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Ultrasound-based tip navigation and tip location during placement of central venous access devices in adult patients: The ECHOTIP protocol revisited

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Abstract

Ultrasound has an important role in many aspects of central venous catheterization. In the last decade, bedside ultrasound has been regarded as a promising tool also for ensuring an accurate and intraprocedural assessment of the location of the catheter tip, as an alternative or complimentary option to intracavitary electrocardiography. In this regard, 5 years ago the Italian Group of Venous Access Devices (GAVeCeLT) developed detailed protocols for the standardization of this methodology in different populations of patients: neonates (Neo-ECHOTIP), children (ECHOTIP-Ped), and adults (ECHOTIP). In the lapse of time since the publication of these protocols, recent clinical studies have brought novel information and new evidence, so that some recommendations included in the original ECHOTIP protocol for adults today may seem incomplete or inappropriate. For this reason, GAVeCeLT has developed an updated version of the protocol, nick-named ECHOTIP-2, which includes new recommendations in regards of some technical aspects of the procedure of bubble test and of the application of the method to femorally inserted central catheters.

Keywords

Central venous access devices, tip location, intracavitary electrocardiography, transthoracic echocardiography, pulse wave Doppler, bubble test

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Introduction

During the last decade, several studies have focused on the adoption of ultrasound for the proper detection of the location of the catheter tip during central venous catheterization.[1,2] Ultrasound methodologies appear particularly attractive in this regard, and they are recommended since they are less invasive, less expensive, and more precise if compared to radiological methods[3–5]: they can be utilized both for the intra-procedural assessment of the correct direction of the guidewire (and/or of the catheter) as it progresses into the vasculature ("tip navigation"), and for the intraprocedural verification of the correct location of the tip of the catheter at the end of the maneuver ("tip location").

Five years ago, the Italian Group of Venous Access Devices (GAVeCeLT) developed standardized protocols for ultrasound-based tip navigation and tip location. Such protocols ("ECHOTIP" protocols) addressed practical issues such as the choice of the probe and of the acoustic

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window and the definition of the best technique for ultrasound visualization of the guidewire and/or catheter and/or catheter tip in different types of central venous access devices and in different patient populations. Three protocols were published in 2020–21, focusing on central venous catheterization in neonates,[6] in children,[7] and in adults.[8] Since then, the protocols have been incorporated into the GAVeCeLT recommendations for proper central venous catheterization in adults,[5,9–14] as well as in children and neonates.[15]

The ECHOTIP protocols were developed on the basis of the best evidence available 5 years ago; though, during the last few years, several new studies on ultrasound-based tip location have been published,[16–23] so that some recommendations of the original ECHOTIP protocol sound today incomplete or outdated. For this reason, a group of GAVeCeLT experts has developed an update of the ECHOTIP protocol—nick-named ECHOTIP-2—which includes additional information about three new interesting aspects of ultrasound-based tip location, that is, (a) the appropriate interpretation of the "bubble test" when used for estimating the distance between catheter tip and right atrium, with special regard to the delay time of appearance of the micro-bubbles; (b) the application of the pulsed-wave doppler as an alternative option for visualizing the appearance of the flow in the right atrium during the "bubble test"; (c) the adoption of the trans-hepatic acoustic window for the visualization of the catheter in the subdiaphragmatic tract of the inferior vena cava.

These novelties have been integrated in the original protocol, developing a new set of recommendations (ECHOTIP-2; Table 1).

Interpretation of the time delay during the bubble test

The so-called "bubble test"—or "swirl sign"—has been included in the ECHOTIP protocols as an aid in the proper identification of the position of the tip.[6–8] When the tip of the catheter is presumably in the vascular area scanned by ultrasound, but its identification is difficult or uncertain, the rapid injection of few milliliters of agitated saline (1–2 ml in neonates, 5 ml in children, 5–10 ml in adults) may confirm precisely the presence of the tip, as the appearance of the micro-bubbles is more easily visualized than the tip itself. On the other hand, the bubble test is also useful in predicting the location of the tip when the catheter tip is not in the area of vasculature visualized by ultrasound. This technique of "indirect" localization of the tip requires an evaluation of the delay time between the moment of saline injection and the moment when the micro-bubbles appear in the area scanned by ultrasound; the longer the delay, the bigger the distance between the actual position of the tip and the area scanned by ultrasound.

