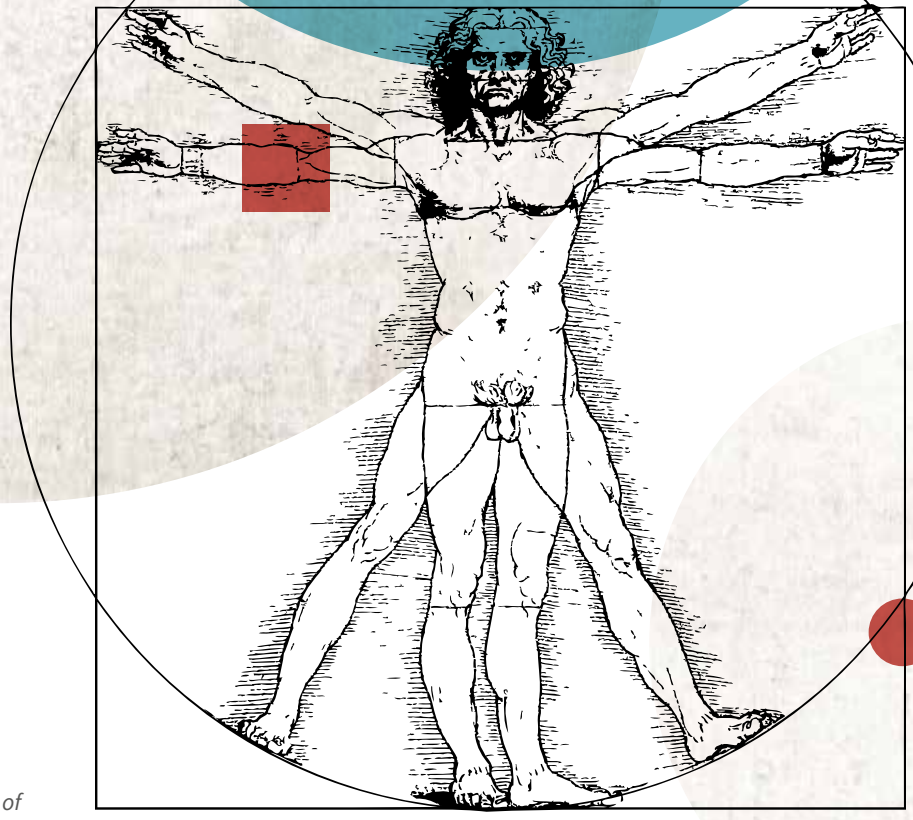
Optimum Use of ***Peripherally Inserted Central Catheters*** (PICC Lines) in Oncology and Hematology



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Optimum Use of ***Peripherally Inserted Central Catheters*** (PICC Lines) in Oncology and Hematology

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Medicine is constantly-evolving science. In this volume, we discuss the “state of the art”, as it may be defined at the time of writing, based on data taken from the most authoritative international literature. It is precisely within the field of treatment that the most rapid developments are to be found, due to both the advent of new drugs and procedures, and changes in the approaches to circumstances and usage of those that have already been in use for some time, as a result of experience gained. However, the authors, editors and all others who have contributed to the drafting or production of this publication may not be held in any way responsible for any conceptual errors that depend on the evolution of clinical thought, or for any material or printing errors that may occur, despite every effort being made to avoid them. Readers who intend to apply any of the therapeutic notions reported must therefore always ascertain that they are up to date and accurate, by consulting reliable sources and directly checking all relevant information in the summary of product characteristics enclosed with each pharmaceutical product, with regard to its clinical indications, contraindications, side effects and, especially, dosage.

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Preface

FAVO (*Federazione italiana delle Associazioni di Volontariato in Oncologia* [the Italian Federation of Volunteer-based Cancer Organisations]) has always promoted ethical values and supported the multidimensional planning of patients' care needs, to achieve the best possible quality of life.
This publication is the outcome of this vision. The purely technical aspects are incorporated into a framework that assumes the correct choice of device type, with the active involvement of the patient, whose preferences must be taken into account, as well as the type of treatment and its duration, the care setting and the presence of a caregiver. The introduction provides certain information that warrants attention: the use of PICC lines has increased significantly in Italy, putting the country at second place in Europe. The use of ports, on the other hand, is below the European average, and the overall number of central venous catheters used is lower than the estimated need for oncology and haematology patients.
There is a tendency towards both inappropriate overuse and inappropriate underuse.
Organisational aspects, availability of human resources, training and the approaches adopted by the healthcare facility that the patient is referred to can make a difference, as can the availability of a team of vascular access specialists to optimise the quality of care and treatment.
The FAVO believes that the Italian acronym "PDTA" (Percorsi Diagnostico-Terapeutici Assistenziali [Diagnostic and Therapeutic Care Pathways]) is all too often lacking the "A" for "assistenziale" (care) and this is certainly the case for central venous catheters.
To what extent does the type of venous access have an impact in terms of the number of hospital visits, personal relationships, complications and distress for the patient?
As a Federation, in all the round tables we partake in, we promote the definition of high-quality standards of care that should be included amongst the priority objectives of the Local Health Authorities of the Italian National Health Service.
We guarantee our support to the Scientific Societies that back this project in all training initiatives aimed at increasing the appropriateness of the patient journey, starting with devices.
It is our mission to raise awareness regarding this issue on behalf of our patient advocacy groups, which will contribute to planning the various regional PDTAs. We would like to thank the authors and the Scientific Societies for their commitment and perseverance in promoting discussions on the ethical repercussions of organisational decision-making.
Together, and as always, by working in synergy with the Scientific Societies, we can overcome the many challenges that face us in the post-COVID healthcare scenario.

FAVO - Federazione Italiana delle Associazioni di Volontariato in Oncologia

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Chapter 1 – Introduction

1.1 Vascular Access in Oncology and Oncohaematology: the Italian scenario

The placement of vascular access devices is an invasive practice that is commonly performed in specialised ("second level") facilities, to allow diagnostic and therapeutic procedures such as collection of specimens, haemodynamic monitoring, supportive treatments (electrolyte infusions, hydration, transfusion therapy, parenteral nutrition, etc.) and pharmacological therapy (chemotherapy, anti-infectives, analgesics, etc.) or apheresis/dialysis.

The choice of venous access device from the variety of available options should be based on the level of clinical complexity and the care needs of the patient, considering the type of infusion, and the anticipated duration and frequency of treatment.[1]
In clinical practice, almost all hospitalised patients have a vascular access device fitted; in 90% of cases the device used is a peripheral IV catheter (PIV), and central venous catheters (CVC), such as totally implantable devices (ports) and PICCs (peripherally inserted central catheters), are only used in a minority of cases.[2]

Several published studies report an average PIV failure rate of between 46 and 59%, due to placement difficulties or the occurrence of complications such as extravasation, occlusion, phlebitis, displacement and infection (including sepsis from methicillin-resistant strains of *Staphylococcus Aureus*, MRSA), requiring device removal. Loss of function of the vascular access means the treatment cannot go ahead.

Although the incorporation of PICC lines into the range of vascular access devices available, partially replacing PIVs, CVCs and implantable ports, is a relatively recent development, there has been a rapid increase in their usage in Italy, which has meant that the country currently occupies second place in the European market, after the United Kingdom, with 82,371 PICCs used each year, whereas the annual usage of ports (40,100) and CVCs in general (610,689) is lower than the European average.[3]

Although this widespread use of PICC lines in Italy is testament to an overall improvement in the selection criteria for vascular access devices, the usage of central venous access devices is still lower than warranted by the actual clinical and healthcare needs of patients and by the criteria of appropriateness in many fields, including oncohaematology.
The need for a stable vascular access device should be an integral part of effective diagnostic and therapeutic patient management throughout the course of the disease, from the early stages, in which the availability of a CVC allows neoadjuvant chemotherapy or post-surgical adjuvant thera-

py to be administered, through to the rehabilitation, advanced and final stages, in which CVCs may be used for palliative and supportive care. This requirement does not only concern hospital care, but also the numerically significantly outpatient setting, and all the other community and home care settings (hospices, residential nursing and rehabilitation facilities, integrated home care]) that increasingly appear to provide the healthcare of these patients, both in Italy and elsewhere.[4]

It is known that PIVs should not be used to infuse irritant solutions, chemotherapy, continuous vesicants, parenteral nutrition, solutions with a high osmolarity (above 900 mOsm/L) or solutions that may be harmful for the peripheral veins (pH <5 or >9), and yet even today, 45% of oncology patients receive chemotherapy by cannula needle, at least during the initial cycles, which exposes them to the risk of serious, perhaps irreversible, harm. If we consider that the incidence of oncological disease in Italy is approximately 371,000 newly-diagnosed cases each year,[5] the extent of the problem is apparent, showing that the importance of preserving the peripheral vascular tree of these patients is not adequately perceived by healthcare professionals and that the suitability of vascular access devices is a critical issue in the care of cancer patients that is still widespread in Italy, although it varies greatly from one geographical area to another.

1.2 Critical Issues in Current Clinical Practice and Document Objectives

This research paints a rather fragmented picture of the use of vascular access devices in the Italian oncology and haematology setting, and it highlights a certain amount of cultural uncertainty regarding the process for selecting the most suitable type of vascular access device, as well as regarding the characteristics of the various devices, the associated complications, the insertion techniques and the correct management of the devices, with training disparities among professionals with different levels of expertise.

Overall, clinical practice in these settings appears to be characterised by the lack of a decision-making algorithm for choosing which device to insert. All too often, the choice of device is dictated by a depletion of peripheral venous access sites, organisational difficulties or even patient preferences, rather than by scientific evidence or specific guidelines.

Consistent variability can be observed between centres regarding the provision of documents that are formally approved by the competent facility, and when they are present, they mainly take the form of operational protocols intended to regulate the insertion and management of vascular access devices, and do not redress the lack of recommendations regarding device selection criteria or the discrepancy between the guidelines and the degree to which they are implemented in clinical practice.

Vascular access teams allow professionals to operate according to a multidisciplinary approach, promoting a collaborative and proactive attitude, as required by cost-effectiveness assessments. The proactive choice of a device must take into account:

- type of treatment;
- duration of the treatment;

- patient needs and wishes;
- the healthcare setting.

However, the current situation shows that the choice still tends to be all too often constituted empirically, on the basis of an operational need as perceived by professionals, and only more rarely constitutes an actual organisational framework formalised by Healthcare Directorates and provided with dedicated resources.

With regard to the criteria that guide the decision to use a PICC rather than other types of central venous access devices, the simplicity of the procedure, the fact that it can be fitted by a nurse without the need for an operating theatre and with shorter organisation times, which allow costs to be kept down and treatment to be started sooner, are some of the main factors that have led to the rapid and widespread use that is seen today in oncology and haematology units. One important factor of the current popularity of PICC lines is precisely the direct involvement of nursing staff in the highly vocational activity of the PICC team, which is perfectly in step with the therapeutic and organisational needs of Departments, particularly in the field of oncology, where the use of PICC lines has changed the waiting times for the start of treatment associated with central venous access.

This document was therefore drawn up by a multidisciplinary group of experts from the Scientific Societies IVAS (Italian Vascular Access Society) and AIOM (*Associazione Italiana di Oncologia Medica* [Italian Association of Medical Oncology), and aims to establish the guidelines for the optimum selection and use of PICC lines, within the early clinical journey of the oncology and haematology patient.

As a matter of fact, the authors believe that the planning of vascular access should constitute an integral part of the patient journey and that the choice of the most appropriate device should be based on multidisciplinary team skill-sharing and a collaborative process that takes the patient's needs into account.

Considering that there are multiple variables at play when choosing a vascular access device, this publication aims to guide healthcare professionals in the overall assessment of the specific case and to help resolve the critical issues that arise with regard to the correct application of vascular access guidelines in current oncological and haematological practice, while fully taking into account the specific operational and regulatory characteristics of the Italian healthcare setting.

In order to disseminate best practice guidelines on the use of PICCs that are based exclusively on solid scientific evidence and may help streamline and improve the standards of care and the criteria of appropriateness in oncology and onco-haematology, the contents of this publication have been formulated on the basis of evidence from a reasoned analysis of the literature, conducted in accordance with the scientific rigour of the Grade6 method used to draw up the guidelines.

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Chapter 2 – Choosing a PICC

2.1 Choosing a venous access device for an oncology patient

Choosing the vascular access device is an integral part of the patient journey in oncology and oncohaematology. The availability of a suitable venous access is an essential criteria for proper patient management for the entire duration of the treatment pathway, in order to protect the veins and ensure justified and systematic delivery of therapies.[1]
Evidence shows that choosing an unsuitable venous access device may lead to:[2]

- venous damage;
- delayed start to the treatment plan;
- prolonged hospitalisation;
- increase in device-related phlebitic and thrombotic complications;
- healthcare professionals taking longer to locate the vascular access devices.
- increased infusion therapy-related costs;
- discomfort and stress for the patient, with a poorer quality of care.

