

9. Venous Access

METHODS

Literature Search

Timeframe: Publications from 1992 until 2004, single publications from 1981 were considered.

Type of publications: original articles, case-control and cohort studies, randomised trials, meta-analyses, systematic reviews, case studies.

Key Words: catheterisation, catheter, Broviac, Hickman, ultrasound, replacement, complications, bacteraemia, parenteral nutrition, central venous catheter, central line, venous access, heparin, catheter handling, skin hygiene, dressing type, frequency of dressing change, intravenous infusions, catheter infections.

Language: English, French.

VENOUS ACCESS

Introduction

The use of central venous catheters (CVCs) to provide venous access has become increasingly common for the purpose of administration of different treatment regimens, intravenous nutrition and blood products, preventing at the same time trauma associated with repeated punctures. However, their insertion and usage may be associated with complications. Therefore, educated personnel should insert and look after the catheter, provide aseptic conditions in handling the catheter and maintain appropriate skin hygiene around the catheter.

The terminology used to identify various types of catheters differs and may be confusing. However, for the purpose of providing parenteral nutrition (PN), it is necessary to differentiate peripheral from central venous access, and among the central venous catheters (CVC) those non-tunnelled i.e. inserted either peripherally (PICC) or directly percutaneously, from tunnelled central catheters.

Intravascular Catheters for Parenteral Nutrition

Types of Catheters

Establishing a peripheral venous access is defined as placement of a needle or short catheter in a subcutaneous vein. As phlebitis of peripheral veins can be expected when the osmolality of i.v. solution exceeds 600 mOsm (1 (LOE 2+)), peripheral veins are only used for short-term venous access and for providing partial nutritional supplementation. Initiation of full PN requires the placement of a CVC. Central venous access is obtained by advancing a catheter into the superior or inferior vena cava or outside of the right atrium. A percutaneously

placed CVC can be inserted directly through one of the deep veins e.g. subclavian, internal jugular, or femoral. Another option is a peripherally inserted central catheter (PICC), which uses a subcutaneous vein as the entry site to reach the central vein (2,3, LOE 3). For long-term continuous or frequent use, tunnelled catheters, such as Broviac or Hickman CVC's, are usually placed ((4) (LOE 2+), (5) (LOE 2+)). The extra vascular portion of these devices is tunnelled subcutaneously. A Dacron cuff is implanted subcutaneously, allowing for better fixation and, because of the distance between the insertion site and the entry into the vein, inhibits migration of micro organisms ((6) (LOE 1+); (7) (LOE 2+)). Totally implantable devices i.e. subcutaneous ports, are ideal for long-term but intermittent vascular access. Each port access requires needle sticking and, therefore, their value for PN is limited ((8) (LOE 2+)).

Recommendation

- Peripherally inserted central catheters (PICC's) and tunnelled central venous catheters (CVCs) should be used preferentially to provide central venous access in neonates and children receiving prolonged PN. **GOR C**

Catheter Material

Catheters made of stiffer material (polyvinylchloride, polypropylene, polyethylene) are easier to insert, but have been associated with more infectious and mechanical complications ((9) (LOE 2+)). Softer catheters (silicone and polyurethane) are less thrombogenic and less traumatic, and are, therefore, preferable for long-term use ((10) (LOE 2+); (11) (LOE 3)).

In adults, catheters coated with chlorhexidine/silver sulfadiazine and minocycline/rifampin, on both the external and internal surfaces, reduce the rate of catheter-related bloodstream infections ((12) (LOE 1+), (13) (LOE 1+)). In adults, in settings associated with high risk for infections (e.g. ICU patients), the use of these expensive devices might be cost-effective, and may justify the possible emergence of resistant bacterial strains ((14) (LOE 1+)).

Recommendation

- Silicone and polyurethane coated with hydromers are preferable materials for catheters used for long-term PN. **GOR C**

Insertion Sites

When a CVC is inserted into a deep vein, the choice of insertion site depends on the expected risk for thrombophlebitis, for mechanical complications and/or for catheter infection, which may all be specific for each insertion site.

The subclavian site is widely accepted as the preferred site of insertion, as it causes less patient discomfort, and in adult patients, carries the lowest risk of infection risk ((15) (LOE 2+), (16) (LOE 1-)).

In children, the subclavian site is also the most common site for insertion of tunnelled CVC's, although it has not been proven to carry less infection risk ((17) (LOE 1+); (18) (LOE 3)); (5) (LOE 2+)). Cannulation of the subclavian vein might be associated with dangerous complications such as pneumothorax and haemothorax. However, with adequate experience of the physician performing the procedure and sufficient sedation or general anaesthesia, the risk of mechanical complications in children at subclavian sites does not exceed the rate of complications at other insertion sites ((19) (LOE 3); (20) (LOE 3)). In contrast to adults, femoral catheters in children have not been shown to have a higher incidence of mechanical and infectious complications compared to jugular and subclavian sites ((21) (LOE 2+); (22) (LOE 3); (17) (LOE 1+); (23) (LOE 3); (24) (LOE 3)). However, femoral access is uncomfortable for the child while the consequences of potential inferior vena cava thrombosis may be severe. The insertion of a CVC is customarily followed by chest radiography for verification of the catheter's course and the position of its tip. In addition, ECG-monitoring may be helpful.

Statements and Recommendations

- In infants and children, in contrast to adults, femoral catheters do not show a higher incidence of mechanical and infectious complications in comparison with jugular and subclavian sites. **LOE 2**
- In children the risk of mechanical complications of subclavian venous access does not exceed the rate of complications with other insertion sites under appropriate conditions of insertion. **GOR C**

Positioning of the Catheter Tip

Cardiac tamponade is a rare but life threatening complication of CVC's ((25) (LOE 3), (26) (LOE 3)). There may be an increased risk of pericardial tamponade when the tip is placed within the heart outline as seen on chest x-ray ((27) (LOE 3), (28) (LOE 4)). It is, therefore, advisable that the CVC tip lies outside the pericardial sac and should be repositioned whenever possible ((27) (LOE 3); (29) (LOE 3)). The preferable position for the

catheter tip on the chest x-ray is at least 0.5 cm outside the cardiac outline for the small infant, and 1.0 cm in larger infants ((28) (LOE 4)). For older children and adults, positioning above the carina, which can be used as an anatomic landmark, suggests that the catheter tip of the CVC placed in the superior vena cava is likely to be outside the pericardial sack ((30) (LOE 4)). The risk of perforation depends on the angle of the catheter and the vessel wall; therefore, the catheter should be parallel with the long axis of the vein ((31) (LOE 4)).

