Review

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A GAVeCeLT consensus on the indication, insertion, and management of central venous access devices in the critically ill

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Abstract

Central venous access devices are essential for the management of critically ill patients, but they are potentially associated with many complications, which may occur during or after insertion. Many evidence-based documents—consensus and guidelines—suggest practical recommendations for reducing catheter-related complications, but they have some limitations. Some documents are not focused on critically ill patients; other documents address only some special strategies, such as the use of ultrasound; other documents are biased by obsolete concepts, inappropriate terminology, and lack of considerations for new technologies and new methods. Thus, the Italian Group of Venous Access Devices (GAVeCeLT) has decided to offer an updated compendium of the main strategies—old and new—that should be adopted for minimizing catheter-related complications in the adult critically ill patient. The project has been planned as a consensus, rather than a guideline, since many issues in this field are relatively recent, and few high-quality randomized clinical studies are currently available, particularly in the area of indications and choice of the device. Panelists were chosen between the Italian vascular access experts who had published papers on peer-reviewed journals about this topic in the last few

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years. The consensus process was carried out according to the RAND/University of California at Los Angeles (UCLA) Appropriateness Methodology, a modification of the Delphi method, that is, a structured process for collecting knowledge from groups of experts through a series of questionnaires. The final document has been structured as statements which answer to four major sets of questions regarding central venous access in the critically ill: (1) before insertion (seven questions), (2) during insertion (eight questions), (3) after insertion (three questions), and (4) at removal (three questions).

Keywords
Critically ill, acutely ill, intensive care, central venous catheters, PICC, central venous access, dialysis catheters, ultrasound

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Introduction

Central Venous Access Devices (VAD) are essential for the management of critically ill patients, both in intensive care units (ICU) and in other sub-intensive or non-intensive settings. Though, central VAD are potentially associated with many complications,[1–4] which may occur during or after insertion, and which may be of different nature (infective, thrombotic, mechanical, etc.). Healthcare improvement programs and quality improvement strategies have been shown to be effective in preventing most of these complications, especially when there is proper compliance and proper adoption of evidence-based interventions.[5,6]

Many evidence-based documents—consensus and guidelines—address the effectiveness of such improvement strategies, with the purpose of offering good quality recommendations, but they have some limitations. Some evidence-based documents offer practical recommendations, but are not focused on critically ill patients[7]; other documents address only some particular aspects, such as the use of ultrasound[8]; other documents offer recommendations on management of central VADs in critically ill patients,[9,10] but are biased by obsolete concepts, inappropriate terminology, and lack of considerations for new technologies and new methods. The MAGIC paper,[9] released in 2015, still reports the antiquate concept that peripherally inserted central catheters (PICCs) may be contraindicated in ICU because of increased risk of catheter related thrombosis. Both the MAGIC paper and the more recent consensus published by the French Society of Intensive Care Medicine[10] ignore new technologies in the field of VADs—such as non-cuffed tunneled catheters, cyanoacrylate glue, micro-puncture kits, subcutaneous anchorage—and do not consider new methodologies such as ultrasound-based tip location or ultrasound-guided approach to the axillary vein or to the brachiocephalic vein or to the superficial femoral vein. Also, in many of these evidence-based documents, there is an ongoing confusion between venous approach and exit site, so that the approach to the subclavian vein is automatically and inappropriately identified with an exit site in the infraclavicular area, the approach to the internal jugular vein with an exit site in the cervical area, and the approach to the femoral vein to an exit site at the groin.

Thus, the Italian Group of Venous Access Devices (GAVeCeLT) has decided to offer an updated compendium of the main strategies—old and new—that should be adopted for minimizing catheter-related complications in the adult critically ill patient. The project has been planned with the methodology of a consensus, rather than a guideline, since many issues in this field are relatively recent, and few high-quality randomized clinical studies are currently available, particularly in the area of indications and choice of the device. The project has been focused only on adult patients, since pediatric and neonatal patients have special characteristics in terms of device and techniques of insertion and management, which cannot be extended to adults. Also, the consensus has been focused exclusively on central VADs, since a detailed summary of all the recommendations for indication, insertion, and management of peripheral VADs has already been published in a recent consensus developed by WoCoVA (World Conference of Vascular Access).[11] As suggested by current guidelines,[7,8,11] any venous access device that has its tip located inside the superior vena cava, the right atrium, or the inferior vena cava, has been considered a "central" VAD: this definition includes centrally inserted central catheters (CICC), peripherally inserted central catheters (PICC), and femorally inserted central catheters (FICC). The consensus has been planned so to address all aspects related to the indication, choice, insertion, management, and removal of central VADs in hospitalized critically ill patients.

Methods

Considering the limited evidence from high-quality studies for many issues concerning central venous access in the acutely ill, a consensus was thought to be the most appropriate tool for providing robust and detailed recommendations. The consensus was promoted and coordinated by two members of GAVeCeLT (MP and FP). A panel of experts was identified. Panelists were chosen between the Italian vascular access experts who had published papers on peer-reviewed journals about this topic in the last few

years: 24 experts were identified as potential panelists and all of them accepted the task.

The consensus was structured in different steps, mainly using e-mails and web-based meetings. Initially, a literature search was performed independently by the promoters of the panel (MP and FP), with the assistance of a clinician with specific experience in bibliography search (GP). The search was carried out using PubMed, OVID, Elsevier, and Cochrane Library, evaluating all randomized and observational studies on central venous access in the critically ill published in English language from January 2000 to April 2023. Keywords such as "venous catheter," "central venous catheter," "tunneled catheter," "peripherally inserted central venous catheter," "centrally inserted central catheter," "femorally inserted central catheter," "dialysis catheters," etc., were matched with "critically ill patients," "acutely ill," "intensive care," and "ICU." Papers regarding pediatric or neonatal patients were excluded. Studies focusing on peripheral venous access, peripheral arterial catheters, and pulmonary artery catheters were also excluded. References of articles, previous reviews, and meta-analyses were also analyzed, so as not to miss relevant papers. A total of 329 papers were initially retrieved. After a selection based on the above criteria, performed by GP and MP, 138 papers were eventually delivered to the panelists, divided in eight folders, according to the type of study and the topics covered.

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.[12] 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 two coordinators of the panel proposed to develop the document as answers to four major sets of questions regarding central venous access in the critically ill: (1) before insertion (seven questions), (2) during insertion (eight questions), (3) after insertion (three questions), and (4) at removal (three questions). After a preliminary email-based discussion, the whole panel agreed to structure the recommendations as answers to these four sets of questions, and the 21 questions proposed by the promoters were approved. The panel decided to exclude questions addressing a few special central VADs used infrequently—such as ECMO cannulas, and catheters for extracorporeal blood purification—considering that the available literature and the clinical experience are still scarce in regard.

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 21 questions. These preliminary statements were e-mailed to the whole panel and each panelist was asked to state her/his level of agreement with each statement (disagree, uncertain, agree) and to provide additional comments, especially in cases of uncertainty or disagreement, and to propose changes to the statement. 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 final survey was sent to each panelist, asking each one to state her/his level of agreement with each new statement (disagree, uncertain, agree). Statements which received 70%–90% of "agree" were considered to be expression of "agreement," statements with 91%–100% of "agree" were considered as "strong agreement." As the voting members of the panel were 26 (24 panelists plus two promoters), "agreement" on a statement corresponded to 19–23 "agree" and "strong agreement" to 24–26 "agree." All statements qualified as "agreement" or "strong agreement"; therefore, all of them were included in the recommendations. After the final vote, a preliminary manuscript was 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 the recommendations into clinical practice.

Results

Before insertion (questions 1–7)

Question 1: Which are the appropriate indications to a central venous access device in the critically ill patient?

