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An Italian expert consensus on the choice of the method of tip location for central venous access devices

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Abstract

Tip location of central venous access devices is considered highly relevant for the purpose of reducing catheter-related complications and prolong the duration of the access. Though, the choice of the method of tip location currently relies upon the operator's experience, preference, and training, on the local availability of specific resources and technologies, and on local policies. On the contrary, considering the relevance of tip location, such clinical choice should preferably be based on the best available evidence. Though current guidelines recommend intra-procedural rather than post-procedural methods of tip location, many clinicians still adopt the strategy of assessing the position of the tip by radiological methods after the completion of the procedure. Also, though current guidelines and evidence-based documents recommend the intra-cavitary electrocardiography and/or trans-thoracic echocardiography as preferred methods of intraprocedural tip location, many clinicians still adopt fluoroscopy. While the pros and cons of each different method of tip location are well known, there is no evidence-based document that offer robust recommendations about the choice of tip location of different central venous access devices in different population of patients (neonates, children, adults). Therefore, the Italian Group of Long-Term Venous Access Devices (GAVeCeLT) and the Italian Vascular Access Society (IVAS) have

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developed a national consensus on the choice of the most appropriate method of tip location. After a systematic review of the available evidence, the panel of the consensus (which included 22 Italian experts with documented competence in this area) has provided structured recommendations answering six key questions regarding the choice between intra-procedural and post-procedural tip location, as well as the appropriate indication of the four different methods of intra-procedural tip location currently available (trans-esophageal echocardiography, trans-thoracic echocardiography, intracavitary electrocardiography, and fluoroscopy). Only statements reaching a 100% agreement were included in the final recommendations.

Keywords

Central venous catheterization, peripherally inserted central catheters, umbilical venous catheters, epicutaneo-cava catheters, port, tip location, fluoroscopy, intracavitary electrocardiography, trans-esophageal echocardiography, trans-thoracic echocardiography

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Introduction

The proper tip location of central venous access devices (CVADs) is of paramount important for the purpose of reducing complications and prolong the duration of the access.[1–4]

Historically, the most widely adopted method of tip location has been the post-procedural radiological examination: though quite inaccurate, since it is based on radiological landmarks,[5,6] such method has been used for all types of CVADs, either in neonates, in children, or in adults, both for CVADs coming from the superior vena cava (centrally inserted central catheters, peripherally inserted central catheters, chest-ports, brachial ports, epicutaneo-cava catheters inserted in vein of the upper limb or of the scalp) and for CVADs coming from the inferior vena cava (femorally inserted central catheters, umbilical venous catheters, femoral ports, epicutaneo-cava catheters inserted in vein of the lower limb).

Though, current guidelines recommend that the proper location of the tip should be assessed during the insertion of the device (intra-procedural tip location) rather than after the maneuver (post-procedural tip location).[1–4] Thus, there are four options for intra-procedural tip location: trans-esophageal echocardiography (TEE), trans-thoracic echocardiography (TTE), intracavitary electrocardiography (IC-ECG), and fluoroscopy.

(1) TEE is used for tip location only in very selected cases, since it is invasive and expensive, as it implies the insertion of a trans-esophageal probe; nonetheless, it is considered the most accurate method of tip location, at least for CVADs with the tip located inside the right atrium or at the junction between superior vena cava and right atrium;
(2) TTE is a non-invasive, accurate method that can be adopted for assessing the location of the tip in the right atrium or in the superior vena cava (using subcostal or apical acoustic windows),[7] but also in the inferior vena cava (using a trans-hepatic acoustic window)[8–10]; it should be preferably coupled with the so-called “bubble test” (a rapid injection of saline, which is associated with the appearance of micro-bubbles at the tip of the CVAD); the bubble test increases the accuracy of TTE and it allows the location of the tip even when it is not included in the acoustic window, by estimating the delay between the injection of saline and the appearance of microbubbles[7];
(3) IC-ECG is an old method of tip location developed in Europe in the last decades of the 20th century, and then introduced into clinical practice in many non-European Countries in the last 15 years[11]; it is a very accurate method—many studies suggest that it may be as accurate as TEE[12]—but it can be applied mainly to CVADs coming from the superior vena cava; also, in its original form, it can be applied only to patients with sinus rhythm; only recently, a “modified” IC-ECG method has been developed, which can be useful in patients with atrial fibrillation[13];
(4) fluoroscopy is a very old method of tip location with no clinical advantage and many disadvantages[1–4,14,15]: it is inaccurate (since it is based on radiological landmarks), expensive (since it requires expensive equipment and dedicated environment), and unsafe (since it implies x-ray exposure of both the patient and the clinician); though, it is still adopted by some centers for insertion of CVADs such as chest-port and dialysis catheters.