Statement and Recommendations

- The CVC tip should lie outside the pericardial sac to avoid the risk of pericardial tamponade. **GOR D**
- In small infants the catheter tip of a jugular or subclavian CVC should lie at least 0.5 cm outside the cardiac outline on a chest x-ray, while in older/larger infants that distance should be at least 1.0 cm. The catheter tip of a femoral catheter should lie above the renal veins. **GOR D**
- In older children, as in adults, positioning above the carina suggests that the catheter tip lying in the superior vena cava is likely to be outside the pericardial sack. **LOE 4**
- The risk of perforation increases with the acute angle of the catheter and the vessel wall. Therefore, the catheter should be parallel with the long axis of the vein. **GOR D**

Ultrasonic Guidance

The ultrasound-guided technique can significantly increase the precision and safety of CVC placement in children and newborns when the internal jugular vein is cannulated ((32) (LOE 3); (33) (LOE 3)).

Statement

- Ultrasound guidance may help reducing complications during internal jugular venous catheterization in children and in newborns. **LOE 3**

Methods of Insertion

Methods of insertion of CVCs, including tunnelled CVC's, are percutaneous placement and the surgical cut-down technique. The chance of permanent damage to the vein is increased when the cut-down method is used ((34) (LOE 2+)). The percutaneous insertion method is as effective as the surgical cut-down ((34) (LOE 2+), (35) (LOE 2+)).

Also, the diameter of the inserted catheter should be as small as possible to minimize the risk of scarring,

stricture, occlusion and distortion of the cannulated vein ((36) (LOE 3)).

In adults, administration of antibiotics before CVC insertion or the CVC flush with a combination of an antibiotic and heparin has been justified ((37) (LOE 1+)). In children, the use of vancomycin concurrent with catheter insertion was associated with decreased incidence of CVC blood stream infections ((38) (LOE 2+), (39) (LOE 2+)).

Statement and Recommendation

- Percutaneous, radiologically controlled, insertion method is equally effective as surgical cut-down, and carries less risk of damaging the vein. **LOE 2+**
- CVC placement should be done under strict aseptic environment, and preferably under general anesthesia and by an experienced team. **GOR D**

Umbilical Catheters

In neonates, umbilical vessels may be directly accessed in the first few days of life and, therefore, this route of central venous approach can regularly be used for PN. However, the risk of expected thrombotic complications limits the use of umbilical catheters to being a bridge procedure while awaiting placement of a long-term device ((40) (LOE 2+); (41) (LOE 2+); (42) (LOE 2+); (43) (LOE 2+)). Umbilical artery catheters placed above the diaphragm are associated with a lower incidence of vascular complications ((44) (LOE 1+)).

Statements

- In neonates, umbilical vessels can be used for PN.
- The risk of complications increases if umbilical artery catheters are being left in place for more than 5 days. **LOE 2++**
- The risk of complications increases if umbilical venous catheters are being left in place for more than 14 days. **LOE 1+**
- Umbilical artery catheters placed above the diaphragm are associated with a lower incidence of vascular complications. **LOE 1+**

Replacement Schedule

Routine replacement of CVC's and PICC's does not prevent catheter-related bloodstream infections ((45) (LOE 2+); (46) (LOE 1+); (47) (LOE 1+)). Functioning CVC's without evident complications should, therefore, be left in place as long as needed. A malfunctioning CVC can be replaced using a guide-wire insertion

technique ((47) (LOE 1+)). This technique lowers the risk of mechanical complications associated with CVC replacement and may make chest radiography unnecessary in adult patients ((48) (LOE 2+)). Replacement over the guide-wire should, however, not be performed in the presence of bacteraemia or in patients suspected to have catheter related infection ((47) (LOE 1+)).

Recommendations

- CVC's and PICC's should not be replaced routinely. **GOR B**
- Malfunctioning non-tunelled CVCs can be replaced by using a guide-wire exchange technique, if there is no evidence of bacteraemia or catheter related infection. **GOR B**

Alternative Sites for CVC Placement

CVC complications following multiple catheterisations can lead to thrombosis and depletion of commonly used venous access sites. Alternative approaches in these children should be regarded as rescue accesses and include the transhepatic, translumbar, intercostal ((49) (LOE 3); (50) (LOE 3) (51) (LOE 3)), and the arteriovenous fistula (52). Preferences among the alternative sites depend on the experience of the physician performing the procedure and the condition of each individual patient.

Lines Designated Only to PN

In order to prevent catheter related infections, several recommendations have been suggested, including dedicating the CVC to PN only, i.e. not using it for blood sampling or for delivering other fluids or drugs ((53) (LOE 2++)). However, many of the patients who require PN are critically ill and have poor venous access, so the use of multiple lumen catheters allows additional access ports for the provision of compatible medications. Double and triple lumen catheters seem to be associated with an increased risk of bacteraemia compared to single lumen devices ((54) (LOE 2+); (55) (LOE 2++); (56) (LOE 2++)). They also seem to be more prone to the development of catheter-related sepsis, possibly because of more frequent catheter manipulations ((53) (LOE 2++); (57) (LOE 2+); (58) (LOE 1+)). The rate of catheter related sepsis has been reported to be as high as 10–20% compared to 0–5% associated with single lumen catheters ((53) (LOE 2++); (59) (LOE 1+); (58) (LOE 1+)).

