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ESPEN Guidelines on Parenteral Nutrition: Central Venous Catheters (access, care, diagnosis and therapy of complications)

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SUMMARY

When planning parenteral nutrition (PN), the proper choice, insertion, and nursing of the venous access are of paramount importance. In hospitalized patients, PN can be delivered through short-term, non-tunneled central venous catheters, through peripherally inserted central catheters (PICC), or – for limited period of time and with limitation in the osmolarity and composition of the solution – through peripheral venous access devices (short cannulas and midline catheters). Home PN usually requires PICCs or – if planned for an extended or unlimited time – long-term venous access devices (tunneled catheters and totally implantable ports).

The most appropriate site for central venous access will take into account many factors, including the patient's conditions and the relative risk of infective and non-infective complications associated with each site. Ultrasound-guided venepuncture is strongly recommended for access to all central veins. For parenteral nutrition, the ideal position of the catheter tip is between the lower third of the superior cava vein and the upper third of the right atrium; this should preferably be checked during the procedure.

Catheter-related bloodstream infection is an important and still too common complication of parenteral nutrition. The risk of infection can be reduced by adopting cost-effective, evidence-based interventions such as proper education and specific training of the staff, an adequate hand washing policy, proper choices of the type of device and the site of insertion, use of maximal barrier protection during insertion, use of chlorhexidine as antiseptic prior to insertion and for disinfecting the exit site thereafter, appropriate policies for the dressing of the exit site, routine changes of administration sets, and removal of central lines as soon as they are no longer necessary.

Most non-infective complications of central venous access devices can also be prevented by appropriate, standardized protocols for line insertion and maintenance. These too depend on appropriate choice of device, skilled implantation and correct positioning of the catheter, adequate stabilization of the device (preferably avoiding stitches), and the use of infusion pumps, as well as adequate policies for flushing and locking lines which are not in use.

General recommendations about the indications for and the use of the different types of venous access devices available for parenteral nutrition

1. What is the role of peripheral parenteral nutrition?

Central venous access (i.e.,venous access which allows delivery of nutrients directly into the superior vena cava or the right atrium) is needed in most patients who are candidates for parenteral nutrition (PN).

In some situations however PN may be safely delivered by peripheral access (short cannula or midline catheter), as when using a solution with low osmolarity, with a substantial proportion of the non-protein calories given as lipid.

It is recommended (Grade C) that peripheral PN (given through a short peripheral cannula or through a midline catheter) should be used only for a limited period of time, and only when using nutrient solutions whose osmolarity does not exceed 850 mOsm/L.

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Summary of statements: Central Venous Catheters			
Subject	**Recommendations**	**Grade**	**Number**
Choice of route for intravenous nutrition	Central venous access (i.e., venous access which allows delivery of nutrients directly into the superior vena cava or the right atrium) is needed in most patients who are candidates for parenteral nutrition (PN). In some situations however PN may be safely delivered by peripheral access (short cannula or midline catheter), as when using a solution with low osmolarity, with a substantial proportion of the non-protein calories given as lipid. It is recommended that peripheral PN (given through a short peripheral cannula or through a midline catheter) should be used only for a limited period of time, and only when using nutrient solutions whose osmolarity does not exceed 850 mOsm/L. Home PN should not normally be given via short cannulas as these carry a high risk of dislocation and complications. Peripheral PN, whether through short cannulas or midline catheters, demands careful surveillance for thrombophlebitis.	C	1
Choice of PN catheter device	Short-term: many non-tunneled central venous catheters (CVCs), as well as peripherally inserted central catheters (PICCs), and peripheral catheters are suitable for in-patient PN. Medium-term: PICCs, Hohn catheters, and tunneled catheters and ports are appropriate. Non-tunneled central venous catheters are discouraged in HPN, because of high rates of infection, obstruction, dislocation, and venous thrombosis. Prolonged use and HPN (>3 months) usually require a long-term device. There is a choice between tunneled catheters and totally implantable devices. In those requiring frequent (daily) access a tunneled device is generally preferable.	B	2
Choice of vein for PN	The choice of vein is affected by several factors including venepuncture technique, the risk of related mechanical complications, the feasibility of appropriate nursing of the catheter site, and the risk of thrombotic and infective complications. The use of the femoral vein for PN is relatively contraindicated, since this is associated with a high risk of contamination at the exit site in the groin, and a high risk of venous thrombosis. High approaches to the internal jugular vein (either anterior or posterior to the sternoclavicular muscle) are not recommended, since the exit site is difficult to nurse, and there is thus a high risk of catheter contamination and catheter-related infection.	C	3
Insertion of CVCs	There is compelling evidence that ultrasound-guided venepuncture (by real-time ultrasonography) is associated with a lower incidence of complications and a higher rate of success than 'blind' venepuncture. Ultrasound support is therefore strongly recommended for all CVC insertions. Placement by surgical cutdown is not recommended, in terms of cost-effectiveness and risk of infection. In placement of PICCs, percutaneous cannulation of the basilic vein or the brachial vein in the midarm, utilizing ultrasound guidance and the micro-introducer technique, is the preferred option	A B	4 4
Position of CVC tip	High osmolarity PN requires central venous access and should be delivered through a catheter whose tip is in the lower third of the superior vena cava, at the atrio-caval junction, or in the upper portion of the right atrium (Grade A). The position of the tip should preferably be checked during the procedure, especially when an infraclavicular approach to the subclavian vein has been used. Postoperative X-ray is mandatory (a) when the position of the tip has not been checked during the procedure, and/or (b) when the device has been placed using blind subclavian approach or other techniques which carry the risk of pleuropulmonary damage.	C, B	5
Choice of material for CVC	There is limited evidence to suggest that the catheter material is important in the etiology of catheter-related sepsis. Teflon, silicone and polyurethane (PUR) have been associated with fewer infections than polyvinyl chloride or polyethylene. Currently all available CVCs are made either of PUR (short-term and medium-term) or silicone (medium-term and long-term); no specific recommendation for clinical practice is made.	B	6
Reducing the risk of catheter-related infection	Evidence indicates that the risk of catheter-related infection is reduced by: • Using tunneled and implanted catheters (value only confirmed in long-term use) • Using antimicrobial coated catheters (value only shown in short-term use) • Using single-lumen catheters • Using peripheral access (PICC) when possible • Appropriate choice of the insertion site • Ultrasound-guided venepuncture • Use of maximal barrier precautions during insertion • Proper education and specific training of the staff • An adequate policy of hand washing • Use of 2% chlorhexidine as skin antiseptic • Appropriate dressing of the exit site • Disinfection of hubs, stopcocks and needle-free connectors • Regular change of administration sets Some interventions are not effective in reducing the risk of infection, and should not be adopted for this purpose; these include: • in-line filters • routine replacement of central lines on a scheduled basis • antibiotic prophylaxis • the use of heparin	B	6
Diagnosis of catheter-related sepsis	Diagnosis of CRBSI is best achieved (a) by quantitative or semi-quantitative culture of the catheter (when the CVC is removed or exchanged over a guide wire), or (b) by paired quantitative blood cultures or paired qualitative blood cultures from a peripheral vein and from the catheter, with continuously monitoring of the differential time to positivity (if the catheter is left in place).	A	7

Table (*continued*)

Summary of statements: Central Venous Catheters			
Subject	**Recommendations**	**Grade**	**Number**
Treatment of catheter-related sepsis (short-term lines)	A short-term central line should be removed in the case of (a) evident signs of local infection at the exit site, (b) clinical signs of sepsis, (c) positive culture of the catheter exchanged over guide wire, or (d) positive paired blood cultures (from peripheral blood and blood drawn from the catheter). Appropriate antibiotic therapy should be continued after catheter removal.	B	8
Treatment of catheter-related sepsis (long-term lines)	Removal of the long-term venous access is required in case of (a) tunnel infection or port abscess, (b) clinical signs of septic shock, (c) paired blood cultures positive for fungi or highly virulent bacteria, and/or (d) complicated infection (e.g., evidence of endocarditis, septic thrombosis, or other metastatic infections). In other cases, an attempt to save the device may be tried, using the antibiotic lock technique.	B	9
Routine care of central catheters	Most central venous access devices for PN can be safely flushed and locked with saline solution when not in use. Heparinized solutions may be used as a lock (after flushing with saline), when recommended by the manufacturer, in the case of implanted ports or opened-ended catheter lumens which are scheduled to remain closed for more than 8 h.	C	10
Prevention of line occlusion	Intraluminal obstruction of the central venous access can be prevented by appropriate nursing protocols in maintenance of the line, including the use of nutritional pumps.	C	11
Prevention of catheter-related central venous thrombosis	Thrombosis is avoided by the use of insertion techniques designed to limit damage to the vein, including • Ultrasound guidance at insertion • choice of a catheter with the smallest caliber compatible with the infusion therapy needed • position of the tip of the catheter at or near to the atrio-caval junction Prophylaxis with a daily subcutaneous dose of low molecular weight heparin is effective only in patients at high risk for thrombosis.	B	12

Home PN should not be given only via short catheters, as these carry a high risk of dislocation and complications (Grade C).

