Considerations on the use of vascular access devices in patients with COVID-19 (and some practical recommendations)

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The health emergency linked to the COVID-19 pandemic has led to a series of dramatic changes in the routine of our clinical practice, requiring the revision of many decision-making processes, the re-organization of treatment units, and the reformulation of protocols and procedures. In this regard, in the practice of venous access - which is essential for the appropriate treatment of COVID-19 patients - it was necessary to review the criteria for the selection, insertion and maintenance of the various devices currently present in our Italian hospitals.

In these pages, a group of experts from GAVeCeLT (Long Term Central Venous Access Group) has tried to point out some important aspects concerning vascular access in COVID-19 patients, based on their current experience in the treatment of these patients, identifying those strategies that simultaneously take into account the need to protect the operator, to ensure the effectiveness of the maneuver, to reduce the risk of complications for the patient, and to avoid a waste of resources. These considerations and recommendations have not yet been published or reviewed. They reflect the views and experiences of the authors and have been drafted to provide a potentially useful tool for all colleagues who need to treat critical or non-critical COVID-19 patients.

Along the lines of an editorial on the subject currently being published in the *Journal of Vascular Access* (1), the topic has been addressed taking into account four key points.

1) Choice of peripheral venous access

Patients with suspected or confirmed diagnosis of COVID-19 - but who do not require hospitalization in the ICU - can be initially treated with peripheral venous access to be used for hydration and supportive therapies, but only for infusion of drugs and solutions compatible with the peripheral venous route (lists of drugs compatible and incompatible with intravenous peripheral infusion are easily available at the GAVeCeLT website) (2).

Currently there are three peripheral venous access devices available: short peripheral cannulas (<6cm); long peripheral cannulas or 'mini-Midline' (6-15cm) and Midline catheters (>15cm long) (3). In some COVID-19 patients **Midline catheters** may be recommended - especially if power injectable and polyurethane. These devices have numerous advantages:

(a) due to their longer dwell time, they reduce the number of peripheral venous access insertions required (with obvious benefits in terms of saving resources and reducing risks for the operator);

(b) they allow high flow infusions;

(c) Midlines allow blood sampling (which is difficult in long peripheral catheters and impossible in short peripheral catheters); in order to optimize the possibility of blood sampling, it is advisable to check by ultrasound that the tip of the Midline is located in the axillary vein, in the infra-clavicular area, just before the passage of the vein under the clavicle (4);

(d) Midlines can be easily replaced over guidewire with a peripherally inserted central catheter (PICC) if indicated.

In order to reduce the risk of catheter-related venous thrombosis, in addition to the mandatory use of ultrasound-guided venipuncture, it should be verified that the size of the cannulated vein (brachial or basilica) is at least three times the external diameter of the Midline (e.g.: 4 mm vein, 4Fr catheter; 5 mm vein, 5Fr catheter; etc.); as already mentioned, it is advisable to use Midline catheters (as well as short cannulas and mini-Midline catheters) exclusively for infusions compatible with the peripheral route. Given the hyper-coagulability of the COVID-19 patient, the subcutaneous administration of low molecular weight heparin at prophylactic (100 units/kg/24h) or therapeutic (100 units/kg/12h) dose should be always taken into consideration, as already foreseen by many centers, even in the absence of venous catheterization.

Ultrasound-guided insertion of **long peripheral catheters** (also called 'mini-Midline', 6-15 cm) may play a role, albeit limited, in these patients, for example on arrival in the emergency room. If compared to Midlines, the advantages of mini-Midlines - lower cost and simpler insertion - should be weighed against the shorter dwell time, the higher risk for local complications (dislocation and infiltration/extravasation) and greater difficulty in performing blood sampling (therefore, in this case, it is advisable to have another sample collection site, such as a peripheral arterial catheter, based upon level of illness).