In contrast, some adult studies showed that the use of multi lumen catheters for PN is safe and that they did not result in an increased incidence of catheter related sepsis ((60) (LOE 2+); (61) (LOE 2+); (62) (LOE 2++); (63) (LOE 1+); (64) (LOE 2++); (65) (LOE 1+)). It is

important to emphasize that in most of these studies either one port of the multiple lumen catheter was reserved only for PN, or the catheter was limited to administration of compatible medications and solutions while administration of blood products, withdrawal of blood and measurement of central venous pressure were prohibited. The authors concluded that PN can safely be given through multiple lumen catheters provided that these measures are strictly followed ((63) (LOE 1+), (64) (LOE 2++), (65) (LOE 1+)).

Statements and Recommendations

- Where possible a central venous line should be dedicated for the administration of PN. **GOR B**
- If a CVC is used to administer PN, use a catheter with the minimal number of ports or lumens essential for the management of the patient. **GOR B**
- If a multi lumen catheter is used to administer PN, designate one port exclusively for PN. Blood administration and central intravenous pressure monitoring from the designated line should be avoided. **GOR B** (from adult studies)
- If single lumen catheters are used, the risk of complications increases with blood sampling from the catheter. **GOR B** (from adult studies). However, to improve the quality of life of patients on long-term or home PN, blood sampling could be done from single lumen catheters, provided that the procedure is aseptic. **LOE 4**

Catheter Heparinisation

In children, central venous lines are the most frequent cause of venous thromboembolism and are responsible for over 80% of venous thromboembolism in newborns and 40% in other children ((66) (LOE 2++); (67) (LOE 2+)). Furthermore, CVC related thrombosis is, alongside sepsis, the most common clinically significant complication of PN ((68) (LOE 2+), (69) (LOE 2+)). Factors that have been associated with initiation and propagation of thrombosis include endothelial damage during catheter placement, blood vessel occlusion, low flow states, blood stasis, turbulent flow, blood hyperviscosity or hypercoagulability, patients' and infusates' characteristics and catheter composition ((70) (LOE 2++), (71) (LOE 1+)).

In an attempt to prolong the duration of catheter patency and to prevent venous thromboembolism as well as its potentially fatal complications, the use of heparin has been suggested ((72) (LOE 2+), (73) (LOE 2+)). Heparin is a glycosaminoglycan with anticoagulant effects mediated largely through its interaction with antithrombin III that markedly accelerates its ability to inactivate coagulation enzymes (thrombin, factor Xa and factor IXa) ((74) (LOE 2++)).

In providing PN, heparin could have the following potential benefits:

1. *anticoagulant action* – besides reducing fibronectin deposition, heparin makes the line hydrophobic, giving it a negative charge, both of which may influence the catheter thrombogenicity ((70) (LOE 2++); (75) (LOE 1+); (76) (LOE 1++));
2. *prevention of infection* – a thrombus might serve as a nidus for microbial colonization of intravascular catheters ((77) (LOE 1+); (78) (LOE 2++)). Heparin bonded catheters were reported to diminish bacterial adherence ((79) (LOE 2++)), as well as to lower the incidence of positive blood cultures, presumably related to the lower incidence of thrombosis ((70) (LOE 2++)) or to a reduced number of microorganisms attached to the surface of the catheter ((75) (LOE 1+));
3. *activation of lipoprotein lipase* - given in infusion, heparin also activates lipoprotein lipase and increases lipolysis and reesterification of infused triglycerides, but has no effect on lipid oxidation and net energy gain ((80) (LOE 1+); (81) (LOE 1+); (82) (LOE 2++); (83) (LOE 2++)).

There are certain possible complications related to the use of heparin in PN, notably bleeding, heparin induced thrombocytopenia, allergic reactions, osteoporosis, which all may result in serious long-term sequelae ((84) (LOE 2+); (85) (LOE 1++); (74) (LOE 2++); (86) (LOE 3)). In addition, neonates are unique in their sensitivity and resistance to heparin and in their higher propensity to develop intracranial haemorrhage ((87) (LOE 2-); (88) (LOE 2+)). Both low molecular weight heparin and heparin used as a catheter coating agent are associated with these complications, although the risk associated with low molecular weight heparin is reduced compared to unfractionated heparin ((85) (1++), (89) (2++), (90) (3)).

Another risk of adding heparin to PN solutions is the possibility of inducing incompatibility. Calcium and heparin can destabilize lipid emulsions leading to flocculation and separation of the lipid from the aqueous phase (91). However, this is unlikely if low heparin concentrations are used (0.5 to 1 U/ml) ((92) (LOE 2+)). Together with minimizing their contact time (having the delivery tube between the point of mixing lipid and amino acid solutions as short as possible), co-administration of vitamin preparations will further decrease this effect ((92) (LOE 2+)).

The current attitude towards prescribing heparin, therefore, differs with regard to whether to use it at all or not, and if yes, in what way (as a flush or in PN infusion), how often and how much. In practice, wide variations are observed in volumes of provided heparin ranging from 5 to 10 ml ((93) (LOE 2+), (94) (LOE 1+), (95) (LOE 1-)), concentration of heparin ranging from 10 U/ml to 200 U/ml ((93) (LOE 2+), (94) (LOE 1+), (69) (LOE 2+)) as well as in the frequency of

heparinisation that ranges from daily infusions ((96) (LOE 2++)) to flushes once or twice daily ((94) (LOE 1+); (97) (LOE 2+)) to once a week ((98) (LOE 2-)) or even once in three weeks ((99) (2+)). Boluses in children frequently contain 200 to 300 U of heparin, and for infants weighing less than 10 kg, a dose of 10 U/kg is frequently used ((89) (2+)). In a meta-analysis evaluating the benefit of heparin prophylaxis (3 U/ml in PN solution; 5000 U every 6 to 12 hours flush or 2500 U of low molecular weight heparin subcutaneously) in patients with CVC's, the risk of central venous thrombosis was significantly reduced. Although bacterial colonization was also decreased, no substantial difference in the rate of catheter related infection was observed ((100) (LOE 1+)). Of the 11 studies included in this meta-analysis only one was performed in the paediatric population. This randomised cross-over study showed that there was no significant difference in the incidence of blocked catheters or other complications between the group of paediatric patients whose CVC's were flushed twice daily with a heparin solution and the group with isotonic saline flushes applied once a week ((94) (LOE 1+)).

