ESPEN Guidelines for Parenteral Nutrition

Central Venous Catheter (access, care, diagnosis and therapy of complications)

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Comments from reviewers that are outstanding include the request for guidance on
1) the use of taurolidine to (treat and) prevent catheter infection
2) the use of arteriovenous fistula creation for vascular access

a) General recommendations about the indication and the use of the different types of central venous catheters in parenteral nutrition
b) Insertion of central venous access devices
c) Prevention of catheter-related bloodstream infections
d) Management of catheter related bloodstream infections
e) Recommendations for prevention, diagnosis and treatment of non-infectious complications

Guidelines
References
a) General recommendations about the indication and the use of the different types of central venous catheters in parenteral nutrition

Which is the role of peripheral parenteral nutrition?

A central venous access (i.e., a venous access which allows delivery of nutrients directly in the superior vena cava or in the right atrium) is needed in most patients candidate to parenteral nutrition (PN).

Though, there are some situations in which PN may be safely delivered by a peripheral access (short cannula or midline catheter), i.e. when using a solution with low osmolarity, when a significant portion of the non-protein calories are given as lipids.

We recommend (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 exclusively when using nutrient solutions – possibly with lipids - whose osmolarity does not exceed 800 mOsm/L.

Peripheral home PN should be given only via midline catheters, since short cannulas carry a high risk of dislocation and infiltration (Grade C).

There are not enough evidence in the literature apt to indicate a clear cut-off osmolarity for central vs. peripheral PN. According to INS Standards (INS 2006), RNAO Guidelines (RNAO 2004) and to RCN Standards (RCN 2005), a 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 (RNAO 2004); 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 i.v. treatment; need for dialysis/pheresis; need for central venous pressure monitoring; venous access needed for > 3 months. According to ASPEN (ASPEN 2002) and SINPE (SINPE 2002) recommendations, a central line is needed for PN whose osmolarity exceeds 800-850 mOsm/L.

One of the few clinical studies on this subject showed that, in most patients, it is possible to give PN with an osmolality around 1100 mOsm/Kg for up to 10 days via peripheral veins (Hoffmann1989). In a recent clinical study on short term PN, increasing osmolarity did not increase episodes of thrombophlebitis and did not affect the success rate of lines (Kane 1996). 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 (Matsusue 1995) – and to the final pH of the solution.

More randomized studies are needed, to clarify the range of indication of peripheral PN, specially considering the increasing use of peripheral lines which can stay safely in place for weeks (midline catheters).

According to CDC Guidelines (CDC 2002), midline catheters should be taken into consideration as a preferable option every time that peripheral i.v. therapy is expected for more than 6 days (Class B recommendation according to CDC Guidelines); since this is the case for most intra-hospital PN treatments, midline catheters are bound to play a major role in this setting.
How to choose the central venous access device for PN?

Central venous access devices suitable for intra-hospital PN include short term non-tunnelled central venous catheters, as well as peripherally inserted central catheters (PICCs).

PICCs, Hohn catheters and long term venous devices (tunnelled catheters and ports) are appropriate for home PN (HPN). The use of short term central venous catheters for home PN should be discouraged, considering their high susceptibility to infection, obstruction of the device, dislocation, and catheter related venous thrombosis (Grade B).

Prolonged HPN (> 3 months) usually requires a long term venous access: the choice between tunnelled catheters and totally implantable device depends on many factors, though in patients requiring frequent (daily) access a tunnelled device is generally preferable (Grade B).

Central venous accesses (i.e., venous devices whose tip is centrally placed) can be classified as short term, medium term and long term accesses.

Short term central catheters are non-tunnelled, 20 – 30 cm long polyurethane (PUR) catheters inserted in a central vein (subclavian vein, internar jugular vein, innominate vein, axillary vein or femoral vein): they may have a single lumen or multiple lumens, and they should be used only in hospitalized patients (Ryder 2006).

Medium term central catheters are non-tunnelled central venous devices specifically planned for discontinuous use: they include PICCs (peripherally inserted central catheters) and Hohn catheters. PICCs are non-tunnelled central catheters inserted through a peripheral vein of the arm (basilica or brachial or cephalic vein); they are 50 – 60 cm long and usually made of silicone or 2nd-3rd generation PUR. Hohn catheters are non-tunnelled 20 cm long centrally inserted silicon catheters (Raad 1993). Both PICCs and Hohn catheters can be used for prolonged parenteral nutrition (up to 3-6 months) both in hospitalized patients and in patients treated in day hospital, in hospice or at home (Home PN) (Ryder 2006).

With regards to PN in the hospitalized patient, there are no clear data showing significant advantages of PICCs vs. centrally inserted CVC. Some evidence suggests that PICC may be preferable because associated with fewer mechanical complications at insertion, lower costs of insertion, and a lower rate of infection (Raad 1993) (Ryder 1995); though this last issue is under debate (Safdar 2005), it is accepted that placement in the antecubital fussa or at midarm carries the important advantage of removing the exit site of the catheter away from endotracheal, oral and nasal secretions (EPIC 2007).