A particular problem related to the use of peripheral venous access devices (short cannulas, mini-Midline and Midline catheters) is their compatibility with the use of helmets for CPAP or non-invasive ventilation (NIV), often used in COVID-19 patients. The problem may arise when using a helmet with tight straps under the armpits, thus inevitably compressing the axillary veins; this maneuver may be associated with edema, paresthesia and risk of venous thrombosis, as well as considerable discomfort for the patient (5). The placement of a peripheral access - whether short cannula or mini-midline or midline - in a limb with venous stasis can theoretically lead to a further increase in the risk of local edema and thrombosis, also considering the increased thrombotic risk of COVID patients. Under normal conditions, about 75% of the venous blood in the arm flows via the axillary vein (via brachial veins and basilic vein), while only 25% flows via the cephalic vein, which can, however, be a collateral route of outflow in the case of compression of the axillary vein. Although there are no reliable literature data available in this regard, it is necessary to keep this problem in mind and prefer CPAP/NIV systems with face mask or with a type of helmet that does not include anchoring under the armpits, or even the adoption of helmet fastening systems using straps connected to the edges of the bed or with counterweights. However, there are still no certain data on the actual incidence of venous thrombosis, in the presence or absence of peripheral brachial catheters (mini-Midline or Midline), directly or indirectly related to the underarm anchorage of the helmet.

2) Choice of central venous access

The COVID patient requiring hospitalization in intensive care unit needs a central venous access for several reasons: multiple and high-flow infusion therapies, administration of vasopressor drugs and other drugs not compatible with the peripheral route, parenteral nutrition, hemodynamic monitoring, repeated daily blood sampling. In adult patients, central venous access devices are now classified as PICC (peripherally inserted central catheters), CICC (centrally inserted central catheters), FICC (femorally inserted central catheters) (6).

Recently, several studies have highlighted the potential benefits of using **peripherally inserted central catheters (PICC),** if power injectable and in polyurethane (non-valved, open-ended) in intensive care unit (7)(8)(9). In the acutely ill patient with COVID-19, the use of these devices -

especially if double-lumen (5Fr) and triple lumen (5Fr or 6Fr) - may be particularly suitable, based on the following considerations:

- the insertion of a PICC is completely free of risk of pleuropulmonary complications (pneumothorax, hemothorax), which can be fatal in patients with COVID-19 pneumonia;
- the insertion of a PICC does not require that the patient is in supine position (which may be impossible in some COVID-19 patients), but can also be performed in patients in a sitting position, and in extreme cases even in pronated patients;
- the insertion of a PICC is theoretically safer for the operator than the insertion of a CICC, where the operator dangerously close to the patient's face and to his oral, nasal and tracheal secretions;
- in patients on non-invasive ventilation (with mask or helmet), keeping the neck free from CICC is undoubtedly an advantage in terms of managing respiratory therapy and venous access;
- in the pronated COVID-19 patient, the dressing of a CICC is inevitably more uncomfortable to manage (think of the difficulty in periodic monitoring of the exit site and in the connection/disconnection of the infusion lines) and it may be flooded by the patient's oral and tracheal secretions during the whole period of pronation, which can be very long (at least 12-16 hours/day);
- in tracheostomized patients, PICC management will be safer than a CICC, both for the patient (lower risk of contamination of the emergency catheter site) and the operator (lower risk of exposure to patient tracheal secretions);
- several protocols recommend anticoagulation in COVID-19 patients - due to the high thrombotic risk - and this is also a factor that makes the insertion of a PICC more desirable than a CICC; in fact, the placement of PICC has no contraindications even in the heavily anticoagulated patient;
- the most severe COVID-19 patients have an average stay of almost 3 weeks and also for this reason PICCs offer considerable advantages, given the longer life expectancy of such devices;
- a pre-existing Midline catheter can be used for the insertion of a PICC by simple replacement over guidewire (if no infection is suspected and no signs of thrombosis are visible at ultrasound);
- also, the insertion of a PICC leaves the venous vessels in the supraclavicular and inguinal area free for ECMO cannulation.

It should be noted that there are no differences in thrombotic risk between CICC and PICC in the patient in ICU (some old studies that had suggested a higher risk in PICC have been rebutted): it is now commonly accepted that one of the most important determining factor in increasing the thrombotic risk, both for CICC and PICC, is the insertion technique (10). Moreover, recent studies have also demonstrated the reliability of PICCs in ICUs both for the detection of central venous pressure (11) and for the measurement of cardiac output by thermodilution (12); in particular, with regard to the latter method, the results obtained using the main lumen of a triple lumen 6Fr PICC are not significantly different from those obtained by infusion in the distal lumen of triple lumen 7Fr CICC (13). Power injectable, multiple lumen PICCs have the same *performance* as a multiple lumen CICC in terms of comfort and infusion flow rate. The main limitation for PICC insertion is the availability of a vein of proper inner diameter (at least 5 mm vein for a 5Fr PICC; at least 6 mm for a 6Fr PICC), so to decrease the thrombotic risk.