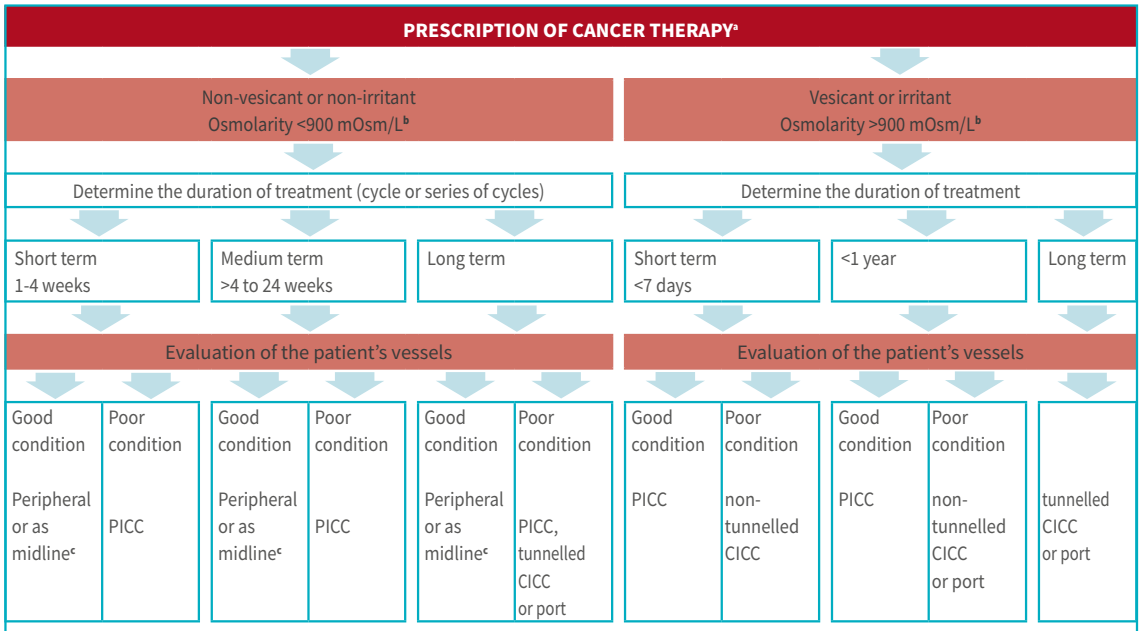
The need to fit a venous access device should be assessed at the start of the patient journey, when he/she is first admitted for care.[3,4]
The choice of suitable venous access is made by integrating the various multidisciplinary skills, from the care team to the vascular access team, also involving the patient and his or her caregivers.[5]

When choosing the device, the VAT (Vascular Access Team) in particular, draws on its training and detailed knowledge of the various devices in terms of indications to provide a reasoned assessment in order to identify the best solution with the least impact on the patient and as few complications as possible, while respecting specific criteria of appropriateness, defined on the basis of objective scientific evidence, considering proven safety, cost-effectiveness and efficiency parameters.
The choice of a peripheral or central venous access device must be based on the evaluation of a series of fundamental factors that can be broken down into four aspects:[3]

- The characteristics of the treatment plan (in particular the type of therapy prescribed and the expected duration of treatment).

- The characteristics of the device (invasiveness, indications, ease and safety of placement, duration of use in situ, possible associated complications, cost-effectiveness, management, material, diameter, number of lumens, etc.).
- Patient characteristics (age, comorbidities, venous characteristics, previous infusion therapy, preference in terms of type or site of the device, lifestyle, capacity and resources available for management of the device).
- The usage setting (emergency or elective).

Although these criteria may be guided by a decision-making algorithm, it is crucial for each patient to be assessed individually and according to therapeutic needs.[3]
Figure 1 illustrates an algorithm for selecting a venous catheter based on infusion characteristics, duration of treatment and the patient's clinical and vascular status, as proposed by the guidelines on infusion therapy safety in cancer patients published by the ECO-SEOM-SEEO (Foundation for Excellence and Quality in Oncology, Spanish Society of Medical Oncology, Spanish Society of Oncology Nursing).[6]



[a]Other criteria to consider are the number of lumens required, the required flow rate, the need for blood draws, patient preferences, availability at the hospital and the patient's capacity for self-care and to comply with treatment after discharge.
[b]There are diverse recommendations on the osmolarity limits for solutions for peripheral infusion in the literature available.
[c]The maximum time the catheter can remain in the vein is 4 days for short-term peripheral catheters, and 28 days for midline catheters. The use of devices with a longer duration of use should be taken into consideration depending on the need for other concomitant drugs or blood sampling that require vascular access between treatment cycles.

Figure 1. Algorithm for selection of a venous access device for cancer patients.

2.2 The treatment characteristics that guide the choice towards a PICC

PICCs (Peripherally Inserted Central Catheters) are by definition peripherally inserted central venous access devices, i.e. intravascular catheters inserted through a peripheral vein in the arm and introduced until the tip is positioned close to the junction between the superior vena cava and the right atrium (cavoatrial junction, more specifically, in the lower third of the superior vena cava or in the upper third of the right atrium).
In oncology, PICCs serve all the uses that central venous catheters are intended for, such as infusion of drugs, solutions and blood products, blood sampling and haemodynamic monitoring to measure central venous blood pressure.[7-9]

PICCs are indicated for the infusion of acidic (pH <5), basic (pH >9) or hypertonic (osmolarity >800 mOsm/L) solutions of medicinal products with vesicant or irritant effects on the endothelium (associated with intimal injury). Infusing vesicant drugs into a peripheral vein is potentially dangerous, as it is associated with a high risk of extravasation, phlebitis, infiltration and local tissue damage, and it may lead to a progressive depletion of the peripheral veins available. Since many cancer drugs are known to be vesicant, in oncology patients undergoing chemotherapy, the recommended venous access device is a CVC such as a PICC, rather than a peripheral device. Although the Infusion Nurses Society (INS) guidelines recommend central venous access (including PICCs) for the administration of vesicant drug boluses, in many oncology units, chemotherapy is still administered mainly via a peripheral route; however, this requires use of a different access site for each administration and recording of the access site to avoid repeated use. In any case, the continuous infusion of vesicant substances may only be performed via a central route.[10]

Therefore, in this setting, the placement of a CVC is often the best option available to ensure effective treatment management and to offer quality clinical care throughout the course of the disease, from the initial stages, for administering neoadjuvant chemotherapy or post-surgical adjuvant therapy, to the advanced stages, for palliative and supportive care, in order to reduce patient discomfort. The type and duration of infusion therapy, device characteristics in terms of safe duration in situ and patient characteristics are the main factors that should be considered in the decision-making process for the choice of the most appropriate catheter in each specific situation.[7]

One large-scale Italian multicentre, retrospective, observational study conducted on 2,477 adult patients who were monitored for 7 years recently showed that PICC lines are a safe option for the delivery of chemotherapy in oncology and onco-haematology in both inpatients and outpatients, as they are associated with a low adverse event rate (16.9%; 1.09 adverse events per 1,000 days of PICC placement), particularly in the most elderly patients, which confirms the results of previous studies conducted in the same setting.[11]
In this study, PICC lines were also used to deliver parenteral supportive treatments (parenteral nutrition, IV fluids, blood derivatives or antibiotics) for a duration of up to 6 months, proving to be a safe alternative for this type of medium-term therapy, when compared with centrally inserted catheters. Valved PICCs that prevent endoluminal blood reflux proved to be superior in terms of the need for removal due to complications, expressed in

terms of days of catheterisation, compared to open-ended PICC lines.[12] These results confirm the findings of previous studies on cancer patients treated at home with parenteral nutrition.[13]

As far as treatment duration characteristics are concerned, it is essential to choose a catheter that can remain in situ safely for the whole anticipated duration of the treatment. PICCs are medium- to long-term venous access devices that are indicated for infusions compatible with central delivery, are expected to be long-lasting and they are suitable for both continuous and intermittent, intra- or extra-hospital use, in compliance with the manufacturer's indications for use, in order to preserve the peripheral veins.
The Atlanta CDC guidelines strongly recommend (category IB) the use of midline or mini-midline PICC catheters (when the duration of the intravenous therapy is expected to be longer than 6 days).[14]
PICC lines are to be preferred over tunnelled catheters and ports for infusion therapy lasting between 15 and 30 days. In cancer patients, PICCs have been classified as appropriate for the infusion of irritant and vesicant drugs, regardless of duration.[15]

Although the maximum time that a PICC can remain safely in place has not been definitively established, the data indicate that placement of this type of catheter ensures long-term functionality, and it may remain in situ for a year or more without causing problems, thus constituting a sound alternative to traditional CVCs for administering therapy for a duration of between 6 months and 1 year.
The INS recommends that CVCs be considered a long-term alternative to PICCs if the patient requires the treatment for more than a year.[16]

2.3 PICC characteristics influencing choice

PICCs are long, thin and flexible central venous catheters that are placed via percutaneous access into a peripheral vein in the arm, such as the basilic, cephalic or brachial veins, usually under ultrasound guidance.

Given their characteristics, PICCs are used to administer medium- and long-term infusion therapy in various types of patient, especially in the presence of specific clinical conditions such as obesity or diabetes, as well as in cancer patients receiving chemotherapy treatments and in patients who require total parenteral nutrition.[17]
The safety and efficacy of PICCs have been demonstrated in a broad range of treatment settings, in cancer patients with both solid and blood tumours.[11,18,19]

PICCs are also indicated when a direct central venous approach is not possible or is contraindicated, in patients with clotting disorders or when it is believed that infectious complications can be reduced.[3]

In patients with blood cancers, PICCs are often chosen for outpatient or home treatment because they can be used safely even when the platelet count is extremely low or there is a high risk of bleeding.[8]

PICCs are a safe and effective alternative to conventional central venous catheters even in oncohaematology patients who are particularly prone to infectious and haemorrhagic complications, such as those who have undergone autologous stem cell transplantation.[20]

The availability of numerous types of PICC with special characteristics (distal valves, proximal valves, high-flow and high-pressure resistance, repair kits, single, double or triple lumen, etc.) makes these devices versatile and suitable for a wide variety of clinical uses and patients.16 As they are vascular access devices with a duration of over 30 days, PICCs are supplied with technical documentation that ensures traceability and provides manufacturer's guidance for correct and safe use by healthcare professionals.[3]

As they boast certain unique characteristics among central venous catheters, such as limited placement technique invasiveness, which is associated with a reduced rate of mechanical complications, a high degree of safety, and probably also a lower percentage of infection and easier removal, PICCs have rapidly become popular and their use has become more widespread over time, exceeding that of traditional CVCs in all clinical settings, including oncology, where they are extensively used in patients with solid or blood cancers.[17]

As a matter of fact, PICC lines are a sound alternative to traditional CVCs for many indications, being linked to the same possibility of infusing solutions of any osmolarity, at high flow rates and high pressure, bringing some significant benefits, starting with the safety and simplicity of the placement procedure, which can be performed by adequately trained nursing staff and at the patient's bedside, without the need for an operating theatre, consequently saving resources, cutting costs and reducing the time to the start of infusion therapy.[11]

The placement of a centrally or femorally inserted catheter may be associated with a significant risk of complications, some of which serious, such as pneumothorax, accidental artery puncture, haemothorax, stroke, arrythmias and nerve damage. The procedure must therefore be performed by a suitably trained doctor, usually in an intensive care unit or an operating theatre.[21]
Due to the particular peripheral insertion route, PICC placement is accompanied not only by a lower rate of mechanical complications, but also greater patient tolerability than CICCs (Centrally Inserted Central Catheters).[22]

Overall, these characteristics make PICCs compatible with use both inside and outside the hospital, including home use, due to their capacity for self-medication, generally less severe complications than those experienced with CICCs, and, if necessary, they can be inserted even at the patient's home, using a strict sterile procedure and portable instrumentation to confirm the correct positioning of the tip, including ECG-guided verification.[23]

For all venous access devices, ultrasound guidance increases the efficiency and safety of the placement procedure, whilst keeping the cost-effectiveness ratio favourable, through a reduced number of attempts and the associated complications. However, the data on clinical practice in Europe suggest that the incidence of ultrasound (echography) use is only high for PICCs, and is much lower for other types of CVC and minimal for PIVs (Figure 2).[3]

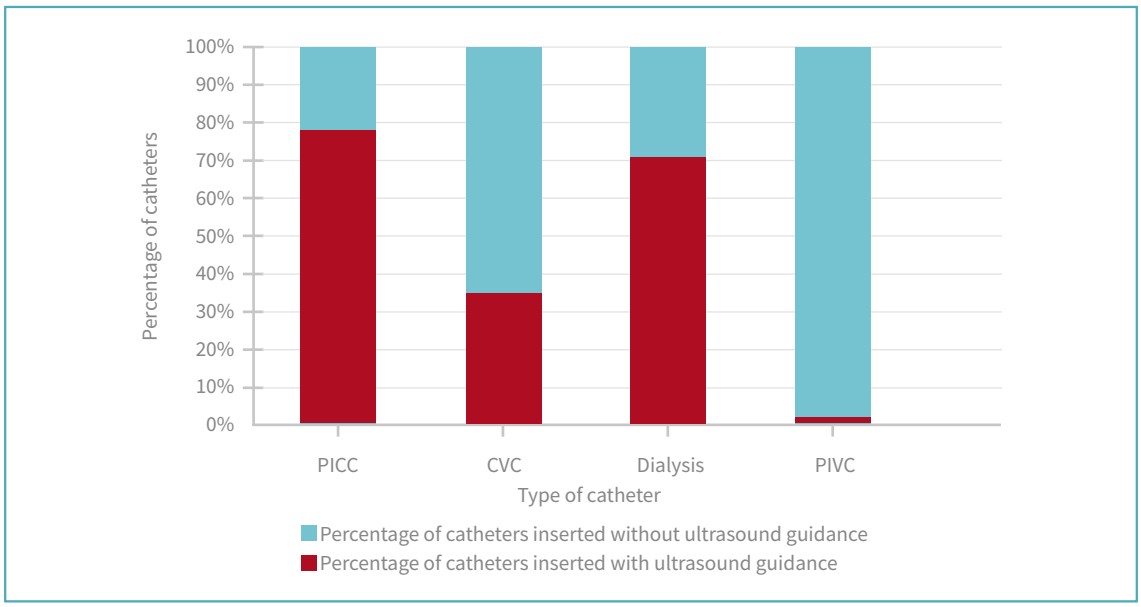


Figure 2. Percentage of placements performed using ultrasound guidance in European clinical practice for the different types of vascular access device.[24]

Ultrasound-guided PICC placement by nursing staff in oncology and haematology patients has been shown to be associated with a high procedure success rate (89.7%), prolonged time in situ (on average, 92 days) and very low complication rates.[25]

The use of specialised nursing staff and the possibility for the procedure to be performed directly at the patient's bedside, thanks to the availability of new technologies such as integrated tip navigation and tip location systems, which reduce intervention times and the need for post-placement repositioning, allow greater rationalisation of radiology resources and reduce operating theatre use.[3] The availability of devices specifically designed to identify the correct positioning of the catheters is a bonus in terms of both patient safety in all settings and cost-effectiveness.