Background. While most hospitalized patients can be treated by a peripheral venous access, there are clinical conditions which necessarily require a central line (hemodynamic monitoring, hemodialysis, etc.), and some other conditions where a central line should be preferred for reducing the risk of complications and for ensuring optimal delivery of the intravenous treatments (infusion of solutions associated with endothelial damage, repeated daily blood sampling, multiple simultaneous solutions). The appropriate indications to central access are described and discussed in detail in a recent European consensus developed by WoCoVA,[11] in the standards of the Infusion Nursing Society (INS),[7] and in many evidence-based documents of different vascular access associations. Patients with DIVA (Difficult Intra-Venous Access) are not currently regarded as inevitable candidates to central access, since they may benefit of peripheral venous catheters inserted by ultrasound guidance.[13–16] On the other hand, the critically ill patient has almost invariably indication to a central venous access, particularly when requiring intensive treatments, for delivering multiple infusions often not

compatible with the peripheral route (e.g. vasopressors), for frequent blood sampling and for hemodynamic monitoring (e.g. measurement of central venous pressure or of oxygen saturation in mixed venous blood; estimate of cardiac output by the thermodilution method). Most of the times, the acutely ill patient has not a single, but multiple reasons for requiring a central venous access.

Panel recommendation. In the critically ill patient, indications to a central venous access are often multiple, and may include one or more of the following: (a) infusion of intravenous solutions which are not compatible with the peripheral route, (b) hemodynamic monitoring, (c) multiple simultaneous infusions, (d) frequent blood sampling, (e) hemodialysis or other techniques of extracorporeal purification. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations. Solutions infused intravenously may be neutral, or irritant, or vesicant, in terms of their risk of inducing endothelial damage; neutral solutions can be delivered by a peripheral route, irritant solutions preferably require a central access, and vesicant solutions must be administered centrally, with the possible exception of the infusion in emergency and/or for a limited period of time (e.g. <24 h). A recent joint document[17] by several Spanish medical associations contains a detailed and updated list of intravenous drugs, reporting for each one if it is neutral, irritant, or vesicant. Such document—or similar—should be available for reference and included in the policies of the hospital or of the ICU.

- Not all central VADs are appropriate for dialysis or apheresis or other techniques of extracorporeal exchange/purification (see below).
- Not all central VADs can be used for hemodynamic monitoring; measurement of central venous pressure and estimate of cardiac output by thermodilution method both require that the tip of the catheter is in the superior vena cava or in the right atrium; measurement of oxygen saturation in mixed venous blood is reliable when the tip is in the right atrium, but not when the tip is in the superior or inferior vena cava.
- Blood sampling can be performed by a central venous line, though the maneuver must be done with proper aseptic technique and must be followed by proper flushing of the lumen. In ICU patients with a peripheral arterial catheter, blood sampling may be easier and safer using such device, rather than via a central VAD.

Question 2: Which are the criteria for choosing the type of central venous access (CICC vs PICC vs FICC)?

Background. During the last two decades, this question has been addressed in countless documents and clinical studies, with controversial results. In particular, the attention has been focused on the specific risk of infection and of thrombosis associated with CICCs versus PICCs versus FICCs.[2–4,18,19] The collective opinion of the panel is that the risk of such complications is not related per se to the type of central VAD, but to other factors. For example, the risk of infection is mostly related to the location of the exit site, since the nearness of a tracheostomy, of an open wound, of a humid and hairy skin area, etc., are all conditions associated with potential bacterial contamination of the catheter.[20] A common misconception—ubiquitous in the literature—has implied an automatic identification of FICCs (via the common femoral vein) as catheters with the exit site at the groin, supraclavicular CICCs (e.g. via the internal jugular vein) as catheters with the exit site at the neck, and so on. On the contrary, current techniques of ultrasound venipuncture and of tunneling allow us to choose independently the venipuncture site and the exit site.[8,21] Also, the risk of thrombosis is now known to be related to the catheter/vein ratio, to the magnitude of venous wall damage during cannulation, to the central or not central position of the tip, and to the stability of the securement.[22] In this regard, PICCs are particularly prone to catheter-related thrombosis when the catheter/vein ratio is not considered[23,24]; CICCs are prone to thrombosis when inserted in the neck, where the stability is poor[25,26]; FICCs with exit site at the groin are also characterized by a high thrombotic risk because of the mobility of the catheter and the uncertainty of the position of the tip, which is often not "central" (i.e. not inside the inferior vena cava).[25–27] Therefore, criteria for choosing between PICCs, CICCs, and FICCs are more complex.

Panel recommendation. The choice between CICC, PICC, and FICC should be based on the availability and patency of the deep veins (as evaluated by ultrasound scan), as well as on some key clinical considerations, which include—for example—the location of the exit site, the risk of puncture-related complications, the presence of chronic renal failure, the expected duration of the access, and whether the device is inserted in emergency or not. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- In non-emergency situations, central VADs should be inserted evaluating the different options in terms of venipuncture and in terms of exit site. The best site of venipuncture (i.e. the easiest, considering that an easy venipuncture is usually the safest for the patient); the site of venipuncture is chosen after the pre-procedural ultrasound scan (see below), while the criteria for choosing the exit site will also be discussed below. Appropriate exit sites can be obtained for each central VAD (the middle third of the arm for PICCs; the infraclavicular area for CICCs; the mid-thigh for FICCs), while each VAD

may have an increased risk of infection if the exit site is an inappropriate location (close to the axilla for PICCs; at the neck for CICCs; at the groin for FICCs). The exit site can be planned independently from the puncture site, adopting tunneling as described in the RAVESTO protocol.[21]

- PICCs are generally contraindicated (a) in chronic renal failure (though each patient should be individually evaluated in this regard),[28] (b) in patients with bilateral issues which contraindicate cannulation of the deep veins of the arm (paresis, lymphatic edema, skin ulcers, etc.), (c) in patients with non-availability of the superior vena cava, and (d) in emergency situations.
- CICCs are generally contraindicated (a) when the approach to infra/supraclavicular veins appears to be associated with high risk of puncture-related complications, (b) when there is a high risk of bleeding due to disease-related or treatment-related abnormalities of the coagulation (see the recent GAVeCeLT consensus on the risk of bleeding associated with venous access),[29] (c) in patients treated with ventilation in prone position, (d) in patients with expected difficulty in insertion/management of infra/supraclavicular catheters (collars, complicated tracheostomies, cervical wounds, etc.), and (e) in patient with non-availability of the superior vena cava.
- FICCs are generally contraindicated (a) in patients with high contamination of the skin of the groin and of the thigh, (b) in patients with non-availability of the inferior vena cava (e.g. because of thrombosis or presence of a cava filter), (c) in patients with kidney transplant, and (d) in patients with bilateral issues of the lower limbs which contraindicate femoral vein cannulation (severe edema, local thrombosis, trauma, etc.).
- In emergency situations, non-tunneled FICC at the groin (via puncture of the common femoral vein) or non-tunneled CICC at neck (via puncture of the internal jugular vein) are acceptable, but they should be removed within 24–48 h, because of the risk of infective and thrombotic complications.[7,30,31]

Question 3: Which is the relevance of the location of the catheter exit site?

Background. The importance of the exit site of central VADs has been identified only in the last 15 years.[32] An exit site in a contaminated area (close to natural orifices, close to stomas or tube drainages, in humid or hairy skin areas, etc.) will increase the risk of catheter-related infections due to extraluminal contamination.[3,20,33,34] An exit site in an unstable area (at the neck, or at the groin, or at the antecubital fossa) will be associated with a high risk of both dislodgment and of catheter-related thrombosis (due to ongoing friction of the catheter on the vein wall). Previous clinical studies have shown that CICCs have an increased risk of infection and thrombosis if the exit site is at the neck rather in the infraclavicular area,[18,34,35] and that FICCs with exit site at mid-thigh have less risk of complications if compared to FICCs with exit site at the groin.[33,36,37] Much confusion exists in the literature, even in some important guidelines,[10,38] because of wrong and misleading terminology; the inguinal site is often called "femoral site," whereas cannulation of the common femoral vein is not necessarily associated with an exit site in that area, and cannulation of the superficial femoral vein never implies an exit site at the groin; the infraclavicular exit site is improperly called "subclavian site," as a vestigial memory of the obsolete (and currently discouraged) infra-clavicular approach to the subclavian vein without ultrasound guidance; the exit site at the neck is inappropriately called "jugular site," while it is currently recommended—in case of puncture/cannulation of the supraclavicular veins (internal jugular, brachiocephalic, subclavian vein)—to obtain an exit site in the supraclavicular area rather than in the cervical region.