Obviously, in the absence of medical and nursing staff appropriately trained to PICC insertion, this option cannot be considered; however, it is not impossible to plan a rapid training course for professionals already skilled in ultrasound-guided venipuncture, so to make them able to insert also Midline and PICCs.

As an alternative to PICCs, in case of specific contraindications, or in the absence of specifically trained personnel, **central insertion catheters (CICCs)** will be used, obviously using ultrasound guidance. In the presence of helmets, face masks, tracheostomies, etc., an infra-clavicular approach (ultrasound-guided puncture and cannulation of the axillary vein) rather than a supraclavicular approach is recommended, in order to provide greater protection and stability of the catheter at the exit site. An important indication for the preferential use of CICCs is the need for a central route with more than three lumens.

In COVID-19 patients, the use of **femorally inserted central catheters (FICCs)** may also be considered. The advantage of FICCs is, of course, the ability to perform the insertion maneuver while further minimizing the risk of operator contamination by the patient's oral, nasal and tracheal secretions, if compared to PICCs and CICCs. When inserting a FICC (usually we recommend adopting a power injectable, polyurethane, open-ended, non-valved PICC, used *off-label* as FICC) some precautions must be taken into account:

- the exit site should preferably be at mid-thigh, away from the groin, which is possible either (a) by puncturing the common femoral vein and then tunneling to mid-thigh, or (b) by directly puncturing the superficial femoral vein at mid-thigh;
- if monitoring of central venous pressure or of mixed venous blood oxygen saturation is required, the tip of the FICC should be in the right atrium, verifying the location of the tip by intracavitary ECG or echocardiography (see below);
- if the FICC will be used exclusively for blood withdrawals and infusions, and not for monitoring, the tip may be placed in the middle tract of the inferior vena cava (above the bifurcation of the iliac veins and below the renal veins). A good anthropometric length estimation is to consider that the tip must be below the navel.

To reduce the risk of thrombosis, it is advisable to choose femoral veins of adequate diameter (5Fr catheter: vein at least 5mm, etc.; as already described for PICCs). In addition, it is highly advisable to protect the emergency site from local contamination from the groin, not only by moving it to the middle of the thigh, but also by sealing the site with cyanoacrylate glue before applying the transparent semi-permeable dressing. Finally, it should be noted that FICC (as opposed to PICC and CICC) cannot usually be used for the measurement of cardiac output by thermodilution.

Although there are no clear clinical data yet, it is possible that the COVID-19 patient - due to his hyper-coagulability status - may have a **high risk of catheter-related thrombosis** (either after PICC, CICC or FICC insertion). In the absence of contraindications, then, for all central venous catheters in COVID-19 patients, subcutaneous administration of low molecular weight heparin at prophylactic (100 units/kg/24h) or even therapeutic (100 units/kg/12h or 150 units/kg/24h) dose should be considered. In many centers, anticoagulation is already given to any COVID-19 patient, regardless of whether a central venous catheter is present or not, as a prevention of pulmonary vascular thrombosis.

Finally, through a femoral or supraclavicular venous access it is possible to place specific catheters for **dialysis and hemodiafiltration,** which are sometimes required in COVID-19 patients; these devices can be inserted *ex novo* or also through replacement of pre-existing FICC or CICC catheters over guidewire.

3) Appropriate choice of insertion technique

All central venous accesses (PICC, CICC, FICC) should of course be positioned by **ultrasound-guidance,** as recommended by all international guidelines (14)(15): ultrasound will play a fundamental role in the whole maneuver, allowing (a) to choose the most appropriate vein, (b) to perform the venipuncture safely, (c) to exclude immediately some possible complications related to the puncture, (d) to verify the correct direction of the guidewire and/or of the catheter (*tip navigation)* and (e) to verify the correct final position (*tip location)* (16). In the COVID-19 patient, **wireless ultrasound probes** should preferably be used, as they allow maximal cleaning of the probe between patients and minimal risk of contamination. These wireless probes are inexpensive and quite widespread in our Country; they consist of a portable transducer connected via Wi-Fi technology with the display of a smartphone or a tablet (obviously both keyboard-less). Wireless probes have always had the advantage of extreme portability, which makes them particularly useful in bedside insertion of long dwelling peripheral catheters (mini-midline and midline) and of central venous catheters. In the COVID-19 patient they become desirable - if not perhaps indispensable - for minimizing the risk of contamination. During the maneuver, the probe is covered by a sterile probe cover, while the display (i.e. the smartphone or tablet) is contained in a non-sterile transparent envelope and supported by a