This technique has been substantiated by clinical evidence, demonstrating its high degree of reliability,[1,2,24–31] and it has been included in the 2021 version of the ECHOTIP protocol.[8] The cut-off time for establishing that the tip may be very close (<1 cm) from the point where the bubbles appear had been set at less than 1 s for centrally inserted central catheters (CICCs) and less than 2 s for peripherally inserted central catheters (PICCs) on the basis of the evidence available in 2020.[24,25,31] New findings lead to a reconsideration of such cut-off times.

A recent clinical study[17] has shown that the delay of appearance of the bubbles in the right atrium was less than 2 s in one-third (29.5%) of midline catheters with tip localized in the thoracic tract of the axillary vein, that is, quite far from the cavo-atrial junction. Also, a recent bench study[18] has shown that the delay time between rapid injection of saline and its appearance at the catheter tip is less than 500 ms, and that it is not significantly different for devices with different lengths (20, 40, or 60 cm). In this study, substantial discrepancies were observed between different operators concerning the rapidity of saline injection, potentially compromising the accuracy of the test. These findings suggested that the technique of bubble test should be integrated into training programs on ultrasound-based tip location, and that the procedure should be further standardized in terms of volume of saline injected, necessary equipment, and method of injection. Last, in a very recent study on PICCs with tip placed at the cavo-atrial junction,[20] the delay was less than 500 ms in 75.5% of cases.

In conclusion, these recent findings suggest that the 1–2 s cut-off previously proposed in the literature[24,25,31] and adopted by the 2021 ECHOTIP protocol[8] is excessively long and thus inappropriate for the indirect estimation of tip location. The cut-off most likely to be accurate is 500 ms, as originally suggested by Meggiolaro et al.,[29] since such delay is associated with a very high probability of the presence of the tip at less than 1 cm from the point where the bubbles appear. Although 500 ms seem to be a suitable and efficient cut-off, this duration is notably very brief and hard to measure (e.g. a blink of an eye lasts approximately the same time).[32] For the practical purposes, this new version of the ECHOTIP protocol—as regards tip location of PICCs and CICCs—recommends to consider that the tip is at the cavo-atrial junction when the micro-bubbles appear in the right atrium "immediately" (i.e. within 500 ms) after the start of saline injection, independently from the catheter type or length.

Use of pulsed-wave doppler

Another recent advancement is the possibility of using pulsed-wave doppler during the bubble test, as a means for identifying the flow coming out of the catheter tip after rapid injection of saline. Pulsed wave doppler has been

Table 1. The ECHOTIP-2 protocol.

ECHOTIP protocol for CICCs		
Tip navigation	7–12 MHz linear probe	Visualization of wire/catheter inside the veins according to the RaCeVA protocol.
Tip location	2–6 MHz sectorial probe or 3–8 MHz convex probe	Immediate visualization (<500 ms) of the bubbles in right atrium, preferably using the subcostal views (apical view is regarded as second choice). Alternative option: immediate visualization of micro-embolic signals by pulsed wave doppler (using the same views).
ECHOTIP protocol for PICCs		
Tip navigation	7–12 MHz linear probe	Visualization of wire/catheter inside the veins according to the RaPeVA and RaCeVA protocols.
Tip location	2–6 MHz sectorial probe or 3–8 MHz convex probe	Immediate visualization (<500 ms) of the bubbles in right atrium, preferably using the subcostal views (apical view is regarded as second choice). Alternative option: immediate visualization of micro-embolic signals by pulsed wave doppler (using the same views).
ECHOTIP protocol for FICCs		
Tip navigation	7–12 MHz linear probe (femoral and external iliac veins) 3–8 MHz convex probe (inferior vena cava)	Visualization of wire/catheter inside the veins of the lower limb according to the RaFeVA protocol. Visualization of wire/catheter inside the subdiaphragmatic tract of the inferior vena cava, using the transhepatic view.
Tip location	2–6 MHz sectorial probe or 3–8 MHz convex probe	Tip in inferior vena cava: immediate visualization (<500 ms) of the bubbles in the subdiaphragmatic tract of the inferior vena cava (using the transhepatic view). Tip in right atrium: immediate visualization (<500 ms) of the bubbles in the right atrium (using the subcostal views). Alternative option: immediate visualization of micro-embolic signals by pulsed wave doppler.