Another randomized double blind trial on paediatric patients demonstrated that the use of normal saline compared to heparinised infusion (saline + 1U of heparin/ml) did not significantly adversely affect patency of CVC's ((101) (LOE 1+)). The proportion of non patent catheters was smaller in the heparinised group but the difference was not statistically significant. However, both studies had a small sample size and thus not enough statistical power to draw definitive conclusions.

Shah et al performed a systematic review on the prophylactic use of heparin for prevention of complications related to peripherally placed percutaneous central venous catheters in neonates but not even one well designed randomized controlled trial was found. Therefore, the routine use of heparin for this purpose could not be recommended ((102) (LOE 1+)).

Later, Kamala et al performed a randomized, double-blind controlled study of heparin infusion (1 U/ml) for prevention of blockage of peripherally inserted central catheter in neonates and found no significant difference in the incidence of blocked catheters, catheter sepsis, hypertriglyceridaemia, hyperbilirubinaemia, coagulopathy or intraventricular haemorrhage between treated and untreated group ((103) (LOE 1-)). However, the study sample was again too small and with a high risk of bias.

Statements and Recommendation

- There is no proven benefit of heparin for the prevention of thrombotic occlusion of CVC's under regular use in children. Therefore its routine use is not recommended. **LOE 1-**

- With respect to CVC's not in regular use, in adults, flushing with 5 to 10 U/ml of heparinised saline once to twice weekly was useful in maintaining CVCs patency and is recommended. **GOR D**
- Routine use of heparin has not been shown to be useful in prevention of complications related to peripherally placed percutaneous CVCs in neonates. **LOE 1-**

Skin hygiene, Dressing Methods and Frequency of Dressing Changes

Skin Antisepsis and Hygiene

Extensive studies have been done to determine which antiseptic solution is the most effective way of removing micro organisms from the skin surface before catheter insertion and during catheter care. The best option appears to be 2% chlorhexidine, which was found to significantly reduce catheter related infections (CRI) ((104) (LOE 1+); (105) (LOE 2+)). In a comparison of 2% chlorhexidine to povidone-iodine and 70% alcohol, it was shown that the two latter solutions were associated with a fourfold higher incidence of CRI ((106) (LOE 1+)). However, when 0.5% chlorhexidine was applied and compared to 10% povidone-iodine no difference in prevention of catheter related bacteriemia could be demonstrated ((107) (LOE 1+)).

Recommendations

- Before insertion of an intravascular device and for post-insertion site care, a clean skin should be disinfected. Application of 2% chlorhexidine is preferred, rather than 10% povidone-iodine or 70% alcohol. **GOR A**
- Antiseptic solution should remain on the insertion site and air dry before catheter insertion or dressing application. **GOR D**
- Organic solvents (acetone, ether, etc.) should not be applied on the skin before insertion of a catheter or during dressing changes. **GOR D**

Dressing Methods and Frequency of Dressing Changes

Apart from providing protection from external contamination, the purpose of the dressing is to secure the CVC and to prevent dislodgement and trauma. Traditionally it was common to dress the CVC site with dry gauze and tape. This method gave way to transparent polyurethane film dressings, defined as dressing composed of a thin

polyurethane membrane coated with a layer of acrylic adhesive. Potential advantages of these dressings include improved security of the catheter, visibility of the wound site, provision of an effective barrier to micro organisms and, therefore, less frequent need for dressing changing. However, there is a concern that the polyurethane dressings may increase the skin surface humidity, resulting in increased colonization of the micro organisms at the catheter insertion site ((108) (LOE 1+); (109) (LOE 1+); (110) (LOE 1+)), thereby increasing the risk of catheter related infections ((108) (LOE 1+), (111) (LOE 2+)).

Numerous studies have investigated the differences between dressing regimens (incidence of CVC-related infection, catheter security, dressing condition and ease of application, tolerance to dressing materials). The first meta-analysis that compared the effect of two different dressing types concluded that the risk of catheter tip infection, but not sepsis, was significantly increased with transparent CVC dressings compared to gauze and tape ((113) (LOE 1-)). However, according to the recent Cochrane Systematic Review by Gillies, et al., several factors could have biased the results of the above mentioned meta-analysis (114). This review failed to demonstrate any difference in the incidence of infectious complications between any dressing types compared (gauze and tape vs Opsite IV300, Opsite vs Opsite IV300, Tegaderm vs Opsite IV300, Tegaderm vs Opsite). As most of the included studies were performed on a small patient sample, they probably did not have a sufficient power to detect any differences between the groups. The authors, therefore, concluded that at this stage the choice of dressing for CVC can be based on patient preference, while the answer on "What is the appropriate dressing to use for CVC" requires further research ((114) (LOE 1++)).

Most of the studies mentioned have been done in adult populations, as there are very few studies involving children. A trial looking at the prevention of CVC infections in neonates concluded that the use of alcohol for cutaneous antiseptics with a subsequent placement of a chlorhexidine-impregnated dressing (Biopatch) over the insertion site of CVC (which should be left on for up to 7 days between dressing changes), provides protection against catheter tip colonisation. The rates of catheter related blood stream infections and blood stream infections without a source were, however, similar among treatment groups. A substantial risk of contact dermatitis at the dressing site may limit its use in low birth weight infants in the first 2 weeks of life ((115) (LOE 1+)).

Taylor et al, conducted a study on paediatric population with the aim of determining whether "microbial growth increased significantly over time when occlusive dressings were used to cover CVC insertion sites". They concluded that occlusive dressings, changed every 3 to 4 days using an aseptic technique, are safe and efficient and provide a barrier that prevents CVC exit site contamination with children's body fluids, food, and surgical wound drainage, and helps to anchor and stabilise the tubing ((116)

(LOE 2-)). Although tunnelled central venous catheters with well-healed exit sites do not require any dressing to prevent dislodgement, it is useful to have them covered.