This operational possibility can translate into a 65% reduction in costs compared to fluoroscopy-controlled insertion performed by interventional radiologists,26 as well as reducing patient and staff exposure to radiation, in accordance with directive 2013/59/Euratom of 5 December 2013.
The establishment of an access team with staff who are qualified to fit and manage venous access devices has proven to be effective in reducing the incidence of catheter-related complications, including infections, and the associated costs.[27]

In addition, the creation of a PICC team run by nursing staff has been seen to have a beneficial cost-effectiveness ratio, as well as being associated with a higher procedure success rate, whilst obtaining greater patient satisfaction regarding the quality of care and the time taken.[28]
If we examine the costs involved in the purchase of these devices and insertion procedures alone, the use of PICC lines is associate with higher costs than PIVs; however, it is important to

note that the cost-effectiveness ratio for PICCs appears to be favourable overall if the analysis takes into account parameters such as:

- procedure failure rate;
- rate of removal and of associated complications;
- the higher number of insertion attempts and devices used;
- the lower number of total days of usage;[29]
- the statistically higher incidence of phlebitis and catheter occlusions associated with PIVs.[30]

Being tunnelled catheters, PICCs come with special kits that allow them to be repaired without having to resort to a new catheter (for silicone valved catheters only), with savings associated with use of a new device and a new placement procedure, entailing further discomfort for the patient.
In an economic evaluation comparing PICCs and other CVCs based on an Italian model supported by real hospital practice taking into account the costs of the device, the placement procedure and possible complications, the cost-effectiveness ratio appeared to be closely associated with the number of accesses the patient has to undergo. The placement of more CVCs for a shorter duration than with PICCs involved higher costs, due to resource utilisation and hospital time, as well as an increased risk of adverse events and a deterioration in quality of life.[30] Moreover, CICCs cannot be managed at home and must be systematically removed before discharge from hospital.

2.4 The role of the patient in the choice of PICC

The choice of a venous access device must comply with precise criteria of appropriateness, particularly with regard to the type and duration of infusion therapy; however, it should also take into account the actual clinical need and the unique characteristics of the patient, with the primary aim of preserving the peripheral vessels and ensuring safety and comfort, together with a good quality of life.[5]
Choosing the device best suited to the patient's needs requires a thorough assessment of all related factors, such as age, site of the primary tumour and any metastases, comorbidities, allergies, the characteristics of the veins, any anatomical peculiarities, performance status, infusion therapy and previous venous catheters. It is also essential to consider factors such as any preferences regarding the type or site of the device, compatibility with lifestyle and family organisation, personal capacity and resources available for management of the device at home, such as support from family and caregivers, and the practical opportunities of access to the medication. These elements can be adequately evaluated at the initial assessment by the specialised nursing staff, through direct observation and discussion with the patient, and recorded on a form to be shared with the multidisciplinary vascular access team, in order to include the patient's characteristics and requests in the decision-making process that results in the choice of the most appropriate device for the individual case.[1]
Before the catheter can be inserted, the patient must sign the informed consent form, which, far from being a mere formality, should be considered the ultimate act of "conscious deci-

sion-making" on the patient's part, within the principle of the doctor-patient alliance, which is aimed at identifying the best treatment and includes the patient's right to understand and take part in the decisions regarding his or her treatment.

To be able to make an "informed" decision, patients who are candidates for infusion therapy, and any family members and/or caregivers involved, must receive all the necessary information on the characteristics of the most suitable device, the procedure for its placement, how to manage it, and any complications associated with its use, as well as any alternative options available. In the case of patients who are not hospitalised (outpatients or those receiving home care), the training of the patient and caregiver must be sufficiently thorough to allow correct device management and timely recognition of malfunctions or signs and symptoms consistent with infection or other complications. Effective and comprehensive communication helps guarantee safe infusion therapy and reduces the risk of complications. Therefore, the information must be provided in an accessible manner, using simple language and taking into account the age, cultural level, any language difficulties, and cognitive or functional limitations, and the achievement of the educational objectives must be suitably verified.[3]

Patient satisfaction with the device is an essential factor for improving compliance with infusion therapy and an integral part of the criteria used to assess the quality of the care provided. Several studies evaluating the experiences of cancer patients who have PICC lines fitted have indicated a high level of patient satisfaction and compatibility with a good quality of life.[31-34]

KEY POINTS

- ***It is important to preserve the patient's venous resources by choosing the right device before starting treatment and not once it is under way, when the venous bloodstream is already depleted.***
- ***The patient must be assessed with a proactive approach, taking into account various factors, such as the duration and type of therapy, the clinical setting, etc.***
- ***There must be a standardised procedure that is in line with literature and includes a decision-making algorithm.***
- ***The use of dedicated tip navigation and tip location technologies improves the clinical and process outcomes, with a consequent improvement in patient safety.***

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Chapter 3 – Types of PICC

Italy is one of the European countries that makes greatest use of PICCs, which would appear to suggest that it is developing a greater capability to choose venous access devices that better meet the actual clinical needs of patients and to comply with the criteria of appropriateness. More specifically, the more widespread use of PICCs in Italy than in other European countries can be attributed to the thorough training of healthcare staff and involvement of nursing staff in the placement of these devices, with the creation of specific teams for the placement and management of vascular access devices (VAD).[1]

Among the various types of PICC on the market, a list of medical devices from the Italian Ministry of Health that is updated weekly lists the models and the manufacturers of devices used nationwide. The list classifies the devices according to the features and nomenclature of the product. In Italy, the devices currently placed on the market are supplied by numerous manufacturers and the models that are most commonly used are open- or closed-tipped, polyurethane or silicone, valved or non-valved PICCs.

3.1 PICC: General characteristics and introduction

PICCs are a type of central venous catheter that is inserted peripherally. They were first placed on the market in the 1970s and are a sound and minimally invasive option that is indicated where a direct central venous approach would be impossible or contraindicated, or when it is believed that it may reduce complications due to infection.[1] Since they are inserted peripherally and with ultrasound guidance, PICCs, which may also be fitted by nursing staff, present an extremely low risk of harming the particularly delicate fine structures. They may also be fitted with confidence in patients with exceptionally low platelet counts and immunocompromised (haematology) patients and are especially commonly used in cancer patients. According to the Atlanta guidelines[2], the use of PICCs is justified when the duration of intravenous therapy is expected to be longer than 6 days. If the expected duration of therapy is less than 6 days, it is advisable to choose a short peripheral venous catheter.

In general, PICCs are flexible and versatile for different types of infusion and use, including for measuring central venous pressure (CVP) and the infusion of vesicant and urticant drugs with a pH above 9 or below 5 and osmolarity above 900 mOsm/L.[3]
PICCs possess a number of characteristics that determine their classification, namely: calibre (expressed in Frenches [F] or gauges [G], indicating the diameter of the lumen), length, flow rate, material, device architecture, insertion technique, ease of use, safety for the professional and cost. The combination of these characteristics determines the performance and provides guidelines on the use of each device.4 PICCs can be classified as single, double and triple lu-

men, and the material used to manufacture them can be radiopaque silicone or polyurethane. Another of the main characteristics is the type of tip, which can be open or closed depending on the model. PICCs can also be classified by whether or not they have a valve, which can be proximal or distal.

3.2 PICC Models

As mentioned above, there are various categories and models of PICC, each having specific characteristics. One particularly important type of PICC is the recently developed power-injectable PICC, which is made from particularly durable polyurethane (third-generation polyurethane) and has superior biocompatibility properties. The use of power-injectable PICCs allows the high-pressure infusion of contrast medium during CT and MRI scans.[5] The issue is also, and especially, relevant to intensive care patients, who often require contrast-enhanced examinations. Power-injectable PICCs are available with various gauges: 3 Fr single-lumen and 4 Fr double-lumen (ideal for paediatric patients), 4 or 5 Fr single-lumen, 5 Fr double-lumen and 5 and 6 Fr triple-lumen. The use of power-injectable PICCs is recommended for severe acute paediatric patients who are candidates for intravenous contrast-enhanced radiology examinations, the injection of which is performed by pumps that generate high pressure (known as power injectors).[6]

Another type of catheter that is better suited to the oncology setting is the partially implanted valved silicone PICC, with a closed tip and distal anti-reflux valve. These devices are available in both single-lumen and double-lumen versions; after placement, they are secured and stabilised using a sutureless system. Valved silicone PICCs, unlike open-tipped catheters, have a three-way valve that allows fluids to flow in and out but remains closed when not in use, thus avoiding blood reflux and the risk of air embolisms. The steps involved in the operation of this three-way valve are listed below:

- The negative pressure in the catheter causes the valve to open inwards, allowing aspiration of the blood.
- When the luminal pressure of the catheter returns to normal levels, the valve closes.
- The positive pressure inside the catheter due to the drop pressure, or the action of a pump or syringe, allows the valve to open outwards, enabling the infusion of the fluids into the bloodstream. When the luminal pressure of the catheter returns to normal values, the valve closes.

When not in use, the valve prevents blood reflux or bleeding towards the exterior and air embolisms, remaining closed, maintaining catheter patency and reducing the need for clamping and the use of heparin. This helps reduce the costs of managing the catheter. This valve model is designed to remain closed at a pressure of between –7 and 80 mmHg. In this situation, as the normal pressure values in the central vein are between 0 and 5 mmHg, the valve remains closed.

Lastly, if the placement of a thoracic port is not feasible, due to the episodic use of catheters (once a week) or for cosmetic reasons, brachial devices, called PICC-ports (originally called

brachial ports) should be adopted. The use of the term "PICC-port" is particularly appropriate, because it makes it clear that it refers to a brachial port in which the catheter is placed with the same technique as when inserting a PICC line, using a special provided kit.[6]

3.3 Single-lumen and double-lumen catheters

The guidelines of the US Centers for Disease Control and Prevention (CDC)2 state that multi-lumen catheters have a higher incidence of infection than single-lumen catheters. This aspect also formed the subject-matter of a meta-analysis study[7] and a review,[8] comparing the rates of microbial colonisation and CRBSIs (catheter-related bloodstream infections) for single-lumen and double- or multi-lumen catheters. The meta-analysis showed that multi-lumen central venous access devices are not an independent variable for higher microbial colonisation and CRBSI rates. The review, on the other hand, demonstrated that the use of single-lumen catheters avoided the onset of CRBSI, which instead appeared to occur with the use of multi-lumen catheters. When a multi-lumen catheter is used, it is advisable to dedicate just one lumen to parenteral nutrition. As a matter of fact, if the emulsion of nutrients comes into contact with pharmacological agents or with any parenteral infusion with a different pH, the possibility of precipitates, and therefore infections, forming increases. Furthermore, nutrient emulsions containing lipids should be infused using catheters that have a lumen with a fairly wide gauge in order to reduce the possibility of obstructions. Although further studies are required, at the current time, single lumen catheters are preferable for general clinical practice except in particular situations requiring the use of multi-lumen catheters.[9]

Multi-lumen catheters have been designed to be able to administer several treatments at once using the same device. Some models may have more than 3 lumens; however, these catheters are relatively new and are not widely used; indeed, they are reserved for patients undergoing intensive care, who need multiple therapies simultaneously. We now also have triple-lumen power-injectable PICCs, with high flow performance. These catheters have one lumen with smaller diameter lumens enclosed within it. However, the market share that these products occupy is rather small.

3.4 Medicated Catheters

Since catheter insertion involves the creation of a route of communication between the interior and exterior of the body, infections occurring at the outlet site should be limited as far as possible.
The most effective impregnated catheters are polyurethane ones coated with antibiotics (minocycline + rifampicin), or with antiseptics (chlorhexidine + sulfadiazine). The official guidelines2,11 (CDC 2011, EPIC3 2014) suggest their use, as their safety and efficacy have been proven by several scientific studies in recent years. These recommendations suggest that the use of central venous catheters impregnated with antimicrobial and antiseptic agents in adult patients in whom it is expected that the catheter must remain in situ for more than 5 days may reduce the risk of CRBSIs (catheter-related bloodstream infections). This appears to be advantageous from a cost-effectiveness perspective, especially in high-risk patients (intensive care, burns or neutropenic patients) and in other patient populations in which the CRBSI incidence rate exceeds 3.3 episodes per 1,000 catheter days, in spite of the adoption of a global strategy

to reduce the risk of CRBSI.11 It is useful to remember that chlorhexidine is a potentially allergenic antiseptic; therefore, it is advisable to assess the patient's susceptibility before use.[11]

3.5 Valved and non-valved, open-tipped or closed-tipped catheters

The choice of catheter type and its characteristics is fundamental, from a clinical perspective, for both patient health and the correct use and maintenance of the devices themselves. In addition to ordinary maintenance, such as heparin infusions and appropriate flushing, CVC manufacturers have extensively proposed and sponsored the use of valved catheters. These devices should prevent the reflux of blood into the distal part of the catheter, avoiding the build-up of fibrin and therefore the risk of clots.

The "ELeCTRiC" study (The Effect of Line/Catheter Type on Risk of Complications),12 conducted on 102 intensive care patients who had various types of catheter fitted, evaluated the influence of the presence or absence of the valve on PICC-related complication incidence rates. One study group received a valved silicone PICC, the second group were fitted with a Navilyst Medical Vaxcel PICC, with a pressure-activated safety valve (PASV), and for the last study group, the non-valved Turbo-Flo PICC, manufactured by Cook Medical, was used. The results of this study showed that the presence of the valve did not adversely affect occlusion and thrombus rates, suggesting that the use of this catheter model is a viable and safe alternative, with average complication rates compared to other catheter models. However, there are limitations to the study, as the critically ill patients concerned required multiple infusions due to the nature of their condition, putting them at greater risk of occlusion. A second limitation relates to the fact that the study was stopped prematurely for ethical reasons due to numerous episodes of haemolysis among the patients implanted with the PASV valve catheter, which reduced the statistical power of the results obtained.[12]

A second study,13published in 2014, found similar results after comparing three different PICC models in patients who were candidates for chemotherapy. The patients were randomised to three groups. The first group received the chemotherapy treatment using the Power PICC Solo central venous catheter, an open-tipped polyurethane power-injectable catheter with a "Solo-2" proximal valve. In the second group of patients, an Xcela PICC power injectable open-tipped polyurethane catheter with a proximal valve with PASV technology was used. Finally, the third group received therapy using a ProPICC non-valved, open-tipped polyurethane catheter.
All the PICCs used were single-lumen catheters with a diameter of 4 Fr, and the GAVeCeLT protocol was used for their insertion. During the study, the incidence of occlusion and malfunctioning of the catheters were evaluated as primary endpoints. The results of this study also demonstrated that the presence of the valve in PICCs did not increase the onset of complications and obstructions compared to non-valved catheters.[13]

A more recent retrospective cohort study[14], conducted on patients with haematological malignancies, evaluated the influence of the type of PICC on the rates and incidence of complications. According to the authors, patients with these haematological conditions are more susceptible to central line-associated bloodstream infections (CLABSI) and deep vein thrombosis (DVT) events, and therefore this patient population requires further study to understand whether the type of PICC can affect the occurrence of complications and to identify additional

risk factors. The study examined 485 double-lumen PICC catheters, inserted in 469 patients with blood cancers. Of these, 161 were silicone PICC lines with a distal valve, 60 were PowerPICC® Solo polyurethane catheters with a proximal valve, 165 were BioFLo® polyurethane catheters with a proximal valve and 99 were Arrow® antimicrobial-impregnated open-tipped catheters. All PICCs were inserted according to "Safer Healthcare Now" protocols, with ultrasound-guided procedures and x-ray confirmation of insertion. The primary endpoints of this study were: the evaluation of CLABSI incidence rates, defined according to the CDC guidelines,[15] the deep vein thrombosis rates, and the rates of mechanical complications such as displacement or the complete occlusion of the catheter.

