

Peripherally inserted central catheters in infants and children – indications, techniques, complications and clinical recommendations

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Venous access required both for blood sampling and for the delivery of medicines and nutrition is an integral element in the care of sick infants and children. Peripherally inserted central catheters (PICCs) have been shown to be a valuable alternative to traditional central venous devices in adults and neonates. However, the evidence may not extrapolate directly to older paediatric patients. In this study, we therefore review the indications, methods of insertion and complications of PICC lines for children beyond the neonatal age to provide clinical recommendations based on a search of the current literature. Although the literature is heterogeneous with few randomised studies, PICCs emerge as a safe and valuable option for intermediate- to long-term central venous access in children both in and out of hospital. Insertion can often be performed in light or no sedation, with

little risk of perioperative complications. Assisted visualisation, preferably with ultrasound, yields high rates of insertion success. With good catheter care, rates of mechanical, infectious and thrombotic complications are low and compare favourably with those of traditional central venous catheters. Even in the case of occlusion or infection, fibrinolytics and antibiotic locks often allow the catheter to be retained.

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IN the paediatric population, intravenous (IV) access represents a unique challenge. Small veins and poor visualisation can make cannulation difficult, and repeated venipunctures are often a source of significant stress in children requiring IV infusions over a prolonged time span.¹

Peripherally inserted central catheters (PICCs) have been used for decades in neonatal populations for intermediate- to long-term IV medical and fluid therapy, where they have been associated with a high insertion success and a low risk of catheter-related complications.^{2,3} New materials, improved insertion techniques and a variety of catheter types, including low-diameter, high-volume catheters, have resulted in PICCs now being used increasingly for a variety of purposes in broader paediatric populations. However, infants, as well as older children, may not be directly comparable with neonates in respect to choice of IV access because of differences in underlying conditions, immunocompetence, general activity level, size and location of available veins, and, accordingly, feasible catheter diameters.

The purpose of this study is to review the current literature concerning indications, methods of insertion and maintenance related to PICC lines in children beyond the neonatal age in order to provide recommendations for clinical practice. Special attention is given to the topic of catheter-related complications, which may play a deciding role in the choice between different IV devices.

Methods

A literature search was performed in PubMed using the search terms 'peripherally inserted central catheter OR PICC AND children', last updated on 19 September 2012. Relevant original articles were identified, including observational studies, clinical trials and meta-analyses. Articles not written in English were excluded, as were initially review articles, case reports, studies concerning adult or neonatal populations, and studies concerning other types of IV access. The latter were only considered where no more relevant studies were available.

Table 1

Comparison of PICCs with other IV access devices.

	PICC	PIV	CVC	TCVC or implantable port
Necessitate GA	Sometimes	Rare	Always	Always
Serious insertion complications	Very rare	No	Potential	Potential
Serious systemic complications	Potential	No	Potential	Potential
Mechanical problems*	Sometimes	Often	Sometimes	Sometimes
Patency	Weeks	Days	Weeks	Months
Catheter cost	+++	+	++	++++
Patient compliance	++	+	+	+++
Necessitate surgical removal	No	No	No	Yes
Insertion difficulty	Easy	Easy	Difficult	Difficult

*Occlusion, dislodgment, fracture.

CVC, central venous catheter; GA, general anaesthesia; IV, intravenous; PICC, peripherally inserted central catheter; PIV, peripheral IV catheter; TCVC, tunnelled CVC.

Further studies were found by manually reviewing references, and key studies were subsequently considered in the formulation of evidence-based recommendations. The presentation of local methods was based on the practices at our own institution.

Indications for PICC in the paediatric population

PICCs may be indicated when intermediate- to long-term IV access is needed for medications and fluid therapy, blood sampling or parenteral nutrition. Peripheral IV catheters (PIVs) have a short patency, and insertion sites may often become exhausted during extended IV therapy. Alternatives include conventional central venous catheters (CVCs) placed in the jugular or subclavian vein, or surgically placed long-term central venous devices, such as tunnelled and cuffed CVCs (TCVCs) and implantable venous port systems. While PICCs can often be inserted with light or even no sedation, the insertion of other central venous devices often requires general anaesthesia during the procedure. Additionally, these procedures are associated with a risk of serious perioperative complications such as pneumo/haemothorax, air embolism or severe haematomas (summarised in Table 1). In one pilot study and one randomised controlled study, the authors recommended considering the use of PICCs rather than PIVs in paediatric surgical patients requiring more than 4–10 days of follow-up IV therapy.^{4,5} In these studies, PICCs were shown to be cost-effective, associated with significantly greater patient satisfaction and resulted in fewer needle punctures. Intermediate-term IV access is often required for prolonged antibiotic therapy, and