At present, national and international guidelines offer conflicting recommendations about the choice of the most appropriate method of tip location. While the most recent guidelines discourage the use of fluoroscopy and of post-procedural x-ray,[1–3,16] other guidelines and hospital policies still leave to the clinicians the choice of the method of tip location, based on their experience or preference.[17]

This is somehow inappropriate, since many clinical studies of the last two decades have addressed clearly the pros and cons of each method. In fact, to achieve maximal patient safety and maximal accuracy of the procedure, it is advisable to develop a frame of recommendations stating which are the most appropriate methods of tip location in different clinical situations.

With this purpose in mind, the Italian Group of Long-Term Venous Access Devices (GAVeCeLT) and the Italian Vascular Access Society (IVAS) have decided to develop a joint consensus document that may assist the clinicians in the choice of the safest, most accurate, and most cost-effective method of tip location in different categories of patients requiring a CVAD.

To achieve a comprehensive document, we chose to expand the field of our investigation to include any type of CVAD (i.e. any venous access device with the tip located in the superior vena cava, or in the right atrium, or in the inferior vena cava), in any population of patients (neonates, children, and adults), both in emergency and non-emergency clinical settings.

Methods

Considering the impact of this topic on the daily clinical practice but an expected low grade of evidence, a consensus of experts was thought to be the most appropriate tool for providing robust recommendations on the choice of the method of tip location. The consensus was promoted by the Italian Group of Long-Term Venous Access Devices (GAVeCeLT) and by the Italian Vascular Access Society (IVAS) and coordinated by the GAVeCeLT chairman (MP) and by the IVAS chairman (VF). The consensus was structured and conducted by a clinician expert in methodology (DGB) following the ACCORD checklist (ACCORD =ACCurate COnsensus Reporting Document), a guideline for consensus methods developed via a modified Delphi.[18]

Panel composition

The Steering Committee was composed by the two co-chairs (MP and VF) and a methodologist (DGB). The Committee decided the methodology, drafted the protocol, established the criteria for panelists' selection, identified the items and managed the voting process.

A panel of experts was identified, choosing the panelists among Italian vascular access experts having both established clinical know-how and research activity in the field of tip location of venous access devices. The latter criterion consisted in at least three published papers on peer-reviewed journals about tip location of central venous access devices in the last 5 years: 21 experts were identified as potential panelists and all of them accepted the task. The experts' panel included clinicians with significant clinical experience in different population of patients (neonates, children, adults) and different settings (oncology, intensive care, parenteral nutrition, emergency, etc.). No patient or caregiver representatives were invited due to the technical and specific nature of the consensus. Before starting the voting process, two members of the panel left the working group, so that the final number of invited panelists consisted in 19 experts.

Literature search

Initially, a literature search was performed independently by the chairs of the panel (MP, and VF), with the assistance of a clinician with specific experience in bibliography search (GP). The search was carried out using PubMed, EMBASE, OVID, Elsevier, and Cochrane Library, evaluating all randomized and observational studies on tip location of central venous access devices published in English language from January 2010 to April 2024. Keywords such as "central venous catheter," "tunneled catheter," "dialysis catheter," "peripherally inserted central venous catheter," "centrally inserted central catheter," "femorally inserted central catheter," "ports," "umbilical venous catheter," etc., were matched with "tip location," "intracavitary ECG," "fluoroscopy," "echocardiography," and others. References of articles, previous reviews, and meta-analyses were also analyzed, so as not to miss relevant papers. Case reports and conference abstracts were excluded. The two chairs independently verified inclusion and exclusion criteria. Discrepancies were solved by discussion within the Steering Committee. A total of 138 papers were retrieved, in different population of patients (41 in neonates, 13 in children, 84 in adults).

Clinical questions and voting process

The consensus process was carried out according to the RAND/University of California at Los Angeles (UCLA) Appropriateness Methodology as a three-step consensus process.[19] The method is a modification of the Delphi method, a structured process for collecting knowledge from groups of experts through a series of questionnaires. First, the coordinators of the panel proposed to develop the document as answers to six questions regarding tip location of central venous access: (1) In which cases is intraprocedural tip location of CVADs indicated? (2) In which cases is post-procedural tip location of CVADs indicated? (3) In which cases is the IC-ECG method indicated? (4) In which cases is tip location by fluoroscopy indicated? (5) In which cases is tip location by TEE indicated? (6) In which cases is tip location by TTE with bubble test indicated?