The secondary endpoints assessed were the rate and incidence in the use of tissue plasminogen activator (tPA) to resolve the occlusions and the time of occurrence of complications. As reported in the results of this study, two PICCs of the same model were inserted in 15 patients; in only one patient, three were inserted, and in 4 patients, two different types of PICC were inserted. All the PICCs used had a calibre of 5 Fr and most were inserted via the patient's right arm. The patients who received Groshohng® PICC catheters recorded a longer duration of catheterisation (expressed in days) that the other 3 types of PICC. Furthermore, although complications were reported in all groups, the use of valved silicone catheters is associated with a significantly lower rate of complications and incidence than the other PICCs used. In patients who received this type of PICC, the rates of occurrence and incidence of deep vein thrombosis and complete occlusion of the catheter were also significantly lower than with the other types of PICC. In addition, the times of occurrence of the first complications from the day of insertion were found to be significantly longer for valved silicone PICC catheters (146 days).[14]

Another characteristic that may influence and alter the functionality and safety of PICC catheters is the proximal or distal location of the valve. A randomised, prospective, comparative study[16] published in 2010 attempted to clarify this issue by comparing polyurethane PICC catheters with a proximal valve located internally near the catheter hubs (Vaxcel with PASV technology) and silicone PICC catheters with a distal valve located near the closed, rounded tip of the catheter.[16] Both catheters were 4 Fr in diameter and 60 cm in length, with 17- and 18-gauge lumens for the proximal and distal valves, respectively. As mentioned above, the critical difference between the two types of PICC, in addition to the manufacturing material, is the design and the location of the valve. All catheters were inserted and positioned by interventional radiologists under radiographic guidance. The results of this study did not find any significant differences in the occlusion rates for the two PICC models; also, compared with other studies conducted on both models, lower catheter failure and displacement rates were observed for both models. Lastly, no significant differences between them were recorded in terms of the complications associated with parenteral nutrition infusions.[16]
As mentioned above, the type of tip can be open or closed depending on the model. This feature may be more significant for the occurrence of complications due to obstructions and consequent removal and catheter replacement.

A team of doctors and nurses from Azienda Ospedaliera di Melegnano (Milan) collected and published data regarding a comparative analysis of closed-ended and open-ended PICC lines used for administering chemotherapy in cancer patients.

The single-centre, retrospective, analytical study[17] evaluated the performance of 5 different types of PICC CVC focusing on the occurrence of thrombotic infections and complications and mechanical complications in general. The closed-ended catheters used were single-lumen valved silicone PICC lines, whereas the open-ended ones were single-lumen polyurethane Power Injectable PICCs.
The results of this study, which involved the placement of 1,416 catheters (including 623 midlines catheters) in 1,341 patients, found that the closed-ended valved catheters were clearly superior in terms of reliability, with fewer cases of complications, despite being used for longer periods in complex patients (cancer patients).
Compared to open-ended catheters, closed-ended valved silicone catheters had a lower complication-induced removal rate (92% vs 11%, respectively). According to this study, the valved catheters were the best solution for avoiding removal due to occlusion.[17]

A recent extension of the study,[18] conducted by the same authors, involved a statistical review of the comparison between silicone catheters with and without a proximal valve. In this extension, the observation period was 9 years, 5 more than the previous study, with a total of 3,700 adult oncohaematology patients, equal to 453,442 catheter days and 64,777 vascular access dressing changes. The results of the study provided new quantitative evidence that showed long overall PICC survival times in oncohaematology patients. They also allowed an in-depth investigation of the risk factors that can lead to catheter removal, based on patient characteristics and PICC type. In particular, valved closed-ended silicone catheters performed better than open-ended PICCs. Even after adjustment for various covariates, the risk of PICC removal due to complications was three times higher in patients with open-ended PICCs than those with closed-ended catheters and the probability of removal was 5 times higher with an open-ended PICC.[18]

A recent retrospective study,[19] conducted in 6 different Italian public hospitals on patients receiving chemotherapy treatment demonstrated that PICC catheters are a safe and effective device for delivering chemotherapy in these patients. Specifically, given the absence of specific recommendations on the use of central venous catheters in cancer patients, the authors evaluated the complication rates, and consequent PICC line removal in 2,477 patients who were fitted with both valved and open-ended PICC lines, used especially in patients who needed high-pressure (contrast agent) or high-osmolarity (parenteral nutrition) infusions. The primary endpoint of the study was evaluation of the removal of PICC lines based on the occurrence of complications, while the secondary endpoint was measurement of the frequency of complications (occlusions, infections at the outlet site or symptomatic thrombosis) during the study period. The results of the study showed that PICC catheters can be used safely for chemotherapy treatment in cancer patients, with a low incidence of major complications such as infections or thrombosis. The most common complications that led to the decision to remove the PICCs were occlusions (about two thirds of all cases of removal). However, the occlusion rates were substantially lower than in other similar studies. The rates of PICC removal due to infections at the outlet site were found to be consistent with the current literature, whereas the incidence of thrombotic complications was found to be lower.
Although the retrospective nature of the study poses certain limitations, the study showed that the use of PICCs in cancer patients appears to be a safe strategy for medium- to long-term chemotherapy treatments.[19]

3.6 Polyurethane and silicone catheters

The first PICC catheters were used in the early 1940s for haemodynamic measurements and they became established in clinical practice in the early 1970s, particularly for administering parenteral nutrition to patients. The main complications associated with their use were related to the poor quality of the materials used at the time (first-generation polyethylene and polyurethane), which greatly reduced their adoption in patients. Since the 1990s, with the advent of new materials, including silicone, and the improvement in existing materials (polyurethane), PICC catheters have once again become widely used.[5]

The choice of materials is associated with the advantages and disadvantages of each one.
The advantages of using silicone to manufacture PICCs, in addition to its biocompatibility, lie in its softness and flexibility, low risk of thrombosis, resistance to biological fluids and finally, its reduced roughness, which reduces bacterial adhesion. The disadvantages include a high risk of intravasal kinking and the "internal lumen:wall thickness" ratio, although this is rather low.
By contrast, the benefits of using polyurethane are its greater consistency, which facilitates its insertion, good biocompatibility and a high "internal lumen:wall thickness" ratio. However, the use of polyurethane can cause kinking.

Currently, the main difficulty in comparing silicone PICC catheters with polyurethane PICC catheters is that the silicone products are almost exclusively silicone catheters with distal valves, which severely limits the choice. This can be attributed to the fact that this material allows infusions at high pressure with minimal risk of failure. However, complications are also possible with this material.

In terms of safety and the incidence of complications, the comparison between the two types of material has been extensively discussed in various clinical studies.
A systematic review collected data from prospective and retrospective studies published between January 2000 and October 2013 in order to evaluate post-insertion PICC complication rates in the general population and in cancer patients, according to the type of catheter material.[20]

The study focused on the overall complication rates for both models of PICC but also classified the rates into different complication categories, such as phlebitis, infections, occlusions, displacement, thrombi and catheter breakage. The overall complication rates for the two materials were almost identical (29.53% for polyurethane PICCs and 24.46% for silicone PICCs).

Interesting results emerged when complications were divided into different classes, showing that, in the studies reviewed, polyurethane PICCs had higher phlebitis and occlusion rates, whereas silicone PICCs had higher infection, dislocation and thrombus rates than polyurethane PICCs.
To conclude, the study shows that, in general, both silicone and polyurethane PICCs are safe and well tolerated, but that the choice of material may be important to minimising the risk of complications in certain patient categories.

A second retrospective study[21] published in 2016 analysed the occurrence of complications of polyurethane or silicone catheters used with totally implantable venous access ports (TIVAP) in the forearm in the short and long term. Out of a total of 698 implants, 396 were fitted with polyurethane catheters, and 302 with silicone catheters. The early (occurring in the first 30 days after insertion) and delayed (occurring after 30 days of insertion) complications were divided into different categories depending on severity and the necessary treatment.
Mild complications (which did not require treatment), moderate complications (which may have even required hospitalisation) and severe complications (with permanent debilitating consequences, through to death of the patient) were considered. Both catheter models had a similar diameter and length and were inserted following the same procedures. The demographic features of the patients did not show any differences between the two groups.

The results of this study highlight the fact that devices equipped with polyurethane catheters showed early complications in 4.5% of cases, versus 0.7% of devices equipped with silicone catheters. Consistent with this finding, delayed complications occurred in 41.6% of devices with polyurethane catheters compared to 8.6% of devices with silicone catheters, suggesting an association between catheter material and the timing of complications.

Polyurethane catheters were associated with a greater risk of thrombotic events; in particular, there was a greater incidence of thrombotic occlusions in the catheter tip. Similarly, the occurrence of infections was higher in devices with polyurethane catheters.

This result is explained by the fact that thrombi, which are more frequent with this type of material, may serve as a platform for bacterial growth and that the surface of the polyurethane catheter, which is rougher and more uneven, may favour the possibility of micro-organism adhesion and growth.[21]
To conclude, this study highlights the importance of the choice of catheter material and that, on the one hand, polyurethane catheters are associated with a high risk of thrombosis and infection, and on the other, silicone catheters are more prone to mechanical-type complications.

3.7 Conclusions

To sum up, the procedure for choosing the right venous access device requires a thorough analysis of the patient's needs, the anatomy and health of the veins and the patient's medical history. It is also necessary to take into account the chemical and physical characteristics of the therapy prescribed and its role in the treatment. However, the first step is to understand whether there is a route for delivering the therapy that is safer and less invasive for the patient, such as oral administration. In certain situations, the risk-benefit ratio for the use of venous access devices is unfavourable for patient health. An important aid for choosing the right device can be found in the Vessel Health and Preservation Programme: The Right Approach for Vascular Access22 , which describes the steps and clinical guidance from the choice of device through to discharge. The aim of the programme is to make these steps as standardised as possible, so as to avoid delays in therapy and increase patient comfort, while keeping his or her vascular system healthy and intact.

KEY POINTS

- ***PICCs are a versatile option both in and out of hospital.***
- ***PICCs are most appropriate for oncological and haematological settings, where it is preferable to choose a valved silicone catheter.18***
- ***There are several types of PICC available and they should be chosen according to clinical need and the specific setting. A proactive assessment is paramount in the choice of the device in order to ensure the best care for the patient.***
- ***The standardisation of the procedures, in terms of placement and management of vascular access devices is the strategy indicated in the latest guidelines for ensuring safety and improving the clinical outcomes for the patient.***

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Chapter 4 – PICC Placement

4.1 General considerations

Venous access is used for the administration of medicinal products or fluids as part of clinical care. The ultrasound-guided procedure was initially used following the failure of conventional techniques.[1]
The ultrasound technique has now been used for some time in interventional radiology, as an aid for access to various organs in combination with venipuncture. Using the ultrasound technique, the vein can be visualised in two modes, a real-time ultrasound mode (which generates a two-dimensional greyscale image) and a colour Doppler mode, which generates a sound to detect blood flow in the vein but does not make it possible to locate its depth.[2]

Current international guidelines suggest using the ultrasound-guided insertion procedure as the primary technique, because of its many advantages.[1] As a matter of fact, inserting PICCs at the elbow or in the distal third of the arm after non-ultrasound-guided cannulation of a visible or palpable vein is not recommended, as it is associated with a high risk of failure, malposition, thrombotic and infectious complications.[3] There are numerous positive aspects of ultrasound-guided insertion procedures. These include the ease with which the target (vessel or nerve) can be viewed, and the real-time visualisation of the needle trajectory. This minimises complications such as arterial puncture or pneumothorax.[1] At the same time, this type of procedure has been seen to bring superior patient satisfaction.[1]
The procedure must ensure patient safety and successful placement, which calls for standardisation, consisting in the use of qualified staff and the implementation of a series of measures for preventing infection.

This type of procedure requires the use of highly-skilled staff who have received structured training before being able to perform the procedure unsupervised.[1] The presence of highly skilled staff assigned exclusively to this type of procedure would increase the success rate and reduce complications.[4] More specifically, a study conducted by Carr and colleagues in 2019 showed that first-time insertion success rates were associated with greater confidence and specialisation on the part of the staff involved.[5] Infection prevention and control is another key aspect that should not be underestimated during PICC insertion procedures, especially in cancer patients who, due to immune system impairment and concomitant conditions, may be subject to an increased risk of infection.[6] During this procedure, the PICC is inserted using a modified version of the Seldinger technique.[7] The Seldinger technique originally involved access to a vein with a very fine needle followed by a metal guide, which was advanced along the vessel following removal of the needle. With the introduction of soft

catheters, the Seldinger technique was modified, to include the use of a sheath and a dilator to ensure access to the vein.[6,7]
In the past, all procedures associated with venous catheter insertion were performed in the operating theatre. Now, however, due partly to the introduction of the modified Seldinger technique and partly to the use of ultrasound machines that combine high performance with compact dimensions,[6] this procedure can also be performed at the patient's bedside (even at home) without sedation,[8] provided, of course, that appropriate sterile conditions are maintained.[4]

4.2 The procedure

For correct implantation of the catheter, the procedure must be performed by a dedicated venous access team, who must have adequate knowledge and skills on venous imaging techniques, adequate ability in assessing the calibre, depth and position of the veins, as well as the anatomical relationships with arteries and nerves, and, of course, knowledge of the possible complications associated with the anatomy of the area.[3] At the time of placement, the practitioner should preferably have a checklist containing all the recommendations that can optimise the performance of the procedure and prevent all potential immediate, early or delayed complications.[3] This checklist must contain a few simple, scientific evidence-based recommendations that are easily applicable in clinical practice.[3]

The PICC insertion procedure involves the following stages:

- information and informed consent;
- assessment and evaluation of the patient's vessels;
- ultrasound-guided procedure;
- verification of the course of the catheter;
- verification of correct positioning;
- report-writing and medico-legal aspects.