Panel recommendation. The location of the exit site plays a major role in the prevention of catheter-related complications. Insertion of central venous access devices should be planned so to obtain an exit site in a clean and stable location; exit site in contaminated and unstable areas such as the neck or the groin are acceptable only for CICCs and FICCs inserted in emergency and for non-tunneled dialysis catheters. *(Strong agreement: 25 agree, 1 uncertain, 0 disagree)*

Special considerations

- The choice of the exit site should consider the Zone Insertion Methods developed by Dawson[39] (as regards PICCs) and by GAVeCeLT (as regards CICCs and FICCs). A detailed description is reported in the papers published by GAVeCeLT and discussing the SIP protocol (Safe Insertion of PICCs),[40] the SIC protocol (Safe Insertion of CICCs),[41] the SIF protocol (Safe Insertion of FICCs).[42] In non-emergency situations, every effort should be done to obtain an acceptable exit site, considering the opportunity of tunneling, according to the different options reported in the RAVESTO protocol.[21]
- The Dawson's ZIM[39] recommends the exit site in the middle third of upper arm for PICCs; if the best site for venipuncture is in the proximal third, the catheter should be tunneled.
- The Central ZIM[41] considers "unacceptable" the exit site at the neck (with the only exception of a CICC inserted in emergency), "acceptable" the supraclavicular site, and "ideal" the infraclavicular

site; a CICC inserted in the supraclavicular veins, especially if a long duration is expected, should be preferably tunneled to the infraclavicular area; on the other hand, an infraclavicular exit site may not be ideal, for example if too close to the tracheostomy, and tunneling to the arm or to the lower chest might be indicated, according to the RAVESTO protocol.
- The Femoral ZIM[43] suggests that the best location of the exit site is in the middle third of the thigh; the groin site is considered acceptable only for non-tunneled dialysis catheters or for FICCs inserted in emergency.
- The only clinically relevant contraindication to tunneling is the presence of a severe disturbance of the coagulation (see GAVeCeLT Consensus).[29]

Question 4: Which is the relevance of the number of lumens of the central venous access device?

Background. All current guidelines recommend to use the smallest number of lumens still compatible with the infusions required by the patient.[31,43] While the risk of infection is related to the total number of lumens (considering the sum of lumens of all the central VADs placed on the patient), to deliver the required intravenous treatments with too few lumens may be difficult or impossible in the critically ill patient, and it may be associated with lumen occlusion due to the simultaneous infusion of incompatible drugs via the same line.

Panel recommendation: The number of lumens of each central venous access device (and the total number of lumens of all devices simultaneously in place) should be kept to a minimum to meet the clinical requirements. *(Strong agreement: 25 agree, 1 uncertain, 0 disagree)*

Special considerations
- The policy of inserting 4-lumen or 5-lumen CICCs in the critically ill may not be ideal, considering that after the acute phase of emergency treatments and complex intensive care, the patient might not need so many lumens. In clinical practice, one or more of these lumens often remain unutilized, which may carry the risk of irreversible lumen occlusion and clinically significant colonization, with the risk of subsequent catheter-related infection. A more reasonable approach may be to insert two or more central VADs in the phase of intensive treatment (for instance, a triple lumen CICC + a double lumen PICC), and then—when the clinical needs change—to reduce the number of lumens by removing one of the devices.

Question 5: Which are the preferred structural features of the central venous access device in terms of design and material?

Background. Central VADs are available in different materials (different types of silicone, different types of polyurethane), but the current recommendations[26,44] and decades of clinical experience suggest that fragile materials should be abandoned and—particularly in intensive care—all central VAD should be in new generation polyurethanes (e.g. polycarbonate-urethanes with aliphatic rather than aromatic bridges, so to be both rigid and alcohol-resistant) and that they should be power-injectable, as this feature improves the performance of the catheter in terms of flow. Interestingly, no clinical study of the last three decades has ever demonstrated any advantage of silicone catheters over polyurethane catheters, as regards the risk of infection or thrombosis. At the same time, no clinical study has ever demonstrated any advantage of having a valve in-built inside the catheter, either proximally or distally located. On the contrary, close-ended catheters with distal valve seem to be associated with high rate of malfunction.

Panel recommendation. For an optimal performance in the critically ill, all central venous access devices (CICC, PICC, and FICC) should be non-valved, open-ended, power-injectable, and made of polyurethane. *(Strong agreement: 25 agree, 0 uncertain, 1 disagree)*

Special considerations
- In ICU, central VADs are likely to be utilized for measurement of central venous pressure (which may be difficult or impossible with valved catheters) and for high flow delivery of fluids, which can be guaranteed only by non-valved power-injectable polyurethane catheters (1–5 ml/s, depending on the gauge of the lumen).
- Also, the critically ill patient is often candidate to radiologic studies (typically, CT or MR) in which the contrast medium is delivered by power injector at high pressure (200–300 PSI), so that a power-injectable device is highly recommended.

Question 6: Which central venous access devices should be used for hemodialysis in intensive care unit?

Background. All dialysis catheters consist of a minimum of two large bore lumens, and they are made of rigid, non-collapsing material (in most cases, polyurethane). Hemodialysis needs high flows (250–350 ml/min), which can be obtained only with large bore double lumen catheters with the tip located in a "central" position (superior vena cava, right atrium, or inferior vena cava): a peripheral location of the tip (for instance, in the common iliac vein) will be associated with an impaired efficiency of the procedure. This implies that the dialysis catheters should be of appropriate length, so to reach the proper tip position: for dialysis catheter inserted in the right supraclavicular area, the length may range between 13 and 19 cm, depending on the body size; for dialysis catheters inserted in the common femoral vein at the groin, 24–25 cm are usually necessary to reach the inferior vena cava. The efficiency of

the dialysis may be also impaired by a curved trajectory of the catheter, since each bending significantly reduces the flow of the lumen; this is the rationale for considering the left supraclavicular approach for dialysis catheter only as a rescue option (when the right supraclavicular approach and both inguinal approaches are not feasible), and for discouraging the use of any infraclavicular approach (which is also associated with risk of venous thrombosis and central venous stenosis).

Panel recommendation. In intensive care unit, hemodialysis requires large bore non-tunneled CICCs or FICCs, with two or three lumens, specifically designed for this purpose, preferably inserted in the right supraclavicular area or in the groin. *(Strong agreement: 24 agree, 2 uncertain, 0 disagree)*

Special considerations

- In ICU, only non-tunneled dialysis catheters are used, though a chronic renal failure patient may already have a previous tunneled-cuffed dialysis catheter.
- Some dialysis catheters have a third lumen, which may be used to deliver drugs and infusions during or after the dialytic procedure.
- The first option for placing a non-tunneled dialysis catheter is the right supraclavicular approach (ultrasound guided venipuncture of the right internal jugular vein or—better—of the right brachiocephalic vein); secondary options are (in order of preference) the right inguinal and the left inguinal approach, and—in selected cases, the left supraclavicular approach (in this case, a catheter of appropriate length—20–25 cm—and not too rigid should be chosen).
- Interestingly, dialysis catheters, because of their high flow, are sometimes used "off label" not for dialytic procedures but as emergency central VADs in hypovolemic/trauma patients, usually inserted via the common femoral vein.

Question 7: Which are the current indications of antimicrobial or antithrombotic central VADs?

