PICC): un "bundle" di otto raccomandazioni per minimizzare le complicanze legate all'impianto dei cateteri centrali ad inserimento periferico (PICC) [The ISP (Safe Insertion of PICCs) protocol: a bundle of 8 recommendations to minimize the complications related to the peripherally inserted central venous catheters (PICC)]. *Assist Inferm Ric* 2014; 33(2): 82–89.
4. Brescia F, Pittiruti M, Ostroff M, et al. Rapid Femoral Vein Assessment (RaFeVA): a systematic protocol for ultrasound evaluation of the veins of the lower limb, so to optimize the insertion of femorally inserted central catheters. *J Vasc Access*. Epub ahead of print 16 October 2020. DOI: 10.1177/1129729820965063.
5. Lamperti M, Bodenham AR, Pittiruti M, et al. International evidence-based recommendations on ultrasound-guided vascular access. *Intensive Care Med* 2012; 38(7): 1105–1117.
6. Passaro G, Pittiruti M and La Greca A. The fibroblastic sleeve, the neglected complication of venous access devices: a narrative review. *J Vasc Access*. Epub ahead of print 23 August 2020. DOI: 10.1177/1129729820951035.
7. Biasucci DG, La Greca A, Scoppettuolo G, et al. What's really new in the field of vascular access? Towards a global use of ultrasound. *Intensive Care Med* 2015; 41(4): 731–733.
8. Brescia F, Pittiruti M, Ostroff M, et al. The SIC protocol: a seven-step strategy to minimize complications potentially related to the insertion of centrally inserted central catheters. *J Vasc Access*. Epub ahead of print 29 July 2021. DOI: 10.1177/11297298211036002.
9. Gorski LA, Hadaway L, Hagle ME, et al. Infusion therapy standards of practice, 8th edition. *J Infus Nurs* 2021; 44(1S Suppl 1): S1–S224.
10. Pittiruti M, Scoppettuolo G, Dolcetti L, et al. Clinical use of sherlock-3CG[®] for positioning peripherally inserted central catheters. *J Vasc Access* 2019; 20(4): 356–361.
11. Pittiruti M, Pelagatti F and Pinelli F. Intracavitary electrocardiography for tip location during central venous catheterization: a narrative review of 70 years of clinical studies. *J Vasc Access*. Epub ahead of print 24 June 2020. DOI: 10.1177/1129729820929835.
12. Calabrese M, Montini L, Arlotta G, et al. A modified intracavitary electrocardiographic method for detecting the location of the tip of central venous catheters in atrial fibrillation patients. *J Vasc Access* 2019; 20(5): 516–523.
13. Zito Marinosci G, Biasucci DG, Barone G, et al. ECHOTIP-Ped: a structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in pediatric patients. *J Vasc Access*. Epub ahead of print 13 July 2021. DOI: 10.1177/11297298211031391.
14. Barone G, Pittiruti M, Biasucci DG, et al. Neo-ECHOTIP: a structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in neonates. *J Vasc Access*. Epub ahead of print 5 April 2021. DOI: 10.1177/11297298211007703.
15. Maury E, Guglielminotti J, Alzieu M, et al. Ultrasonic examination: an alternative to chest radiography after central venous catheter insertion? *Am J Respir Crit Care Med* 2001; 164(3): 403–405.
16. Bedel J, Vallée F, Mari A, et al. Guidewire localization by transthoracic echocardiography during central venous catheter insertion: a periprocedural method to evaluate catheter placement. *Intensive Care Med* 2013; 39(11): 1932–1937.
17. Zanobetti M, Coppa A, Bulletti F, et al. Verification of correct central venous catheter placement in the emergency department: comparison between ultrasonography and chest radiography. *Intern Emerg Med* 2013; 8(2): 173–180.
18. Matsushima K and Frankel HL. Bedside ultrasound can safely eliminate the need for chest radiographs after central venous catheter placement: CVC sono in the surgical ICU (SICU). *J Surg Res* 2010; 163(1): 155–161.
19. Miccini M, Cassini D, Gregori M, et al. Ultrasound-guided placement of central venous port systems via the right internal jugular vein: are chest X-ray and/or fluoroscopy needed to confirm the correct placement of the device? *World J Surg* 2016; 40(10): 2353–2358.
20. Kim SC, Heinze I, Schmiedel A, et al. Ultrasound confirmation of central venous catheter position via a right supraclavicular fossa view using a microconvex probe: an observational pilot study. *Eur J Anaesthesiol* 2015; 32(1): 29–36.
21. Kim SC, Gräff I, Sommer A, et al. Ultrasound-guided supraclavicular central venous catheter tip positioning via the right subclavian vein using a microconvex probe. *J Vasc Access* 2016; 17(5): 435–439.
22. Nakamuta S, Nishizawa T, Matsuhashi S, et al. Real-time ultrasound-guided placement of peripherally inserted central venous catheter without fluoroscopy. *J Vasc Access* 2018; 19(6): 609–614.