CICCs: centrally inserted central catheters; PICCs: peripherally inserted central catheters; FICCs: femorally inserted central catheters; RaCeVA: rapid central vein assessment; RaPeVA: rapid peripheral vein assessment; RaFeVA: rapid femoral vein assessment.

used successfully for the diagnosis of right-to-left cardiac shunt, based on the detection of at least one micro-embolic signal in the middle cerebral or the carotid artery following saline injection.[33]

This variant of the bubble test has been reported in a small case series (eight patients), as a possible method of tip location during central venous catheterization.[16] In this study, the reading of pulse wave doppler at the level of the tricuspid valve was used for detecting the passage of micro-embolic signals following rapid injection of saline through the catheter. Micro-embolic signals are high-intensity signals within the doppler spectrum, and they can be regarded as the acoustic equivalent of the micro-bubbles. The study included six patients with sinus rhythm and two with atrial fibrillation. Seven patients were examined using a subcostal view, whereas one was examined using an apical four-chamber view. One patient had a femorally inserted central catheter (FICC) inserted at mid-thigh, while the others had a PICC. The results showed a strong agreement between the reference standard method of tip location (intracavitary ECG) and the ultrasound-based tip location by pulsed wave doppler, as well between the pulsed wave doppler and the standard bubble test (detection of both micro-embolic signals and micro-bubbles within 1 s after infusion).

The detection of micro-embolic signals by pulse wave doppler may have some advantages if compared to the standard bubble test based on the appearance of micro-bubbles, possibly increasing the sensitivity and specificity of the procedure: (a) the time delay between start of the infusion and appearance of the flow in the right atrium can be accurately defined, since the appearance of specific signals in the pulsed wave spectrum is more evident than the appearance of bubbles in B-mode ultrasound; (b) on pulsed wave doppler, the operator receives both a visual and an acoustic feedback, which may help to identify with the greatest certainty the result of the test. The accuracy and reliability of the pulse waved doppler must still be verified in more extensive prospective studies, so to standardize the technical details and further confirm the specificity and sensitivity of the method not only for detecting the bubbles in the right atrium (during placement of CICCs and PICCs) but also in the inferior vena cava (during placement of FICC; see Figure 1). However, pulse wave doppler appear quite promising and deserved a mention in the updated