After a preliminary email-based discussion, the whole panel agreed to structure the recommendations as answers to these six questions, which were formally approved by each panelist. Based on the collected literature—which had been previously shared with the whole panel—the two coordinators wrote a preliminary draft of statements, specifically answering the six questions. These preliminary statements were e-mailed to the whole panel; each panelist was asked to state anonymously her/his level of agreement with each statement using a 5-points Likert scale (strongly disagree, disagree, uncertain, agree, strongly agree) and to provide additional comments, or propose changes to the statements, especially in cases of uncertainty. The Likert-type scale was classified as "agreement/support/appropriate" (median score 4–5 and with no individual score <4), "uncertainty" (median score 3), or "disagreement/rejection" (median score 1–2). Consensus was reached when 80% or more of the voting panelists assigned a score within the 1–2 or 4–5 ranges, which rejected or accepted the statements, respectively.

After collecting the answers of each member of the panel, a first web-based meeting was organized, and all the controversies were discussed collegially. At this point, a second document was arranged, modifying the statements according to the suggestions of the panel, and presented to the panel for approval. After a second web-based meeting, the final statements were defined and a second survey was sent to each panelist, asking each one to state anonymously her/his level of agreement with each new statement using the same 5-points Likert scale (strongly disagree, disagree, uncertain, agree, strongly agree). Panelists were encouraged to provide written comments for their responses, which were then circulated to facilitate informed discussions. In cases where consensus was not achieved, the Steering Committee reviewed the contentious items, considered the underlying evidence, and proposed revised statements for further voting. After two rounds of voting, all statements received >80% of score in the range of 4–5 (agree or strongly agree), so all of them were included in the recommendations. After the final vote, a preliminary manuscript was drafted and sent to the whole panel for review and final approval.

The results of the consensus are presented in the following section, question by question, offering the background knowledge behind each question, the recommendations of the panel, plus some special additional considerations that the panel considered relevant for the proper translation of these recommendations into clinical practice.

Results

Question #1: In which cases is intraprocedural tip location of CVADs indicated?

Background. According to the most recent guidelines,[1–3,16,20] assessment of tip location should be performed during any maneuver of central venous catheterization. The two most popular intra-procedural methods, IC-ECG and TTE, are simple and rapid enough to be performed in most cases—even when the central access is placed in emergency[21]—since they require just an ECG monitor with a sterile cable (IC-ECG) or a sectorial or convex ultrasound probe (TTE). Though, in conditions of extreme emergency (i.e. during resuscitation maneuvers) tip location may be impossible or difficult to perform. In such conditions, the assessment of the location of the tip of a centrally inserted central catheter (CICC) in adults or children or of an umbilical venous catheter (UVC) in neonates should be postponed. If the CVAD has been inserted in extreme urgency, without the proper strategies of infection prevention (hand hygiene, appropriate skin antisepsis, maximal barrier precautions), the post-procedural tip location may be even omitted, since the device must be removed within 24–48 h, as recommended by current guidelines.[2,3]

Panel recommendation

Statement 1.1: Intraprocedural verification of tip position is always indicated: it should be performed during insertion/implantation of any CVAD, whether in neonate, child, or adult, whether in election or emergency, with the possible exception of CVADs inserted under conditions of extreme clinical emergency (e.g. UVC placement during neonatal resuscitation or CICC placement in children/adults in cardiorespiratory arrest).

(100% agreement: 95.5% strongly agree, 4.5% agree)

Special considerations

- If insertion has occurred under conditions of extreme clinical emergency, it is best to (a) perform a post-procedural tip location as soon as allowed by the patient's condition (see below) or (b) remove the device.
- Urgent placement of a 20- to 25-cm femoral catheter in an adult patient does not necessarily involve tip location, since such a device is unlikely to reach the inferior cava and it cannot be classified as "central."

Question #2: In which cases is post-procedural tip location of CVADs indicated?