Background. Several types of VADs treated (coated or impregnated) with antimicrobial agents (silver ions, antibiotics, chlorhexidine, etc.) have been tested and used in clinical practice in the last two decades. Though, the only antimicrobial catheters with evidence of efficacy in reducing the risk of excessive catheter colonization and consequent catheter-related infections in adult patients are CICCs coated with chlorhexidine and silver-sulfadiazine and CICCs coated with rifampicin and minocycline.[45,46] The critically ill patient is at high risk of catheter-related blood stream infections (CRBSI), and obviously the adoption of an antimicrobial central VAD is an attractive option. Though, the actual cost-effectiveness of such devices is still a matter of debate. Some concerns also exist about their safety (possible allergy to chlorhexidine and to antibiotics) and about the potential induction of antibiotic resistance. For this reason, all current guidelines recommend their use only in some specific conditions.[7,38,43,47] More recently, some antithrombotic catheters (impregnated of a special compounds) have become available,[48,49] but there is no hard evidence of their effectiveness and cost-effectiveness.

Panel recommendation. Some antimicrobial central VADs may have a role in the acutely ill; specific indications include (a) high risk of CRBSI (neutropenia, burns, etc.), (b) recurrent CRBSI, (c) expected high incidence of CRBSI even with adoption of standard preventive strategies, (d) high risk of severe sequelae should CRBSI occur (patients with long term implanted intravascular devices such as cardiac valves or pacemaker). Antimicrobial CICCs should be considered also in presence of blood cultures positive for germs or yeasts. At present, there is no hard evidence about the effectiveness and cost-effectiveness of antithrombotic central VADs. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- The panel recommendation is consistent with the current guidelines about the indication of antimicrobial CICCs. Also, the panel has added another possible indication, based on low evidence: antimicrobial CICCs may be useful in some blood stream infections, when a central access is required for antibiotic therapy and supportive treatment, but a standard central VAD might be at risk of secondary colonization.
- It must be stated clearly that the adoption of antimicrobial central VAD does not imply a reduced attention to all the other strategy of infection prevention that will be discussed below.

During insertion (questions 8–15)

Question 8: Which is the role of insertion bundles and insertion checklists?

Background. Insertion bundles are currently considered a very important tool for the standardization of the procedure, in particular for facilitating the consistent and systematic adoption of all those strategies which are known to increase the safety and the cost-effectiveness of the maneuver. The bundles are also a useful and important educational tool during clinical training, since they help to memorize all the different steps of a specific maneuver. On the other hand, the checklist is a simple and powerful instrument of controlling the performance of a procedure. Provided as hardcopy or digital document, it's a list of all the steps which are meant to be completed during or soon after the procedure, so as to ensure that the insertion bundle

has been fully adopted. In this regard, in ideal conditions, the checklist should be completed by an observer, empowered to stop the procedure if something is not adherent to the checklist.

Panel recommendation. All placements of central VADs should be performed adopting a well-defined specific insertion bundle (such as the SIC, SIP, or SIF protocols) and according to an appropriate checklist. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- The panel strongly recommends the adoption of the bundles for PICC insertion (the SIP protocol),[40] for CICC insertion (the SIC protocol),[41] and for FICC insertion (the SIF protocol),[42] developed by GAVeCeLT, since they are updated, properly structured, and easy to apply.
- In emergency, if the insertion of the central VAD is an urgent, life-saving maneuver that must be completed as soon as possible, it may be unfeasible or unwise to follow all the steps of the bundle, and some key aspects may be left behind (such as the maximal barrier precautions or the intra-procedural tip location). At any case, central VADs placed in emergency should be removed within 24–48 h, as recommended by the current guidelines.[50]

Question 9: Which are the criteria for choosing the venipuncture site?

Background. The clinician inserting a central VAD should be trained in CICC, PICC, and FICC insertion and should be familiar with systematic protocols for the choice of the venipuncture site as developed by GAVeCeLT: the Rapid Central Vein Assessment (RaCeVA),[51] the Rapid Peripheral Vein Assessment (RaPeVA),[40] and the Rapid Femoral Vein Assessment (RaFeVA).[52] This patient-centered approach is quite different from the clinician-centered approach of the XX Century, when the site of venipuncture was not based on the actual verification of all alternative options, but on a pre-defined decision of the operator, based on his personal experience and preference.

Today, clinicians should take into considerations all possible sites of venipuncture for placing a central VAD: a pre-procedural ultrasound scan allows to evaluate each vein considering its morphology (caliber, collapsibility, possible abnormalities, etc.) and its location (depth, relationship with the surrounding structures, etc.); the easiest vein to puncture is usually the safest for the patient.

Panel recommendation. The site of venipuncture must always be chosen after a systematic and bilateral ultrasound evaluation of all deep veins (preferably, using the RaPeVA, RaCeVA, and RaFeVA protocols). *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- While protocols for systematic pre-preprocedural ultrasound evaluation of the vasculature offer a robust framework for choosing the best venous approach, the final decision is also modulated by many other clinical factors: the presence of a severe coagulation disorder may be indication for a PICC or for a FICC inserted into the superficial femoral vein (see the GAVeCeLT consensus on this topic)[29]; a severe cardiorespiratory impairment might be indication to FICC insertion; as already mentioned, in the emergency setting, a non-tunneled FICC via the common femoral vein or a non-tunneled CICC via a supraclavicular vein may be the best choice; and so on.

Question 10: Which is the current role of ultrasound guided venipuncture?

Background. Since the beginning of the XXI Century, ultrasound has progressively changed the world of vascular access. The first application of ultrasound was during the venipuncture. The overwhelming evidence in favor of ultrasound-guided venipuncture if compared to "blind" venipuncture (euphemistically called "landmark-based" venipuncture) was so strong that since the first decade of the century all guidelines have included this strategy as a relevant option. The first important evidence-based document on ultrasound-guided venous access—developed by GAVeCeLT and WoCoVA—was published in 2012,[53] and this technique was rapidly applied to all devices inserted in deep vessels. At present, the most complete and structured guidelines on the use of ultrasound for vascular access have been developed by the European Society of Anesthesiology (ESA) and published in 2020.[8] The recommendations of our panel are aligned with the ESA guidelines: ultrasound guided venipuncture must be adopted for all central venous access of any type in the adult patient, either PICC or CICC or FICC, either in emergency or in elective situations.

Panel recommendation: All central VADs in the adult patient must be inserted exclusively by "real time" ultrasound-guided venipuncture: the most common veins utilized for central venous access are the basilica, brachial, and axillary vein (for PICC placement), the axillary vein (for CICC placement in the infraclavicular area), the internal jugular, brachiocephalic, and subclavian veins (for CICC placement in the supraclavicular area), and the common and superficial femoral veins (for FICC placement). *(Strong agreement: 25 agree, 1 uncertain, 0 disagree)*

Special considerations

- Some other veins, not mentioned in the statements, may be cannulated by ultrasound in selected, rare clinical conditions: for example, the cephalic vein at mid-arm (for PICC insertion), the cephalic vein in the infraclavicular area or the final tract of the

external jugular vein in the supraclavicular area (for CICC insertion), and the saphenous vein (for FICC insertion).
- As recommended by the ESA guidelines,[8] only "real-time" ultrasound guidance will bring the best clinical outcome (i.e. direct visualization of the needle while it enters the vein); the so-called "ultrasound-assisted" puncture has no role anymore in clinical practice.
- Also, according to the ESA guidelines,[8] the technique of ultrasound-guided venipuncture—in terms of spatial relationship between the probe and the vein (short axis vs oblique axis vs long axis) and in terms of angle between axis of the needle and plane of the probe (in-plane vs out-of-plane)—must be decided depending on the vein to cannulate.

Question 11: Which should be the preferred methods for assessment of tip location?