4.2.1 Information and informed consent

The patient and family members involved in the treatment must be informed regarding all aspects of the treatment plan, the objectives, risk and benefits, potential side effects and adverse events associated with the procedure.[4] The information must therefore be tailored to the patient's and the family's ability to understand it and consequently the language and style used must be adapted to suit the cultural background of the addressees. This can make a considerable contribution to the granting of informed consent.[4] Informed consent must be issued by the patient or whoever is acting on his or her behalf, before any infusion and vascular access procedures (in accordance with national and local regulations), after a discussion with the person in charge of the procedure.[4] Once the patient or person acting on his/her behalf has received exhaustive information regarding the procedure and has understood this information, he/she must be free to give consent without being subjected to any obligation or persuasion. The consent form must be signed.[4] For further information on informed consent, please see the Appendix.

4.2.2 Assessment and evaluation of the patient's vessels

The VHP (Vessel Health and Preservation) framework is applied for vascular access management and the administration of intravenous therapies, basing the practices within 4 quadrants of medical care: vascular assessment and vessel selection, insertion, management and evaluation of vascular access devices. The framework includes procedures supported by scientific evidence, guidelines and international recommendations that provide a guide from the admission of the patient to hospital through to the completion of the treatment. Before the patient undergoes the device implantation procedure, it is essential to evaluate his/her medical history, since any previous surgery, concomitant and oncological diseases, as well as previous complications associated with the use of venous accesses, may influence the choice of device and its insertion. A physical assessment of the patient should also be conducted, and clotting, electrolyte and complete blood count parameters must be thoroughly monitored.

The correct assessment and selection of the best vein and its location is the first step in vascular assessment. Clinical assessment of the blood vessel be carried out by palpation (a technique that is now obsolete and not recommended), or by ultrasound imaging, which facilitates correct positioning inside the vessel.
The vessels may be naturally kinked, or present bifurcations or even thrombi and as all of these situations can make it difficult to place a venous catheter, they should be avoided when assessing the vessels.[8] The factors that increase the difficulty in locating the veins through observation and palpation (known as benchmark techniques) include, among other things:[4]

- medical conditions that modify the vascular structure (diabetes mellitus, hypertension);
- previous frequent venipuncture and/or long-term infusion therapy;
- specific characteristics of the patient's skin (dark or very hairy skin);
- skin abnormalities, such as scars or tattoos;
- age of the patient (both new-borns and the elderly);
- obesity;
- fluid volume deficits.

The scientific community strongly recommends the use of ultrasound imaging techniques for the placement of central and peripheral venous accesses, which make the implantation procedure safer, increase the chances of successful placement at the first attempt and reduce the risk of complications (accidental arterial puncture, haematoma and haemothorax).[9]

The Italian Group for Vascular Access Devices (GAVeCeLT) has developed the RaPeVA (Rapid Assessment of the Peripheral Veins) protocol, which is used and followed to assess the vessels and the adjacent areas. The RaPeVA protocol is well-defined and systematic, maps the veins of the arm and the supra-/subclavicular area and provides useful information for selecting the vein. There is no pre-defined choice, rather each patient presents anatomical and clinical characteristics that require a justified choice on a case-by-case basis. These protocols are followed during the catheter pre-implantation phase and provide a detailed map of the major blood

vessels, reducing complication rates and increasing success rates. According to the RaPeVA protocol, it is preferable to choose a vein with a diameter at least double or triple that of the catheter to be inserted, in order to minimise the risk of PICC-related thrombosis. Assessment by ultrasound identifies and maps the most suitable vein sites for device insertion in the arm, neck, chest and legs. Due to the enormous benefit its use brings the patient, ultrasound is widely used for implanting central venous catheters, PICCs, midlines and, albeit recently, peripheral intravenous catheters.[9]
The 2021 INS guidelines4 also suggest using infrared and ultrasound imaging techniques to increase the likelihood of successful insertion in patients with problematic venous access. These vessel imaging techniques, using an ultrasound-guided needle, allow easy assessment of the essential parameters for choosing the device and the candidate vessel for implantation. These parameters are: shape, dimensions, the vein path and patency, pressure and flow rate.

- The shape of the vessel should be even, both in terms of lumen and vessel wall thickness. This type of unevenness can be better identified on the sagittal plane.
- Vessel dimensions are measured without the use of a tourniquet and the diameter may be measured in-plane and out-of-plane. These measurements determine the calibre and the number of lumens of the catheter to be inserted.
- The vein path must be even, with no kinking, or areas of dilation or stenosis. Similarly, the vessel wall should also be free from irregularities.
- To assess the patency of the vessel, it is necessary to compress the vein. Resistance to compression may indicate thrombosis or the presence of other tissues, such as nerves or arteries.
- In a patient with normal heart function, arterial blood flow is pulsatile and rhythmic. Venous flow is slower and does not pulsate.[8]

In addition to complete mapping of the vessels, these protocols combined with ultrasound imaging techniques are the most effective way of avoiding accidental damage to the median nerve, as nerve areas can be identified during ultrasound-guided venipuncture. Ultrasound also makes it possible to distinguish the arteries, and consequently avoid accidentally puncturing them. Appropriate training and ultrasound equipment suited to the implementation of these protocols and procedures are essential. Poorly performed PICC implantation can have serious consequences consisting in deep vein thrombosis, pulmonary embolism, catheter-related blood infections and post-thrombotic syndrome. For this reason, a key contribution comes from standardisation of the PICC implantation manoeuvre, starting with the choice of the ideal area for insertion.[9]

The PICC Zone Insertion Method (ZIM®) is a system that has been proposed to promote patient safety during PICC insertion and is implemented to optimise and organise the clinical approach. The purpose of the technique is to identify the ideal area for insertion of the needle in the upper arm with ultrasound guidance. The ZIM® system divides the anatomical area affected into red, yellow or green zones, according to the characteristics of the skin, muscle and vessels, and indicates which zones are exposed to a greater risk of complications and which

are not, using a traffic light system. The ideal area for needle insertion is identified in the upper half of the green zone, between the red zone (proximal to the elbow) and the yellow zone (proximal to the axillary cavity). The point of needle insertion is not established by measuring alone, but also through the analysis of the vessels using ultrasound within the green zone. The significance of a systematic approach that is repeatable and measurable reduces the variability and risks of the practice of PICC insertion.[10]

Once the ideal insertion point has been identified, anthropometric measurement is used to define the length of the catheter by measuring the distance between the insertion point and the projection site at the cavoatrial junction. The most commonly used method is to measure the distance between the puncture site and the clavicular midpoint and the distance between the midpoint of the clavicle and the third intercostal space on the right parasternal border and add the two measurements together.[2]

4.2.3 Ultrasound-guided procedure

The PICC must be inserted using a deep peripheral venous puncture located above the elbow, in order to reduce the probability of thrombotic and infectious complications. In order of preference, the veins used are the basilic vein, the brachial veins and the cephalic vein. Preferably, placement is in the veins of the patient's dominant arm and in a non-paretic arm to reduce the possibility of thrombosis.[2]

The environment used should be arranged so as to ensure it is used exclusively for this type of manoeuvre.[3] In addition, all surfaces involved in the procedure should be cleaned and disinfected frequently using appropriate products.[11]
Hand-washing is the first step that must be performed by the staff involved before starting any procedure. As a rule, an alcohol-based solution containing at least 60% ethanol or 70% isopropyl alcohol should be used for washing, which should last at least twenty seconds.[4] All staff must wear personal protective equipment, which must be carefully chosen depending on the interaction with the patient and the potential exposure of the professional to blood, biological fluids and infectious agents.[4] The equipment used during the procedure must be removed afterwards and before leaving the room where the patient is.[3] Hand-washing is also necessary each time protective equipment is removed.[4]
Once the environment and the professional have been prepared, it is necessary to disinfect the skin at the catheter insertion site with 2% chlorhexidine7 in 70% isopropyl alcohol[3] and to prepare the materials to be used. Recently, all-in-one kits have provided an effective aid in the prevention of infection. These kits contain all the components necessary for catheter insertion using an aseptic technique and should be available and readily accessible in all units where PICCs are inserted.[12]

The two main approaches for the ultrasound-guided procedure are the “in-plane” and “out-of-plane” methods. With the in-plane (long-axis) approach, the needle is advanced "in-plane" according to a longitudinal view of the vessel along the entire path of the target; this is done independently of the view of the vessel. With the out-of-plane (short-axis) approach, the needle advances longitudinally and appears as a hyperechoic dot.[1]

Ultrasound-guided PICC insertion is performed using the short-axis, out-of-plane venipuncture technique. This approach provides an accurate panoramic view of the vein's relationship with other adjacent structures, consequently minimising the risk of potential accidental puncture of the median nerve or brachial artery.[3]
Ultrasound-guided vein puncture can be performed either freehand or with special grooved needle holders. In the former case, which is more suitable for experienced practitioners, there is a greater possibility of variability and pliability of the puncture. In the latter, once the candidate vein for puncture and its depth have been identified with ultrasound, a holder with a central groove is mounted onto the probe, and acts as an obligatory guide for the descent of the needle.[2]
After puncture, the cannulation manoeuvre is performed with the modified Seldinger technique using a micro-introducer. The puncture is performed with a fine 21G echogenic-tipped needle, into which a fine metal guide with a straight but soft Nitinol tip, known as a floppy straight tip, is fed.[3] The needle is slowly introduced under ultrasound guidance, directing it parallel to the axis of the vessel and perpendicular to the ultrasound beam.[2] The practitioner's experience and the high quality of the ultrasound scanner and the micro-introduction kit are the most important factors in determining the success of the procedure.[3] More specifically, the ultrasound scanners used must be portable devices specifically designed for this type of procedure and equipped with high-frequency linear probes for the imaging of the superficial tissues.[2]

According to the guidelines, the ultrasound-guided procedure is recommended in adults in particular, both in emergency and routine situations. This type of procedure is safer and more effective than the other techniques and procedures used, in terms of reducing complications, increasing the success rate and reducing the time taken to complete the procedure.[1]
Verification of the position of the tip is strongly recommended during this initial stage: in optimal conditions the tip must be located close to the cavoatrial junction.[3]

4.2.4 Verification of the catheter path – tip navigation

During catheter insertion, locating the path of the tip plays a key role.[3] However, not all of these methods may be performed by all specialists, as not all staff have the necessary skill sets, and this can jeopardise the standardisation of the procedure.
The catheter is introduced to a length of 15-20 cm.[2] At this point, it is advisable to visualise the internal jugular vein by compressing it with the ultrasound probe, which allows and facilitates the passage of the catheter from the subclavian vein to the innominate vein.[11] After the manoeuvre, it is nevertheless recommended to check the absence of the catheter in both jugular veins.[3] This procedure makes it possible to identify any misplacement, such failure to enter the innominate vein, without the need for fluoroscopic manoeuvres or other localisation systems.[3]

Another method for complete control of the route covered by the catheter is PICC placement under fluoroscopic guidance. This type of technique is no longer recommended in routine clinical practice, as it exposes the patient and practitioner to radiation, and involves high costs and logistical difficulties.[3] There are also various devices specially designed for tip navigation. One of these is based on an electromagnetic pulse identification system that enables the position of the catheter tip to be identified directly below the cutaneous and subcutaneous

planes. This method, together with ultrasound and fluoroscopy, is classified under direct visual methods.[3]
The tip navigation method that is recommended today is the intracavitary electrocardiogram combined with dedicated and validated systems. The use of these two systems simultaneously allows not only intra-procedural tip navigation but also confirmation of the tip location with intracavitary ECG.[3]

4.2.5 Verification of correct positioning – tip location

Having reached the desired length, device function is tested by simple suction and pulsed washing with saline solution.[2]
Verification that the catheter is correctly positioned in the vicinity of the cavoatrial junction is fundamental.[2] Tip location methods can be categorised into intraprocedural and postprocedural techniques. Until a few years ago, the most commonly used postprocedural technique for checking the position of the catheter tip was post-insertion chest x-ray. The length of the catheter was estimated using various anthropometric measurement systems, the direction was checked by placing the ultrasound machine over the internal jugular vein (to check for misplacement in this venous district homolaterally to the implantation site) and an antero-posterior chest x-ray was taken at the end of the manoeuvre to visualise the correct direction and position of the tip near the cavoatrial junction. However, as this was a post-insertion verification technique, in the event of misplacement, it was necessary to perform a new insertion manoeuvre.[3]
Intraprocedural tip location can be performed using various techniques such as fluoroscopy, transthoracic echocardiography (TTE), transoesophageal echocardiography (TEE) or intracavitary electrocardiography.[3] Tip location by fluoroscopy is excessively expensive and logistically complicated, as it must be performed in an interventional radiology facility.[13] Fluoroscopy insertion also involves exposing both patient and practitioner to ionising radiation.[4]
TTE is a possible option for accurate verification of the tip location. However, it has never become part of clinical practice for PICC placement in adult patients for a number of reasons, mainly due to the technical difficulties in obese patients, suboptimal visualisation of the superior vena cava, the need to use a different type of probe to that used for venipuncture or the need for training to be able to successfully interpret the echocardiographic image.[3]
Although TTE is a highly accurate method (it allows the catheter to be placed precisely at the cavoatrial junction) for checking the correct central positioning of the tip, as it allows direct visualisation of the catheter, in most cases, it is not clinically viable due to its invasiveness and cost. For this very reason, the technique is used exclusively for research purposes, or occasionally for CICC placement during heart surgery which also involves the presence of an oesophageal ultrasound probe for intraoperative haemodynamic monitoring.[3]

TTE is a feasible and effective option for accurate verification of tip location. However, it has never entered clinical practice for PICC placement in the adult patient for a number of reasons, mainly due to technical difficulties in obese patients, suboptimal visualisation of the superior vena cava, the need to use a different type of probe to that used for venipuncture or the need for training to be able to successfully interpret the echocardiographic image.[3]
In recent months, there has been a great deal of scientific evidence validating this technique

with the aid of an echogenic contrast agent. As a matter of fact, as a method of verifying the correct positioning of the tip, which is useful intra-operatively and in emergency situations and can be applied to both adult and paediatric/neonatal patients, a bubble test is used.[16,17,18] This test is based on a rapid infusion of a mixture of air and saline solution through the catheter (9 mL of saline solution is mixed with 1 mL of air to form microbubbles in solution). The correct positioning of the catheter is confirmed by the appearance of microbubbles in the right atrium under TTE echocardiographic control immediately after the start of the infusion.[16,17] If microbubbles visualisation is delayed or absent, central venous catheter misplacement may be inferred. This method is equally effective and predictive also in patients with abnormal heart rhythm, as in the case of patients in atrial fibrillation;18 however, it requires adequate training and dedicated diagnostic tools.