Peripheral PN, whether through short cannulas or midline catheters, demands careful surveillance for thrombophlebitis (Grade C).

Comments: There is not enough evidence in the literature to indicate a clear cut-off osmolarity for central versus peripheral PN, and experimental data obtained in animal models are not completely transferable to humans.[1] Central venous access is usually indicated in the following conditions: administration of solutions with pH < 5 or pH > 9; administration of drugs with osmolarity >600 mOsm/L (INS 2006) or 500 mOsm/L; PN with solution whose osmolarity is equal or superior to 10% glucose or 5% aminoacids; administration of vesicant drugs or drugs associated with intimal damage; need for multiple lumen intravenous treatment; need for dialysis/apheresis; need for central venous pressure monitoring; venous access needed for > 3 months. PN whose osmolarity exceeds 800–900 mOsm/L has been widely thought (several guideline statements) to warrant use of a central line, the upper limit based on a clinical study published 30 years ago.[2] However, in another clinical study on this subject it proved possible to give PN with an osmolality around 1100 mOsm/kg for up to 10 days via peripheral veins in most patients.[3] In short-term PN, increasing osmolarity did not increase the incidence of thrombophlebitis and did not affect the success rate of lines.[4] Also, it appears that the risk of thrombophlebitis is related not only to the osmolarity, but also to the lipid content – which may have a protective effect on the endothelium[5] – and to the final pH of the solution. Finally, volume load and osmolarity appear to have equal relevance in determining phlebitis: the osmolarity rate, defined as the number of milliOsmols infused per hour, correlated well with the phlebitis rate ($r = 0.95$) in clinical trial.[6]

Thus, more randomized studies are needed, to clarify the range of indication of peripheral PN, especially considering the increasing use of peripheral lines which can stay safely in place for weeks (midline catheters). These are 20–25 cm long polyurethane or silicone catheters, whose diameter is usually between 3 and 5 Fr, inserted[1] in the superficial veins of the antecubital area, by a simple percutaneous technique, or[2] in the deep veins of the midarm, with ultrasound guidance.

Midline catheters should be taken into consideration as a potential option every time that peripheral therapy is expected for more than 6 days (Grade B). Since this is the case for most in-hospital PN treatments, midline catheters are bound to play a major role in this setting. In the case of home PN, short cannulas carry a high risk of dislocation and infiltration, so in the unusual event of home peripheral PN being indicated it should be delivered through midline catheters.

Nonetheless, it is important to stress that peripheral PN, both through short cannulas and through midline catheters, has major limitations (a) in the availability of peripheral veins and (b) in the risk of peripheral vein thrombophlebitis.[7] The first problem can be overcome by the routine use of ultrasound guidance, which allows positioning of midline catheters in deep veins of the upper arm (basilic and brachial) even when no superficial veins can be found. The prevention of peripheral vein thrombophlebitis is based on several interventions: aseptic technique during catheter placement and catheter care; choice of the smallest gauge possible (ideally, the diameter of the catheter should be one third or less of the diameter of the vein, as checked by ultrasound); use of polyurethane (PUR) and silicone catheters rather than Teflon cannulas; appropriate osmolarity of the solution; use of lipid-based solutions (fat emulsion may have a protective effect on the vein wall); pH higher than 5 and lower than 9; adequate fixation of the catheter (by transparent adhesive membranes and/or sutureless fixation devices).

2. How to choose the central venous access device for PN?

Short-term: many non-tunneled central venous catheters (CVCs), as well as peripherally inserted central catheters (PICCs) are suitable for in-patient PN.

Medium-term: PICCs, Hohn catheters, and tunneled catheters and ports are appropriate. Non-tunneled central venous catheters are discouraged in HPN, because of high rates of infection, obstruction, dislocation, and venous thrombosis (Grade B).

Prolonged use and HPN (>3 months) usually require a long-term device. There is a choice between tunneled catheters and totally implantable device. In those requiring frequent (daily) access a tunneled device is generally preferable (Grade B).

Comments: Central venous access devices (i.e., venous devices whose tip is centrally placed) can be classified as those used for short-, medium- and long-term access.

Short-term central catheters are usually non-tunneled, 20–30 cm polyurethane (PUR) catheters inserted in a central vein (subclavian vein, internal jugular vein, innominate vein, axillary vein or femoral vein); they may have a single-lumen or multiple lumens; they are designed for continuous use and they should normally be used only in hospitalized patients,[8] for a limited period of time (days to weeks).

Medium-term central catheters are usually non-tunneled central venous devices intended for discontinuous use: they include PICCs (peripherally inserted central catheters) and non-tunneled centrally inserted silicone catheters (such as Hohn catheters). PICCs are non-tunneled central catheters inserted through a peripheral vein of the arm (basilic, brachial or cephalic); they are 50–60 cm in length and usually made of silicone or PUR. Hohn catheters are non-tunneled 20 cm centrally inserted silicon catheters.[9] Both PICCs and Hohn catheters can be used for prolonged parenteral nutrition (up to 3 months) in hospitalized patients and in non-hospitalized patients treated in day hospitals, in hospices or at home.[8] PICCs are acceptable for short–medium-term HPN, but – since the exit position effectively disables one hand – self care may be difficult.

With regards to PN in the hospitalized patient, there are no clear data showing significant advantages of PICCs versus centrally inserted CVC. Some evidence suggests that PICC use may be preferable because associated with fewer mechanical complications at insertion, lower costs of insertion, and a lower rate of infection.[9,10] Although this last issue is under debate,[11] it is accepted that placement in the antecubital fossa or the midarm carries the important advantage of removing the exit site of the catheter further away from endotracheal, oral and nasal secretions (Grade C).

Long-term (>3 months) home parenteral nutrition (HPN) requires a long-term venous access device, such as a cuffed tunneled central catheter (Hickman, Broviac, Groshong, and Hickman-like catheters such as Lifecath, RedoTPN, etc.) or a totally implanted port. The choice between tunneled catheters and ports depends on many factors, mainly related to patient's compliance and choice, the experience of the nursing staff, and the frequency of venous access required. Implantable access devices have been recommended only for patients who require long-term, intermittent vascular access, while for patients requiring long-term frequent or continuous access, a tunneled CVC is preferable, but the evidence base for this is weak (Grade C).

Arteriovenous fistulae have been used episodically as a route for delivery of long-term home PN, when central venous access had become impossible; there is insufficient evidence to give recommendations in this regard.

b) Insertion of central venous access devices

3. Which is the preferred site for placement of a central venous access device?

The choice of vein is affected by several factors including venepuncture technique, the risk of related mechanical complications, the feasibility of appropriate nursing of the catheter site, and the risk of thrombotic and infective complications (Grade B).

The use of the femoral vein for PN is relatively contraindicated, since this is associated with a high risk of contamination at the exit site at the groin, and a high risk of venous thrombosis (Grade B).

High approaches to the internal jugular vein (either anterior or posterior to the sternoclavicular muscle) are not recommended, since the exit site is difficult to nurse, and there is thus a high risk of catheter contamination and catheter-related infection (Grade C).