Background. For any central VAD (PICC, CICC, or FICC) the proper "central" position of the tip should be verified before use. For PICCs and CICCs, acceptable tip locations include the lower third of the superior vena cava, the cava-atrial junction, and the upper part of the right atrium[7]; for specific purposes (hemodynamic monitoring, dialysis, etc.) the latter is preferred. For FICCs, acceptable tip locations include the inferior vena cava, the junction between inferior vena cava and the right atrium, and the right atrium (the latter, if hemodynamic monitoring is required).[36] Current guidelines[7,8] recommend that assessment of tip location should be performed during the procedure. The old-fashioned strategy of post-procedural tip location by chest-X-ray is associated with waste of time and resources, delay in starting the intravenous treatments, and potential damage to the patient. Also, chest-X-ray has been proven to be relatively inaccurate. The current intra-procedural methods of tip location include intracavitary ECG (IC-ECG), trans-thoracic echocardiography (TTE), trans-esophageal echocardiography (TEE), and fluoroscopy. Fluoroscopy is expensive, unsafe (because of X-ray exposure), relatively inaccurate (as much as chest X-ray), and logistically difficult or impossible, so that it should not be taken into consideration in ICU. TEE is the most accurate method of tip location, but it is invasive, expensive, and logistically difficult: it has little or no role in ICU. Therefore, the most appropriate intraprocedural methods of tip location are IC-ECG and TTE.

The IC-ECG method can be easily applied in ICU using any ECG monitor: it may be applied to any PICC, or CICC, or even to those FICCs with the tip in the right atrium. In the case of patients with atrial fibrillation (AF), a particular variant of IC-ECG (modified IC-ECG) should be utilized.[54] Though, in patients without sinus rhythm and without AF, the IC-ECG cannot be applied. TTE, on the contrary, is theoretically applicable to all patients, and to any type of central VADs. The GAVeCeLT has recently developed a protocol for the standardization of TTE for tip location (the ECHOTIP protocol),[55] which describes the probes and the acoustic windows to adopt during the maneuver, and explains the method of the "bubble test," for a better localization of the tip. In case of difficult tip location (such as difficult or abnormal progression of the catheter), the trajectory of the catheter through the vasculature may be followed by ultrasound-based tip location, as recommended in the ECHOTIP protocol[55]; there is no evidence to support the effectiveness and the cost-effectiveness of the methods of tip navigation based on electromagnetic tracking or doppler flow measurements. In some complex cases, while navigating the tip through the venous system, the use of a floppy straight tip micro-guidewire may be helpful in directing the catheter.

Panel recommendation. The position of the tip of any central VAD must be assessed by intra-procedural, non-invasive methods such as intracavitary ECG or ultrasound-based tip location (preferably, according to the ECHOTIP protocol). *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations
- In most ICU patients, IC-ECG (in its conventional version or in its modified version for AF patients) is the first option for tip location during PICC and CICC insertion. When IC-ECG is not applicable (patients with no visible P wave and no AF), the ECHOTIP protocol should be used (visualization of the right atrium by subxiphoid or apical acoustic window, using a convex or sectorial probe + "bubble test").[55]
- During FICC insertion, the ECHOTIP protocol may confirm the presence of the tip in the right atrium or in the tract of inferior vena cava between the renal veins and the hepatic veins, using a convex probe and a subxiphoid or transhepatic window, using the "bubble test."[56]
- For PICCs, CICCs, and FICCs, post-procedural tip location by X-ray is to be considered only in selected cases, when the intra-procedural methods (IC-ECG and TTE) could not be adopted due to logistical or technical difficulties.
- Should tip navigation be required, the best choice is to adopt ultrasound-based tip navigation, as described in the ECHOTIP protocol.[55]
- In emergency insertion of central VADs, as mentioned above, there might not be time for intra-procedural tip location: in these cases, tip location may be assessed after the procedure, as soon as the patient is stable, either by radiological methods or, preferably, by TTE.

Question 12: Which intra-procedural strategies may minimize the risk of bleeding during and soon after the maneuver of central venous catheterization?

Background. Vascular access procedures are generally considered at low risk of bleeding. Still, some clinical conditions may be associated with significant bleeding during or after insertion of a PICC, a CICC, or a FICC: for example, an altered coagulation state—either secondary to disease or to pharmacological treatment—or a puncture-related complication (accidental arterial injury; disruption of the vein wall; etc.). A recent GAVeCeLT consensus[29] has classified the venous access procedures according to their invasiveness: non-tunneled PICC and non-tunneled FICC inserted in the superficial femoral vein are considered of minimal invasiveness, and should be considered as the first option in patients with severe abnormalities of the coagulation. In these patients, tunneling should preferably be avoided.

Panel recommendation. Intra-procedural or early post-procedural bleeding may be minimized by strategies such as: (a) proper choice of the venipuncture site, (b) adoption of a device with minimal invasiveness, (c) ultrasound guided venipuncture, (d) adoption of micro-introduction kits, (e) sutureless securement, (f) application of cyanoacrylate glue over the exit site. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- The micro-introduction kits (which consist of 21G needles, 0.018″ mini-guidewires, and micro-introducer-dilators tapered to the mini-guidewire) are commonly available in the kits of PICCs. They are associated with less tissue trauma and less risk of bleeding. When inserting a CICC, it is possible to use a PICC kit ("off label") or also use the CICC kit, opening an additional kit containing only the micro-introducer kit.
- Cyanoacrylate glue has been shown to be highly effective in stopping the bleeding of the exit site.[57] When the breech of the venipuncture has been enlarged using a surgical blade, the risk of bleeding from the exit site is increased, and the use of cyanoacrylate glue is highly recommended.

Question 13: Which intra-procedural strategies may minimize the risk of catheter-related infection?

Background. Several guidelines published by different institutions[38,43,50,58] have defined in the last two decades the main strategies to adopt during insertion of a central VAD for the purpose of reducing the risk of infection. All of these strategies—that are strongly supported by scientific evidence—are also included in the insertion protocols (SIP, SIC, SIF)[40–42] developed by GAVeCeLT.

Panel recommendation. The risk of catheter-related infections may be reduced by adopting intra-procedural strategies such as: (a) proper hand hygiene, (b) adoption of pre-assembled insertion kits, (c) maximal barrier precautions, (d) skin antisepsis with 2% chlorhexidine in 70% isopropyl-alcohol (preferably using one-dose disposable dispenser), (e) proper choice of the location of the exit site (considering tunneling the catheter—if required—according to the RAVESTO protocol), (f) ultrasound guided venipuncture, (g) sutureless securement of the catheter, (h) protection of the exit site with cyanoacrylate glue and semipermeable transparent dressing. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- As regards hand hygiene, it should be performed preferably by hydroalcoholic gel, following the guidelines recommendations,[7,38] that is, extending the antisepsis up to the operator's elbow and scrubbing for a prolonged time.
- As regards skin antisepsis, patients with known allergy to chlorhexidine should have the skin prepped by iodine povidone in alcohol; the duration of disinfection and drying time will depend on the type of antiseptic used.
- As regards the maximal barrier precautions, several recent documents have focused the attention on the proper cover of the probes.[38] Wireless probes are probably easier to cover efficiently; they are also easier to clean appropriately, which may reduce the accidental cross-contamination of pathogens among patients.
- As regards cyanoacrylate glue, the panel recommends using it for protection of the exit site soon after insertion. The glue appears to be as effective as chlorhexidine-releasing sponge dressing in reducing bacterial contamination by the extraluminal route, but it has the additional advantage of stopping any local oozing or bleeding.[57]
- In the 2020 GAVeCeLT document on vascular access in COVID-19 patients,[59] both wireless probe and cyanoacrylate glue were considered as important strategies for preventing complications.

Question 14: Which intra-procedural strategies may minimize the risk of catheter-related venous thrombosis?