Background. Post-procedural tip location soon after insertion of the CVAD is acceptable as alternative option only when intra-procedural methods of tip location could not be adopted.[2,3] Furthermore, tip location may be required not only during/after insertion, but also after some time, in case of suspected inappropriate position of the tip: for example, in case of malfunction,[22] or in case of dislodgment of the external tract of the catheter,[2] or in some

CVADs with notoriously high risk of tip migration, such as epicutaneo-cava catheters (ECC) or UVCs in the neonate.[23,24] Though the literature on this issue is scarce, the panel has agreed on a list of indications to post-procedural tip location.

Panel recommendation

Statement 2.1: Post-procedural tip location is indicated:

a. **When intraprocedural tip location was impossible due to clinical emergency.**
b. **In rare but possible cases in which the main intraprocedural tip location methods (IC-ECG and TTE) were both found to be inapplicable or infeasible or associated with uncertain results.**
c. **In case of a CVAD placed in another hospital, or not used for a long time, or with history of previous tip migration (secondary tip malposition).**
d. **In case of device malfunction (e.g. persistent withdrawal occlusion).**
e. **In the case of dislocation of the extracutaneous tract of the device (unless the dislocation is obviously incompatible with a central position of the tip).**
f. **In the newborn with CVADs at high risk of dislocation and/or tip migration, such as UVC (where tip location should be checked every 48 h) or ECC (where tip location should be checked weekly).**
g. **In infants/children with long-term CVADs whose tip may no longer be central, due to patient growth.**

(100% agreement: 95.5% strongly agree, 4.5% agree)

Special considerations

- Post-procedural control may be conducted by different methods, with preference given to control by TTE with bubble test (accurate, rapid, safe, bedside, inexpensive) over radiological control (less accurate, logistically more challenging, more expensive, and unsafe). Radiologic control may be indicated in cases where TTE with bubble test is negative or not applicable or not feasible, or in cases where the integrity of the catheter and its entire trajectory must also be investigated.
- In the newborn, post-procedural tip location of CVADs is exclusively performed by TTE (with or without bubble test).
- Post-procedural tip location by IC-ECG is applicable only in case of external catheters in which at least one lumen has only one distal opening (this excludes ports and chronic dialysis catheters with multi-fenestrated lumens); moreover, the accuracy of the method is limited in the post-procedural setting, because dynamic interpretation of P-wave changes during intravascular catheter movements is not possible.

Question #3: In which cases is the IC-ECG method indicated?

Background. Most current guidelines recommend IC-ECG as the first option for intra-procedural tip location,[1–3,16] but only if the tip of the CVAD must be located at the junction between superior vena cava and right atrium (maximal P wave) or in the right atrium (biphasic P wave). If the tip of a catheter inserted via the inferior vena cava must be located in the sub-diaphragmatic cava or at the junction between inferior vena cava and right atrium, IC-ECG cannot be adopted because the pattern of P changes associated with these two locations of the tip is unpredictable.[12]

The accuracy, safety and cost-effectiveness of IC-ECG for tip location of PICCs and CICCs has been proven in many clinical studies in different population of patients and in different types of CVADs.[11,25–37] The recent introduction of wireless devices for IC-ECG[38] has made the method easily available at bedside also in non-intensive ward.

As mentioned above, the development of a modified IC-ECG method for atrial fibrillation[13,39] has further expanded the applicability of the method. Nonetheless, in atrial fibrillation and in any situation where the results of IC-ECG are uncertain or questionable, it is wise to adopt also TTE.[7]

For ECC inserted in veins of the scalp or of the upper limb, IC-ECG is applicable,[40–42] but may not always be feasible, so that TTE is considered the first option.

Tip location by IC-ECG has been included in the insertion bundles of different types of CVADs: PICC,[43] CICC,[44] FICC,[45] port,[46] and PICC-port,[47] ultrasound-guided CVADs in neonates and children.[48,49]

Panel recommendation

Statement 3.1: The IC-ECG method is recommended as the intraprocedural method of first choice for the tip location of any CVAD whose tip is to be placed near the junction between superior vena cava and right atrium, or inside the right atrium (with the exception of ECC in the newborn).

- In its conventional version, the method is applicable only when a P wave is well identifiable on the surface ECG tracing.
- In its modified version, the IC-ECG method is applicable in atrial fibrillation, if f-wave amplitudes are clearly distinguishable; however, in such a situation it is also recommended to combine the

modified IC-ECG method with an intraprocedural tip location by TTE with bubble test, or—if this is not applicable or not feasible—with a post-procedural radiological tip location.
- The IC-ECG method is also applicable in ECC from the superior vena cava, although in this case the method of first choice is TTE with bubble test.