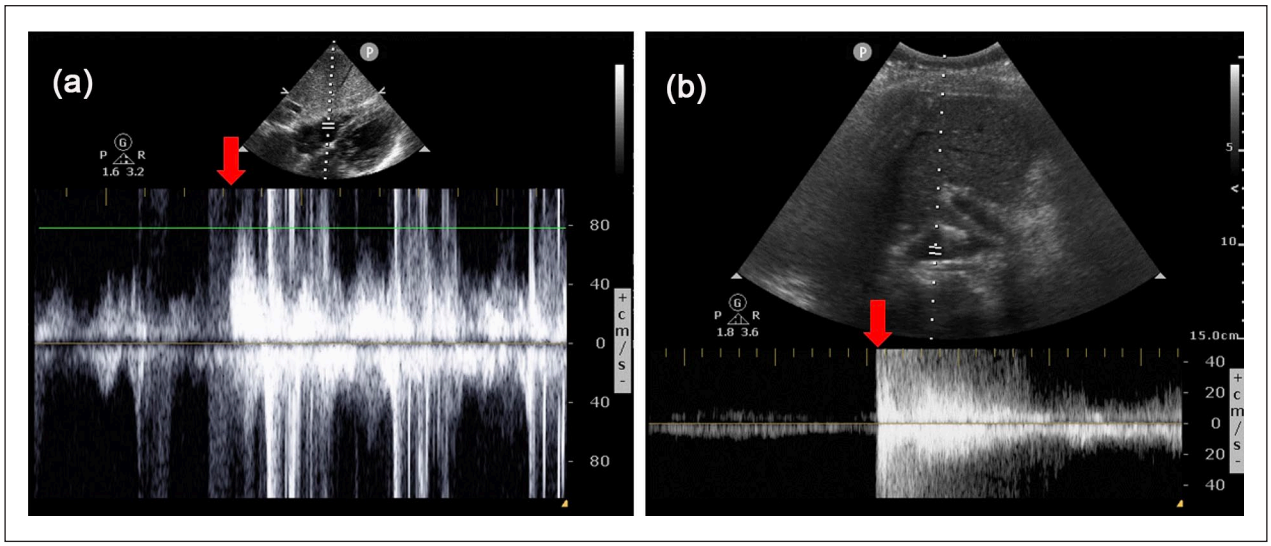


Figure 1. Example of bubble test with pulsed wave doppler: (a) subcostal view with pulsed doppler at the level of the tricuspid valve: the micro-embolic signals appear immediately after injection (red arrow) and (b) trans-hepatic view with pulsed doppler in the inferior vena cava: the micro-embolic signals appear immediately after injection (red arrow).

version of the ECHOTIP protocol, ECHOTIP-2, as a complementary method for the detection of the micro-bubbles during the bubble test.

Trans-hepatic visualization of the inferior vena cava

In recent years, the use of FICCs has become increasingly widespread in clinical practice, initially driven by the needs dictated by the COVID-19 pandemic, and subsequently due to the evidence of a favorable risk/benefit ratio in many patient populations.[21,34,35]

Thus, accurate methods of tip location during FICC insertion have been investigated. Radiological methods (intra-procedural fluoroscopy and post-procedural X-ray of the abdomen) are quite inaccurate, since the position of the tip is estimated indirectly on the basis of radiological landmarks, which are quite uncertain and variable from patient to patient. Thus, whether the tip is at the junction between right atrium and inferior vena cava or in the sub-diaphragmatic tract of the inferior vena cava can only be guessed with a large margin of uncertainty.

Also, both intraprocedural fluoroscopy and post-procedural X-ray are unsafe, since they imply radiological exposure; furthermore, they may fail to identify the malposition of the tip of the FICC inside the right ascending lumbar vein.[21,36]

Therefore, when the tip of the FICC is planned to be in the right atrium or at the junction between right atrium and inferior vena cava, ultrasound-based tip location using the subcostal view is probably the best option; the position of the tip in the middle of the right atrium can also be accurately verified by intracavitary ECG (mid-atrium = presence of biphasic P wave). Such tip location methods have been used—for example—in neonatal intensive care unit and pediatric intensive care unit during FICC insertion.

Though, in many adult patients the planned position of the tip of the FICC may be the subdiaphragmatic tract of the inferior vena cava, rather than the right atrium. In this situation, the ideal method of tip location is ultrasound, adopting the transhepatic window.

This acoustic window has already been described in the literature, but it has often been considered only as a "rescue" window in case of inaccessibility of the sub-xiphoid area.[37] Recently, Annetta et al. have proposed the use of the trans-hepatic acoustic window (more precisely: "the right transhepatic coronal long axis view") as a reliable and easy method of tip location during FICC placement.[21–23] The transhepatic window allows for the visualization of the catheter inside the inferior vena cava, in the tract between the renal veins and the hepatic veins (see Figure 2). If the direct identification of the tip is uncertain, the bubble test may be used.