Comments: Short-term non-tunneled CVC and Hohn catheters are inserted by percutaneous venepuncture of central veins, either by the so-called 'blind' method (using anatomical landmarks) or by ultrasound (US) guidance/ assistance.

Blind positioning of CVCs is usually achieved by direct venepuncture of the subclavian vein (via a supraclavicular or infraclavicular approach), or the internal jugular vein (high posterior approach; high anterior approach; axial approach, between the two heads of the sternoclavicular muscle; low lateral approach; etc.); or the femoral vein. Venepuncture of the internal jugular vein carries less risk of insertion-related complications if compared to the subclavian vein[12]; in particular, the low lateral approach to the internal jugular vein (or Jernigan's approach) appears to be the technique of blind venepuncture associated with the lowest risk of mechanical complications.[13]

US-guided positioning of short-term CVCs may be achieved by supraclavicular venepuncture of the subclavian vein, of the internal jugular vein, or of the innominate vein; by infraclavicular venepuncture of the axillary/subclavian vein; or by femoral venepuncture.

Though positioning of central venous catheters on the left side is usually associated with a higher risk of malposition than on the right side, there are no evidence-based recommendations in this regard. Also (a) there may be specific clinical and anatomic conditions which enforce use of one or other side (poor visualization of the veins on the other side, skin abnormalities, etc.), and (b) the risk of malposition may be minimized by using a technique for intraoperative control of the position of the catheter tip (including fluoroscopy and ECG-based methods).

Since the presence of a non-tunneled CVC in the femoral vein is associated with a high risk of infection and of catheter-related venous thrombosis, this route is relatively contraindicated in parenteral nutrition (Grade C).

Increased difficulty in nursing of the exit site of the catheter is to be expected when the exit site of the CVC is in the neck area[14]; therefore, it is preferable to employ approaches that facilitate dressing changes, such as the infraclavicular area (subclavian or axillary venepuncture) or the area just above the clavicle (low approach to the internal jugular vein; supraclavicular approach to the innominate vein or to the internal jugular vein).

4. Which is the best technique for placement of a central venous access?

There is compelling evidence that ultrasound-guided venepuncture (by real-time ultrasonography) is associated with a lower incidence of complications and a higher rate of success than 'blind' venepuncture. Ultrasound support is therefore strongly recommended for all CVC insertions (Grade A). Placement by surgical cutdown is not recommended, in terms of cost-effectiveness and risk of infection (Grade A).

Comments: The advantages of US-guidance for placement of CVCs have been demonstrated in many RCTs and confirmed by all the meta-analyses on this subject. In a 1996 meta-analysis of eight RCTs, US-guidance was characterized by a lower rate of failure and complications and by a higher rate of success at the first attempt if compared to the landmark technique.[15] In 2001, the Stanford Evidence Based Practice Center at the UCSF published the results of the project 'Making Health Care Safer: A critical analysis of patient

safety practices', identifying US-guidance for CVC placement as one of eleven evidence-based clinical tools which should be enforced in clinical practice.[16] In 2002 the British National Institute for Clinical Excellence made the following recommendations: 'imaging US-guidance should be the preferred method when inserting a CVC into the internal jugular vein in adults and children in elective situations' and that 'imaging US-guidance should be considered in most clinical situations where CVC insertion is necessary, whether the situation is elective or an emergency' (Table 1). A meta-analysis of 18 RCTs showed that US-guidance is highly effective in reducing the rate of failure, the rate of complications, and the rate of accidental arterial puncture, thus 'clearly improving patient safety'.[17] Similar results were shown in a 2003 meta-analysis,[18] which also showed that US-guided venepuncture takes less time to perform than blind venepuncture. The same authors concluded that 'economic modeling indicates that US is likely to save health service resources as well as improve failure and complication rates,' and that 'for every 1000 procedures, a resource saving of £2000 (~2200€) is suggested'.[19] More recently, several randomized studies have confirmed – with no exception – the superiority of US-guided venepuncture, not only as an elective procedure, but also in the emergency department.[20] A randomized study of US-guided versus blind catheterization of the internal jugular vein in critical care patients showed that US-guidance was also associated with a decrease of catheter-related infections.[21] The uniform use of real-time ultrasound guidance for the placement of CVCs is clearly supported by the literature (Grade A).

In summary there is strong statistical evidence to indicate that US-guided insertion of central catheters is more effective and safer than blind techniques in both adults and children. It may therefore now be considered unethical or lacking in common sense to withhold the use of this option.[22]

In placement of PICCs, percutaneous cannulation of the basilic vein or the brachial vein in the midarm, utilizing ultrasound guidance and the micro-introducer technique, is the preferred option (Grade C).

Comments: PICCs may be inserted either in the antecubital fossa, by 'blind' percutaneous cannulation of cephalic or basilic vein, or in the midarm, by ultrasound-guided cannulation of the basilic, brachial or cephalic vein; the results of ultrasound technique are optimal if used in conjunction with the micro-introducer technique. Evidence suggests that US insertion in the midarm significantly increases the rate of success, reduces the incidence of local complications such as thrombophlebitis, and also positively affects the compliance of the patient[23–25]: US-guided PICC insertion is also recommended in other guidelines.

Long-term venous devices (tunneled catheters or ports) usually consist of large bore silicone catheters, which are particularly prone to malfunction and damage if compressed between the clavicle and the first rib (the so-called 'pinch-off syndrome'). Thus, when inserting a long-term venous access, the 'blind' infraclavicular approach to the subclavian vein – and particularly the 'medial' infraclavicular approach – is not recommended. It is noteworthy that US-guided CVC placement does not seem associated with the risk of pinch-off, even when using the infraclavicular approach.

US-guided venepuncture of the internal jugular, subclavian, innominate or axillary vein, plus subcutaneous tunneling to the infraclavicular area, is now the best option for long-term venous access. Other less satisfactory options include 'blind' cannulation of internal jugular vein (possibly by the low lateral approach) and surgical cutdown onto the cephalic vein at the delto-pectoral fossa or the external jugular vein in the neck. Surgical cutdown is associated with higher costs and a higher risk of infection when compared to percutaneous venepuncture.[26]

In selected patients (such as when there is obstruction of the superior vena cava), long-term venous access devices may be placed in the inferior vena cava, by femoral venepuncture: in these cases, the catheter exit site or the port must be placed at a proper distance from the groin, to minimize the risk of contamination.

5. Which is the most appropriate position of the tip of a central venous access for parenteral nutrition?

High osmolarity PN requires central venous access and should be delivered through a catheter whose tip is in the lower third of the superior vena cava, at the atrio-caval junction, or in the upper portion of the right atrium (Grade A). The position of the tip should preferably be checked during the procedure, especially when an infraclavicular approach to the subclavian vein has been used (Grade C).

Postoperative X-ray is mandatory (a) when the position of the tip has not been checked during the procedure, and/or (b) when the devise been placed using a blind subclavian approach or other technique which carries the risk of pleuropulmonary damage (Grade B).

Comments: For any central venous access (short-, medium- or long-term), the position of the tip of the catheter plays a critical role. The ideal position has been said to be between the lower third of the superior cava vein and the upper third of the right atrium. In fact, evidence shows that infusion of high osmolarity PN in the lower third of the superior vena cava or at the atrio-caval junction is associated with the least incidence of mechanical and thrombotic complications. On the other hand, if the catheter is too deep into the atrium, in proximity to the tricuspid valve, or even deeper, it may be associated with these complications.

Ideally, the position of the tip should be checked during the procedure,[27] either by fluoroscopy or by the ECG method.[28,29] If the position has not been checked intraoperatively, a post-procedural chest X-ray should be performed to check the position of the tip. A chest X-ray should always be performed if the venepuncture has been performed by the 'blind' technique, and especially so with an approach which carries the risk of pleuro-pulmonary damage (pneumothorax, hemothorax, etc.). A very early X-ray (within 1 h after the procedure) may not be sufficient, since a pneumothorax may not become apparent for 12–24 h.

c) Prevention of catheter-related bloodstream infections

6. Which evidence-based interventions effectively reduce the risk of catheter-related bloodstream infections?

There is limited evidence to suggest that the catheter material is important in the etiology of catheter-related sepsis. Teflon, silicone and polyurethane (PUR) have been associated with fewer infections than polyvinyl chloride or polyethylene. Currently all available CVCs are made either of PUR (short-term and medium-term) or silicone (medium-term and long-term); no specific recommendation for clinical practice is made.