Long term (> 3 months) home parenteral nutrition (HPN) requires a long term venous access device, such as a tunnelled central catheter (Hickman, Broviac, Groshong, etc.) or a totally implanted port. The choice between a tunnelled catheter vs. a port depends on many factors, mainly related to patient’s compliance, experience of the nursing staff, and frequency of venous access. According to CDC Guidelines (CDC 2002) totally implantable access devices should be reserved for patients who require long-term, intermittent vascular access, while for patients requiring long term frequent or continuous access (which is the case of PN), a tunnelled CVC is preferable (Class C recommendation according to CDC).
b) Insertion of central venous access devices

Which is the site preferable for placement of a short term central venous access?

The choice of the site for placement of a short term non-tunnelled central venous access is affected by several factors, such as the technique of venipuncture, the risk of venipuncture-related mechanical complications, the feasibility of an appropriate nursing of the catheter site care, and the overall risk of thrombotic and infective complications (Grade B).

Placement of a short term CVC for PN in the femoral vein is contraindicated, since it is associated with a high risk of contamination of the catheter exit site at the groin, as well as with a high risk of catheter-related venous thrombosis (Grade B).

The high approaches to the internal jugular vein (either anterior or posterior to the sternoclavicular muscle) are not recommended, since they are associated with difficult care of the exit site and thus a high risk of catheter contamination and catheter related bloodstream infection (Grade C).

Short term non-tunnelled CVC and Hohn catheters are inserted by percutaneous venipuncture of central veins, either by the so called ‘blind’ method (using anatomical landmarks) or by ultrasound (US) guidance/ assistance.

Blind positioning of CVC usually is achieved by venipuncture 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. Venipuncture of the internal jugular vein carries less risk of insertion-related complications if compared to the subclavian vein (McDonald 2000); in particular, the low lateral approach to the internal jugular vein (or Jernigan’s approach) appears to be the technique of blind venipuncture associated with the minimal risk of mechanical complications (Pittiruti 2000).

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

Since the presence of a non-tunnelled CVC in the femoral vein is associated with a high risk of infection and of catheter-related venous thrombosis, this route is contraindicated for parenteral nutrition (Class B recommendation in ASPEN guidelines).

Also, an 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 (EPIC 2007) (Pittiruti 2007); therefore, venous approaches which imply an exit site in the infraclavicular area (subclavian or axillary vein) or just above the clavicle (low approach to the internal jugular vein; or supraclavicular approach to the innominate vein or to the internal jugular vein) should be preferred.
Which is the best technique for placement of a central venous access?

With regards to the placement of short term CVCs, there is a wide and compelling evidence that US guided venipuncture (by real time ultrasonography) is overall associated with a significantly lower incidence of complications and a higher rate of success if compared to ‘blind’ venipuncture. Ultrasound support is strongly recommended for all CVC insertions (Grade A).

The advantages of US guidance for placement of CVC have been demonstrated in many RCTs and confirmed by all meta-analyses on this subject: in 1996, in a 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 (Randolph 1996). Few years later, 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 enforced in clinical practice (Rothschild, 2001). In 2002, the National Institute for Clinical Excellence (NICE 2002) 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’. Also, ‘imaging US guidance should be considered in most clinical situations where CVC insertion is necessary, whether the situation is elective or an emergency’. An other meta-analysis of 18 RCT showed that US guidance is highly effective in reducing the rate of failure, the rate of complications, the rate of accidental arterial puncture, thus ‘clearly improving patient’s safety’ (Keenan 2002). Similar results are shown in a 2003 meta-analysis (Hind 2003), which also showed that US guided venipuncture takes less time to perform that blind venipuncture; the same Authors concluded that ‘economic modelling indicates that US is likely to save NHS resources as well as improve failure and complication rates,’ and that ‘for every 1000 procedures, a resource saving of 2000 pounds is suggested’ (Calvert 2004). More recently, many randomized studies have confirmed – with no exception - the superiority of US guided venipuncture, non only as an elective procedure, but also in the emergency department (Leung 2006). A wide, randomized study on US guided vs. blind catheterization of the internal jugular vein has also shown that in critical patients US guidance is associated also with a decrease of CR BSI (Karakitsos 2006). According to the BCSH guidelines (BCSH 2006), ‘ultrasound guided insertion is recommended for all routes of central venous catheterisation’.

In summary, as stated during the 2007 Congress of the Association for Vascular Access, ‘there is now strong statistical evidence that US is more effective than the landmark method for CVA in both adults and children. It may be considered unethical or lacking in common sense to withhold the use of available machines that will certainly help operators determine the location and patency of target vessels. The evidence is extensive, randomized, controlled and compelling in favor of ultrasound guidance’ (LeDonne 2007).

With regards to the placement of PICCs, percutaneous cannulation of the basilic vein or the brachial vein at midarm, by utilizing ultrasound guidance and the micro-introducer technique, is the preferable option (Grade C).

PICCs may be inserted either in the antecubital fossa, by ‘blind’ percutaneous cannulation of cephalic or basilic vein, or at midarm, by ultrasound guided cannulation of 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 at 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 (Parkinson 1998) (Pittiruti 2006): US guided PICC insertion is recommended by INS (INS 2006) and BCSH (BCSH 2006) guidelines (Class C recommendation in both guidelines).