Concerning catheter submerging, according to Robbins et al, swimming does not increase the risk of catheter-related infections in children with tunnelled catheters ((117) (LOE 2-)).

The use of topical antibiotic ointments to clean the insertion sites at dressing changes is not recommended, as such ointments are associated with an increased frequency of fungal infections ((118) (LOE 1-)), antibiotic resistance ((119) (LOE 3)), and might adversely affect the integrity of polyurethane catheters ((120) (LOE 3), (120) (LOE 3)).

Recommendations

- Both, sterile gauze + tape and various transparent polyurethane film dressings can be used for the catheter site. **GOR A**
- If the catheter site is bleeding or oozing, a gauze dressing is preferable to a transparent, semi-permeable dressing. **LOE 4**
- The catheter-site dressing should be replaced when it becomes damp, loosened, or when inspection of the site is necessary. **GOR D**
- On short term CVC sites dressings should be replaced every 2 days for gauze dressings and at least every 7 days for transparent dressings, except in those paediatric patients in which the risk for dislodging the catheter outweighs the benefit of changing the dressing. **GOR B**
- Topical antimicrobial ointments should not be used routinely at the insertion site as they may promote fungal infection, antimicrobial resistance and damage the surface of the catheters. **GOR D**
- With tunneled catheters swimming is possible if the catheter is secured with water resistant dressing. **LOE 4**

REFERENCES

1. Gazitua R, Wilson K, Bistran BR, et al. Factors determining peripheral vein tolerance to amino acid infusions. *Arch Surg* 1979; 114:897-900.
2. Puntis JW. Percutaneous insertion of central venous feeding catheters. *Arch Dis Child* 1986;61:1138-40.
3. Thiagarajan RR, Ramamoorthy C, Gettmann T, et al. Survey of the use of peripherally inserted central venous catheters in children. *Pediatrics* 1997;99:E4.
4. Ladefoged K, Efsen F, Krogh Christoffersen J, et al. Long-term parenteral nutrition. II. Catheter-related complications. *Scand J Gastroenterol* 1981;16:913-9.
5. Murai DT. Are femoral Broviac catheters effective and safe? A prospective comparison of femoral and jugular venous broviac catheters in newborn infants. *Chest* 2002;121:1527-30.