several observational studies have documented that PICCs are suitable in both inpatient and outpatient settings for up to 6 weeks.^{6–8} Additionally, recent studies have shown the value of PICCs even in long-term treatment of oncological children.^{9–12} PICCs were used for both infusion and blood sampling for maximum dwell times of 390–575 days. Although manufacturers do not support blood sampling through smaller PICCs, a non-randomised observational study has shown that the use of 3 French PICCs for repeated blood sampling is possible without a significant increase in catheter occlusion.¹³

Contraindications

Contraindications for PICC placement are few. Infection, burns or radiation damage at the insertion site may increase the risk of catheter colonisation or bacteraemia, and make catheter securement difficult. Local oedema may reduce venous visibility and insertion success. Small, damaged or thrombosed vessels caused by previous catheter insertions or repeated attempts at cannulation may hinder catheter placement. A recent retrospective study by Yang et al. showed that successive PICC insertions were associated with progressively increased difficulty of access.¹⁴ Likewise, central thrombosis, stenosis, congenital or idiopathic venous anomalies of the ipsilateral subclavian vein or of the superior vena cava (SVC) may hamper catheter advancement to the correct target position. Special consideration should be given to children with chronic renal failure or end-stage renal disease. In these patients, other alternatives should be considered in order to prioritise the preservation of veins for the formation of an arteriovenous fistula for dialysis.

Table 2

Sedation strategy for peripherally inserted central catheter placement.

Age < 6–8 years	Age 6–8 years	Age > 6–8 years
General anaesthesia	Pre-medication, local anaesthesia, nitrous oxide	Pre-medication Local anaesthesia

PICC placement

PICCs can be placed by a variety of trained personnel, including anaesthesiologists, interventional radiologists, paediatricians or specialised IV nurses. Insertion can be performed in a variety of settings, including bedside, in the operating theatre or in a specialised angiography suite.^{15–18} The veins of the antecubital fossa can often be identified visually or by palpation. Deeper veins can be visualised by high-resolution ultrasound (US)^{19,20} or by fluoroscopic venography with contrast injected via a PIV distal to the insertion site.^{18,21–23} Assisted visualisation significantly improves insertion success,^{15,24} and several studies have reported success rates of 90–100% using these techniques.^{9–11,18,21,22} No direct comparisons of fluoroscopy and US exist in the paediatric population, and the choice of strategy should reflect local organisation, resources and the needs of individual patients. US is probably preferable in most cases. It is easy to learn, transportable and provides good visualisation of veins and adjacent structures. Even so, probe compression of the vein may impede puncture and advancement of the guide wire. Fluoroscopy provides superior visualisation of the veins in their entirety including occlusions or collaterals. It is, however, limited to the angiography suite and requires an increased radiation exposure, IV contrast and an existing PIV.

Sedation

Most children need to be sedated in order to reduce patient discomfort, to optimise the positioning of the insertion arm and to keep it in place. There are many different sedation protocols,^{25,26} but in the paediatric population, it is necessary to individualise the analgo-sedative strategy. Table 2 outlines a suggestion for strategies depending on the age of the child. Most sedation protocols include spontaneous breathing with supplemental oxygen via the nasal route or a laryngeal mask airway. With older children (> 10–12 years), it may be possible to perform a PICC insertion using local anaesthesia alone. Options include eutectic mixture of local anaesthetic