23. Vezzani A, Brusasco C, Palermo S, et al. Ultrasound localization of central vein catheter and detection of postprocedural pneumothorax: an alternative to chest radiography. *Crit Care Med* 2010; 38(2): 533–538.
24. Meggiolaro M, Scatto A, Zorzi A, et al. Confirmation of correct central venous catheter position in the preoperative setting by echocardiographic "bubble-test". *Minerva Anesthesiol* 2015; 81(9): 989–1000.
25. Megahed MM, Zakhary TN, AbdElHady MA, et al. Validity of ultrasonography in detection of central venous catheter position and pneumothorax compared to portable chest X-ray. *Biolife* 2016; 4(4): 687–692.
26. Blans MJ, Endeman H and Bosch FH. The use of ultrasound during and after central venous catheter insertion versus conventional chest X-ray after insertion of a central venous catheter. *Neth J Med* 2016; 74(8): 353–357.
27. Arellano R, Nurmohamed A, Rumman A, et al. The utility of transthoracic echocardiography to confirm central line placement: an observational study. *Can J Anaesth* 2014; 61(4): 340–346.
28. Cortellaro F, Mellace L, Paglia S, et al. Contrast enhanced ultrasound vs chest X-ray to determine correct central venous catheter position. *Am J Emerg Med* 2014; 32(1): 78–81.

29. Vezzani A, Manca T, Vercelli A, et al. Ultrasonography as a guide during vascular access procedures and in the diagnosis of complications. *J Ultrasound* 2013; 16(4): 161–170.
30. Haskins SC, Tanaka CY, Boublik J, et al. Focused cardiac ultrasound for the regional anesthesiologist and pain specialist. *Reg Anesth Pain Med* 2017; 42(5): 632–644.
31. Weekes AJ, Johnson DA, Keller SM, et al. Central vascular catheter placement evaluation using saline flush and bedside echocardiography. *Acad Emerg Med* 2014; 21(1): 65–72.
32. Weekes AJ, Keller SM, Efuno B, et al. Prospective comparison of ultrasound and CXR for confirmation of central vascular catheter placement. *Emerg Med J* 2016; 33(3): 176–180.
33. Duran-Gehring PE, Guirgis FW, McKee KC, et al. The bubble study: ultrasound confirmation of central venous catheter placement. *Am J Emerg Med* 2015; 33(3): 315–319.
34. Amir R, Knio ZO, Mahmood F, et al. Ultrasound as a screening tool for central venous catheter positioning and exclusion of pneumothorax. *Crit Care Med* 2017; 45(7): 1192–1198.
35. American College of Emergency Physicians. Emergency ultrasound guidelines. *Ann Emerg Med* 2009; 53(4): 550–570.
36. Ablordeppey EA, Drewry AM, Beyer AB, et al. Diagnostic accuracy of central venous catheter confirmation by bedside ultrasound versus chest radiography in critically ill patients: a systematic review and meta-analysis. *Crit Care Med* 2017; 45(4): 715–724.
37. Smit JM, Raadsen R, Blans MJ, et al. Bedside ultrasound to detect central venous catheter misplacement and associated iatrogenic complications: a systematic review and meta-analysis. *Crit Care* 2018; 22(1): 65.
38. Gekle R, Dubensky L, Haddad S, et al. Saline flush test: can bedside sonography replace conventional radiography for confirmation of above-the-diaphragm central venous catheter placement? *J Ultrasound Med* 2015; 34(7): 1295–1299.
39. Wen M, Stock K, Heemann U, et al. Agitated saline bubble-enhanced transthoracic echocardiography: a novel method to visualize the position of central venous catheter. *Crit Care Med* 2014; 42(3): e231–e233.
40. Baviskar AS, Khatib KI, Bhoi S, et al. Confirmation of endovenous placement of central catheter using the ultrasonographic “bubble test”. *Indian J Crit Care Med* 2015; 19(1): 38–41.
41. Kamalipour H, Ahmadi S, Kamali K, et al. Ultrasound for localization of central venous catheter: a good alternative to chest X-ray? *Anesth Pain Med* 2016; 6(5): e38834.
42. Passos RDH, Ribeiro M, da Conceição LFMR, et al. Agitated saline bubble-enhanced ultrasound for the positioning of cuffed, tunneled dialysis catheters in patients with end-stage renal disease. *J Vasc Access* 2019; 20(4): 362–367.
43. Iacobone E, Elisei D, Gattari D, et al. Transthoracic echocardiography as bedside technique to verify tip location of central venous catheters in patients with atrial arrhythmia. *J Vasc Access* 2020; 21(6): 861–867.
44. D’Arrigo S, Annetta MG and Pittiruti M. An ultrasound-based technique in the management of totally implantable venous access devices with persistent withdrawal occlusion. *J Vasc Access*. Epub ahead of print 6 June 2021. DOI: 10.1177/11297298211023275.
45. Annetta MG, Marche B, Dolcetti L, et al. Ultrasound-guided cannulation of the superficial femoral vein for central venous access. *J Vasc Access*. Epub ahead of print 21 March 2021. DOI: 10.1177/11297298211003745.