Background. Many guidelines of the last 15 years have identified the intra-procedural strategies that may reduce the risk of thrombosis, the most important being the appropriate ratio between external caliber of the catheter and inner diameter of the vein.[31,53] Though, other strategies are recommended, such as minimizing the trauma to the vein wall (by using ultrasound guidance and micro-introducer kits) and adopting intraprocedural methods for optimal tip location.[26,60] In fact, inappropriate position of the tip is a

frequent cause of catheter related thrombosis, typically localized at the tip of the device.[7,22,26,60] The presumed high incidence of thrombosis in femoral catheters is probably explained by a failure of the tip to get to the inferior vena cava (in the adult patient, a 20 cm catheter inserted in the inguinal groove cannot reach the inferior vena cava). Also, the often-reported higher incidence of thrombosis for CICCs inserted on the left side if compared to right side may be explained by the fact that 20 cm catheters inserted in the infraclavicular area would have the tip in a suboptimal position, in the upper part of the superior vena cava, or even more proximally.[27] Proper stabilization of the catheter (by appropriate choice of the exit site and adequate securement) also plays a role in reducing thrombosis: central venous catheters that are particularly unstable (CICC with exit site at the neck, FICC with exit site at the groin) have a high incidence of venous thrombosis.[25,26,61]

Panel recommendation. The risk of catheter-related thrombosis may be reduced by adopting intra-procedural strategies such as: (a) choice of an adequate ratio between catheter caliber and vein diameter (1:3 or less), (b) adoption of micro-introducer kits, (c) ultrasound-guided venipuncture, (d) intra-procedural tip location, (e) proper securement of the catheter. *(Strong agreement: 25 agree, 1 uncertain, 0 disagree)*

Special considerations

- The ideal catheter/vein ratio (1:3 according to GAVeCeLT and WoCoVA) has not been defined by solid randomized clinical trials, but on the basis of in vitro studies and retrospective reports.[62,63] It is most likely that slightly higher ratio (as suggested by INS)[7] might also be associated with low risk of thrombosis.
- Obviously, a 1:3 catheter/vein ratio cannot be adopted in all situations; for placement of large bore dialysis catheters (11–13 Fr), sometimes it may be difficult to find a vein of appropriate diameter.
- Prevention of catheter-related thrombosis might include pharmacological intervention. Though, this prevention is seldom taken into consideration in the acutely ill patient with short-medium term central VAD, while it has a role in selected populations of cancer patients with long term VADs for chemotherapy.[27,64]

Question 15: Which intra-procedural strategies may minimize the risk of catheter dislodgment?

Background. Dislodgment of central VADs is not infrequent in ICU,[4] considering that these patients are often mobilized for therapeutic and diagnostic procedures. Pronation of the patient for optimizing lung ventilation is also associated with risk of dislodgment. Also, high perspiration (as it occurs in the septic patient with fever and sweating) may impair the adhesiveness of traditional sutureless devices and of semipermeable transparent dressings. Securement with stitches is discouraged by all guidelines,[7,38,43,58] since it is associated with increased risk of infection, possible injury to the operator, and pain for the patient. Glue has been considered as securement, but in adult patients it is apparently effective—if combined with transparent dressing—only for securement of short peripheral catheters.[11]

Panel recommendation. The risk of catheter dislodgment may be reduced by adopting intra-procedural strategies such as: (a) proper choice of the location of the exit site (considering tunneling the catheter—if required—according to the RAVESTO protocol), (b) sutureless securement, (c) use of semipermeable transparent dressing to cover the exit site. In patients with high risk of dislodgment, the catheter should be preferably secured by subcutaneous anchorage. *(Agreement: 21 agree, 5 uncertain, 0 disagree)*

Special considerations

- Subcutaneous anchorage is certainly the most reliable securement for any catheter of caliber ranging from 3 Fr to 12 Fr. Its efficacy and safety have been discussed in the WoCoVA consensus on subcutaneous anchorage published few years ago.[61] Its main advantages include: (a) it does not require periodic replacement, (b) it is highly effective in reducing dislodgment, (c) it simplifies the management of the exit site, (d) it cancels any "micro-movement" of the catheter inside the exit site.
- Considering its cost, the subcutaneous anchoring device has its indication in population of patients at high risk of dislodgment, or in patients in whom dislodgment may be associated with particularly unfavorable consequences (for instance, patients with limited options of venous access). In ICU, many patients may have these characteristics, so that subcutaneous anchorage should be taken into consideration. The 2020 GAVeCeLT document on vascular access in COVID-19[59] recommends the use of this type of securement in this population of patients.

After insertion (questions 16–18)

Question 16: Which are the basic post-procedural strategies that reduce the risk of catheter-related infections?

Background. Several guidelines of the last two decades have analyzed the post-procedural strategies that may reduce the risk of catheter-related infections. As suggested by recent guidelines,[38] these strategies can be classified as "basic" strategies (methods and technologies), with proven evidence of effectiveness and cost-effectiveness, and "additional" strategies, which may be conditionally useful in some environments. The panel has reviewed the basic strategies largely supported by strong evidence from

randomized clinical studies and high-quality prospective studies and has provided a recommendation that summarized the most important of such intervention for infection prevention.

Panel recommendation. The risk of catheter-related infections can be reduced by adopting basic post-procedural strategies such as: (a) staff education, (b) adequate nurse/patient ratio, (c) hand hygiene, (d) scheduled dressing change every 7 days, with skin antisepsis using 2% chlorhexidine in 70% isopropyl alcohol, weekly replacement of the sutureless device (unless the catheter is anchored subcutaneously), and weekly replacement of the semipermeable transparent dressing, (e) adoption of chlorhexidine releasing sponge dressing for non-tunneled central VADs; (f) disinfection of catheter hubs and of needle-free connectors (NFC) at each use, preferably using disinfecting caps (port-protectors), (g) scheduled replacement of infusion lines and NFC, at different intervals, depending on the type of infusion, and (h) early removal of central lines that are not strictly necessary or that have been placed in emergency. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- Most of the strategies listed by the panel are also recommended by the most recent guidelines in this field.[7,38,58]
- The optimal nurse/patient ratio is 1:1 or 1.2, though shortage of nursing staff in ICU may yield a suboptimal ratio.
- The effectiveness of chlorhexidine releasing sponge dressing is supported by many randomized clinical trials,[65,66] but their use should be limited to non-tunneled central VADs; also, they have a role since the first dressing change, but not at the time of VAD insertion, when cyanoacrylate glue should be preferably applied on the exit site. The effectiveness of chlorhexidine-releasing gel pad dressing is controversial, since it is supported only by one randomized clinical study,[67] but it was not demonstrated by other randomized trials[68,69]; also, the reduced transpirability of the gel dressing is a matter of concern, since it may be associated with skin damage, particularly in the ICU patient with high perspiration.[70,71]
- The studies comparing different outcomes associated with the use of NFC with negative versus neutral versus positive displacement do not yield definitive conclusions[72,73]; though, the panel recommends to use preferably neutral displacement NFC, since they are most likely to be associated with the lowest incidence of complications. The neutral displacement NFCs with an added valve cannot be recommended since their cost-effectiveness is still uncertain.
- The panel strongly recommends that all the hubs of the catheter and of the infusion line, if used intermittently, should be closed with NFC (including the hubs of the stopcocks).
- Whenever possible, a no-touch technique[7] should be used during dressing change; this is facilitated by the consistent use of subcutaneous anchorage (which does not imply replacement of the sutureless device) and of one-dose disposable dispenser of 2% chlorhexidine in alcohol.

Question 17: Which additional strategies may be also considered to reduce the risk of catheter-related infections?

Background. Some additional strategies with undefined profile of effectiveness and cost-effectiveness were also considered by the panel.

Panel recommendation. The risk of catheter-related infections might also be reduced by adopting additional strategies such as: (a) adoption of pre-filled syringes for flushing the lumen of the catheters, (b) pre-assembled kits for dressing change, (c) adoption of maintenance checklists. *(Strong agreement: 24 agree, 2 uncertain, 0 disagree)*

Special considerations

- The effectiveness of pre-filled syringes for flushing is proven by clinical studies, though their cost-effectiveness may be uncertain in the setting of intensive care.[74]
- While pre-assembled kits are strongly recommended at the time of central VAD insertion, pre-assembled kits for dressing change may have a limited cost-effectiveness in ICU.
- Taurolidine lock is certainly effective for infection prevention in outpatients with medium-long term central VADs,[75,76] but its applicability and feasibility in the acutely ill, whose central lines are utilized continuously, is probably scarce.

Question 18: Which post-procedural strategies may minimize the risk of lumen occlusion?