6. Timsit JF, Bruneel F, Cheval C, et al. Use of tunneled femoral catheters to prevent catheter-related infection. A randomized, controlled trial. *Ann Intern Med* 1999;130:729–35.
7. Nahum E, Levy I, Katz J, et al. Efficacy of subcutaneous tunneling for prevention of bacterial colonization of femoral central venous catheters in critically ill children. *Pediatr Infect Dis J* 2002;21:1000–4.
8. Flynn PM, Willis B, Gaur AH, et al. Catheter design influences recurrence of catheter-related bloodstream infection in children with cancer. *J Clin Oncol* 2003;21:3520–5.
9. Sheth NK, Franson TR, Rose HD, et al. Colonization of bacteria on polyvinyl chloride and Teflon intravascular catheters in hospitalized patients. *J Clin Microbiol* 1983;18:1061–3.
10. Sank A, Chalabian-Baliozian J, Ertl D, et al. Cellular responses to silicone and polyurethane prosthetic surfaces. *J Surg Res* 1993;54:12–20.
11. Polderman KH, Girbes AJ. Central venous catheter use. Part 1: mechanical complications. *Intensive Care Med* 2002;28:1–17.
12. Maki DG, Stolz SM, Wheeler S, et al. Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomized, controlled trial. *Ann Intern Med* 1997;127:257–66.
13. Raad I, Darouiche R, Dupuis J, et al. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. A randomized, double-blind trial. The Texas Medical Center Catheter Study Group. *Ann Intern Med* 1997;127:267–74.
14. Veenstra DL, Saint S, Sullivan SD. Cost-effectiveness of antiseptic-impregnated central venous catheters for the prevention of catheter-related bloodstream infection. *JAMA* 1999;282:554–60.
15. Goetz AM, Wagener MM, Miller JM, et al. Risk of infection due to central venous catheters: effect of site of placement and catheter type. *Infect Control Hosp Epidemiol* 1998;19:842–5.
16. Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 2001;286:700–7.
17. Venkataraman ST, Thompson AE, Orr RA. Femoral vascular catheterization in critically ill infants and children. *Clin Pediatr (Phila)* 1997;36:311–9.
18. Sovinz P, Urban C, Lackner H, et al. Tunneled femoral central venous catheters in children with cancer. *Pediatrics* 2001;107:E104.
19. Johnson EM, Saltzman DA, Suh G, et al. Complications and risks of central venous catheter placement in children. *Surgery* 1998;124:911–6.
20. Citak A, Karabocuoğlu M, Ucsel R, et al. Central venous catheters in pediatric patients-subclavian venous approach as the first choice. *Pediatr Int* 2002;44:83–6.
21. Stenzel JP, Green TP, Fuhrman BP, et al. Percutaneous femoral venous catheterizations: a prospective study of complications. *J Pediatr* 1989;114:411–5.
22. Goldstein AM, Weber JM, Sheridan RL. Femoral venous access is safe in burned children: an analysis of 224 catheters. *J Pediatr* 1997;130:442–6.
23. Chen KB. Clinical experience of percutaneous femoral venous catheterization in critically ill preterm infants less than 1,000 grams. *Anesthesiology* 2001;95:637–9.
24. Wardle SP, Kelsall AW, Yoxall CW, et al. Percutaneous femoral arterial and venous catheterisation during neonatal intensive care. *Arch Dis Child Fetal Neonatal Ed* 2001;85:F119–22.
25. van Engelenburg KC, Festen C. Cardiac tamponade: a rare but life-threatening complication of central venous catheters in children. *J Pediatr Surg* 1998;33:1822–4.
26. Nowlen TT, Rosenthal GL, Johnson GL, et al. Pericardial effusion and tamponade in infants with central catheters. *Pediatrics* 2002;100:137–42.
27. Collier PE, Blocker SH, Graff DM, et al. Cardiac tamponade from central venous catheters. *Am J Surg* 1998;176:212–4.
28. Darling JC, Newell SJ, Dear PR. Placement of neonatal central venous catheter tips in the right atrium: a practice to be avoided. *Arch Dis Child Fetal Neonatal Ed* 2001;85:F146.
29. Menon G. Neonatal long lines. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F260–2.
30. Schuster M, Nave H, Piepenbrock S, et al. The carina as a landmark in central venous catheter placement. *Br J Anaesth* 2000;85:192–4.
31. Fletcher SJ, Bodenham AR. Safe placement of central venous catheters: where should the tip of the catheter lie? *Br J Anaesth* 2000;85:188–91.
32. Amram S, Zeraffatourkine MH, Bourgeois JM, et al. Ultrasound-guided percutaneous central venous catheterization in preterm infants. *Ann Pediatr* 1995;42:55–9.
33. Asheim P, Mostad U, Aadahl P. Ultrasound-guided central venous cannulation in infants and children. *Acta Anaesthesiol Scand* 2002;46:390–2.
34. Davis SJ, Thompson JS, Edney JA. Insertion of Hickman's catheters in total parenteral nutrition: a prospective study of 200 consecutive patients. *Am Surg* 1984;50:673–6.
35. Noshier JL, Shami MM, Siegel RL, et al. Tunneled central venous access catheter placement in the pediatric population: comparison of radiologic and surgical results. *Radiology* 1994;192:265–8.
36. Alderson PJ, Burrows FA, Stemp LI, et al. Use of ultrasound to evaluate internal jugular vein anatomy and to facilitate central venous cannulation in paediatric patients. *Br J Anaesth* 1993;70:145–8.
37. van de Wetering MD, van Woensel JB. Prophylactic antibiotics for preventing early central venous catheter Gram positive infections in oncology patients. *Cochrane Database Syst Rev* 2003; CD003295.
38. Fallat ME, Gallinaro RN, Stover BH, et al. Central venous catheter bloodstream infections in the neonatal intensive care unit. *J Pediatr Surg* 1998;33:1383–7.
39. Shaul DB, Scheer B, Rokhsar S, et al. Risk factors for early infection of central venous catheters in pediatric patients. *J Am Coll Surg* 1998;186:654–8.
40. Fletcher MA, Brown DR, Landers S, et al. Umbilical arterial catheter use: report of an audit conducted by the Study Group for Complications of Perinatal Care. *Am J Perinatol* 1994;11:94–9.
41. Seguin J, Fletcher MA, Landers S, et al. Umbilical venous catheterizations: audit by the Study Group for Complications of Perinatal Care. *Am J Perinatol* 1994;11:67–70.
42. Loisel DB, Smith MM, MacDonald MG, et al. Intravenous access in newborn infants: impact of extended umbilical venous catheter use on requirement for peripheral venous lines. *J Perinatol* 1996;16:461–6.
43. Boo NY, Wong NC, Zulkifli SS, et al. Risk factors associated with umbilical vascular catheter-associated thrombosis in newborn infants. *J Paediatr Child Health* 1999;35:460–5.
44. Barrington KJ. Umbilical artery catheters in the newborn: effects of position of the catheter tip. *Cochrane Database Syst Rev* 2000; 2:CD000505.
45. Eyer S, Brummitt C, Crossley K, et al. Catheter-related sepsis: prospective, randomized study of three methods of long-term catheter maintenance. *Crit Care Med* 1990;18:1073–9.
46. Cobb DK, High KP, Sawyer RG, et al. A controlled trial of scheduled replacement of central venous and pulmonary-artery catheters. *N Engl J Med* 1992;327:1062–8.
47. Cook D, Randolph A, Kernerman P, et al. Central venous catheter replacement strategies: systematic review of the literature. *Crit Care Med* 1997;25:1417–24.
48. Palesty JA, Amshel CE, Dudrick SJ. Routine chest radiographs following central venous recatheterization over a wire are not justified. *Am J Surg* 1998;176:618–21.
49. Azizkhan RG, Taylor LA, Jaques PF, et al. Percutaneous trans-lumbar and transhepatic inferior vena cava catheters for prolonged vascular access in children. *J Pediatr Surg* 1992;27:165–9.
50. Cheatham JP, McCowan TC, Fletcher SE. Percutaneous trans-lumbar catheterization and central venous line insertion: an