The safest option for placement of a long term venous access device - a tunneled catheter or a totally implantable port - is the US guided cannulation of the internal jugular, subclavian, innominate or axillary vein (Grade A).

Blind venipuncture of the subclavian vein by the infraclavicular route is not recommended, considering the risk of mechanical complications (pneumothorax, pinch-off syndrome, etc.) (Grade B).

Placement by surgical cutdown is not recommended, in terms of cost-effectiveness and risk of infection (Grade A).

Long term venous devices (tunneled catheters or ports) usually consists of large bore silicone catheters, which are particularly prone to malfunction and damage if compressed between the clavicle and the first rib (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: see also SINPE and ASPEN guidelines (Class C recommendation), plus a specific 1999 warning of the French Ministry of Health. It is noteworthy that US guided CVC placement is never associated with the risk of pinch-off, not even using the infraclavicular approach.

US guided venipuncture of internal jugular, subclavian, innominate or axillary vein, plus tunnellization to the infraclavicular area, is now the best option for long term venous access insertion; other possible options include ‘blind’ cannulation of internal jugular vein (possibly by the low lateral approach) and surgical cutdown of the cephalic vein at the delto-pectoral fossa or of the external jugular vein at the neck. Nonetheless, surgical cutdown is associated with higher costs and a higher risk of infection if compared to percutaneous venipuncture (Povoski 2000). As CDC Guidelines (CDC 2002) recommends: ‘do not routinely use arterial or venous cutdown procedures as a method to insert catheters’ (Class A recommendation according to CDC).

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

PN requiring a central venous access (i.e., high osmolarity PN) should be delivered through a catheter whose tip is 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). The position of the tip should be preferably checked during the procedure, specially when using an infraclavicular approach to the subclavian vein (Grade C).

Postoperative Xray is mandatory (a) when the position of the tip has not been checked during the procedure, and/or (b) when the central venous access has been placed using a technique which carries the risk of pleuropulmonary damage (i.e.: blind subclavian venipuncture) (Grade B).

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 is apparently between the lower third of the superior cava vein and the upper third of the right atrium. According to both SINPE guidelines (SINPE 2002) and ASPEN guidelines (ASPEN 2002) ‘PN should be delivered through a catheter located with its distal tip in the SVC or right atrium’ (Class A recommendation); 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 of the tricuspid valve, or even deeper, it may be associated with mechanical and thrombotic complications.

Ideally, the position of the tip should be checked during the procedure (Silberzweig 2003), either by fluoroscopy or by the EKG method (Francis 1992). According to ASPEN ‘chest Xray should be obtained after CVC insertion, unless the access is obtained by interventional radiology techniques’ (ASPEN 2002). If the position has not been checked intraoperatively, a postoperative chest Xray should be performed so to check the position of the tip. Nevertheless, when the central venous access is placed via an infraclavicular approach (i.e., ‘blind’ or US-guided venipuncture of the subclavian or the axillary vein), intraoperative control of the position of the tip is recommended, since the risk of malposition is relevant.

Also, a postoperative chest Xray should always be performed if the venipuncture has been performed by the ‘blind’ technique, and specially with an approach which carries the risk of pleuro-pulmonary damage (pneumothorax, haemothorax, etc.) (Class B recommendation according to ASPEN and SINPE). A very ‘early’ Xray (within 1 hour after the procedure) may not be enough, since a delayed pneumothorax may occur in the first 12-24 hrs.
c) Prevention of catheter-related bloodstream infections

Which are the evidence based interventions which effectively reduce the risk of catheter related bloodstream infections?

Although catheter material may be an important determinant of catheter related bloodstream infections (CR-BSI), evidence available is limited. Teflon, silicone and polyurethane (PUR) have been associated with fewer infections than polyvinyl chloride or polyethylene. As all available CVCs are made either of PUR (short term and medium term) or silicone (medium term and long term), there is no specific recommendation for the clinical practice (EPIC 2007).

On the other hand, the type of the catheter itself may significantly affect the risk of catheter-related Infection, as shown by Maki in a important systematic review of 200 prospective studies (Maki 2006).

Tunnelling the extravascular portion of the catheter and/or connecting the catheter to a totally implanted subcutaneous port do surely reduce the risk of CRBSI, by decreasing the extent of extraluminal contamination. Though there are no conclusive evidence-based data, such manoeuvres do not appear to be cost effective for short and medium term access, and should be reserved for long term HPN (Class B).