stand. After the procedure, the covers are easily removed, and the probe and the display are cleaned with an appropriate solution. The lack of grooves and keypads facilitate the disinfection of both.

In the absence of wireless ultrasound probes, the most advisable strategy is to dedicate an ultrasound device exclusively to maneuvers on COVID-19 patients; this does not, of course, exempt from an accurate disinfection of the ultrasound device and of the probes, after each procedure, according to the current recommendations provided by the manufacturer and available on specific web sites (17).

The recommendations on the mandatory use of ultrasound also concern **peripheral arterial catheters**, which are essential in the COVID-19 patient admitted to the intensive care unit - but also frequently necessary in non-intensive care settings - for continuous monitoring of blood pressure and/or for performing arterial blood gas analysis and blood sampling. The forthcoming guidelines of the European Society of Anesthesiology (ESA) (18) recommend the use of ultrasound (level of evidence IB) also for arterial cannulation. Ultrasound guidance is particularly important in COVID-19 patients, since the difficulty of palpating the arterial pulsation, due to the presence of double gloves, may make blind cannulation impossible.

Another important point in COVID patients is to **avoid radiology after central venous cannulation:** whether you transport the patient to the radiology department or bring the radiological equipment to the patient's bed, the risk of contamination of operators and machinery is very high. In these patients, it is imperative to check the location of the tip of the central venous catheter by non-radiological methods, such as **intracavitary electrocardiography** (IC-ECG) and **transthoracic echocardiography** (TTE). These two methods for tip location have been strongly recommended by recent studies and guidelines, as they are considered safer, more accurate and more cost effective than chest x-ray (15). The fact that both methods are not yet being used on a large scale is exclusively related to cultural issues; in fact, reasoning in terms of resource savings, clinical effectiveness and patient safety, chest X-ray after CICC or PICC insertion should logically be abandoned in favor of intra-procedural verification by IC-ECG and/or TTE. Tip location by TTE can be performed rapidly at bedside using wireless probes with convex, micro-convex or sectorial transducers and using the so-called ‘bubble test’ or contrast-enhanced method (rapid infusion of saline with the addition of micro-bubbles of air, visualized by subxiphoid or apical echocardiography) (19). Tip location by IC-ECG can also be performed at bedside minimizing the risk of contamination: if the patient is not already connected to an ECG monitor (as it usually occurs when the COVID-19 patient is in ICU), a dedicated wireless ECG monitor can be used, connected to a smartphone or tablet using Bluetooth technology.

In the case of CICC insertion, it will also be necessary to **verify the absence of pneumothorax**: also in this case, it is not recommended to use radiological methods. Many studies have shown that the sensitivity of the ultrasound examination of the pleural space is greater than that of chest x-ray in the diagnosis of pneumothorax (16). The ultrasound examination of the pleural movement will be done (preferably with a wireless probe) immediately after the insertion of the CICC to optimize the time of verification of complications and the patient’s safety.

Another important precaution in the COVID-19 patient concerns the **prevention of central venous catheter dislocation**. In fact, the risk of dislodgment is particularly high in this type of patient, particularly during the maneuvers of pronation-supination. The loss of a central line where vasoactive amines are infused is certainly a serious event and requires a new emergency insertion that can be difficult and associated with additional risks. Moreover, the partial or total dislocation of a CICC or PICC in a COVID-19 patient (and therefore the need for repositioning it) not only implies a waste of resources (as in the non-COVID-19 patient, with the addition of the valuable personal protective equipment, unfortunately limited in its availability), but also to a new risk of contamination of the operator when repeating the procedure. It is therefore necessary to consider the use of **subcutaneously anchored securement**, which will make the dislocation less likely especially in the agitated patient or in the patient undergoing periodic pronation.