Background. The critically ill patients typically receive many different infusions, with different drugs that may be incompatible if administered simultaneously, so that the risk of lumen occlusion due to precipitates is high. Also, blood sampling and administration of blood and blood derivatives increase the risk of lumen occlusion due to clots. Contrast media used for TC scan and MR have a very high viscosity, and they represent another possible cause of lumen occlusion.

Panel recommendation. The risk of lumen occlusion is reduced by adopting post-procedural strategies such as: (a) adequate protocols of flushing the lumen with saline, before and after each infusion, and (b) adequate protocols of locking the lumen when not in use, locking non-dialysis catheters with saline only and locking catheters utilized for dialysis or apheresis with heparin or citrate. *(Strong agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- These recommendations are based on the GAVeCeLT consensus on catheter lock published in 2016,[75] which stated the main principles behind flushing and locking central VADs: (a) all central VADs should be flushed with saline only; (b) flushing should be performed using the "start and stop" technique (pulsatile technique); (c) central VADs not utilized for dialysis or apheresis should be locked, if not used, with saline only; (d) central VADs utilized for dialysis or apheresis should be locked, if not used, with heparinized solution or with 4% citrate.

At removal (questions 19–21)

Question 19: Which strategies may reduce the risk of air embolism during the removal of a central VAD?

Background. Air embolism has been described during removal of large bore non-tunneled CICCs, particularly if the patient is hypovolemic and/or in a semi-upright/sitting position and/or if the patient is breathing deeply. The risk may be even higher in large bore CICCs used for temporary dialysis in ICU. Once penetrated into the veins, air emboli can migrate in different areas following three major routes: into the pulmonary circulation, into the arterial circulation through a patent *foramen ovale* (paradoxical embolism), or into the cerebral venous system (retrograde ascension). Clinical manifestation may include loss of consciousness, sudden acute ventricular failure, cardiac arrest, cardiac ischemia and infarction, focal neurological deficits, and so on.[77]

Panel recommendation. The risk of embolism during removal exists only for CICCs, and can be reduced by performing the maneuver with the patient in supine position, and sealing rapidly the skin breech by cyanoacrylate glue after proper local compression. *(Agreement: 23 agree, 3 uncertain, 0 disagree)*

Special considerations

- The use of cyanoacrylate glue for this purpose is based on clinical experience and experts' opinion, but it is not supported by evidence. Still, if available, its use should be considered.
- Air-occlusive dressing should also be considered.

Question 20: Which strategies may reduce the risk of bleeding during the removal of a central VAD?

Background. Bleeding may occur during/after removal of central VADs, in some special situations: (a) removal of large bore tunneled or non-tunneled catheters; (b) removal of central VADs in patients with abnormal coagulative state (either because of the disease itself, or because of pharmacological treatments); (c) more infrequently, removal of catheters which had been inserted with some technical complications (for instance, accidental arterial injury during venipuncture).

Panel recommendation. The risk of bleeding during removal of central VADs can be reduced by sealing rapidly the skin breech by cyanoacrylate glue after proper local compression. *(Agreement: 23 agree, 3 uncertain, 0 disagree)*

Special considerations

- The use of cyanoacrylate glue for this purpose is based on clinical experience, and experts' opinion, and it is also supported by clinical studies.[57] If glue is available, its use is recommended. Other empirical local treatments of bleeding of the exit site (tranexamic acid, adrenaline, hemostatic sponges, etc.) are ineffective and should be avoided.

Question 21: Which strategies may reduce the risk of thromboembolism during the removal of a central VAD?

Background. In the literature, a few cases of thromboembolism at removal of central VADs are reported.[78,79] Most of these cases (which include also some fatalities) regarded CICCs or FICCs with undiagnosed recent asymptomatic catheter-related thrombosis.[79,80] Risk is higher if the thrombosis is relatively recent. Although the incidence of this complication is very low, its prevention is very easy and implies an ultrasound scan of the local veins before removal. A recent editorial has addressed the actual indication of pre-removal ultrasound scan before removal of PICCs, providing algorithms of good clinical practice.[81] Though, the issue may be different in the acutely ill patient, who is characterized by high risk of catheter related thrombosis.[82]

Panel recommendation. The risk of thrombo-embolism during removal of central VADs can be reduced by performing an ultrasound evaluation of the veins soon before removal, so to rule out the presence of an undiagnosed asymptomatic venous thrombosis. *(Agreement: 26 agree, 0 uncertain, 0 disagree)*

Special considerations

- Pre-removal ultrasound should be considered mainly in patients at high risk of catheter related thrombosis (COVID-19, onco-hematologic, cancer patients, sepsis, etc.) or in patients with recent insertion of central VADs (1–2 weeks).

Conclusions

The goal of the present consensus is to offer a systematic set of recommendations for the adoption of appropriate strategies (methods and technologies) to reduce the risk of complications associated with the insertion, maintenance, and removal of central venous catheters. Most of these recommendations are aligned with what is currently recommended by most guidelines, but this consensus carries the additional value of being specifically focused on adult critically ill patients; also, it includes comments and suggestions about new methods and new technologies that have been introduced in the clinical practice only in the last decade (non-cuffed tunneled catheters, cyanoacrylate glue, micro-puncture kits, subcutaneous anchorage, ultrasound-based tip location, ultrasound-guided puncture of the axillary vein or of the brachiocephalic vein or of the superficial femoral vein). The recommendations of the panel are summarized in Table 1 (indication and choice of the central VAD), in Table 2 (insertion of the central VAD), and in Table 3 (maintenance and removal of the central VAD).

Table 1. Panel recommendations: indications and choice of the central VAD in the critically ill.

Questions	Panel recommendation
Question 1: Which are the appropriate indications to a central venous access device in the critically ill patient?	In the critically ill patient, indications to central venous access are often multiple, and may include one or more of the following: (a) infusion of intravenous solutions which are not compatible with the peripheral route, (b) hemodynamic monitoring, (c) multiple simultaneous infusions, (d) frequent blood sampling, (e) hemodialysis or other techniques of extracorporeal purification. *(Strong agreement)*
Question 2: Which are the criteria for choosing the type of central venous access (CICC vs PICC vs FICC)?	The choice between CICC, PICC, and FICC should be based on the availability and patency of the deep veins (as evaluated by ultrasound scan), as well as on some key clinical considerations, which include—for example—the location of the exit site, the risk of puncture-related complications, the presence of chronic renal failure, the expected duration of the access, and whether the device is inserted in emergency or not. *(Strong agreement)*
Question 3: Which is the relevance of the location of the catheter exit site?	The location of the exit site plays a major role in the prevention of catheter-related complications. Insertion of central venous access devices should be planned so to obtain an exit site in a clean and stable location; exit site in contaminated and unstable areas such as the neck or the groin are acceptable only for CICCs and FICCs inserted in emergency and for non-tunneled dialysis catheters. *(Strong agreement)*
Question 4: Which is the relevance of the number of lumens of the central venous access device?	The number of lumens of each central venous access device (and the total number of lumens of all devices simultaneously in place) should be kept to a minimum to meet the clinical requirements. *(Strong agreement)*
Question 5: Which are the preferred structural features of the central venous access device in terms of design and material?	For an optimal performance in the critically ill, all central venous access devices (CICC, PICC, and FICC) should be non-valved, open-ended, power-injectable, and made of polyurethane. *(Strong agreement)*
Question 6: Which central venous access devices should be used for hemodialysis in intensive care unit?	In intensive care unit, hemodialysis requires large bore non-tunneled CICCs or FICCs, with two or three lumens, specifically designed for this purpose, preferably inserted in the right supraclavicular area or in the groin. *(Strong agreement)*
Question 7: Which are the current indications of antimicrobial or antithrombotic central VADs?	Some antimicrobial central VADs may have a role in the acutely ill; specific indications include (a) high risk of CRBSI (neutropenia, burns, etc.), (b) recurrent CRBSI, (c) expected high incidence of CRBSI even with adoption of standard preventive strategies, (d) high risk of severe sequelae should CRBSI occur (patients with long term implanted intravascular devices such as cardiac valves or pacemaker). Antimicrobial CICCs should be considered also in presence of blood cultures positive for germs or yeasts. At present, there is no hard evidence about the effectiveness and cost-effectiveness of antithrombotic central VADs. *(Strong agreement)*

Table 2. Panel recommendations: insertion of central VADs in the critically ill.