Tunnelled catheters and totally implanted venous access devices are associated with a low rate of infection, since they are specifically protected from extraluminal contamination. Though, tunnelling and subcutaneous implantation require a minor surgical procedure, which is contraindicated in patients with low platelet count or coagulation abnormalities (see BCSH guidelines) (BCSH 2006); 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 to long term home parenteral nutrition (Class A recommendation according to CDC). As stated by CDC guidelines: ‘Use a tunnelled or implanted central venous access device (one with a subcutaneous port) for patients in whom long-term vascular access is anticipated’ (CDC 2002). Nonetheless, no randomized clinical trial has definitely proven such contention in adult patients; in pediatric patients, some paper suggest a benefit of tunnelling 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 chlorexidine/sulfadiazine or coated with rifampicin/minocycline have an infection rate significantly lower of catheter related infections, as shown in the systematic review of Maki and coworkers (Maki 2006). In a recent systematic review and economic evaluation conducted by the Liverpool Reviews and Implementation Group (Hockenhull 2006), the Authors conclude that rates of CR-BSI are statistically significantly reduced by catheters coated with minocycline/rifampin, or
internally and externally coated with chlorhexidine/silver sulfadiazine (only a trend to statistical significance was seen in catheters only extraluminally coated).

Thus, as suggested by EPIC guidelines (EPIC 2007), the use of an antimicrobial coated central venous access device is to be considered for adult patients who require short-term central venous catheterisation and who are at high risk for catheter-related bloodstream infection (CR-BSI) if rates of CR-BSI remain high despite implementing a comprehensive strategy to reduce rates of CR-BSI. (Class A recommendation according to EPIC guidelines).

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 may be associated with an increased rate of infection if compared to single lumen CVCs as shown by several randomised controlled trials and stated by CDC guidelines (CDC 2002); nonetheless, this contention has been questioned by recent papers. Two recent systematic review and quantitative meta-analysis have focused on the risk of CR-BSI and catheter colonisation in multilumen catheters compared with single-lumen catheters. The first one (Dezfulian 2004) concluded that multilumen catheters are not a significant risk factor for increased CR-BSI or local catheter colonisation compared with single-lumen CVAD. The second one (Zürcher 2004) concluded that there is some evidence - from 5 randomised controlled trials (RCTs) with data on 530 CVAD - 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 (Class B recommendation). Also, if a multilumen catheter is used, it is recommended to identify and designate one port 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 if compared to non-tunnelled 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 abnormalities of the coagulation, (d) in patients candidate to HPN (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 (Ryder 1995); though, no randomized control studies has yet proven such contention (EPIC 2007). At present, it is reasonable to consider PICC insertion (Class D recommendation according to EPIC) 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 extremely low platelet count (below 9000, according to BCSH guidelines), and (d) in patients candidate to home parenteral nutrition for prolonged periods of time (months). On the other hand, PICC 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. Anyway, 'the assumption that PICC are safer than conventional CVC 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 thrombo-phlebitis, PICC-related thrombosis, and premature dislodgment, as well as CR-BSI (Safdar 2005).

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-tunnelled CVC in the femoral vein is not recommended in adult patients, since it is associated with a relevant risk of venous thrombosis, as well as a high risk of extraluminal contamination and CRBSI, due to poor nursing of the exit site (Grade B).

Placement of a non-tunnelled 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 poor nursing of the exit site (Grade C).

No RCT satisfactorily has compared CR-infection rates for catheters placed in jugular, subclavian, and femoral sites. However, previous evidence suggested that non-tunnelled catheters inserted into the internal jugular vein were associated with higher risks for CR-infection than those inserted into a subclavian vein (CDC 2002).

This might be secondary not to the choice of the vein itself, but to feasibility of an adequate dressing of catheter exit site (EPIC 2007); 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 (Pittiruti 2000).

A recent clinical study in intensive care patients have failed to demonstrate any advantage of the subclavian route if compared to the internal jugular vein in terms of infection rate (Deshpande 2005): in a recent prospective study in 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 (Lorente 2004).

On the other hand, non-tunnelled femoral catheters have been demonstrated to have relatively high colonization rates when used in adults (Durbec 1997) and should be avoided because they are presumed to be associated with a higher risk of deep vein thrombosis (DVT) and CR-infection if compared to internal jugular or subclavian catheters (Class B recommendation according to EPIC).

As already mentioned, with regards to PICCs, the exit site at midarm (typical of US guided PICC insertion) might have relevant advantages in terms of nursing if compared to the exit site at the antecubital fossa (typical of ‘blind’ PICC insertion) (Pittiruti 2007).

In conclusion, with regards to non-tunnelled CVCs, the choice of the insertion site may have relevant implications on the nursing of the exit site: exit sites at the groin (femoral vein), on the neck (high approaches to the internal jugular vein) or in the antecubital fossa (blind PICC insertion) may carry a higher risk of contamination if compared to exit 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 infracclavicular fossa (subclavial or axillary vein) or at 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 venipuncture of the internal jugular vein is apparently associated with a lower rate of CRBSI if compared to ‘blind’ venipuncture, most likely because of less trauma to the tissues and shorter time needed for the procedure, as shown in a recent randomized study (Karakitsos 2006). As stated by EPIC Guidelines: ‘the use of ultrasound may indirectly reduce the risk of infection by facilitating mechanically uncomplicated subclavian placement’ (EPIC 2007).

Also, real time ultrasound guidance allows PICC positioning at midarm, by cannulation of the basilic vein or one of the brachial veins: this seems to be associated with a lower risk of local infection and thrombosis if compared to ‘blind’ positioning at the antecubital fussia (Pittiruti 2006).