- alternative approach in children with congenital heart disease. *Catheter Cardiovasc Interv* 1999;46:187–92.
51. de Csepel J, Stanley P, Padua EM, et al. Maintaining long-term central venous access by repetitive hepatic vein cannulation. *J Pediatr Surg* 1994;29:56–7.
 52. Goldstein SL, Baronette S, Gambrell TV, et al. nPCR assessment and IDPN treatment of malnutrition in pediatric hemodialysis patients. *Pediatr Nephrol* 2002;17:531–4.
 53. Pemberton LB, Lyman B, Lander V, et al. Sepsis from triple- vs single-lumen catheters during total parenteral nutrition in surgical or critically ill patients. *Arch Surg* 1986;121:591–4.
 54. Apelgren KN. Triple lumen catheters. Technological advance or setback? *Am Surg* 1987;53:113–6.
 55. Yeung C, May J, Hughes R. Infection rate for single lumen v triple lumen subclavian catheters. *Infect Control Hosp Epidemiol* 1988; 9:154–8.
 56. Lagro SW, Verdonck LF, Borel Rinkes IH, et al. No effect of nadroparin prophylaxis in the prevention of central venous catheter (CVC)-associated thrombosis in bone marrow transplant recipients. *Bone Marrow Transplant* 2000;26: 1103–6.
 57. Hilton E, Haslett TM, Borenstein MT, et al. Central catheter infections: single- versus triple-lumen catheters. Influence of guide wires on infection rates when used for replacement of catheters. *Am J Med* 1988;84:667–72.
 58. Clark-Christoff N, Watters VA, Sparks W, et al. Use of triple-lumen subclavian catheters for administration of total parenteral nutrition. *JPEN J Parenter Enteral Nutr* 1992;16:403–7.
 59. McCarthy MC, Shives JK, Robison RJ, et al. Prospective evaluation of single and triple lumen catheters in total parenteral nutrition. *JPEN J Parenter Enteral Nutr* 1987;11:259–62.
 60. Kaufman JL, Rodriguez JL, McFadden JA, et al. Clinical experience with the multiple lumen central venous catheter. *JPEN J Parenter Enteral Nutr* 1986;10:487–9.
 61. Lee RB, Buckner M, Sharp KW. Do multi-lumen catheters increase central venous catheter sepsis compared to single-lumen catheters? *J Trauma* 1988;28:1472–5.
 62. Gil RT, Kruse JA, Thill-Baharozian MC, et al. Triple- vs single-lumen central venous catheters. A prospective study in a critically ill population. *Arch Intern Med* 1989;149:1139–43.
 63. Johnson BH, Rypins EB. Single-lumen vs double-lumen catheters for total parenteral nutrition. A randomized, prospective trial. *Arch Surg* 1990;125:990–2.
 64. Savage AP, Picard M, Hopkins CC, et al. Complications and survival of multilumen central venous catheters used for total parenteral nutrition. *Br J Surg* 1993;80:1287–90.
 65. Ma TY, Yoshinaka R, Banaag A, et al. Total parenteral nutrition via multilumen catheters does not increase the risk of catheter-related sepsis: a randomized, prospective study. *Clin Infect Dis* 1998;27:500–3.
 66. Andrew M, David M, Adams M, et al. Venous thromboembolic complications (VTE) in children: first analyses of the Canadian Registry of VTE. *Blood* 1994;83:1251–7.
 67. Schmidt B, Andrew M. Neonatal thrombosis: report of a prospective Canadian and international registry. *Pediatrics* 1995;96: 939–43.
 68. Moukartzel AA, Haddad I, Ament ME, et al. 230 patient years of experience with home long-term parenteral nutrition in childhood: natural history and life of central venous catheters. *J Pediatr Surg* 1994;29:1323–7.
 69. Andrew M, Marzinotto V, Pencharz P, et al. A cross-sectional study of catheter-related thrombosis in children receiving total parenteral nutrition at home. *J Pediatr* 1995;126:358–63.
 70. Krafte-Jacobs B, Sivit CJ, Mejia R, et al. Catheter-related thrombosis in critically ill children: comparison of catheters with and without heparin bonding. *J Pediatr* 1995;126:50–4.
 71. Pottecher T, Forrlor M, Picardat P, et al. Thrombogenicity of central venous catheters: prospective study of polyethylene, silicone and polyurethane catheters with phlebography or post-mortem examination. *Eur J Anaesthesiol* 1984;1:361–5.
 72. Dollery CM, Sullivan ID, Bauraind O, et al. Thrombosis and embolism in long-term central venous access for parenteral nutrition. *Lancet* 1994;344:1043–5.
 73. Pollard AJ, Sreeram N, Wright JG, et al. ECG and echocardiographic diagnosis of pulmonary thromboembolism associated with central venous lines. *Arch Dis Child* 1995;73:147–50.
 74. Hirsh J, Warkentin TE, Raschke R, et al. Heparin and low-molecular-weight heparin: mechanisms of action, pharmacokinetics, dosing considerations, monitoring, efficacy, and safety. *Chest* 1998;114:489S–510.
 75. Appelgren P, Ransjo U, Bindslev L, et al. Surface heparinization of central venous catheters reduces microbial colonization in vitro and in vivo: results from a prospective, randomized trial. *Crit Care Med* 1996;24:1482–9.
 76. Pierce CM, Wade A, Mok Q. Heparin-bonded central venous lines reduce thrombotic and infective complications in critically ill children. *Intensive Care Med* 2000;26:967–72.
 77. Raad II, Luna M, Khalil SA, et al. The relationship between the thrombotic and infectious complications of central venous catheters. *JAMA* 1994;271:1014–6.
 78. Timsit JF, Farkas JC, Boyer JM, et al. Central vein catheter-related thrombosis in intensive care patients: incidence, risks factors, and relationship with catheter-related sepsis. *Chest* 1998;114:207–13.
 79. Goldmann DA, Pier GB. Pathogenesis of infections related to intravascular catheterization. *Clin Microbiol Rev* 1993;6:176–92.
 80. Spear ML, Stahl GE, Hamosh M, et al. Effect of heparin dose and infusion rate on lipid clearance and bilirubin binding in premature infants receiving intravenous fat emulsions. *J Pediatr* 1988;112:94–8.
 81. Roth B, Ekelund M, Fan BG, et al. Effects of heparin and low molecular weight heparin on lipid transport during parenteral feeding in the rat. *Acta Anaesthesiol Scand* 1996;40:102–11.
 82. Chen X, Ruiz J, Boden G. Release, oxidation, and reesterification of fatty acids from infused triglycerides: effect of heparin. *Metabolism* 1995;44:1590–5.
 83. Shulman RJ, Phillips S. Parenteral nutrition in infants and children. *J Pediatr Gastroenterol Nutr* 2003;36:587–60.
 84. Spadone D, Clark F, James E, et al. Heparin-induced thrombocytopenia in the newborn. *J Vasc Surg* 1992;15:306–11.
 85. Warkentin TE, Levine MN, Hirsh J, et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. *N Engl J Med* 1995;332:1330–5.
 86. Ranze O, Rakow A, Ranze P, et al. Low-dose danaparol sodium catheter flushes in an intensive care infant suffering from heparin-induced thrombocytopenia. *Pediatr Crit Care Med* 2001;2:175–7.
 87. Lesko SM, Mitchell AA, Epstein MF, et al. Heparin use as a risk factor for intraventricular hemorrhage in low-birth-weight infants. *N Engl J Med* 1986;314:1156–60.
 88. Vieira A, Berry L, Ofosu F, et al. Heparin sensitivity and resistance in the neonate: an explanation. *Thromb Res* 1991;63:85–98.
 89. Michelson AD, Bovill E, Monagle P, et al. Antithrombotic therapy in children. *Chest* 1998;114:748S–69S.
 90. Nasuno A, Matsubara T, Hori T, et al. Acute pulmonary thromboembolism induced by prophylactic heparin use and a heparin-coated catheter: a case of heparin-induced thrombocytopenia and thrombosis syndrome. *Circ J* 2003;67:96–8.
 91. Johnson OL, Washington C, Davis SS, et al. The destabilization of parenteral feeding emulsions by heparin. *Int J Pharm* 1989;53: 237–40.
 92. Silvers KM, Darlow BA, Winterbourn CC. Pharmacologic levels of heparin do not destabilize neonatal parenteral nutrition. *JPEN J Parenter Enteral Nutr* 1998;22:311–4.
 93. Brown-Smith JK, Stoner MH, Barley ZA. Tunnelled catheter thrombosis: Factors related to incidence. *Oncol Nurs Forum* 1990; 17:543–9.