(100% agreement: 90.9% strongly agree, 9.1% agree)

Special considerations

- The IC-ECG method is accurate, inexpensive, requires minimal training, and is completely harmless.
- If applicable, IC-ECG is therefore the first option—in the infant, child, and adult—for CICCs, for PICCs, for FICCs whose tips must be placed in the right atrium, for chest ports, for brachial ports, and for dialysis catheters whose tip must be placed in the right atrium;
- IC-ECG is not appropriate for CVADs whose tip is to be placed at the junction between inferior vena cava and right atrium (e.g. UVC in the newborn) or in the subdiaphragmatic inferior cava (e.g. FICC-port, or FICC to be used only for infusions and withdrawals but not for hemodynamic monitoring);
- IC-ECG is theoretically applicable in the newborn for tip location of ECC from the superior cava, but often—in terms of feasibility—tip location by TTE and bubble test is preferable;
- The preferred technique for performing the IC-ECG method is the column of saline technique rather than the metal guide technique; the first technique can be easily performed on any CVADs with any ECG monitor, as long as a dedicated sterile cable is available.

Question #4: In which cases is tip location by fluoroscopy indicated?

Background. Most current guidelines recommend to limit the use of fluoroscopy as much as possible, so to reduce the x-ray exposure of patients and clinicians and to save time and resources.[1–3,16] Unnecessary fluoroscopies should be particularly avoided in neonates, infants, and children, who might receive the worst damage from x-ray exposure.[16,50–53]

Panel recommendation

Statement 4.1: Fluoroscopy is generally contraindicated for intraprocedural tip location because (a) it has lower accuracy than IC-ECG and TTE, (b) it is potentially harmful because it exposes both patient and operator to radiation, and (c) it is burdened with significant use of resources (high cost, dedicated room, etc.).

(100% agreement: 90.9% strongly agree, 9.1% agree)

Statement 4.2: In the newborn, the use of fluoroscopy for the purpose of tip location of central venous accesses is never justified.

(100% agreement: 90.9% strongly agree, 9.1% agree)

Statement 4.3: In children and adults, tip location by fluoroscopy may be indicated only in extremely complex cases, such as in some placements of permanent dialysis catheter, (a) if fluoroscopy is necessary for tip navigation, or (b) if simultaneous use of angiographic visualization techniques and/or interventional radiology techniques is planned at the same time as CVAD placement. In these situations, considering the inaccuracy of fluoroscopy as a method of tip location, it is wise to supplement the maneuver—where applicable and feasible—with a tip location by IC-ECG and/or TTE with bubble test.

(100% agreement: 90.9% strongly agree, 9.1% agree)

Special considerations

- The new ultrasound techniques for tip navigation and tip location have now made fluoroscopy unnecessary in the vast majority of cases, considering that both IC-ECG and TTE with bubble test are more accurate, more innocuous, and more cost-effective.
- Fluoroscopy may have a role in the placement/repositioning of cuffed-tunneled catheters for chronic hemodialysis, where the insertion maneuver involves visualization and/or treatment of venous stenosis or other obstacles to catheter progression.

Question #5: In which cases is tip location by TEE indicated?

Background. TEE allows a perfect visualization of the right atrium and of the final tract of the superior and inferior vena cava, as much as a clear visualization of the tip of the catheter. The anatomic landmark of the junction between superior vena cava and right atrium, the crista terminalis, is also visualized clearly, so that the tip of the catheter can be placed with the utmost precision in this location.[53,54]

Being invasive and expensive, TEE has been used only rarely as method of tip location, though it has been used in several clinical studies as "gold standard" to confirm the accuracy of IC-ECG[53] and of TTE.[54]

Panel recommendations

Statement 5.1: Intraprocedural tip location by TEE, while being the "gold standard" in terms of accuracy (if the tip location is planned at the superior cavo-atrial junction, in the right atrium, or at the inferior cavo-atrial junction), has limited clinical indications because it is invasive, expensive, potentially associated with complications, and because it requires specific training.

(100% agreement: 90.9% strongly agree, 9.1% agree)

Statement 5.2: In the newborn, intraprocedural tip location by TEE may have indication only in exceptional cases.

(100% agreement: 90.9% strongly agree, 9.1% agree)

Statement 5.3: Intraprocedural tip location by TEE has potential indication in children and adults, limited to those rare cases where insertion of a CVAD and placement of a transesophageal ultrasound probe are simultaneously indicated.