Evidence indicates that the risk of catheter-related infection is reduced by:

- ***Using tunneled and implanted catheters (value only confirmed in long-term use)***
- ***Using antimicrobial coated catheters (value only shown in short-term use)***
- ***Using single-lumen catheters***
- ***Using peripheral access (PICC) when possible***
- ***Appropriate choice of the insertion site***
- ***Ultrasound-guided venepuncture***

- ***Use of maximal barrier precautions during insertion***
- ***Proper education and specific training of staff***
- ***An adequate policy of hand washing***
- ***Use of 2% chlorhexidine as skin antiseptic***
- ***Appropriate dressing of the exit site***
- ***Disinfection of hubs, stopcocks and needle-free connectors***
- ***Regular change of administration sets***

Some interventions are not effective in reducing the risk of infection, and should not be adopted for this purpose; these include:

- ***in-line filters***
- ***routine replacement of central lines on a scheduled basis***
- ***antibiotic prophylaxis***
- ***the use of heparin***

Comments: Tunneled catheters and totally implanted venous access devices are associated with a low rate of infection, since they are specifically protected from extraluminal contamination. However, tunneling and subcutaneous implantation is in effect a minor surgical procedure, which is relatively contraindicated in patients with a low platelet count or coagulation abnormalities; also, these devices are expensive and are not cost-effective in the setting of short-/medium-term venous access for parenteral nutrition: they should be reserved for long-term home parenteral nutrition. Nonetheless, this view is not yet supported by randomized clinical trial in adult patients. In pediatric patients, some benefit may accrue from tunneling short-term CVCs.

Antimicrobial coated CVCs are effective in reducing CRBSI, and their use is recommended in short-term catheterization of adult patients in clinical settings characterized by a high incidence of CRBSI despite adequate implementation of the other evidence-based interventions (Grade A). Short-term central venous catheters coated with chlorhexidine/sulfadiazine or coated with rifampicin/minocycline have a significantly lower rate of catheter-related infections, as shown in the systematic review of Maki and co-workers.[30] In a recent systematic review and economic evaluation conducted by the Liverpool Reviews and Implementation Group,[31] the authors conclude that rates of CR-BSI are statistically significantly reduced by catheters coated with minocycline/rifampicin, or internally and externally coated with chlorhexidine/silver sulfadiazine (only a trend to statistical significance was seen in catheters only extraluminally coated).

Thus the use of an antimicrobial coated central venous access device is to be considered for adult patients who require short-term central venous catheterization and who are at high risk for catheter-related bloodstream infection if rates of CR-BSI remain high despite implementing a comprehensive strategy to reduce their frequency.

A single-lumen CVC is to be preferred, unless multiple ports are essential for the management of the patient (Grade B). If a multilumen CVC is used, one lumen should be reserved exclusively for PN (Grade C). Central venous catheters with multiple lumens are associated with an increased rate of infection compared to single-lumen CVCs as shown by several randomized controlled trials; nonetheless, this contention has been questioned by recent papers. Two recent systematic review and quantitative meta-analyses have focused on the risk of CR-BSI and catheter colonization in multilumen catheters compared with single-lumen catheters. The first[32] concluded that multilumen catheters are not a significant risk factor for increased CR-BSI or local catheter colonization compared with single-lumen devices. The second review[33] concluded that there is some evidence – from 5 randomized controlled trials (RCTs) with data on 530 catheterizations – that for every 20 single-lumen catheters inserted one CR-BSI will be avoided which would have occurred had multi-lumen catheters been used. Though further research is warranted, in the meantime it is reasonable to recommend a single-lumen catheter unless multiple ports are essential for the management of the patient (Grade B). If a multilumen catheter is used, it is recommended that one lumen is designated exclusively for PN. Of course, all lumens must be handled with the same meticulous attention to aseptic technique.

Though some data suggest that PICCs may be associated with a lower risk of CRBSI compared to non-tunneled short-term CVCs, there is no conclusive evidence on this point. At present, PICCs should be taken into consideration for PN (a) in patients with tracheostomy, (b) when placement of a standard CVC implies an increased risk of insertion-related complications, (c) in patients with coagulation abnormalities (Grade C). Peripherally inserted central venous catheters (PICCs) are apparently associated with a lower risk of infection, most probably because of the exit site on the arm, which is less prone to be contaminated by nasal and oral secretions.[10] In a recent multicenter study analyzing 2101 central venous catheters inserted in critically ill patients, PICCs were associated with a significantly lower rate of bloodstream infection than standard CVCs.[34] No randomized control study has yet proven this. A meta-analysis from Turcotte et al.,[35] including 48 papers published between 1979 and 2004, did not find a clear evidence that PICC is superior to CVC in acute care settings, as each approach offers its own advantages and a different profile of complications. In this meta-analysis infectious complications did not significantly differ between PICC and CVC, but it is important to stress that all the papers included in this analysis reported experience with PICC inserted with the 'blind' technique, and not by ultrasound guidance, which is the method now considered standard for PICC insertion.[24]

In conclusion, at present, it is reasonable to consider PICC insertion for parenteral nutrition (a) in patients with tracheostomy, (b) in patients with severe anatomical abnormalities of neck and thorax, which may be associated with difficult positioning and nursing of a centrally placed CVC, (c) in patients with very low platelet count (e.g., below 9000), and (d) in patients who are candidates for home parenteral nutrition for limited periods of time (e.g., weeks).[10] On the other hand, PICCs are not advisable in patients with renal failure and impending need for dialysis, in whom preservation of upper-extremity veins is needed for fistula or graft implantation. 'The assumption that PICCs are safer than conventional CVCs with regard to the risk of infection is in question and should be assessed by a larger, adequately powered randomized trial that assesses peripheral vein thrombophlebitis, PICC-related thrombosis, and premature dislodgment, as well as CR-BSI'.[11]

In selecting the most appropriate insertion site for a CVC, it is advisable to consider several factors, including patient-specific factors (e.g., pre-existing CVC, anatomic abnormalities, bleeding diathesis, some types of positive-pressure ventilation), the relative risk of mechanical complications (e.g., bleeding, pneumothorax, thrombosis), as well as the risk of infection and the feasibility of an adequate nursing care of the catheter exit site (Grade B).

Placement of a non-tunneled CVC in the femoral vein is not recommended in adult patients receiving PN, since this route is associated with a relevant risk of venous thrombosis, as well as a high risk of extraluminal contamination and CRBSI, due to the difficulties inherent in dressing this exit site (Grade B).

Placement of a non-tunneled CVC whose exit site is in the mid-upper part of the neck (i.e., via a high approach to the internal jugular vein) is not recommended, since it is associated with a high risk of extraluminal contamination and CRBSI, due to neck movement and difficulties inherent in nursing care of this site (Grade C).

No RCT has satisfactorily compared catheter-related infection rates for catheters placed in jugular, subclavian, and femoral sites.

However, previous evidence suggested that non-tunneled catheters inserted into the internal jugular vein were associated with higher risks for CR-infection than those inserted into a subclavian vein.

This might be secondary not to the choice of the vein itself, but to feasibility of an adequate dressing of catheter exit site; thus, the infection risk of a CVC line inserted in the internal jugular vein via the high posterior approach (exit site at midneck) and the infection risk of a CVCs inserted using the low lateral 'Jernigan' approach to the internal jugular vein (exit site in the supraclavicular fossa) may be quite different.[13]

A clinical study in intensive care patients failed to demonstrate any advantage of the subclavian route compared to the internal jugular vein in terms of infection rate.[36] In a prospective study of 988 ICU patients, the internal jugular route and the femoral route were associated with a higher risk of local infection of the exit site, but there was no difference in terms of CRBSI.[37] Non-tunneled femoral catheters have been demonstrated to have relatively high colonization rates when used in adults[38] and should be avoided because they are thought to be associated with a higher risk of deep vein thrombosis (DVT) and CR-infection when compared to internal jugular or subclavian catheters.