The catheter exit site of a non-tunnelled central venous access should be covered preferably with a sterile, transparent, semi-permeable polyurethane dressing, which should be routinely changed every 7 days (Grade C)

According to EPIC guidelines (EPIC 2007), a sterile, transparent, semi-permeable polyurethane dressing should be used to cover the catheter insertion site (Class D recommendation according to EPIC).

These transparent dressings should be changed every 7 days, or sooner if they are no longer intact or moisture collects under the dressing (Class D). If a patient has profuse perspiration or if the insertion site is bleeding or oozing, a sterile gauze dressing is preferable to a transparent, semi-permeable dressing (Class D).

The need for a gauze dressing should be assessed daily and 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 tunnelled 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 (Class D).

Chlorexidine impregnated dressing are effective in reducing the extraluminal contamination of the catheter exit site, and their use should be taken into consideration in adult patients with non-tunnelled CVCs at high risk infection (Grade C).

The efficacy and cost-effectiveness of antimicrobial impregnated dressings in preventing catheter colonisation and CR-BSI is still under investigation. Many prospective trials have demonstrated the effectiveness of chlorexidine-impregnated sponges (Biopatch) in preventing extraluminal contamination of the catheter at the exit site (Hanazaki 1999) (Maki 2000). Their use should be considered in adult patients with non-tunnelled 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 traditional securing the catheter with stitches may be associated with a high risk of contamination of the exit site (INS 2006). 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 (e.g.: Statlock) is preferred (Class C recommendation). Stitches should not be used routinely (BCSH 2006).

It is noteworthy that 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.

The most appropriate skin antiseptic for prevention of catheter related bloodstream infection is chlorexidine 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).

Several recent clinical randomized studies (Mimoz 2007) (EPIC 2007) have indicated that chlorexidine, particularly as 2% chlorhexidine gluconate in 70% isopropyl alcohol, is to be considered the most appropriate antiseptic for preparation of the insertion site (Class A recommendation according to EPIC) as well as for cleansing the entry site once the catheter is in place (Class 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 PUR catheters). Alcoholic povidone-iodine solution should be used in patients with a history of chlorhexidine sensitivity (Class D according to EPIC). 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 (Class D). Also, antimicrobial ointment are not effective for prevention of catheter site infections and should not be applied routinely.

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)

Stopcocks, catheter hubs and sampling ports are important routes of intraluminal contamination and a source of CRBSI, and should be carefully disinfected before access (Class C according to CDC) (CDC 2002).

Needlefree connectors have been introduced in clinical practice for the protection of the health care 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, while – on the contrary – their misuse has been call for responsible of outbreaks of CRBSI (EPIC 2007). On the other hand, appropriate disinfection of needleless connectors significantly reduces external microbial contamination (Casey 2003).

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 (Class D according to EPIC) (EPIC 2007).

When needle-free devices are used, the risk of contamination should be minimised by decontaminating the access port before and after use with a single patient use
application of alcoholic chlorhexidine gluconate solution (preferably 2% chlorhexidine gluconate in 70% isopropyl alcohol) unless contraindicated by the manufacturer’s recommendations (Class D).

In-line filters are not recommended for the prevention of CR-BSI (Grade C)

In the systematic review reported in the CDC guidelines (CDC 2002), no evidence was found to support the use of in-line filters for preventing infusion-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 specific pharmacist’s recommendation, for filtering micro-aggregates possibly occurring in the emulsion. Nonetheless, ‘in-line filters should not be used routinely for infection prevention’ (Class D recommendation according to EPIC guidelines).

Non-tunnelled CVCs should not be removed and replaced routinely (Grade A), and they should not be changed routinely over guidewire (Grade A): such strategies are not associated with a reduction of CRBSI and may actually increase the rate of complications.

Both ASPEN guidelines (ASPEN 2002) and CDC guidelines (CDC 2002) recommend that CVCs should not be exchanged routinely over guide wires as a strategy to prevent infection (Class A recommendation in both guidelines).

Also, a systematic review of the studies available on this subject (EPIC 2007) concluded that routine removal and replacement ‘ex novo’ of the CVC, without specific clinical indication, does not reduce the rate of catheter colonisation or the rate of CR-BSI, but increases the incidence of insertion-related complications. CVCs should be removed only if complicated or not necessary any longer (Class A recommendation according to EPIC).

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. Also, guidewire exchange may have 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. Of course, all fluid administration tubing and connectors must also be replaced when the central venous access device is replaced (Class D recommendation according to CDC).

The intravenous catheter administration set should be changed every 24 hrs (when using lipid PN) or every 72 hrs (if lipids are not infused) (Grade C).

Both CDC guidelines (CDC 2002) and EPIC guidelines (EPIC 2007) agree that administration sets used for total parenteral nutrition infusions should generally be changed every 24 hours (Class D recommendation according to CDC). If the solution contains only glucose and amino acids, administration sets in continuous use do not need to be replaced more frequently than every 72 hours.
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).