The intracavitary ECG method remains the technique of choice for verifying the correct position of the catheter tip, as it is cheap, simple and safe. In addition, it is the only method that can guarantee the desired standardisation for this type of procedure. This method was first described in 1949 and entered mainstream clinical practice in the 1980s and 1990s.[3] It verifies the position of the catheter tip based on observation of the P-wave, its growth and peaks.15 When the tip is at the cavoatrial junction, the P-wave on the intracavitary ECG becomes maximal; in more proximal positions it decreases in amplitude and in more distal positions it becomes biphasic until becoming negative if it reaches the inferior vena cava.[3] An additional advantage of the ECG method is that it can be applied not only during implantation, but also days, weeks or months afterwards (e.g. when it is necessary to verify that the tip has not migrated but is still in the correct position. Correct tip positioning can be easily documented in the medical record by printing the intracavitary ECG tracing. The method has also other advantages: it can be applied in clinical situations where radiological verification is contraindicated (pregnancy) or is logistically difficult (PICC placement at home or in hospices), it is safe and inexpensive as it requires only a cable-transducer and the availability of an ECG monitor and it can be easily performed by skilled nurses.[3]
The ECG system is also used in conjunction with an electromagnetic direct-vision tip navigation and tip location system that is integrated, validated, and has a clear intended use. Using real-time magnetic electrocardiographic tip tracking, it can allow the operator to detect (and subsequently correct) any positioning errors.[6]

4.2.6 Report and medico-legal aspects

The ultrasound-guided procedure is accompanied by a report containing certain information. Specifically, the documents included in the report contain:[4]

A. An information sheet containing the patient's or guardian's informed consent, as well as:

- The patient's response to the insertion and removal procedures.
- The patient's response to treatment, including any symptoms, side effects and adverse events.

B. Documentation regarding the vascular access device:

- A standardised tool ensuring strict observation of the guidelines regarding preparation of the site of insertion, prevention of infections and safety precautions taken.

- Indication for the procedure, date and time of insertion and number of attempts. Similarly, all specifications of the inserted catheter should be indicated: type, length, functionality of the device, identification of the insertion site, brand and batch number of the device, type of anaesthetic used (if applicable) and method of insertion, including imaging and guidance techniques.
- Information about the site of insertion: condition of the site, dressings used, any pain or discomfort experienced by the patient and any event that is attributed to the site of insertion.
- Information on any signs and symptoms of phlebitis and/or infiltration, accompanied by images.
- Verification of the absence of any signs and symptoms of complications.
- Any administration or replacement of material used during the procedure.

PICC insertion also requires additional documentation specifying the external and internal length of the catheter as well as the circumference of the tip (assessing the circumference of the point identified as the site for assessing oedema).[4] All the above documents, in addition to the informed consent can be added to the hospital file as well as home records. It is the clinician's responsibility to retain all of the patient's clinical data. Documentation should be complete and chronologically accurate; it should also be legible and accessible to all authorised staff and should be designed to facilitate communication between the various parties involved in care of the patient.[4] Current guidelines recommend maintaining and preserving patient privacy by making information accessible only to specific parties and accredited facilities.[4]

4.3 Conclusions

To sum up, the ultrasound-guided insertion procedure is currently the technique of choice for PICC placement. The benefits of the ultrasound-guided technique are not only limited to the act of insertion, but also regard all stages of the procedure. A fundamental role is played by the ability to follow standardised protocols requiring all steps to be performed in the same procedure, and the use of high-performance equipment and qualified staff. The combination of these aspects, together with the use of integrated tip navigation and tip location systems, help achieve greater safety for the patient, by reducing the risk of contamination, including of the sterile field. The benefits also extend to the identification of vessel disorders or other anatomical anomalies. With this type of method, the choice of vein is also simpler, as is the prevention of immediate, early and late complications.[1]

Due to the reduced incidence of complications, patients welcome the ultrasound-guided procedure (they can be discharged sooner) and fewer staff are involved. Furthermore, the costs associated with the use of the system are considerably lower, as it avoids additional costs due to problems with incorrect positioning. Likewise, costs for resources from other departments, such as radiology, are reduced.[6] The result is greater efficiency of the process, which optimises the patient care pathway and resources.

KEY POINTS

- ***The presence of a vascular access team at the centre concerned is crucial to obtaining better outcomes.***
- ***A standardised procedure allows a more efficient use of resources.***
- ***It is of the utmost importance that the puncture is ultrasound-guided during insertion.***
- ***The availability of devices for tip location and tip navigation during insertion makes the procedure safer and more cost-effective.***

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Chapter 5 – PICC Management

5.1 Introduction

The correct management of a PICC central venous access device is based on careful and thorough training of the medical and nursing staff involved, starting from the choice of the most appropriate device for the patient. The importance of establishing a multidisciplinary team dedicated to PICC management is unanimously recommended by the current literature. The duties of the multidisciplinary team in charge of PICC management and venous access devices in general range from the choice of device and positioning, dressing and management of any complications, to its correct removal. The team consists of specialised doctors and nurses with advanced skills and is also responsible for the collection of data, standardisation of evidence-based practices, evaluation of the most recent literature, new procedures in use and the education and training of healthcare staff.[1]
Correct management of PICC central venous access devices is essential for good treatment outcomes and for the health and quality of life of the patient. PICC management can be broken down into various operations, each of which must be performed by specialised staff following standardised and validated procedures. Instructions and protocols for the management of venous access devices must be available at corporate level, in accordance with the manufacturer's indications.1 Management of a PICC involves:

- dressing the PICC;
- securing the PICC to the skin;
- washing and closing the PICC;
- managing connection systems and infusion lines;
- drawing blood from the PICC and blood culture tests;
- management of the PICC at home.

Before describing the individual procedures for PICC management in detail, it is useful to consider that PICC management consists of two separate stages, both of which are essential for the correct functioning of the PICC and for the health of the patient. As a matter of fact, PICC management includes daily assessments, during which caregivers and family members, as well as the patient, check the PICC is working properly. This assessment consists of an external visual examination, palpation of the insertion site and checks on catheter patency, to monitor any signs that might indicate obstructions, infections and misplacement of the catheter. The second key aspect of PICC management concerns the management itself, which

includes dressing changes, flushing the catheter, all infusion line management procedures and, when necessary, taking blood draws.

The training of the healthcare professional is crucial in this regard. Perfect insertion and correct management of a vascular access device require appropriate theoretical and practical training of medical and nursing staff, as well as in-depth knowledge of human anatomy and physiology. The insertion procedure requires extreme precision and technique and poor or inadequate training can put the patient's health at risk needlessly. As a matter of fact, several studies show that if the staff involved in PICC insertion are not adequately qualified and trained, there are increased risks of complications. Complications may be infectious or thrombotic and the most serious ones associated with catheter use include nerve damage and damage to large-calibre arteries.[2]
A recent study conducted in 6 different public hospitals in Italy3 suggested the need to implement and improve PICC management in cancer patients.

The results obtained demonstrated that 80% of cases of occlusions occurred within 30 days of PICC insertion and, therefore, are most likely caused by flushes that were not carried out or were not properly performed. Likewise, 70% of catheter exit site infections occur 30 days after PICC insertion, suggesting that their cause may be due to poor management and hygiene rather than the insertion of the PICC itself. For this reason, the authors suggested that it is essential that health authorities promote and improve protocols, including educational and training programmes for the nursing and other staff who manage and check these devices every day.
It has indeed been observed that complications in cancer patients are reduced when the staff have received proper technical and practical training.[3]

The EPIC3 (2014) guidelines suggest that healthcare professionals who assist patients with vascular catheters must be trained in the use of such devices, must also be specifically assessed on their skills in this respect and must constantly follow procedures for the prevention of catheter-related bacterial infections.
A new recommendation in the guidelines states that in order to ensure safe use of the devices, healthcare professionals must be aware of the manufacturers' recommendations for each catheter, the connection and the dwell time for infusion lines, as well as the compatibility of these devices with antiseptics and other liquids. Furthermore, before discharge, patients with an intravascular catheter and their caregivers should be educated on the techniques for preventing infection and for the correct management of the device.[4]

5.2 The PICC Dressing

Management of the PICC dressing involves various steps during which specialised staff inform the patient about the procedure to be performed by obtaining informed consent, preparing a clean environment that is appropriate for the procedure and ensuring privacy at all times.

Hygiene – both that of the professional and that of the patient – is vital to avoiding complications due to infection. It is therefore recommended that staff wash their hands thoroughly

before the procedure and that they use sterile instruments and disposable materials. There are several types of hand-washing – hygienic, or social hand-washing, to remove visible dirt and pathogens using water and soap, preferably of the liquid type; antiseptic hand-washing, to eliminate any pathogens present on the hands using water and detergents containing an antiseptic agent (chlorhexidine gluconate and iodophors); and finally, alcohol hand rub, to eliminate pathogens using a 60-80% alcohol solution, together with emollient and moisturising substances to protect the skin of the hands. It is extremely important to emphasise that the use of gloves is not a substitute for hand-washing. Contaminated gloves used by the professional may, in fact, become a significant and often overlooked vehicle for spreading micro-organisms in the environment.[5] Nevertheless, gloves must always be worn during the procedure.
After careful cleansing of the hands and equipment, the PICC insertion site should be thoroughly examined. The procedure can be carried out at the patient's bedside in the case of hospitalised patients, or, in outpatient or home care settings, with the patient sitting down. Other positions may be used provided they are suitable and comfortable for the patient and make it possible to observe the criteria of asepsis, as recommended and classified by the official international guidelines.

The insertion and exit site of CVC, PICC or midline venous devices must be regularly checked by visual inspection or palpation with the dressing intact. If the patient experiences pain at the site of insertion, fever with no other identified source or other symptoms consistent with a local infection or a bloodstream infection (BSI), the dressing must be removed to allow the site to be examined directly. For the insertion site dressing, it is preferable to use a sterile transparent polyurethane dressing as this allows immediate and ongoing inspection of the site and secures the device so as to allow good adhesion to the skin. If the patient is prone to profuse sweating or if the insertion site is bleeding or secreting, a gauze and plaster dressing should be applied.
Except in particular situations in which the dressing is visibly damaged, dirty or detached, the frequency of replacement varies depending on the type of dressing and the condition of the insertion site: every 7 days for transparent polyurethane dressings and every 24 hours for gauze and plaster dressings.

Once the existing dressing has been removed, the area around the exit site should be cleansed with saline solution and disinfected. The most suitable and recommended antiseptic is 2% chlorhexidine in 70% isopropyl alcohol, possibly in a single-use applicator.
In the case of allergy to chlorhexidine alone, 7-10% povidone-iodine can be used as an alternative. Before applying a new dressing, the affected area must be thoroughly dried, so as to avoid skin irritation due to the interaction between the disinfectant and the adhesive agents in the dressings. Wait for 30 seconds for chlorhexidine and 1.5-2 minutes for povidone-iodine.[6]
The procedure also involves the replacement of the catheter securing system and washing of the site where it is attached to the skin. The catheter securing system of choice is the silicone adhesive sutureless system, as sutures tend to expose the patient to a further risk of infection. Silicone adhesive reduces the risk of skin lesions and tears. The sutureless system must be replaced every 7 days or when the catheter dressing is changed. Bandages must not be used to secure the catheter, as they conceal any signs or symptoms and are harmful

to the bloodstream. Once the exit site has been disinfected and the securing method has been replaced, the sterile transparent dressing (to allow daily inspection of the insertion site) must be easy to apply and remove, to ensure patient comfort, and be an effective barrier against micro-organisms. In adult patients, the use of transparent polyurethane dressings impregnated with slow-release 2% chlorhexidine or a similar system is recommended.[6]
Apart from the classic sutureless systems, catheter securing systems also include a system for stabilising the catheter through the skin.

5.3 PICC flushing and closure

As with the replacement of the dressing and catheter securing system, the flushing of the catheter also requires all operations to be performed under completely sterile and clean conditions. Thorough hygiene is therefore required of both the operator's hands and all necessary equipment. All CVCs/CVPs, excluding fully implantable devices (ports), need regular flushing with 0.9% saline solution (to maintain patency), which must always be carried out before drawing blood, before and after each infusion of blood derivatives, parenteral nutrition, lipids or medicinal products. In the case of prolonged catheter use, flushes must be performed periodically, in order to maintain catheter patency and hygiene.
Flushing with sterile saline solution must be performed with 10 mL/20 mL syringes and never a lower calibre, as this could generate pressure that might damage the catheter. These flushes can also be performed using commercially-available pre-filled syringes of saline solution. The volume required for flushing must be double the empty space in the catheter (internal volume of the catheter).