A review and meta-analysis[39] of non-randomized studies published up to 2000 reported that there were significantly more arterial punctures with jugular access compared to the subclavian approach, but that there were significantly fewer malpositions with jugular access, with no difference in the incidence of hemo- or pneumothorax or of vessel occlusion. The more recent Cochrane systematic review found no adequate randomized trials of subclavian versus jugular central venous access. More evidence is required on whether the subclavian or the jugular access route is to be preferred.[40] Also, since ultrasound guidance is now considered as a standard of care, it is recommended that future comparative trials should incorporate ultrasound-guided venepuncture, as well as taking into account other central routes which have been made possible by ultrasound guidance, such as the axillary or the innominate (brachio-cephalic) vein.

With regards to PICCs, an exit site in the midarm (typical of US-guided PICC insertion) might have relevant advantages in terms of nursing care compared to the antecubital fossa (typical of 'blind' PICC insertion).[14]

In conclusion, with regards to non-tunneled CVCs, the choice of the insertion site has implications to its nursing care. Sites in the groin (femoral vein), on the neck (high approaches to the internal jugular vein) or in the antecubital fossa (blind PICC insertion) probably carry a higher risk of contamination compared to sites in the supraclavicular fossa (low lateral approach to the internal jugular vein, supraclavicular approaches to the subclavian vein or to the innominate vein), in the infraclavicular fossa (subclavian or axillary vein) or the midarm (US-guided PICC insertion).

Ultrasound placement of catheters may indirectly reduce the risk of contamination and infection, and it is recommended for all central venous access (Grade C). Real-time US-guided venepuncture of the internal jugular vein is apparently associated with a lower rate of CRBSI compared to 'blind' venepuncture, most likely because of less trauma to the tissues and the shorter time needed for the procedure, as shown in a recent randomized study.[21] Also, real-time ultrasound guidance allows PICC positioning in the midarm, by cannulation of the basilic vein or one of the brachial veins: this may be associated with a lower risk of local infection and thrombosis as compared to 'blind' positioning in the antecubital fossa.[24,25]

Maximal barrier precautions during CVC insertion are effective in reducing the risk of infection and are recommended (Grade B). Prospective trials suggest that the risk of CRBSI may be reduced by using maximal sterile barriers, including a sterile gown and sterile gloves for the operator, and a large sterile drape for the insertion of central venous access devices (Grade C). Full-barrier precautions during CVC insertion are recommended by most other guidelines, and this practice has been adopted by most 'bundles' of evidence-based interventions aiming to reduce CRBSI, in multicenter prospective trials.

Proper education and specific training of the staff is universally recommended as one of the most important and evidence-based strategy for reducing the risk of catheter-related infections (Grade A). Specialized nursing teams should care for venous access devices in patients receiving PN. There is good evidence demonstrating that the risk of infection declines following the standardization of aseptic care and increases when the maintenance of intravascular catheters is undertaken by inexperienced healthcare workers. Also, it has been proven that relatively simple education programs focused on training healthcare workers to adhere to local evidence-based protocols may decrease the risk to patients of CRBSI.[41,42] In a very important multicenter prospective study carried out in 108 intensive care units, Provonost and coworkers[43] have shown that the adoption of a bundle of a small number of evidence-based interventions (hand washing; full-barrier precautions during the insertion of central venous catheters; skin antisepsis with chlorhexidine; avoiding the femoral site if possible; removing unnecessary catheters as soon as possible) was highly effective in producing a clinically relevant (up to 66%) and persistent reduction in the incidence of CRBSI.

The implementation of an adequate policy of hand washing amongst healthcare workers who have contact with patients on PN is considered one of the most evidence-based and cost-effective maneuvers for reducing the risk of catheter-related infection (Grade A). Good standards of hand hygiene and antiseptic technique can clearly reduce the risk of CR-infection.[8,44] In particular: before accessing or dressing a central venous access device, hands must be decontaminated either by washing with an antimicrobial liquid soap and water, or by using an alcohol hand rub. When washing hands with soap and water, wet hands first with water, apply the amount of product recommended by the manufacturer to hands, and rub hands vigorously for at least 15 s, covering all surfaces of the hands and fingers; rinse hands with water and dry thoroughly with a disposable towel. When decontaminating hands with an alcohol-based hand rub, apply product to palm of one hand and rub hands together, covering all surfaces of hands and fingers, until hands are dry[8]; follow manufacturer's recommendations regarding the volume of product to use. Hands that are visibly soiled or contaminated with dirt or organic material must be washed with liquid soap and water before using an alcohol hand rub. Evidence from RCTs has shown that when accessing a central venous line (for insertion site dressing, line manipulation or intravenous drug administration) there are two possible options: (1) hand antisepsis + clean gloves, and aseptic non-touch technique; (2) hand antisepsis + sterile gloves (Grade C).

The most appropriate skin antiseptic for prevention of catheter-related bloodstream infection is chlorhexidine as 2% solution in 70% isopropyl alcohol, and it should be preferred for both skin preparation before catheter insertion and cleaning of the catheter exit site (Grade A). Recent clinical randomized study[45] indicates that chlorhexidine, particularly as 2% chlorhexidine gluconate in 70% isopropyl alcohol, is the most appropriate antiseptic for preparation of the insertion site as well as for cleansing the entry site once the catheter is in place (Grade A).

An aqueous solution of chlorhexidine gluconate should be used if the manufacturer's recommendations prohibit the use of alcohol with their product (such as in the case of some PUR catheters). Alcoholic povidone–iodine solution should be used in patients with a history of chlorhexidine sensitivity (Grade A).

Antiseptic should be allowed to air dry; organic solvents, e.g., acetone, ether, should not be applied to the skin before or after the antiseptic (Grade C). Antimicrobial ointments are not effective for prevention of catheter site infections and should not be applied routinely (Grade B).

The catheter exit site of a non-tunneled central venous access should preferably be covered with a sterile, transparent, semi-permeable polyurethane dressing, which should be routinely changed every 7 days (Grade C). These should be changed sooner if they are no longer intact or if moisture collects under the dressing (Grade C). If a patient has profuse perspiration or if the insertion site is bleeding or oozing, a sterile gauze dressing is preferred (Grade C). This need should be assessed daily and the gauze changed when inspection of the insertion site is necessary or when the dressing becomes damp, loosened or soiled. A gauze dressing should be replaced by a transparent dressing as soon as possible. Dressings used on tunneled or implanted catheter insertion sites should be replaced every 7 days until the insertion site has healed, unless there is an indication to change them sooner (Grade C). Chlorhexidine-impregnated dressing is effective in reducing the extraluminal contamination of the catheter exit site, and its use should be taken into consideration in adult patients with non-tunneled CVCs at high risk infection (Grade C).

The efficacy and cost-effectiveness of antimicrobial impregnated dressings in preventing catheter colonization and CR-BSI are still under investigation. Many prospective trials have demonstrated the effectiveness of chlorhexidine-impregnated sponges (Biopatch) in preventing extraluminal contamination of the catheter at the exit site (Grade B).[46–48] Their use should be considered in adult patients with non-tunneled CVCs at high risk for infection (after proper evaluation of their cost-effectiveness).

Another important issue is the technique for stabilization of the CVCs. Evidence has accumulated that the traditional securing of the catheter with sutures may be associated with a high risk of contamination of the exit site. Products used to stabilize the catheter should include manufactured catheter stabilization devices, sterile tapes, and surgical strips, but – whenever feasible – using a manufactured catheter stabilization device is preferred (Grade C). Sutures should no longer be used routinely (Grade B). It is noteworthy that (for example) the Statlock and Biopatch can be simultaneously used on the same catheter exit site, both covered with a transparent semi-permeable dressing, and left in place for 1 week.