(100% agreement: 86.4% strongly agree, 13.6% agree)

Special considerations

- Tip location by TEE has been used in clinical trials as a reference method to verify the accuracy of other methods;
- Current clinical indications of tip location by TEE include only certain cardiac surgeries or interventional radiology procedures that also require central venous access.

Question #6: In which cases is tip location by TTE with bubble test indicated?

Background. In the first 20 years of our century, tip location by TTE has been investigated in many clinical studies carried out in adult patients,[55–71] in children,[72–75] and in neonates.[76–85]

The advantages of the method (the accuracy, non-invasiveness, repeatability, and the ability to be used during the procedure) were immediately clear. The method was later improved by the standardization of the technique (in terms of probes and acoustic windows) and by the addition of the so-called bubble test, which allows better identification of the tip position, even if the tip is not framed in the acoustic window, since the delay in the appearance of microbubbles after the rapid injection of physiologic allows estimation of the distance between the tip and the acoustic window.[7,54,86–96] The "bubble test" implies a minimal infusion of micro-bubbles of air and it is considered harmless.[97]

The most structured attempt in standardizing the technique of TTE with bubble test in different settings of patients and devices has led to the development of the so-called ECHOTIP protocols in neonates,[98] in children,[99] and in adults.[100] One of the key points currently under standardization is the interpretation of the delay between injection and appearance of the microbubbles: the most recent evidence suggests that a delay of 500 ms or less is associated with a distance <1 cm between tip and site of appearance of the bubbles.[91,96,101,102]

Also, if compared to all the other methods (TEE, IC-ECG, fluoroscopy), TTE is very accurate in the assessment of tip location of femoral CVADs (FICC and femoral ports), since it allows a proper visualization of the subdiaphragmatic tract of the inferior vena cava (trans-hepatic window) and of the junction between inferior vena cava and right atrium (subcostal window).[8–10]

In addition, TTE is also a method of tip navigation: that is, it allows to follow the path of the catheter into the vasculature during the maneuver.[103] Ultrasound is the most accurate, simplest, and most cost-effective method of tip navigation, compared to fluoroscopy (inaccurate, expensive, potentially harmful), or electromagnetic methods (inaccurate and expensive),[104] or pressure-based methods.[105] In the most recent literature, the combined used of ultrasound for intraprocedural tip navigation and tip location is particularly recommended in neonates during ECC and UVC insertion[106–115] as well in children requiring any type of CVAD.[14,15,48]

In many clinical situations, the simultaneous use of IC-ECG for tip location and of TTE for tip navigation and tip location may be the optimal solution in terms of accuracy and cost-effectiveness, avoiding the need for post-procedural x-ray.[14,116]

Tip navigation and tip location by TTE has been included in the insertion bundles of different types of CVADs: UVC,[117] ECC,[118] PICC,[43] CICC,[44] FICC,[45] ultrasound-guided CVADs in neonates and children,[48,49] port,[46] PICC-port,[47] and femoral ports.[119]

Panel recommendation

Statement 6.1: Intraprocedural tip location by TTE is indicated as the first option in the following situations:

- **In the newborn, for the tip location of UVC, ECC, FICC;**
- **for the tip location of ultrasound-guided CICC in the newborn (in this case, both TTE and IC-ECG may be considered equally appropriate);**
- **in children and adults, for any FICC or FICC-port, if the tip is planned to be either in the right atrium or at the junction of the inferior cava and right atrium or in the subdiaphragmatic cava;**

Table 1. Summary of panel recommendations: indications of intra- and post-procedural tip location.

Intra-procedural tip location

Intraprocedural verification of tip position is always indicated: it should be performed during insertion/implantation of any CVAD, whether in neonate, child, or adult, whether in election or emergency, with the possible exception of CVADs inserted under conditions of extreme clinical emergency (e.g. UVC placement during neonatal resuscitation or CICC placement in children/adults in cardiorespiratory arrest).

Post-procedural tip location

Post-procedural tip location is indicated:

- When intraprocedural tip location was impossible due to clinical emergency.
- In rare but possible cases in which the main intraprocedural tip location methods (IC-ECG and TTE) were both found to be inapplicable or infeasible or associated with uncertain results.
- In case of a CVAD placed in another hospital, or not used for a long time, or with history of previous tip migration (secondary tip malposition).
- In case of device malfunction (e.g. persistent withdrawal occlusion).
- In the case of dislocation of the extracutaneous tract of the device (unless the dislocation is obviously incompatible with a central position of the tip).
- In the newborn with CVADs at high risk of dislocation and/or tip migration, such as UVC (where tip location should be checked every 48 h) or ECC (where tip location should be checked weekly).
- In infants/children with long-term CVADs whose tip may no longer be central, due to patient growth.