CDC guidelines recommend (Class A) to avoid routine administration of systemic antibiotics before insertion or during the use of a central venous access device to prevent catheter colonisation or bloodstream infection. Prophylaxis with antibiotic lock has been effective only in neutropenic patients with long-term venous access. But there is no evidence that routinely using this procedure in all patients with CVC may reduce the risk of CR-BSI. Thus, antibiotic lock solutions should not be used routinely to prevent catheter-related bloodstream infections (Class D recommendation).

Low-dose systemic anticoagulation or catheter flushing with heparin do not reduce the risk of catheter contamination, and are not recommended for prevention of CRBSi (Grade C).

According to review contained in the EPIC Guidelines (EPIC 2007), there is no definite evidence that heparin may reduce the incidence of CR-BSI, but this may reflect the heterogeneity of heparin concentration used and its modality of administration. Systemic anticoagulants should not be used routinely to prevent catheter-related bloodstream infection. (Class D recommendation)

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).

As stated by ASPEN guidelines, specialized nursing teams should care for venous access devices in patients receiving PN. As a matter of fact, evidence demonstrates that the risk of infection declines following the standardisation of aseptic care and increases when the maintenance of intravascular catheters is undertaken by inexperienced healthcare workers (EPIC 2007).

Also, it has been proven that relatively simple education programmes focused on training healthcare workers to adhere to local evidence-based protocols may decrease the risk to patients of CRBSI (Warren 2004) (East 2005).

In a recent and very important multicentric prospective study carried out in 108 intensive care units, Provonost and coworkers (Pronovost 2006) have shown that the adoption of a bundle of few 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 relevant (up to 66%) and persistent reduction in the incidence of CRBSI.

The definition of an adequate policy of hand washing and its implementation among the health care workers which have contact with the patient on PN are considered one of the most evidence based and cost effective manoeuvres for reducing the risk of catheter related infection (Grade A).
Good standards of hand hygiene and antiseptic technique can reduce the risk of CR-infection (EPIC 2007) (Boyce 2002) (Ryder 2006), as shown by many randomized studies. 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 handrub (Class A recommendation according to EPIC). 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 seconds, 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 (Ryder 2006); 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 handrub (Class A according to EPIC).
- Evidence from the most recent RCTs (EPIC 2007) have shown that when accessing a central venous line (for insertion site dressing, or line manipulation or intravenous drug administration) there are two possible options (Class D recommendation): (1) hand antisepsis (washing and/or alcohol-based hand rub: see above) + clean gloves and aseptic non-touch technique; (2) hand antisepsis + sterile gloves.

Maximal barrier precautions during CVC insertion are effective in reducing the risk of infection and are recommended (Grade B)

Many prospective trials suggests that the risk of CRBSI may be reduced by using maximal sterile barriers, including a sterile gown, sterile gloves, and a large sterile drape, for the insertion of central venous access devices (Class C recommendation according to CDC).

At present, full barrier precautions during CVC insertion are recommended by most guidelines (ASPEN 2002) (SINPE 2002) (EPIC 2007); also, this practice has been adopted by most ‘bundles’ of evidence based interventions aiming to reduce CRBSI, in many multicentric prospective trials.
d) Management of catheter related bloodstream infections

Which is the best method for diagnosis of CRBSI?

Diagnosis of CRBSI is best achieved (a) by quantitative or semiquantitative culture of the catheter (when the CVC is removed or exchanged over guidewire), 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).

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 (IDSA 2001).

As regards the diagnosis (Siegman-Igra 1997), it is recommended that culture of catheters should be done only when catheter-related bloodstream infection is suspected, and not on as a routine (Class B recommendation according to IDSA); quantitative or semiquantitative cultures of catheters are preferable to qualitative cultures (Class A according to IDSA).

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 (Blot 1999) are recommended for the diagnosis of catheter-related infection (Class A according to IDSA).

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

A short term central line should be removed in 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 guidewire, or (d) positive paired blood cultures (from peripheral blood and blood drawn from the catheter) highly suggestive for CRBSI (Grade B). Appropriate antibiotic therapy should be continued also after catheter removal.

With regards to non-tunneled CVCs, in patients with fever and mild to moderate disease the catheter should not routinely be removed (Class D according to IDSA); the CVC should be removed and cultured if the patient has erythema or pus overlying the catheter exit site, or clinical signs of sepsis (Class B).

If blood culture results are positive or if the CVC is exchanged over the guidewire and has significant colonization according to results of quantitative or semiquantitative cultures, the catheter should be removed and placed into a new site (Class B).

If not contraindicated, trans-esophageal echocardiography (TEE) should be done to rule out vegetations in patients with catheter-related *Staphylococcus aureus* bloodstream infection (Class B), because of recently reported high rates of complicating endocarditis (LI 2000); if TEE is not available and results of transthoracic echocardiography are negative, the duration of therapy should be decided clinically for each patient.
After removal of a colonized catheter associated with bloodstream infection, if there is persistent bacteremia or fungemia, or a lack of clinical improvement (especially if it is 13 days after catheter withdrawal and initiation of appropriate antimicrobial therapy), aggressive evaluation for septic thrombosis, infective endocarditis, and other metastatic infections should ensue (Class B).