Stopcocks, catheter hubs and sampling ports of needle-free connectors are an important route of intraluminal contamination and subsequent CRBSI, and they should always be disinfected before access, preferably using 2% chlorhexidine gluconate in 70% isopropyl alcohol (Grade C)

Needle-free connectors have been introduced into clinical practice for the protection of the patient and healthcare worker, in order to reduce the risk of accidental needle puncture and/or biological contamination. Their effectiveness in reducing CRBSI has never been proven unequivocally; whilst – in contrast – their misuse may actually increase the incidence of CRBSI. Evidence suggests that appropriate disinfection of needle-free connectors may significantly reduce external microbial contamination.[49] Though there is no conclusive evidence on their protective or permissive role in terms of infection prevention, it is recommended that the introduction of needle-free devices should be monitored for an increase in the occurrence of device associated infection. If needle-free devices are used, the manufacturer's recommendations for changing the needle-free components should be followed (Grade C).

When needle-free devices are used, the risk of contamination should be minimized by decontaminating the access port before and after use with a single patient use application of a 70% alcoholic solution or a 2% chlorhexidine gluconate solution unless contraindicated by the manufacturer's recommendations (Grade C).

The intravenous catheter administration set should be changed every 24 h (when using lipid PN) or every 72 h (if lipids are not infused) (Grade C). In-line filters are not recommended for the prevention of CR-BSI (Grade C). No evidence has been found to support the use of in-line filters for preventing infusate-related CR-BSI. However, there may be a role for the use of in-line filtration of lipid-based PN solutions in selected cases, under a pharmacist's recommendation, for filtering micro-aggregates possibly occurring in the emulsion.

Non-tunneled CVCs should not be removed and replaced routinely (Grade A), and they should not be changed routinely over a guide wire (Grade A). Such strategies are not associated with a reduction of CRBSI and may actually increase the rate of complications. Routine removal and replacement of the CVC without a specific clinical indication does not reduce the rate of catheter colonization or the rate of CR-BSI, but increases the incidence of insertion-related complications. CVCs should be removed only if complications occur or they are no longer necessary (Grade A).

Guide wire assisted catheter exchange has a role in replacing a malfunctioning catheter, but is contraindicated in the presence of infection at the catheter site or proven CRBSI. Guide wire exchange may have a role in diagnosis of CRBSI. If catheter-related infection is suspected, but there is no evidence of infection at the catheter site, the existing catheter may be removed and a new catheter inserted over a guide wire; if tests reveal catheter-related infection, the newly inserted catheter should be removed and, if still required, a new catheter inserted at a different site. If there is evidence of infection at the exit site or evidence of CRBSI, the catheter should be removed and not exchanged over guide wire. All fluid administration tubing and connectors must also be replaced when the central venous access device is replaced (Grade C).

Prophylactic administration of systemic or local antibiotics before or during the use of a CVC is not recommended, since it does not reduce the incidence of CR-BSI (Grade A).[50–52]

Prophylaxis with an antibiotic lock has been shown to be effective only in neutropenic patients with long-term venous access. There is no evidence that routinely using this procedure in all patients with CVC will reduce the risk of catheter-related bloodstream infections, and this is not recommended (Grade C).

Low-dose systemic anticoagulation, periodic flushing with heparin, or heparin lock, do not reduce the risk of catheter contamination, and are not recommended for prevention of CRBSI (Grade C). There is no definite evidence that heparin reduces the incidence of CR-BSI, but this may reflect the heterogeneity of heparin concentration used and its modality of administration.

Many substances (taurolidine, citrate, EDTA, ethanol, etc.) have been proposed for flushing and locking the catheter for the purpose or reducing the formation of biofilm inside the catheter and/or reducing the colonization of the device and/or reducing the risk of CRBSI, but there is not enough evidence to give recommendations in this regard.

d) Management of catheter-related bloodstream infections

7. Which is the best method for diagnosis of CRBSI?

Diagnosis of CRBSI is best achieved (a) by quantitative or semi-quantitative culture of the catheter (when the CVC is removed or exchanged over a guide wire), or (b) by paired quantitative blood cultures or paired qualitative blood cultures from a peripheral vein and from the catheter, with continuously monitoring of the differential time to positivity (if the catheter is left in place) (Grade A).

Comments: The cornerstones of diagnosis and treatment of catheter-related bloodstream infections have been clearly summarized in the very exhaustive and evidence-based guidelines released in 2001 by the Infectious Disease Society of America (Table 1).

As regards the diagnosis, it is recommended[53] that culture of catheters should be done only when catheter-related bloodstream infection is suspected, and not as a routine (Grade B); quantitative or semi-quantitative cultures of catheters are preferable to qualitative cultures (Grade A).

When a CRBSI is suspected, two sets of blood samples for culture, one percutaneously and one from the catheter, should be obtained; paired quantitative blood cultures or paired qualitative blood cultures with a continuously monitored differential time to positivity[54,55] are recommended for the diagnosis of catheter-related infection (Grade A).

8. Which is the best method for the management of CRBSI in non-tunneled CVCs?

A short-term central line should be removed in the case of (a) evident signs of local infection at the exit site, (b) clinical signs of sepsis, (c) positive culture of the catheter exchanged over guide wire, or (d) positive paired blood cultures (from peripheral blood and blood drawn from the catheter) (Grade B). Appropriate antibiotic therapy should be continued after catheter removal.

Comments: With regards to non-tunneled CVCs, in patients with fever and mild to moderate disease the catheter should not routinely be removed (Grade C); the CVC should be removed and cultured if the patient has erythema or pus overlying the catheter exit site, or clinical signs of septic shock (Grade B).

If blood culture results are positive or if the CVC is exchanged over the guide wire and has significant colonization according to results of quantitative or semi-quantitative cultures, the catheter should be removed and replaced at a new site (Grade B).

If not contraindicated, trans-esophageal echocardiography (TEE) should be done to rule out vegetations in patients with catheter-related *Staphylococcus aureus* bloodstream infection (Grade B), because of recently reported high rates of complicating endocarditis[56]; if TEE is not available and results of transthoracic echocardiography are negative, the duration of therapy should be decided for each patient on an individual basis.

After removal of a colonized catheter associated with bloodstream infection, if there is persistent bacteremia or fungemia, or a lack of clinical improvement on appropriate antimicrobial therapy, aggressive evaluation for septic thrombosis, infective endocarditis, and other metastatic infections should ensue (Grade B).

After catheters have been removed from patients with catheter-related bloodstream infection, non-tunneled catheters may be reinserted after appropriate systemic antimicrobial therapy is begun (Grade C).

9. Which is the best method for the management of CRBSI in long-term central venous access devices?

Removal of the long-term venous access device is required in case of (a) tunnel infection or port abscess, (b) clinical signs of septic shock, (c) paired blood cultures positive for fungi or highly virulent bacteria, and/or (d) complicated infection (e.g., evidence of endocarditis, septic thrombosis, or other metastatic infections). In other cases, an attempt to save the device may be tried, using the antibiotic lock technique (Grade B).

Comments: With regards to long-term venous access devices (tunneled CVCs and ports), clinical assessment is recommended to determine whether the device is actually the source of infection or bloodstream infection (Grade B).[57] For complicated infections, the long-term device should be removed (Grade B). For salvage of the device in patients with uncomplicated infections, antibiotic lock therapy[58] should be used for 2 weeks with standard systemic therapy for treatment of catheter-related bacteremia due to *S. aureus*, coagulase-negative staphylococci, and gram-negative bacilli for suspected intraluminal infection, in the absence of tunnel or pocket infection (Grade B)

On the contrary, tunnel infection or port abscess always require removal of the device and usually at least 7–10 days of appropriate antibiotic therapy (Grade C).

Reinsertion of long-term devices should be postponed until after appropriate systemic antimicrobial therapy is begun, based on susceptibilities of the bloodstream isolate, and after repeat cultures of blood samples yield negative results (Grade B); if time permits, insertion of a new device in a stable patient ideally should be done after a systemic antibiotic course of therapy is completed, and repeat blood samples drawn 5–10 days later yield negative results (Grade C).

e) Recommendations for prevention, diagnosis and treatment of non-infectious complications

10. Should the catheter be routinely flushed and if so which solution should be used and how often?

Most central venous access devices for PN can be safely flushed and locked with saline solution when not in use (Grade B).