- **in children and adults, for any CICC, PICC, chest-port, or PICC-port, when IC-ECG has limitations in its applicability and/or feasibility, or as a complement to the IC-ECG method in cases where interpretation is uncertain.**

(100% agreement: 95.5% strongly agree, 4.5% agree)

Special considerations

- As much as IC-ECG, TTE is more accurate, more innocuous, and more cost-effective than fluoroscopy;
- Standardized protocols for the use of TTE, such as the ECHOTIP protocols developed by GAVeCeLT, are recommended;
- Similar to fluoroscopy, TTE can be used during the procedure for both tip navigation and tip location;
- Compared with IC-ECG method, TTE has the advantage of being also an easy method of post-procedural tip location, and of being applicable to all CVADs inserted through the inferior cava (ECC, FICC, FICC-port);
- On the other hand, compared with IC-ECG, TTE has the disadvantage of requiring more training; also, tip location by TTE may be less accurate than IC-ECG in children and adults.

Conclusions

The goal of the present consensus is to offer a systematic set of recommendations on the choice of the most appropriate method of tip location for CVADs. All CVADs—as defined and described in the recent international consensus document developed by WoCoVA/GloVANet[120]—were considered, in all populations of patients (neonates, children, adults).

Current tip location methods (IC-ECG, TEE, TTE, fluoroscopy) differ greatly in accuracy, safety, applicability, feasibility, and cost-effectiveness. Although these differences are well known and well documented in the literature, to the best of our knowledge this consensus is the first attempt to systematically address the choice of the most appropriate method of tip location by including every category of patients, from infants to adults, and every category of central venous access devices, in an attempt to offer recommendations that can be used in clinical practice (see Tables 1 and 2).

Review of the literature from the last decade clearly indicates the need for intraprocedural rather than postprocedural tip location: the strategy of blind placement of the catheter tip (based on surface landmarks) followed by inaccurate post-procedural tip location by x-ray (based on radiological landmarks) is now to be considered antiquated, potentially risky for the patient, and not cost effective.

Among the intraprocedural techniques, clinical studies of the past two decades have increasingly emphasized the need to use fluoroscopy only in very selected cases, in favor of IC-ECG and TTE. The IC-ECG method has now been validated by countless papers over the past three decades, and comparative studies using TEE as a reference have shown that tip location by IC-ECG is more accurate than radiological tip location. However, IC-ECG has limitations in applicability, and the development of tip location methods using TTE has opened up new possibilities. The most important and immediate application of tip location by TTE has been in CVADs in the newborn. Currently, it also finds clinical application in the child and adult, in all cases where the IC-ECG technique appears not applicable or not feasible.

Table 2. Summary of panel recommendations: indications of the different methods of tip location.

Intracavitary ECG (IC-ECG)
The IC-ECG method is recommended as the intraprocedural method of first choice for the tip location of any CVAD whose tip is to be placed near the junction between superior vena cava and right atrium, or inside the right atrium (with the exception of ECC in the newborn). In its conventional version, the method is applicable only when a P wave is well identifiable on the surface ECG tracing. In its modified version, the IC-ECG method is applicable in atrial fibrillation, if f-wave amplitudes are clearly distinguishable; however, in such a situation it is also recommended to combine the modified IC-ECG method with an intraprocedural tip location by TTE with bubble test, or—if this is not applicable or not feasible—with a post-procedural radiological tip location. The IC-ECG method is also applicable in ECC from the superior vena cava, although in this case the method of first choice is TTE with bubble test.

Fluoroscopy
Fluoroscopy is generally contraindicated for intraprocedural tip location because (a) it has lower accuracy than IC-ECG and TTE, (b) it is potentially harmful because it exposes both patient and operator to radiation, and (c) it is burdened with significant use of resources (high cost, dedicated room, etc.). In the newborn, the use of fluoroscopy for the purpose of tip location of central venous accesses is never justified. In children and adults, tip location by fluoroscopy may be indicated only in extremely complex cases, such as in some placements of permanent dialysis catheter, (a) if fluoroscopy is necessary for tip navigation, or (b) if simultaneous use of angiographic visualization techniques and/or interventional radiology techniques is planned at the same time as CVAD placement. In these situations, considering the inaccuracy of fluoroscopy as a method of tip location, it is wise to supplement the maneuver—where applicable and feasible—with a tip location by IC-ECG and/or TTE with bubble test.