This new technique of ultrasound-based tip location during FICC placement is characterized by high applicability (97.6%) and feasibility (100%)[22,23] and it is relatively easy to learn. It is performed using a 2–6 MHz sectorial probe or 3–8 MHz convex probe, placed longitudinally between the anterior and middle axillary lines, at the 9th or 10th intercostal space. Then, the probe is tilted so to visualize the inferior vena cava in its long axis, below the liver, from the junction with the hepatic veins—that can be easily detected inside the liver parenchyma—and the right kidney. If the catheter has reached the subdiaphragmatic tract of the vena cava above the renal veins, the catheter can be easily detected in most cases. If the catheter is not clearly identified, a rapid injection of 5–10 ml of agitated saline can be administered through the catheter to confirm



Figure 2. Direct visualization of the tip of the catheter inside the subdiaphragmatic vena cava, through a trans-hepatic view using a convex probe.

tip placement by bubble test. The direct visualization of the micro-bubbles coming out of the catheter tip confirms the correct placement of the tip in this tract. An immediate appearance of the bubbles (<500 ms) coming from below suggests the tip is just below this segment. A delayed appearance of the bubbles (>500 ms after injection) suggests the location of the tip below the renal veins, either in the lower tract of the inferior vena cava (suboptimal but acceptable central position) or in the iliac veins, or elsewhere (malposition); noteworthily, a catheter looped or coiled within the inferior vena cava will also be associated with a delay in the appearance of the bubbles. If no flush is seen, the tip might be inside the right atrium: a subxiphoid view may detect the tip in this area, and the catheter can be retracted until the tip is visualized in the tract of inferior vena cava between the renal and hepatic veins.

The technique is simple, accurate, and easy to learn. It has been included in the current update version of the ECHOTIP protocol.

Conclusion

Ultrasound-based tip location is a relatively new and promising field of investigation. Studies of the last decade have shown that ultrasound-based tip location is safer, more accurate, and more cost-effective than radiological methods,[1,2] and that it should be considered as an alternative option to intracavitary ECG, in those situations where the intracavitary ECG is not applicable or not feasible.[3] Considering that the main defect of such methodology was the lack of standardization, 5 years ago GAVeCeLT developed detailed protocols[6–8] which reported which probe, which acoustic window and which technique were recommended for detecting tip location in different types of central venous access devices (CICCs, PICCs, or FICCs, either tunneled or non-tunneled; dialysis catheters; ports; etc.) and in different populations of patients (neonates, children, adults). Though, the progress in this field have been so rapid that an update of such protocols became necessary, particularly of the adult protocol (ECHOTIP),[8] in regards of some technical aspects of the procedure of bubble test and of the application of the method to FICCs.

The updated protocol (ECHOTIP-2) is summarized in Table 1. The basic recommendations for tip navigation have not been changed, and are still based on the standardized protocols for ultrasound evaluation of the vasculature developed by GAVeCeLT: the Rapid Central Vein Assessment (RaCeVA),[38] the Rapid Peripheral Vein Assessment (RaPeVA),[12] and the Rapid Femoral Vein Assessment (RaFeVA).[39] In the recommendations about the interpretation of the bubble test, the cut-off for the definition of "immediate visualization" has been changed from 1–2 s to 500 ms. The pulsed wave doppler (visualization of the micro-embolic signals in the right atrium) has been added as possible alternative to the standard bubble test (visualization of the micro-bubbles in B-mode ultrasonography) for tip location of CICCs and PICCs. The transhepatic acoustic view has been included as main option for the visualization of the tip of FICCs in the subdiaphragmatic tract of the inferior vena cava.

It is quite likely that further clinical studies will bring new information, so that the ECHOTIP-2 should be regarded as a work in progress, and not as a final statement of permanent validity; still, it represents the state of the art of ultrasound-based tip navigation and tip location, and it can be used as a guide for the standardization of clinical

practice, as a tool during the training of venous access clinicians, and also as a reference for future scientific studies in this field.

Author contributions

All the authors had an active part in the construction of this update version of the ECHOTIP protocol, writing sections of the manuscript and searching for the related bibliography. The draft of the complete manuscript was written by MGA and MP. All the authors revised and approved the final manuscript.

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