Heparinized solutions should be used as a lock (after proper flushing with saline), when recommended by the manufacturer, in the case of implanted ports or open-ended catheter lumens which are scheduled to remain closed for more than 8 h (Grade C).

Comments: Three different meta-analyses of randomized controlled trials evaluating the effect of heparin on duration of catheter patency have concluded that intermittent flushing with heparin is no more beneficial than flushing with normal saline alone.[59–61] Nevertheless, manufacturers of implanted ports or opened-ended catheter lumens recommend heparin flushes for maintaining catheter patency and many clinicians feel that heparin flushes are appropriate for flushing devices that are infrequently accessed. Most likely, appropriate flushing with saline before heparinization is more important than the use of heparin itself or its concentration. Also, since heparin may facilitate the precipitation of lipids, saline flushing is mandatory during PN with lipids before any flushing with heparin.

According to most other guidelines there is no need for heparinization when the catheter is closed for a short period of time (<8 h). Since most PN treatments in hospital are delivered by continuous infusion or with short intervals, heparinization does not have a relevant role in hospital PN. On the other hand, heparin flushing may be useful in helping to maintain patency in catheter lumens that are infrequently accessed, and is recommended by manufacturers of implantable ports and for devices used for blood processing (e.g., hemodialysis or apheresis). If heparin flushes are used in patients on home PN, attention should be given to the risk of lipid precipitation. Heparin should not be used immediately before or after the administration of lipid-containing PN admixtures: a saline flush should always be interposed (Grade B).

Close ended valve catheters – following manufacturers' instructions – should be flushed and locked with saline only. No randomized clinical trials have ever established the usefulness of heparinization or the ideal heparin concentration, though most

authors suggest using a range of concentration between 50 and 500 units per mL (Grade C).

There are no evidence-based data suggesting the ideal frequency of heparinization for catheter lumens which remain unused for prolonged periods of time, though most authors and most manufacturers suggest flushing and locking devices with small caliber (5 Fr or less) weekly, and devices with large caliber (6 Fr or more) every 3–4 weeks. Sterile 0.9% sodium chloride for injection should be used to flush and lock catheter lumens that are in frequent use (Grade A); when recommended by the manufacturer, implanted ports or opened-ended catheter lumens should be flushed and locked with heparin sodium flush solutions (Grade C).

Regarding the possible effect of needle-free connectors in preventing catheter occlusion, there are not enough data for a clinical recommendation, though some papers[62] suggest that CVCs with a positive-pressure valve device may have a lower incidence of complete catheter occlusion than those with a standard cap. As some clinical reports suggest that positive displacement needle-free connectors may be associated with a higher risk of CRBSI, their use cannot be actively recommended.

11. Are there evidence-based recommendations regarding prevention, diagnosis or treatment of mechanical complications?

Intraluminal obstruction of the central venous access can be prevented by appropriate nursing protocols in maintenance of the line, including the use of nutritional pumps (Grade C).

Comments: The obstruction of a central venous catheter is most often due to intraluminal precipitate of lipid aggregates, drugs, clots, or contrast medium, and it can be effectively prevented by appropriate nursing measures (e.g., continuous infusion of PN by pump; utilization of appropriate protocols for flushing when the catheter is not in use, or after blood withdrawal; avoidance of routine use of the catheter for infusion of blood products, blood withdrawal, or infusion of contrast medium for radiological exams; avoidance of direct contact between lipid PN and heparin solutions). When the lumen of the catheter is obstructed, the most appropriate action will usually be exchange over a guide wire or removal (in the case of a non-tunneled short-term catheter) or an attempt at pharmacological clearance (in the case of PICCs or long-term venous access devices). Clearance should always be performed using a 10 mL syringe (or bigger), so as to avoid inappropriate high pressures which may damage the catheter. The solution most adequate for the presumed type of obstruction should be used (ethanol for lipid aggregates; urokinase or recombinant tissue plasminogen activator (rTPA) for clots; NaOH or HCl for drugs; $NaHCO_3$ for contrast medium) (Grade C).

Damage to the external part of the catheter can be effectively prevented by appropriate nursing protocols (Grade C). Central lines utilized for PN should not be used for infusion of radiological contrast medium during CT or MR. Damage to the external part of the catheter may occur because of inappropriate care of the catheter exit site (e.g., using scissors when changing the dressing; chemical damage to the silicone due to inappropriate use of organic solvents; chemical damage of PUR due to the inappropriate use of ethanol). Damage to PICCs and tunneled catheters can usually be repaired with specific repair kits; for short-term non-tunneled CVCs, exchange over a guide wire is more cost-effective.

A new specific mechanical complication – whose incidence is rapidly increasing – is the rupture of the external portion of the catheters (most frequently, silicone catheters) due to inappropriate use of the central line for infusion of contrast medium at high pressure by 'power injectors', during MR or CT scan. A specific warning of the FDA recommends utilizing power injectors only on peripheral short cannulas or specific venous access devices which have been certified to resist such high pressures (so-called 'pressure injectable' or 'power' devices).

For totally implantable devices, the choice of the port size and its proper positioning are of paramount importance in the prevention of future complications. The necessary non-coring needles (Huber needles) should not be left in place for more than a week (Grade C). Erosion or damage to the skin above the port occurs frequently, and is usually secondary to (a) error during placement (choice of too big a port, or positioning of the port in an area of the body where there is an inadequate layer of subcutaneous fat), or to (b) inappropriate nursing (e.g., a Huber needle left in place for more than a week).

Appropriate catheter stabilization plays a major role in reducing the incidence of local complications at the exit site and the risk of dislocations. Stitches should not be used routinely: whenever possible, the catheter should be stabilized using a manufactured catheter stabilization device (Grade C). Dislocation of non-tunneled catheters (central and PICC) is usually secondary to inappropriate securing of the catheter at the moment of insertion or to inadequate care of the catheter exit site. Products used to stabilize the catheter may include sterile tapes, and surgical strips, but – whenever feasible – using a manufactured catheter stabilization device (e.g., Statlock) is preferred (Grade C). Stitches should not be used routinely (BCSH 2006), since they increase the risk of local thrombosis/phlebitis (in PICCs), as well as the risk of CRBSI (in CVCs) and the risk of dislocation and local infection of the exit site (in all devices) (Grade C).

Dislocation of tunneled catheters can be prevented by locating the cuff at least 2.5 cm inside the tunnel (or more, according to the manufacturer's instruction), and securing the catheter preferably with a manufactured catheter stabilization device for at least 3–4 weeks.

The so-called 'pinch-off' syndrome is a compression of a large bore silicone catheter – tunneled or connected to an implantable port – between the clavicle and the first rib, typically secondary to 'blind' percutaneous placement of the catheter in the subclavian vein via the infraclavicular route. The compression may lead to malfunction, obstruction, damage and even fracture of the catheter, with embolization of part of it into the pulmonary vascular bed. It is a potentially severe complication, yet apparently preventable simply by avoiding placement of silicone catheters via the blind infraclavicular venepuncture of the subclavian vein (Grade C).

The tip of a central venous catheter should be positioned in the lower third of the superior vena cava, or at the atrio-caval junction, or in the upper portion of the right atrium (Grade A). Tip migration is a complication of silicone long-term catheters: this is also termed secondary malposition, and it usually happens when too short a catheter (with its tip in the upper third of superior vena cava) dislocates because of an increase in thoracic pressure or vigorous physical activity drawing the tip out of the vena cava and allowing it to flick back into an unsuitable position in the innominate vein of the opposite side or retrovertly into one of the jugular veins. It can be prevented by initial correct positioning of the catheter tip.

12. Are there evidence-based recommendations regarding prevention, diagnosis or treatment of thrombotic complications?

Thrombosis is avoided by the use of insertion technique designed to limit damage to the vein including: ultrasound guidance (Grade C), choice of a catheter with the smallest caliber compatible with the infusion therapy needed (Grade B), position

of the tip of the catheter at or near to the atrio-caval junction (Grade B). Prophylaxis with a daily subcutaneous dose of low molecular weight heparin is effective only in patients at high risk for thrombosis (Grade C).