Finally, as in all patients with central venous access devices, it is important to **protect the exit site of the catheter** by (a) cyanoacrylate glue or chlorhexidine-releasing sponge dressings, and (b) semi-permeable transparent membranes with good adhesiveness and high transpirability.

4) Taking appropriate precautions to avoid operator contamination

The insertion of central venous accesses or long term peripheral venous accesses should be performed following the CDC recommendations for vascular access in COVID-19 patients (20): For patient protection, the operator should take the **highest 'standard' barrier precautions** (hand hygiene before the maneuver, skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol, non-sterile surgical mask, non-sterile cap, sterile gloves, waterproof sterile gown, wide sterile field on the patient, sterile probe cover of appropriate length around the ultrasound probe).

With regard to the protection of the operator, apart from **personal protective equipment (PPE) for contact protection** (double glove, full suit, goggles or face shield, footwear), in COVID-19 patients the Centers for Disease Control (CDC) recommend the use of the surgical mask for the patient (if not intubated) and for the operator. Protective masks with N95 filter (equivalent to FFP2 of the European nomenclature) are recommended by the CDC only for procedures that generate aerosol (tracheal intubation, extubation, bronchoscopy, tracheostomy packing, etc.). Nevertheless, considering also some recent documents of the World Health Organization (WHO), the Italian 'Istituto Superiore di Sanità' (ISS) and the European Centre of Disease Prevention and Control (ECDC) (21), we strongly recommend the use of a double mask (mask with protective filter type FFP2 + surgical mask) also for the insertion of vascular access devices, considering the high risk of aerosol in the environment, especially in the extubated and symptomatic patient or in NIV. An additional strategy may be to protect the patient's face with a non-sterile transparent waterproof plastic cover that allows the operator to see the patient but at the same time protects him in case of contamination by droplets.

Conclusions

Well aware of the multiform clinical realities present in our Country, we know that not always and not all of these recommendations can be implemented everywhere, even if they are recognized as reasonable. Particularly in this circumstance, no one should attempt procedures and methods that are unfamiliar to him/her and/or for which he/she does not feel to be appropriately trained. In fact, there are some clinical units in Italy that are up to date from a cultural and technological point of view, but there are also clinical units where there is a lack of clinical staff trained for the insertion of some or all of the venous access devices illustrated in this document (mini-midline, Midline, PICC, CICC, FICC); there are (unfortunately) many clinical units where there ultrasound guidance is still scarcely used; there are clinical units where there is an over-indication of radiological controls after the insertion of central venous access devices; there are clinical units where the adoption of international recommendations for the prevention of infective complications during insertion of vascular access devices (hand hygiene, skin antisepsis with chlorhexidine 2% in alcohol, maximum barrier precautions) is inconsistent or defective.

We are also aware that the failure to update the procedures for venous access is not due to a lack of resources, considering that all the strategies listed in this document result in significant cost savings: let us consider - just to give a few examples - the relevant reduction in the incidence of expensive early and late complications when adopting ultrasound guidance, or the low cost of wireless probes compared to traditional ultrasound devices, or the advantage of the tip location by IC-ECG or TTE in terms of time and money. The real issue is a in the area of logistics and of education: it is a lack of willingness to optimize the procedures, caused by an organizational and cultural difficulty in identifying and implementing those strategies that are associated with greater safety of the patient and the operator and greater savings of resources.

The tragic pandemic that has hit us in recent weeks will undoubtedly change many of our clinical behaviors in the future. We hope that, in the field of venous accesses, the positive side effect of this experience can take the form of a new awareness of the need to save resources and increase safety even outside of health emergency situations, adopting winning strategies such as:

(a) to implement vascular access teams trained to insert any short or medium-term venous access device, according to the needs of the individual patient (see in this regard the reasoned guide to the choice of venous access device contained in the 'VAD-Expert' expert system developed by GAVeCeLT (22);

(b) to abandon the routine use of radiology for checking the tip location and ruling out pneumothorax after central venous access insertion, in favor of faster, more accurate, safer and cheaper methods such as intracavitary electrocardiography and echocardiography;

(c) to adopt systematically appropriate technique of infection prevention in order to maximize both patient and operator safety during insertion of vascular access devices.

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