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

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

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

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 (Raad 1998) (Class B). For complicated infections, the long term device should be removed (Class B). For salvage of the device in patients with uncomplicated infections, antibiotic lock therapy (Messing 1990) 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 (Class B). On the contrary, tunnel infection or port abscess always require removal of the device and usually 7–10 days of appropriate antibiotic therapy (Class 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 (Class 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 (Class C).
e) Recommendations for prevention, diagnosis and treatment of non-infectious complications

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 lock with standard 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 opened-ended catheter lumens which are scheduled to remain closed for more than 8 hours (Grade C).

Three different meta-analyses of randomised controlled trials evaluating the effect of heparin on duration of catheter patency have concluded that heparin for intermittent flushing is no more beneficial than flushing with normal saline alone (Randolph 1998) (Goode 1991) (Peterson 1991). 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, an appropriate flushing with saline (preferably with the ‘start and stop’ technique) before heparinization (RCN 2005) (INS 2006) is far 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 guidelines (RCN 2005), there is no need for heparinization when the catheter is closed for a short period of time (< 8 hours). Since most PN treatments are delivered by continuous infusion or with very short free intervals, heparinization does not have a relevant role in PN.

On the other hand, heparin flush solutions may be useful in helping to maintain patency in catheter lumens that are infrequently accessed and are recommended by manufacturers of implantable ports and for devices used for blood processing, e.g., haemodialysis or apheresis.

Close ended valved catheters – following manufacturers’ instructions – should be flushed and locked with saline only.

No randomized clinical trials has ever established the usefulness of heparinization or the ideal heparin concentration, though most Authors suggest to use a range of concentration between 50 and 500 units per ml.

Also, there are no evidence-based data suggesting the ideal frequency of heparinization for catheter lumens which remain not in use for prolonged period of time, though most Authors and most manufacturers suggest to flush and lock the devices with small calibre (5 Fr or less) weekly, and the devices with large calibre (6 Fr or more) every 3-4 weeks.

EPIC guidelines (EPIC 2007) recommend: preferably, sterile 0.9 percent sodium chloride for injection should be used to flush and lock catheter lumens that are in frequent use (Class A recommendation); when recommended by the manufacturer, implanted ports
or opened-ended catheter lumens should be flushed and locked with heparin sodium flush solutions (Class D).

Regarding the possible effect of needlefree connectors in preventing catheter occlusion, there are not enough data for a clinical recommendation, though some papers (Jacobs 2004) suggest that CVCs with a positive-pressure valve device may have a lower incidence of complete catheter occlusion than those with a standard cap.

**Are there evidence based recommendations regarding prevention, diagnosis or treatment of mechanical complications?**

*Intraluminal obstruction of the central venous access can be effectively prevented by appropriate nursing protocols in maintenance of the i.v. line, and by implementing the use of nutritional pumps (Grade C).*

The obstruction of a central venous catheter is most often due to intraluminal precipitate of lipid aggregates, or drugs, or clots, or contrast medium, and it can be effectively prevented by appropriate nursing (provide continuous infusion of PN by i.v. pump; utilize appropriate protocols of flushing when the catheter is not in use, or after blood withdrawal; avoid routine use of the catheter for infusion of blood derivates, blood withdrawal, or infusion of contrast medium for radiological exams; avoid direct contact between lipid PN and heparin solution; etc.). When the lumen of the catheter is obstructed, the most appropriate action is exchange over guidewire or removal (in case of non-tunnelled short term CVC or Hohn) or an attempt of pharmacological disobstruction (in case of PICCs or long term venous access devices). Disobstruction should always be performed using 10 ml syringe (or bigger), so to avoid inappropriate high pressure which may damage the catheter, and using the solution most adequate for the presumed type of obstruction (ethanol for lipid aggregates; urokinasis or rTPA for clots; NaOH or HCl for drugs; Na Bicarbonate for contrast medium).

**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 nursing care of the catheter exit site (e.g.: using scissors changing the dressing; chemical damage of silicone due to inappropriate use of ether; chemical damage of PUR due to inappropriate use of ethanol; etc.) (RCN 2005) (INS 2006). Damages of PICCs and tunnelled catheters are usually repaired with specific repair kits; for short term non-tunnelled CVCs, exchange over 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 to utilize power injectors only on peripheral short cannulas or specific CVCs which have been certified to resist at 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. Also, a non-coring needle (Huber needle) should be 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 a port too big, or positioning of the port in an area too skinny), or to (b) inappropriate nursing, i.e. a Huber needle left in place for more than a week (INS 2006) (RCN 2005).

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-tunnelled catheters (central and PICC) are usually secondary to inappropriate securing of the catheter at the moment of insertion or to inadequate nursing of the catheter exit site. Catheter stabilization shall be used to preserve the integrity of the access device and to prevent catheter dislocation. CVCs shall be stabilized using a method that does not interfere with assessment and monitoring of the access site or impede vascular circulation or delivery of the prescribed therapy (INS 2006).