Questions	Panel recommendation
Question 8: Which is the role of insertion bundles and insertion checklists?	All placements of central VADs should be performed adopting a well-defined specific insertion bundle (such as the SIC, SIP, or SIF protocols) and according to an appropriate checklist. *(Strong agreement)*
Question 9: Which are the criteria for choosing the venipuncture site?	The site of venipuncture must always be chosen after a systematic and bilateral ultrasound evaluation of all deep veins (preferably, using the RaPeVA, RaCeVA, and RaFeVA protocols). *(Strong agreement)*
Question 10: Which is the current role of ultrasound guided venipuncture?	All central VADs in the adult patient must be inserted exclusively by "real time" ultrasound-guided venipuncture: the most common veins utilized for central venous access are the basilica, brachial, and axillary vein (for PICC placement), the axillary vein (for CICC placement in the infraclavicular area), the internal jugular, brachiocephalic, and subclavian veins (for CICC placement in the supraclavicular area), and the common and superficial femoral veins (for FICC placement). *(Strong agreement)*
Question 11: Which should be the preferred methods for assessment of tip location?	The position of the tip of any central VAD must be assessed by intra-procedural, non-invasive methods such as intracavitary ECG or ultrasound-based tip location (preferably, according to the ECHOTIP protocol). *(Strong agreement)*
Question 12: Which intra-procedural strategies may minimize the risk of bleeding during and soon after the maneuver of central venous catheterization?	Intra-procedural or early post-procedural bleeding may be minimized by strategies such as: (a) proper choice of the venipuncture site, (b) adoption of a device with minimal invasiveness, (c) ultrasound guided venipuncture, (d) adoption of micro-introduction kits, (e) sutureless securement, (f) application of cyanoacrylate glue over the exit site. *(Strong agreement)*
Question 13: Which intra-procedural strategies may minimize the risk of catheter-related infection?	The risk of catheter-related infections may be reduced by adopting intra-procedural strategies such as: (a) proper hand hygiene, (b) adoption of pre-assembled insertion kits, (c) maximal barrier precautions, (d) skin antisepsis with 2% chlorhexidine in 70% isopropyl-alcohol (preferably using one-dose disposable dispenser), (e) proper choice of the location of the exit site (considering tunneling the catheter—if required—according to the RAVESTO protocol), (f) ultrasound guided venipuncture, (g) sutureless securement of the catheter, (h) protection of the exit site with cyanoacrylate glue and semipermeable transparent dressing. *(Strong agreement)*
Question 14: Which intra-procedural strategies may minimize the risk of catheter-related venous thrombosis?	The risk of catheter-related thrombosis may be reduced by adopting intra-procedural strategies such as: (a) choice of an adequate ratio between catheter caliber and vein diameter (1:3 or less), (b) adoption of micro-introducer kits, (c) ultrasound-guided venipuncture, (d) intra-procedural tip location, (e) proper securement of the catheter. *(Strong agreement)*
Question 15: Which intra-procedural strategies may minimize the risk of catheter dislodgment?	The risk of catheter dislodgment may be reduced by adopting intra-procedural strategies such as: (a) proper choice of the location of the exit site (considering tunneling the catheter—if required—according to the RAVESTO protocol), (b) sutureless securement, (c) use of semipermeable transparent dressing to cover the exit site. In patients with high risk of dislodgment, the catheter should be preferably secured by subcutaneous anchorage. *(Agreement)*

Table 3. Panel recommendations: maintenance and removal of central VADs.

Questions	Panel recommendations
Question 16: Which are the basic post-procedural strategies that reduce the risk of catheter-related infections?	The risk of catheter-related infections can be reduced by adopting basic post-procedural strategies such as: (a) staff education, (b) adequate nurse/patient ratio, (c) hand hygiene, (d) scheduled dressing change every 7 days, with skin antisepsis using 2% chlorhexidine in 70% isopropyl alcohol, weekly replacement of the sutureless device (unless the catheter is anchored subcutaneously), and weekly replacement of the semipermeable transparent dressing, (e) adoption of chlorhexidine releasing sponge dressing for non-tunneled central VADs; (f) disinfection of catheter hubs and of needle-free connectors (NFC) at each use, preferably using disinfecting caps (port-protectors), (g) scheduled replacement of infusion lines and NFC, at different intervals, depending on the type of infusion, and (h) early removal of central lines that are not strictly necessary or that have been placed in emergency. *(Strong agreement)*

(Continued)

Table 3. (Continued)

Questions	Panel recommendations
Question 17: Which additional strategies may also be considered to reduce the risk of catheter-related infections?	The risk of catheter-related infections could also be reduced by adopting additional post-procedural strategies such as: (a) adoption of pre-filled syringes for flushing the lumen of the catheters, (b) pre-assembled kits for dressing change, (c) adoption of maintenance checklists. *(Strong agreement)*
Question 18: Which post-procedural strategies may minimize the risk of lumen occlusion?	The risk of lumen occlusion is reduced by adopting post-procedural strategies such as: (a) adequate protocols of flushing the lumen with saline, before and after each infusion, and (b) adequate protocols of locking the lumen when not in use, with saline only for non-dialysis catheters and with heparin or citrate for catheters utilized for dialysis or apheresis. *(Strong agreement)*
Question 19: Which strategies may reduce the risk of air embolism during the removal of a central VAD?	The risk of embolism during removal exists only for CICCs and can be reduced by performing the maneuver with the patient in supine position, and rapidly sealing the skin breech with cyanoacrylate glue after proper local compression. *(Agreement)*
Question 20: Which strategies may reduce the risk of bleeding during the removal of a central VAD?	The risk of bleeding during removal of central VADs can be reduced by sealing rapidly the skin breech with cyanoacrylate glue after proper local compression. *(Agreement)*
Question 21: Which strategies may reduce the risk of thrombo-embolism during the removal of a central VAD?	The risk of thrombo-embolism during removal of central VADs can be reduced by performing an ultrasound evaluation of the veins soon before removal, so to rule out the presence of an undiagnosed asymptomatic venous thrombosis. *(Agreement)*

Abbreviation

AF—atrial fibrillation
CICC—centrally inserted central catheter
CRBSI—catheter-related bloodstream infection
CT—computerized tomography
DIVA—difficult intra-venous access
ECHOTIP—structured protocol for tip location by ultrasound, developed by GAVeCeLT
ECMO—extra-corporeal membrane oxygenation
ESA—European Society of Anesthesiology
FICC—femorally inserted central catheters
GAVeCeLT—Gruppo Accessi Venosi Centrali a Lungo Termine (Italian Group of Central Venous Access Devices)
IC-ECG—intracavitary electrocardiography
ICU—intensive care unit
INS—Infusion Nursing Society
MAGIC—Michigan Appropriateness Guide for Intravenous Catheters
MR—magnetic resonance
NFC—needle-free connectors
PICC—peripherally inserted central catheter
RaCeVA—Rapid Central Vein Assessment
RaFeVA—Rapid Femoral Vein Assessment
RaPeVA—Rapid Peripheral Vein Assessment
RAVESTO—Rapid Assessment of Venous Exit Site and Tunneling Options
SIC—Safe Insertion of CICCs
SIF—Safe Insertion of FICCs
SIP—Safe Insertion of PICCs
TEE—trans-esophageal echocardiography
TTE—trans-thoracic echocardiography
VAD—venous access device
WoCoVA—World Conference on Vascular Access
ZIM—Zone Insertion Method

Author contributions

MP and FP contributed to the study's conception and design. MP and GP performed the literature research. All the other authors had an active part in the construction of the recommendations of the present paper, as explained in the methods section. The first draft of the manuscript was written by MP and FP. All authors read and approved the final manuscript.

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