5.4 Connection system and infusion line management

Connection systems include plugs or needle-free connectors or taps. Needle-free connectors are devices that allow connection to infusion lines and aspiration systems without the use of needles, in order to reduce risks of infection from handling. These devices are designed to reduce the risks of system occlusion using a valve mechanism able to generate displacement at the time of disconnection, to prevent blood from being aspirated, or even flush any stagnant blood from the system.[5] According to the 2016 INS guidelines[7], the standards for use suggest that needle-free connectors must be suitable for connection to the device or access port of the infusion line through a luer-lock type closure mechanism, to ensure a secure connection. It is advisable to disinfect needle-free connectors before and after each use of the device and to use the aseptic no-touch technique when replacing the needle-free connector. It is also recommended that needle-free connectors are accessed only with sterile, luer-lock devices (syringes, extensions, infusion lines, etc.).
In the case of oncology and onco-haematology patients receiving antineoplastic drugs, administration sets must be closed-circuit and have several lines (3/6), with flow regulators, one-way anti-reflux valves and luer-lock attachments. Their main feature is that they allow all drugs to be administered through an initial connection to the central venous access, which only occurs after a thorough catheter patency check. The individual drug infusions are delivered progressively by intervention on the clamps and after flushing with

sterile saline solution. The presence of a closed-circuit system makes it possible to work safely, by eliminating the possibility of accidental contamination of the healthcare staff handling the product during preparation, administration and disposal. Once the drug infusion procedure is finished, the catheter is disconnected after flushing of the infusion lines used and the closed-circuit system is then disposed of using the dedicated hospital waste bins. These sets must be replaced every 96 hours in the case of continuous infusion, but also every time contamination or problems of mechanical origin are suspected. If these connectors are not used, they should be replaced every 7 days. In the case of intermittent infusions, continuous handling increases the risk of catheter-related bacterial infections. Therefore, it is advisable to replace the administration set every 24 hours.

For the administration of fluids for parenteral nutrition (including those combined with amino acids and glucose in a 3:1 solution or those infused separately), sets must be replaced within 24 hours of the start of the infusion. Sets for the infusion of lipids must be replaced every 12-24 hours since these solutions encourage the growth of bacteria. It is important to stress that for the infusion of nutritional and lipid fluids the sets must be free from di-2-ethylhexyl phthalate (DEHP) as it is lipophilic. This compound, which is toxic for the health of the patient, is extracted from the polyvinyl chloride (PVC) of which the administration sets and the bags are made. The infusion of blood and blood derivatives also requires specific administration sets, which must be replaced at each transfusion/infusion, or in any case every 12 hours.6 The frequencies for replacement of the administration sets are listed below:

- every 72 hours for infusion lines used for the continuous delivery of solutions containing glucose and amino acids;
- every 96 hours for single- and multi-use transducers used to detect central venous pressure (CVP);
- every 6-12 hours, depending on their use, for propofol infusion lines.

5.5 PICC blood draws and blood cultures

If necessary, PICCs, like other central venous catheters, can be used for blood withdrawal. Before proceeding, it is essential to evaluate the risk and benefits of this operation and base the procedure on consolidated standard protocols. These operations must be performed exclusively by specialised and qualified staff. As with the previous operations, staff must also inform the patient before blood collection about the procedure that is to take place. Before withdrawal, the standard precautions must be taken, following all recommendations for the prevention of infections (hand hygiene, use of gloves, disposable tourniquet, use of disposable blood draw devices), for both the patient and the clinician/healthcare professional.

Blood withdrawal is carried out using vacutainers, vacuum-sealed systems for blood collection. These systems provide a lower risk of blood contamination than manual aspiration using a syringe, ensure the withdrawal of the correct volume and also do away with the need to transfer the blood into test-tubes.

For withdrawal from multi-lumen central venous catheters, it is advisable to choose the lumen with the greatest calibre. If the central venous catheter has lumens with different lengths, the sample must be withdrawn from the most proximal lumen (that furthest from the catheter tip). It is advisable not to collect blood from PICCs used for the infusion of parenteral nutrition due to the increased risk of infection.
The risks associated with blood draws from central venous catheters include potential intra-luminal contamination from handling of the connector, possible occlusion or subocclusion of the catheter lumen, or even errors in the laboratory values, secondary to the effects of the drugs or solutions infused through the catheter.

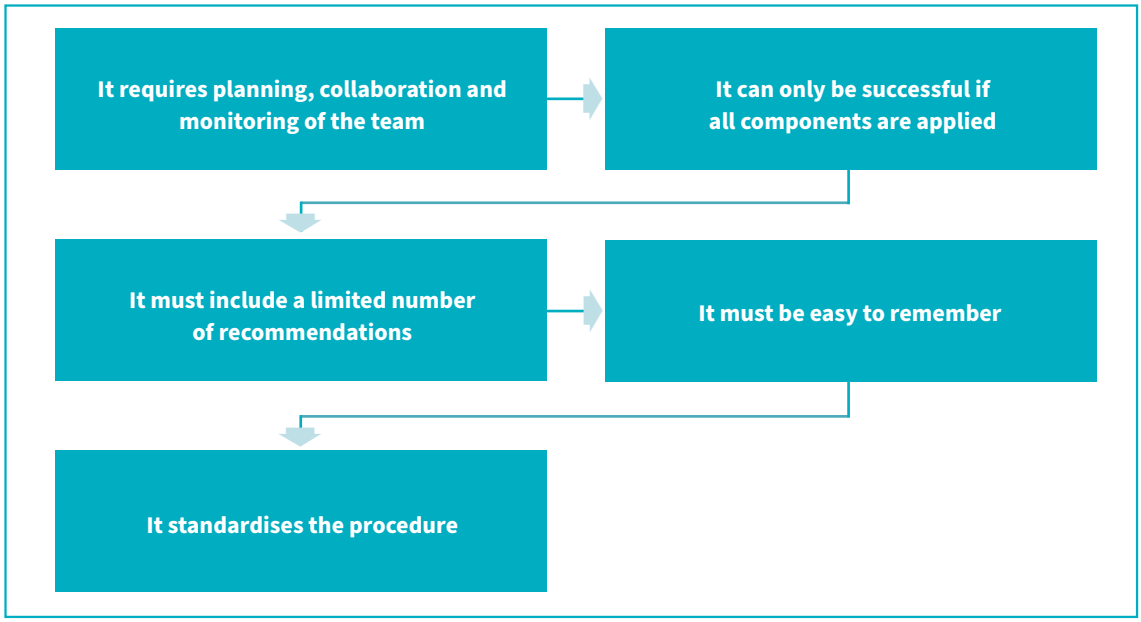
After preparation of the environment, the procedure for blood withdrawal from a PICC requires the operator to place the venous device lumens on a clean cloth and to clean and disinfect the PICC hub with 2% chlorhexidine in a 70% alcohol solution or povidone-iodine, leaving it for the appropriate contact time. The closure connector can be unscrewed with the same gauze. Since no blood samples are taken from the infusion set, if a sample is to be taken from a continuous use device connected to an infusion, the current infusion should first be isolated and discontinued. After flushing with saline solution, approximately 5 mL of blood are drawn and discarded and only afterwards is the vacutainer connected to the catheter to take the sample. For intermittent use catheters and those not connected to an infusion, the waste blood sample can be taken directly and the vacutainer connected. Once the sample has been collected, a second saline solution flush is performed with an intermittent "pulsatile" technique. All test tubes must be labelled with the patient's identifying details, only after having collected the blood samples. The amount of blood collected for the waste sample should be sufficient to avoid errors in the laboratory tests.

Blood sample withdrawal from PICC catheters becomes crucial when a catheter-related bacterial infection is suspected. In this case, following collection, a blood culture must also be performed. For specific samples for blood culture, it is necessary to consider some additional precautions to avoid false negatives and false positives that may invalidate any catheter-related bacterial infection diagnoses. A first precaution is to take the blood culture sample before any other blood sample for clinical chemistry tests, and if a catheter-related infection is suspected, two blood cultures must be performed, the first from the peripheral vein and the second from the catheter. Blood culture samples must be taken before starting antibiotic therapy. The needle-free connector must be removed before taking the blood sample to avoid the risk of false positives and if the sample is collected from a central venous catheter for blood culture there is no need to take a waste sample. The volume of blood taken for a blood culture must be sufficient to isolate the micro-organisms (20-30 mL for adults and not more than 1% of blood volume for infants and children). The samples collected for blood culture must be processed as soon as possible and not refrigerated.[1]
To sum up, the decision to use a CVC to take blood samples must be taken after considering the risks that each passage of blood may cause in the lumen of the catheter. Blood residues that cannot always be removed completely (especially in the port) may favour the formation of micro-clots and subsequently thrombotic formations, leading to occlusion of the catheter and possible infection.

5.6 PICC management at home

As mentioned above, in addition to management dedicated to dressings, flushing and infusion lines, daily PICC management is necessary, consisting in regular checking of its patency and checks to assess the presence of infections or inflammation at the insertion site. In this regard, a crucial point about PICC and venous catheter management is due to the fact that, in many situations, patients needing a venous access device are not always hospitalised or admitted to a facility. Continuity between hospital and community care is a critical aspect for PICC management. Home management of PICC central venous catheters therefore plays a key role. Home management for non-hospitalised patients (outpatients or those under home care) requires correct and complete information of the patient and/or caregivers on various aspects, which may be technical, associated with correct placement and the type of PICC, but also clinical, associated with the early recognition of signs and symptoms of complications. Their task is to recognise and report them promptly and, in the event of an emergency, be able to stop the infusion pump. The patient or caregiver must be taught how to check the catheter exit site at least once a day, to detect any anomalies or possible displacements of the dressing. In case of continuous infusions through peripheral cannulas, the check should be carried out every 4 hours during waking hours.[1]

Bundle: a set of clinically proven interventions which – if applied simultaneously, diligently and in a controlled manner by every professional for every patient – is able to minimise or eliminate certain complications, ensuring a better outcome.[6]



EXAMPLE

Protection of the exit site (prevention of extraluminal contamination and displacement)

Skin disinfection with 2% chlorhexidine and 70% alcohol solution

Sustained-release semi-permeable transparent

CHG-impregnated pad dressing

Securing with sutureless devices

Protection of the infusion line (prevention of endoluminal contamination and occlusion events)

Flushing with saline before and after each infusion.

Use of covered needle-free connectors with port protectors

Catheter lock

KEY POINTS

- *Daily assessment: check on the exit site and the dressing.*
- *Dressing change: 24 hours after insertion and then every 7 days.*
- *Correct and frequent flushing and locking with disposable syringes.*
- *Correct care of the exit site by skin disinfection preferably with single-use 2% chlorhexidine in isopropyl alcohol.*
- *It is important to provide staff with a management bundle.*

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Chapter 6 – PICC-related complications in Onco-haematology

6.1. Introduction

Although PICC devices have been utilised since 1980, their use has increased over the years1to become widespread today. This is due to their advantages over CVCs and totally-implantable venous access devices (TIVADs),[1] i.e. their ease and speed of insertion, the possibility of obtaining long-term venous access, and the lower rate of complaints associated with their use,2 with a difference of 36 percentage points compared to centrally-inserted catheters[3] (13% vs 49%).[4] For these reasons, PICCs also show a generally high level of satisfaction among patients.2 They are also more economical, especially for short-term therapy (under 6 months).5 However, PICCs are unfortunately not without complications.[1] Particular patient groups, such as patients with a BMI >25, have a higher incidence of complications.[6]
From a timing perspective, it is possible to classify complications as early and late. Early complications are all those that occur within 24 hours of the insertion procedure and are a direct consequence of it. Mechanical complications and misplacement, haematoma, arterial puncture and median nerve puncture all fall under this category.

Late complications are those that appear more than 24 hours after the procedure and they can in turn be classified into major late complications and minor late complications. Major late complications include all complications that occur after 24 hours from insertion and require prolonged hospitalisation and the administration of drugs such as anticoagulants or antibiotics. As a matter of fact, bloodstream infections and symptomatic thromboses come under this category. Minor late complications, on the other hand, do not require hospitalisation, can be managed with a second treatment and, unlike the previous ones, do not require removal of the PICC. This category includes phlebitis, insertion and exit site infections and occlusion of the PICC as well as the various mechanical dysfunctions and obstructions,[1] burning, pain caused by inflammation of the tunica intima of the vein, skin reactions, blood loss and resistance at withdrawal (due to the presence of fibrin clots).
Although critical patients are at greater risk of complications, for some PICCs are the only means of receiving chemotherapy during long-term treatment.[2]

6.2. Thrombotic complications

Thrombotic complications consist of the formation of a blood clot inside a vessel following PICC insertion and are today the most common type of complication following PICC insertion (0-71%).[3] Nevertheless, this percentage is lower than that found with centrally-inserted catheters.[5] Young men show a greater risk of developing thrombotic conditions, due to the nature of

the tumour and the treatment, as germ cell tumours are treated with cisplatin, which increases the risk of thrombosis.[7]
The development of thrombosis following insertion of a PICC is probably due to mechanical stimulation of the vessel wall, which results in endothelial cell damage and the formation of a clot.[8]

The most common risk factors are placement in the left arm, history of deep vein thrombosis, diabetes mellitus and advanced disease, accompanied (at transfusion) by the average number of red blood cell and/or platelet units transfused.[1] Generally speaking, the risk factors can be broken down into:

Patient-related risk factors

- history of deep vein thrombosis;
- cancer diagnosis;
- advanced kidney disease (due to the pre-thrombotic state associated with this condition);
- diabetes;
- obesity;
- chronic obstructive pulmonary disease (as reported in various observational studies);
- surgery.

Device-related or infusion-related risk factors[2]

- Calibre and surface area of the catheter:[9] the greater the calibre, the greater the likelihood of developing thrombosis.
- PICCs connected to infusion machines.
- The nature of the infused substance (some antimicrobials such as vancomycin, ceftriaxone, metronidazole or other substances such as mannitol, vasopressors, erythropoietin stimulants, certain chemotherapy agents such as fluorouracil or capecitabine).
- Extreme pH (<5 or >9), osmolarity and concentration of the infusion.
- The presence of fibrin, platelet and collagen clots.
- Crystal formation.

Insertion-related risk factors

- Vein and arm of insertion (according to some studies, insertion into the left basilic vein is more likely to cause the development of thrombi).[6]
- PICC to vein calibre ratio >1:3.