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 (e.g.: Statlock) is preferred (Class C recommendation according to INS guidelines). Stitches should not be use 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).

Dislocation of tunnelled catheters should 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 a manufactured catheter stabilization device (Statlock) for at least 3-4 weeks.

As regards positioning of long term venous access devices, ‘blind’ venipuncture of the subclavian vein by the infraclavicular route is not recommendend (Grade B).

The ‘pinch-off’ syndrome is a compression of a large bore silicone catheter - tunnelled 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 in the lung vascular bed. It is a potentially severe complication, totally preventable simply by avoiding placement of silicone catheters via the infraclavicular ‘blind’ venipuncture of the subclavian vein (Class C recommendation according to SINPE guidelines).
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: it is also defined as a secondary malposition, and it usually happens when a catheter too short (tip in the upper third of superior vena cava) dislocates because of increase of thoracic pressure. It can be prevented by a proper positioning of the tip of the catheter.

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

Catheter-related central venous thrombosis is a frequent complication of CVCs, usually associated to long term venous access devices, specially when positioned with the femoral approach or when the tip of the catheter has not been correctly positioned in the lower third of the superior vena cava or at the cava-atrial junction. A systematic review of the clinical aspects of this complication – which is often asymptomatic – have been discussed in a Consensus of GAVeCeLT (The Italian Group for Long Term Venous Access) published on JAVA in 2007 (GAVeCeLT 2007).

Prevention of catheter-related central venous thrombosis should include (a) choice of an insertion technique associated with minimal damage to the vein, such as US guidance (Grade C), (b) choice of a catheter with the lowest calibre compatible with the infusion therapy needed by the patient (Grade B), (c) appropriate position of the tip of the catheter in proximity of the atrio-caval junction (Grade B), and (d) prophylaxis with a daily single dose of LMWH 100 IU/kg, exclusively in patients at high risk for thrombosis (Grade C).

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 (eg, percutaneous vs venous cut-down, US-guided vs anatomic landmark techniques) and central venous thrombosis rate. Though, prospective, not randomized, studies have suggested a relationship between minimal insertion damage to vein wall, as obtained with US guidance, and low rate of subsequent thrombotic events. (Class C recommendation according to GAVeCeLT).
- silicone and 2nd-3rd-generation, polyurethane catheters are less thrombogenic than polyethylene or PVC ones, and should be preferred for long term venous devices.
- a lower-diameter catheter and a single lumen might be protective against the risk of central venous thrombosis. When the number of therapies demands a multiple-lumen catheter, the number of lumens used should be minimized (Class B according to GAVeCeLT).
- in many prospective studies, tip position emerged as the main independent prognostic factor for malfunction, thrombosis, and reduced duration of the device. The atrial-caval junction appears to be the optimal position of the catheter tip, as it minimizes the risk of central venous thrombotic events (Class B according to GAVeCeLT).
- although some early trials suggested a benefit of oral, low-dose daily warfarin or daily subcutaneous dose of LMWHs, more recent randomized, double-blind, placebo controlled, and sufficiently powered trials did not find any advantages for either of these prevention strategies. The choice to start a prophylaxis of venous thromboembolic events in all oncology patients bearing a CVC, either with LMWHs or with minidose warfarin,
remains unsupported by evidence-based medicine. GAVeCeLT suggests considering prophylaxis with a daily single dose of LMWH 100 IU/kg only in high-risk population (including those who have a family history or previously suffered from idiopathic venous thrombotic events of the upper or lower vena cava district) (Class C according to GAVeCeLT)

Treatment of catheter-related central venous thrombosis should 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 influence the outcome; on the other hand, the presence of the catheter might be useful for local thrombolitic treatment, when indicated;
- in case of clinically overt or imaging-diagnosed DVT , a risk of embolization during or immediately after catheter removal has been reported;
- nonetheless, catheter should be removed in case of infected thrombus, or malposition of the tip, or irreversible occlusion of the lumen (Class B Recommendation);
- thrombolytic drugs should be used only in acute symptomatic cases (diagnosis <24 hours after the first symptoms). Efficacy of systemic versus local thrombolysis is still matter of debate, especially for large thrombi;
- chronic symptomatic cases should be treated with a combination of 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 unit dose without the need for dose monitoring (Class C Recommendation).

With regard to the venous thrombosis (local or more seldom central) which may occasionally be associated with PICCs, it is apparently a multifactorial phenomenon, influenced by the calibre of the catheter (Grove 2000), the technique of placement (US guided vs. blind), the vein cannulated (cephalic vs. brachial vs. basilica), the position of the tip, the stabilization technique (Statlock vs. tape vs. stitches), the type of treatment (Ong 2006), the patient and its disease. It is recommended to prefer PICC placement in the basilica vein or in a brachial vein, at midarm, by the US technique, and to avoid catheter larger than 4 Fr (Class D recommendation).

The fibrin sleeve (or fibrin sheath) is a sleeve of fibroblastic tissue which slowly covers the intraluminal tract of long term catheters; it may be asymptomatic, or it can be associated with a persistent withdrawal occlusion or with a 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.
Guidelines


References


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