94. Smith S, Dawson S, Hennessey R, et al. Maintenance of the patency of indwelling central venous catheters: is heparin necessary? *Am J Pediatr Hematol Oncol* 1991;13:141-3.
95. Buswell L, Beyea SC. Flushing protocols for tunneled central venous catheters: an integrative review of the literature. *Online J Knowl Synth Nurs* 1998;5:U1-9.
96. Hentschel R, Wiescholek U, von Lengerke J, et al. Coagulation-associated complications of indwelling arterial and central venous catheters during heparin prophylaxis - a prospective study. *Eur J Pediatr* 1999;158:S126-9.
97. Rizzari C, Palamone G, Corbetta A, et al. Central venous catheter-related infections in pediatric hematology-oncology patients: role of home and hospital management. *Pediatr Hematol Oncol* 1992;9:115-23.
98. Kelly C, Dumenko L, McGregor SE, et al. A change in flushing protocols of central venous catheters. *Oncol Nurs Forum* 1992;19:599-605.
99. Delva R, Gamelin E, Lortholary A, et al. Suppression of heparinization of central venous catheters between cycles of chemotherapy: Results of a phase I study. *Support Care Cancer* 1998;6:384-8.
100. Randolph AG, Cook DJ, Gonzales CA, et al. Benefit of heparin in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials. *Chest* 1998;113:165-71.
101. de Neef M, Heijboer H, van Woensel JB, et al. The efficacy of heparinization in prolonging patency of arterial and central venous catheters in children: A randomized double-blind trial. *Pediatr Hematol Oncol* 2002;19:553-60.
102. Shah P, Shah V. Continuous heparin infusion to prevent thrombosis and catheter occlusion in neonates with peripherally placed percutaneous central venous catheters. *Cochrane Database Syst Rev* 2001;CD002772.
103. Kamala F, Boo NY, Cheah FC, et al. Randomized controlled trial of heparin for prevention of blockage of peripherally inserted central catheters in neonates. *Acta Paediatr* 2002;91:1350-6.
104. Mimos O, Pieroni L, Lawrence C, et al. Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. *Crit Care Med* 1996;24:1818-23.
105. Elliott TS, Tebbs SE. Prevention of central venous catheter-related infection. *J Hosp Infect* 1998;40:193-201.
106. Maki DG, Ringer M, Alvarado CJ. Prospective randomised trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet* 1991;338:339-43.
107. Humar A, Ostromecki A, Direnfeld J, et al. Prospective randomized trial of 10% povidone-iodine versus 0.5% tincture of chlorhexidine as cutaneous antiseptics for prevention of central venous catheter infection. *Clin Infect Dis* 2000;31:1001-7.
108. Conly JM, Grieves K, Peters B. A prospective randomized study comparing transparent and dry gauze dressings for central venous catheters. *J Infect Dis* 1989;159:310-9.
109. Wille JC, Blusse van Oud Albas A, Thewessen EA. A comparison of two transparent film-type dressings in central venous therapy. *J Hosp Infect* 1993;23:113-21.
110. Maki DG, Stolz SS, Wheeler S, et al. A prospective, randomized trial of gauze and two polyurethane dressings for site care of pulmonary artery catheters: implications for catheter management. *Crit Care Med* 1994;22:1729-37.
111. Richet H, Hubert B, Nitemberg G, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. *J Clin Microbiol* 1990;28:2520-5.
112. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. *Pediatrics* 2002;110:1-24.
113. Hoffmann KK, Weber DJ, Samsa GP, et al. Transparent polyurethane film as an intravenous catheter dressing. A meta-analysis of the infection risks. *JAMA* 1992;267:2072-6.
114. Gillies D, O'Riordan L, Carr D, et al. Gauze and tape and transparent polyurethane dressings for central venous catheters. *Cochrane Database Syst Rev* 2003;CD003827.
115. Garland JS, Alex CP, Mueller CD, et al. A randomised trial comparing Povidone-Iodine to a Chlorhexidine Gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics* 2001;107:1431-6.
116. Taylor D, Myers ST, Monarch K, et al. Use of occlusive dressings on central venous catheter sites in hospitalized children. *J Pediatr Nurs* 1996;11:169-74.
117. Robbins J, Cromwell P, Korones DN. Swimming and central venous catheter-related infections in the child with cancer. *J Pediatr Oncol Nurs* 1999;16:51-6.
118. Maki DG, Band JD. A comparative study of polyantibiotic and iodophor ointments in prevention of vascular catheter-related infection. *Am J Med* 1981;70:739-44.
119. Zakrzewska-Bode A, Muytjens HL, Liem KD, et al. Mupirocin resistance in coagulase-negative staphylococci, after topical prophylaxis for the reduction of colonization of central venous catheters. *J Hosp Infect* 1995;31:189-93.
120. Rao SP, Oreopoulos DG. Unusual complications of a polyurethane PD catheter. *Perit Dial Int* 1997;17:410-2.
121. Riu S, Ruiz CG, Martinez-Vea A, et al. Spontaneous rupture of polyurethane peritoneal catheter. A possible deleterious effect of mupirocin ointment. *Nephrol Dial Transplant* 1998;13:1870-1.