Comments: As regards the prevention of catheter-related central venous thrombosis, to date, to our knowledge, no randomized trials have investigated the relationships between insertion techniques in the long-term setting (e.g., percutaneous versus venous cut-down, US-guided versus anatomic landmark techniques) and central venous thrombosis rate. Prospective, unrandomized, studies have however suggested that minimizing insertion damage to the vein wall, as obtained with US-guidance, helps to yield a low rate of subsequent thrombotic events (Grade C). In vitro and ex vivo data confirm that silicone, and 2nd and 3rd generation polyurethane catheters are less thrombogenic than polyethylene or PVC ones, and should be preferred for long-term use (Grade C).

A lower-diameter catheter with a single-lumen may be protective against the risk of central venous thrombosis. When the number of therapies demands a multiple lumen catheter, it is recommended that the number of lumens is minimized (Grade C). Although some reports suggest that central venous catheters positioned on the left side may be associated with a higher risk of thrombosis if compared to the right side, there is not enough evidence to give recommendations in this regard. Evidence from several prospective studies, indicated that tip position was the main independent prognostic factor for malfunction, thrombosis, and reduced duration of the device. The atrio-caval junction appears to be the optimal position of the catheter tip, as it minimizes the risk of central venous thrombotic events (Grade B).

Although some early trials suggested a benefit of oral, low-dose daily warfarin or daily doses of subcutaneous low molecular weight heparins (LMWH), more recent randomized, double-blind, placebo controlled, and sufficiently powered trials did not find any advantages for either of these prevention strategies. The decision to start prophylaxis against venous thromboembolic events in patients with CVCs, for that reason only, remains unsupported by evidence even in those with underlying malignancy. Prophylaxis with a daily single dose of LMWH 100 IU/kg in those on PN with neoplasia or chronic inflammatory disease, or those with a family or personal past history of idiopathic venous thrombotic events, is however reasonable (Grade C).

Treatment of catheter-related central venous thrombosis should normally include (a) careful removal of the catheter, only if infected or malpositioned or obstructed (Grade B); (b) in acute symptomatic cases, local or systemic thrombolysis; (c) in subacute and chronic symptomatic cases, anticoagulant treatment with LMWH (Grade C). Catheter removal or maintenance does not appear to influence the outcome of the thrombosis; indeed, the presence of the catheter might be useful for local thrombolytic treatment, when indicated. Moreover there is a risk of embolization of clot partially attached to the catheter which may easily become dislodged during catheter removal. The catheter should be removed in the case of infected thrombus, when the tip is malpositioned, and if occlusion proves irreversible (Grade C). The use of thrombolytic drugs is best supported in acute symptomatic cases (diagnosis $<$24 h after the first symptoms) and the efficacy of systemic versus local thrombolysis is still a matter of debate, especially for large thrombi (Grade C). Chronic symptomatic central venous thrombosis should be treated with LMWH and then oral anticoagulants, or LMWH long-term alone, depending on the clinical setting. Compared with warfarin, the LMWHs exhibit a superior safety profile and more predictable antithrombotic effects and can usually be given once daily in a single dose without the need for monitoring (Grade C).

Venous thrombosis (local or more seldom central) is occasionally associated with PICCs; it is apparently a multifactorial phenomenon, influenced by the caliber of the catheter,[63] the technique of placement (US-guided versus blind), the vein cannulated (cephalic versus brachial versus basilic), the position of the tip, the stabilization technique (Statlock versus tape versus stitches), the type of treatment,[64] and factors related to the patient and the underlying disease. Preventative measures are discussed above: PICCs should not be inserted in paretic or immobilized arms, since the risk of thrombosis is particularly high in these conditions (Grade C).

The fibrin sleeve (or fibrin sheath) is a sleeve derived from fibroblastic tissue which slowly covers the intraluminal and extraluminal surfaces of long-term catheters; it may be unapparent, but can be associated with a persistent problem with

Table 1
Guidelines on venous access and venous access devices produced by other national and international bodies. The topics have been widely and repeatedly addressed with considerable conformity in the major conclusions. They are included here to demonstrate this, and also (through their own citation of primary publications) to help limit an otherwise very lengthy list of primary sources.

ACS 2008 – American College of Surgeons. Statement on recommendations for uniform use of real-time ultrasound guidance for placement of central venous catheters. 2008. http://www.facs.org/fellows_info/statements/st-60.html

AVA 2008 – Association for Vascular Access. Position Statement on the Use of Real-Time Imaging Modalities for Placement of Central Venous Access Devices. 2008. www.avainfo.org

ASPEN 2002 – ASPEN Board of Directors and the Clinical Guidelines Task Force: Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 2002, vol. 26 (n. 1, suppl.): pp. 36SA-37SA

ASPEN 2004 – Task Force for the Revision of Safe Practices for Parenteral Nutrition: Safe Practices for Parenteral Nutrition. JPEN 2004, Vol. 8, n. 6: pp. S40–S70

AUSPEN 2008 – Gillanders L, Angstmann K, Ball P et al.: AuSPEN clinical practice guideline for home parenteral nutrition patients in Australia and New Zealand. Nutrition 2008, 24: 998–1012.

BCSH 2006 – British Committee for Standards in Haematology: Guidelines on the insertion and management of central venous access devices in adults. Published in 2006 and diffused by the British Society for Haematology, 100 White Lion Street, London. Available on www.evanetwork.info

CDC 2002 – Centers for Disease Control and Prevention: Guidelines for the Prevention of Intravascular Catheter-Related Infections. MMWR 2002; 51(No. RR-10): pp. 1–32. Available on www.evanetwork.info

EPIC 2007 – Pratt RJ, Pellowe CM, Wilson JA et al.: EPIC2: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. Journal of Hospital Infection (2007) 65S, S1–S64. Available on www.evanetwork.info

GAVeCeLT 2007 – Campisi C, Biffi R, Pittiruti M and the GAVeCeLT Committee for the Consensus: Catheter-Related Central Venous Thrombosis – The Development of a Nationwide Consensus Paper in Italy. JAVA 2007, Vol 12 (No 1): pp. 38–46. Available on www.evanetwork.info

IDSA 2001 – Mermel LA, Farr BM, Sherertz RJ at al.: Guidelines for the Management of Intravascular Catheter-Related Infections. Clinical Infectious Diseases 2001; 32:1249–72. Available on www.evanetwork.info

INS 2006 – Infusion Nurses Society: Infusion Nursing Standards of Practice. Journal of Infusion Nursing, vol. 29 (suppl. 1): pp. S1–S92.

NICE 2002 – National Institute for Clinical Excellence: Guidance on the use of ultrasound locating devices for placing central venous catheters. September 2002. Published and diffused by National Institute for Clinical Excellence, 11 Strand, London. Available on www.nice.org.uk and on www.evanetwork.info

RCN 2005 – Royal College of Nursing I.V. Therapy Forum: Standards for infusion therapy. November 2005. Published by the Royal College of Nursing, 20 Cavendish Square, London. Available on www.rcn.org.uk and on www.evanetwork.info

RNAO 2004 – Registered Nurses Association of Ontario, Nursing Best Practice Guidelines Project: Assessment and Device Selection for Vascular Access. May 2004. Published and diffused by the Registered Nurses Association of Ontario, 111 Richmond Street West, Suite 1100, Toronto, Ontario (Canada). Available on www.rnao.org/bestpractices and on www.evanetwork.info

SINPE 2002 – Linee Guida SINPE per la Nutrizione Artificiale Ospedaliera. RINPE 2002, anno 20 (suppl. 5): pp. S21–S22, pp. S29–S33

SHEA/IDSA 2008 – SHEA/IDSA practice recommendations – Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals. Infect Control Hosp Epidemiol 2008; 29: S22–S30.

withdrawal from, or complete occlusion of the catheter. Its pathogenesis is unknown and there are not enough data to formulate evidence-based recommendations with regards to its prevention and treatment.

Conflict of interest

Conflict of interest on file at ESPEN (espenjournals@espen.org).

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