The PICC team should take preventive measures tailored to the type of patient and treatment, to avoid thrombotic complications.[10] In particular, according to current literature, it is good

practice to insert the PICC into the distal third of the superior vena cava using guided procedures in order to assess correct placement. The device should be as small in calibre as possible but, at the same time adapted to suit the needs of the patient. Healthcare staff should be properly trained and receive refresher sessions on insertion procedures, monitoring, management and catheter selection. The latter should be based on costs but above all on safety, capacity to withstand large volumes, duration and complication rates. Staff therefore have a fundamental role to play, and it is important that nursing staff apply flushing techniques that are appropriate for the type of catheter and its diameter, so as to prevent its obstruction.[2]

Very often, patients who develop this type of complication do not show any symptoms (33-66% of cases[8]). When symptomatic, venous thrombosis caused by PICCs can lead to a range of clinical manifestations, which can be classified according to their frequency. Among the most common symptoms, impairment of the circulatory system (characterised by arm pain and swelling) is certainly significant, followed by erythema, heat at the cannula insertion site and thrombophlebitis. The uncommon clinical symptoms most notably include lower limb embolism.

Diagnosis involves various possible procedures. Firstly, ultrasound, non-compression of the vein and lack of flow on Doppler ultrasound can be useful in detecting the presence of thrombi, and all of these methods have a specificity of 94-100% and a sensitivity of 56-100%, although the latter two parameters tend to decrease in proximal veins, such as the brachiocephalic and subclavian veins.

Contrast-enhanced venography is a more invasive method of diagnosis and should therefore be reserved for cases in which ultrasound does not provide a certain diagnosis.[8] Although CT angiography or magnetic resonance angiography are less invasive alternatives, they have the disadvantages of being expensive and involving risks for the patient due to transportation.[11]

Another diagnostic method is based on the determination of plasma biomarkers (such as D-dimers) or new biomarkers such as P-selectin. The D-dimer test has been seen to have high sensitivity (100%) but low specificity (14%). The diagnostic power of this test is low, especially in patients with tumours or infections, concomitant conditions that can lead to a non-specific increase in these dimers. P-selectin, by contrast, has proved to be the most predictive biomarker.

Prevention should depend on the patient and the characteristics of the PICC.[9] At the current time, the use of prophylactic heparin is still under investigation, but would appear to have great advantages:

- it has little influence on the platelet count;
- it does not affect lipid metabolism;
- it is safe;
- it has a long half-life;
- it does not cause bleeding after use.

A Following administration of low-molecular-weight heparin, reduced mechanical damage to the vein due to catheter insertion was noted in the animal model.

Low-molecular-weight heparin can also act on factor Xa with an antithrombotic effect and release plasminogen activator, which increases fibrinolysis and inhibits platelet aggregation.[8] Another treatment used to prevent thrombotic complications from PICCs is rivaroxaban. This agent is an oral inhibitor of factor Xa and has high selectivity. It also has the advantage that, being an oral agent, it can be administered out of hospital. In addition, rivaroxaban does not have the typical side effect of low-molecular-weight heparin, in that it does not cause thrombocytopenia.[11]
Nevertheless, there is still no certain data on thromboprophylactic therapy and the published data is still conflicting.[9]
The treatment of thrombotic complications is based on the use of three mainstays of therapy:

- anticoagulant therapy;
- removal of the PICC if it is not necessary;
- interventional and thrombolysis procedures.

For cancer patients, anticoagulant therapy is based on the use of low-molecular-weight heparin (fondaparinux, enoxaparin),[9] at a starting dose of 1 mg/kg/day for 6 weeks, which can be adjusted based on renal function and platelet count.[1] Warfarin is generally administered for non-cancer patients, or patients who cannot take heparin for medical or financial reasons. In both cases, treatment should be for at least 3 months, with extensions based on the risk/benefit assessment and until the PICC is removed.[9] Patients with acute myeloid leukaemia, with a higher incidence of thrombocytopenia, are more difficult to treat for thrombosis.[12] However, heparin therapy finds divergent opinions among clinicians, and in any case, the choice is based on a cost-benefit assessment.

The PICC should only be removed when the thrombus has been physically identified and if the device is no longer required, or if anticoagulants are contraindicated.[9] Removal is generally not recommended unless it is essential; it is usually carried out after a treatment with low-molecular-weight heparin of approximately 3-5 days,[1] and is followed by anticoagulant therapy for 3-6 months.

In 2018, a prospective study analysed the sequelae of PICC removal in patients with thrombosis. A total of 83 patients were enrolled in the study, of whom 62 were treated with catheter removal alone and 21 were treated with catheter removal followed by anticoagulant therapy. In patients treated with catheter removal alone, thrombocytopenia and brachial thrombosis were found but few haemorrhages were observed (only 4.8%). By contrast, in patients treated with PICC removal and anticoagulant therapy, there was no brachial thrombosis but haemorrhages (major bleeding, gastrointestinal and/or intracranial haemorrhages) occurred in 2.5% of cases.[13] For this reason, some clinicians prefer to avoid treatment to avoid putting the patient at risk of haemorrhage. It is generally preferable to keep it in place if it is still useful and well positioned.[9] Thrombolysis is indicated in patients with severe syndromes, subclavian or axillary vein thrombosis, who have had symptoms for more than 14 days. These patients should have a life expectancy of at least one year and a low haemorrhage risk. Interventional procedures such as thrombectomy and angioplasty might reduce

the risk of post-thrombotic syndrome in the lower limbs; however, their role still needs to be clarified.[9]

One sequela of thrombotic complications is post-thrombotic syndrome, which is characterised by pain, venous hypertension, swelling and restricted movement. It has an incidence of 36-50% in patients with CVCs but is less common in patients with PICCs.[11]

6.3. Infectious complications

PICC-related infections are fairly common (16.4-28.8%)2 (10%),[12] and are the most common complications among patients on home parenteral nutrition (10%).[12]
Bloodstream infections are caused by the patient's immune status and the adherence and colonisation of biofilm-producing bacteria, which are therefore resistant to antibiotics. The most common include *S. aureus* and *S. epidermidis*.[13]
According to the Infectious Disease Society of America, infectious complications (and therefore, bloodstream infections) are when the same micro-organism is detected by blood culture and PICC culture (after removal), when the bacterial count in the PICC is at least three times that obtained from peripheral blood and when the PICC tests positive at least 2 hours before the peripheral vein.[14]

The gold standards for diagnosis are PICC blood culture and DTP (Differential Time to Positivity). This method has a sensitivity of 90% and a specificity of 80%.[15]
Parenteral nutrition at home is increasingly common: in the US, it concerns about 30% of patients, while in Spain the rate of patients put on home parenteral nutrition is about 6.[6] patients per million inhabitants per year – higher than that observed in the past. 10% of patients who undergo this treatment are prone to developing bloodstream infections. For this very reason, training programmes are necessary for subjects involved in the home care of the patient.[16]

Patients with acute myeloid leukaemia are another category at risk of infection, in which the incidence amongst PICC patients is about 1.4/1000 catheters/day, which is nevertheless lower than amongst CICC patients (where the incidence reaches 7.8/1000 catheters/day[4]).

As adhesion of bacteria to the catheter is the first step in infection, it is the first point for which an alternative solution to antibiotics was sought.[17] A first solution involved the production of materials able to prevent the initial adhesion of the bacteria, while other solutions involved modifying surfaces by adding anti-adhesives, antibiotics and various chemical and biological substances. In this way, it is possible to modify the properties of the surface, such as roughness, chemical characteristics, load and hydrophobicity, so that the surface becomes inert to bacterial adhesion. Antimicrobial substances can still be released.[17] Of the various material characteristics, hydrophobicity and roughness play a key role in inhibiting bacterial adhesion by *S. epidermidis*, *E. Coli*, *P. aeruginosa* and C. albicans.

The use of polyurethane has been shown to be a viable aid in preventing infectious complications compared with silicone catheters.[18] One material in particular, submicron-textured polyurethane, which was initially produced to inhibit platelet aggregation, has proved to be effective in inhibiting adhesion of *S. aureus* and *S. epidermidis* and the formation of biofilm.[19]

PICC teams should adopt personalised measures for each patient, maintaining high levels of sterility before[2] (disinfecting the insertion site with 2% chlorhexidine, handling the catheter in sterile conditions and wearing personal protective equipment), during and after the procedure (using pre-filled syringes, frequently checking the insertion site, changing the dressing – which should be transparent – the day after the procedure and then every 7 days and checking for redness, swelling and pus1 and disinfecting the exit site and catheter hub to prevent infection).[2] As with thrombotic complications, the risk factors for infectious complications can be broken down into:

- factors related to the patient's condition: in immunocompromised patients (with neutrophil count <1x109/L at the time of PICC insertion), in those with neutropenia during monitoring of the PICC and with a platelet count <50x109/L,1 for example, the likelihood of developing infections is greater;[16]
- factors related to vein selection: catheter insertion in the neck, chest and groin increases the risk of infection due to the proximity of the mouth, nose and genital organs;
- factors related to the choice of catheter: silicone catheters are associated with a higher infection rate.[2] Furthermore, as with thrombotic complications, double-lumen catheters also show a greater incidence of infectious complications;[16]
- care-related factors: the lack of adequate training of staff on sterility practices and infection recognition, and also lacking or insufficient hygiene during patient care can increase the risk of infection.[2]

According to these guidelines, in the event of fever or other signs of systemic infection in patients with PICCs, a blood culture should be taken from both the catheter and the peripheral vein, and empirical antibiotic therapy should be initiated while awaiting the results, followed by appropriate treatment. In the case of septicaemia, suppurative thrombophlebitis, endocarditis, persistent bloodstream infections despite 72 hours of antimicrobial therapy (sustained by susceptible organisms) and in the case of infections caused by Candida spp., Mycobacterium spp. and *S. aureus*, the PICC should be removed.[1]

6.4. Mechanical complications

PICC displacement, mechanical occlusion, damage and rupture are typical mechanical complications,[1] accounting on average for approximately 9% of complications.[20]

Secondary malpositioning can occur at any time after insertion and can be intravascular (such as tip migration into a vessel) or extravascular (damage to the vessel by the catheter tip). Some of the typical symptoms are lack of blood return, difficulty in infusing through the catheter, breathing difficulties, paraesthesia, and oedema and pain in the shoulder, neck, chest and back.[21]

PICC displacement involves the migration of the PICC from the point of insertion and can be caused by physiological and/or pathological events such as coughing, vomiting, hyperventilation or high infusion pressure, or by the catheter being too short.[22] Displacement entails clinical and economic issues. Anchoring devices have been developed recently, with the aim of

limiting the occurrence of this type of complication. Another system for preventing displacement of the PICC involves replacement of the classical suture stitches with skin-adhesive sutureless devices, which are able to prevent phenomena associated with decubitus.[21]

Mechanical occlusion is a more common issue with silicone catheters than with polyurethane catheters (indeed, the latter are washed daily even when not in use1). There are three types of occlusion:

- persistent withdrawal occlusion: aspiration is difficult or impossible but infusion is not;
- subocclusion: difficulties are encountered for both infusion and aspiration;
- complete occlusion: both infusion and aspiration are impossible.

The signs and symptoms of occlusion can be broken down into:

- specific: aspiration is difficult, infusion is impossible, possible infusion pump alarms;
- non-specific: oedema and leakage of fluid from the insertion site.

To prevent mechanical occlusion, it is advisable to avoid kneeling, constriction, twisting and pulling, and the catheter should be flushed frequently and positive pressure maintained at all times (by administering fluids via the infusion pump). Catheter failure is associated with its maintenance and insertion. Signs and symptoms attributable to failure are swelling, pain, infusion and aspiration difficulties and leakage from the insertion site.[21]

Polyurethane catheters have been found to have improved performance and safety with regard to damage and failure. Indeed, this type of catheter is more flexible and hard-wearing, with better tolerance of pressure. Again for pressure-related reasons, it is also useful to use syringes that have a volume greater than 10 cc.[1]
Among the risk factors, the patient plays a central role in this type of complication, as certain movements, vomiting and constipation can cause PICC malposition.[2]

KEY POINTS

- ***Correct management of the device is essential for the prevention of catheter-related complications.***
- ***There are various types of complications: thrombotic, infectious, mechanical.***
- ***Use the smallest possible calibre of catheter to maintain the best catheter to vessel ratio ensuring the best flow performance.***
- ***Prevention.***

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Appendix

Informed Consent

Informed Consent is a delicate process of communication between the patient and the doctor that is necessary for the patient to authorise any medical intervention going ahead. Achieving a successful procedure and informed consent depends on the strength of the relationship between doctor and patient. Informed consent does not consist of merely acquiring the patient's signature, rather it is a process based on dialogue between doctor and patient. It is essential to provide appropriate and accessible information to the patient, especially where there may be co-existing disabilities.

Italian law no. 219 of 22 December 2017, setting forth the **"Regulations regarding informed consent and advanced treatment provisions"** came into force on 31 January 2018.
Informed consent forms the fundamental basis for the lawfulness of any treatment, which, except in cases of incapacity or impossibility, must involve medical information regarding the methods, timing and risks of any type of intervention. Informed consent is therefore binding for the doctor, implies a relationship between doctor and patient and has the purpose of making the sick person the focus of the doctor's attention, making information a right rather than a concession.

According to Italian law no. 219/2017 *"Medical informed consent is the process by which the patient decides freely and autonomously whether to begin or continue the proposed medical treatment, after being presented with a specific set of information, made comprehensible to him or her by the doctor or medical team"* (Article 1, paragraphs 2 and 3).

Italian law no. 219/2017 recognises the decision-making autonomy of the patient within the treatment relationship, which has been strengthened and overcomes physical and temporal limits biologically imposed on the patient's conscience. Furthermore, the wishes indicated by the patient remain legally valid even if the patient becomes incapacitated.

Informed consent information is a specific obligation of the healthcare facility (Law 219/17, Article. 1, paragraph 9). The information, which the patient must understand, specified in the third paragraph of the same law, concerns:

- diagnosis;
- prognosis;
- benefits and risks of the diagnostic investigation and the healthcare treatments indicated;
- possible alternatives;
- consequences of any refusal of the healthcare treatment and the diagnostic investigation or of subsequent withdrawal of consent.

Specifically, therefore, for adequate informed consent as provided for by law 219/17, the following different types of information must be provided:

1. patient-specific information (diagnosis);
2. information regarding the treatment identified by the doctor to be the most appropriate for the patient;
3. information regarding any alternatives;
4. further information (likely prognosis, consequences of refusal/withdrawal, any information regarding psychological counselling pursuant to Article 1, paragraph 5).

Refusal or waiving of information, the possible appointment of a representative and the informed consent, in whatever form it is expressed, must be recorded on the patient's medical record and electronic health record.