Trans-esophageal echocardiography (TEE)
Intraprocedural tip location by TEE, while being the "gold standard" in terms of accuracy (if the tip location is planned at the superior cavo-atrial junction, in the right atrium, or at the inferior cavo-atrial junction), has limited clinical indications because it is invasive, expensive, potentially associated with complications, and because it requires specific training. In the newborn, intraprocedural tip location by TEE may have indication only in exceptional cases. Intraprocedural tip location by TEE has potential indication in children and adults, limited to those rare cases where insertion of a CVAD and placement of a transesophageal ultrasound probe are simultaneously indicated.

Trans-thoracic echocardiography (TTE)
Intraprocedural tip location by TTE is indicated as the first option in the following situations:

- In the newborn, for the tip location of UVC, ECC, FICC;
- for the tip location of ultrasound-guided CICC in the newborn (in this case, both TTE and IC-ECG may be considered equally appropriate);
- in children and adults, for any FICC or FICC-port, if the tip is planned to be either in the right atrium or at the junction of the inferior cava and right atrium or in the subdiaphragmatic cava;
- in children and adults, for any CICC, PICC, chest-port, or PICC-port, when IC-ECG has limitations in its applicability and/or feasibility, or as a complement to the IC-ECG method in cases where interpretation is uncertain.

All evidence-based documents that have addressed the issue of tip location of CVADs in the last 5 years[1,2,4,16] have provided recommendations which are aligned with the statements of our consensus, with special emphasis on the adoption of intra-procedural rather than post-procedural methods and on the preference for non-invasive rather than invasive methods.

Since the field of venous access devices is constantly evolving, we can expect further technological innovations also in the methods of tip location; such innovations are likely to be in the direction of greater accuracy, greater patient safety, but also better cost-effectiveness, considering the inevitable limitation of resources in healthcare.

Potential limitations and biases

The consensus is the selection included only Italian panelists, since the purpose was to develop a document immediately and appropriately applicable to the Italian clinical practice of venous access. Though, all the available literature in English language was considered, so that the results of the consensus—developed by experts with clinical experience and scientific publication in the field—may be valid and/or interesting also at an international level.

As for all documents produced according to the Delphi method, the consensus was potentially affected by different types of biases:

Fist, the selection of panelists may have introduced some degree of selection bias. To mitigate this, we ensured a diverse panel comprising experts from various Italian regions, clinical specialties, and practice settings. This approach aimed to balance perspectives and reduce the risk of dominance by a single group or viewpoint.

Also, panelists may have been inclined to favor recommendations that align with their pre-existing beliefs or clinical practices. To address this, we anonymized responses during the voting process and encouraged panelists to provide evidence-based justifications for their ratings. This approach promoted critical evaluation and reduced the influence of individual biases.

Another relevant bias in this type of document is that the desire for consensus may have led to "groupthink," where dissenting opinions were suppressed in favor of harmony. To minimize this risk, we actively encouraged open discussion of disagreements and provided opportunities for minority viewpoints to be heard and considered. Additionally, the use of anonymized voting helped ensure that panelists felt comfortable expressing dissenting opinions.

Last, the recommendations may have been influenced by the availability of published studies or the prominence of certain evidence. To address this, we conducted a comprehensive literature review and included both high-quality studies and real-world clinical experiences to inform the discussions.

To further reduce the impact of biases, we adopted transparency (the Delphi methodology, including the criteria for expert selection, voting process, and consensus thresholds, was clearly documented and reported) and iterative feedback (multiple rounds of voting and discussion allowed for refinement of recommendations and incorporation of diverse perspectives).

We acknowledge that while these measures significantly reduce the risk of bias, no consensus process is entirely free from its influence. By transparently addressing these potential biases, we aim to enhance the trustworthiness and applicability of the recommendations.

Author contributions

MP and VF contributed to the conception and design of the consensus and chair the panel. GP performed the literature research. DGB took care of the methodology. All the other authors had an active part in the construction of the recommendations of the consensus, as explained in the methods section. The first draft of the manuscript was written by MP, VF, and DGB. All authors read and approved the final manuscript.

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