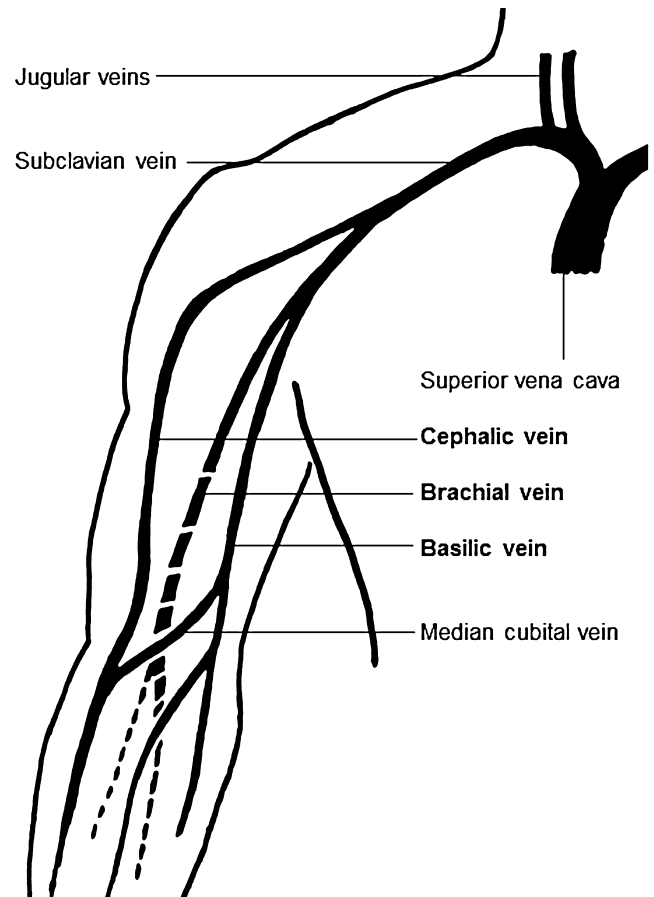


Fig. 1. Veins of the right arm. The veins of choice for peripherally inserted central catheter insertion has been marked in bold.

cream applied over suitable veins and/or infiltration with lignocaine. Some children benefit from midazolam pre-medication or inhalation of 50% nitrous oxide during the procedure.

Vein selection

Suitable veins for PICC insertion include the basilic, brachial and cephalic veins of the arm (Fig. 1). Visualisation by US is generally easy 2–4 cm above the antecubital fossa (Fig. 2), where the indwelling catheter may cause less discomfort to the patient during flexion of the elbow. The basilic and brachial veins usually have a suitable size, making the puncture

Table 3

Choice of catheter size.	Infants	Age 1–6 years	Age 6–10 years	Children > 10 years
Catheter size (French)	2–3	3–4	4	4–5

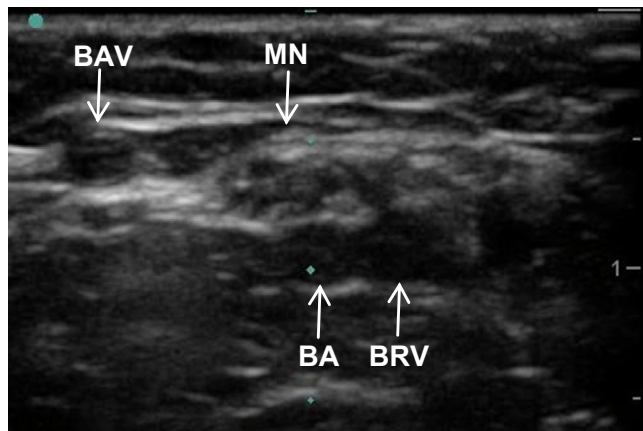


Fig. 2. Ultrasound of the arm veins. BAV, basilic vein; BA, brachial artery; BRV, brachial vein; MN, median nerve.

easier and probably lowering the risk of post-operative complications.¹¹ Furthermore, their out-flow to the axillary vein is normally direct. The cephalic vein sometimes ends in small collaterals in the upper arm, making it difficult or even impossible to advance the catheter to a central location. On the other hand, guide wire insertion into the basilic vein can be difficult in preschool children because of their elastic tissue and the deep localisation of the vein. Although the brachial vein is usually easy to puncture, it is situated close to the brachial plexus and the brachial artery, and therefore should be punctured cautiously. Because of anatomical variation, it may be advisable to evaluate cephalic, basilic and brachial veins along their full length up to the axillary junction by US before puncture.

Choice of catheter

PICCs are made of silicone or polyurethane, the latter being the material increasingly preferred by the manufactures because of its greater flexibility when customising the material to specific requirements. Polyurethane provides the PICC with comparatively greater wall strength, allowing the production of small-sized high-flow catheters with greater inner lumina. In relation to complications after insertion, there seems to be no difference

between silicone and polyurethane catheters, although no randomised clinical studies comparing the two materials have been conducted. PICC size is chosen according to vein dimensions and the age of the child (see Table 3). The ideal catheter seems to be a single-lumen, low-diameter, high-volume, polyurethane catheter. Larger PICCs may increase the incidence of venous occlusion and thrombosis, although this has not been confirmed in randomised studies. Conversely, smaller catheters can cause more mechanical problems with luminal occlusion and other dysfunctions.²⁷ Unless multiple ports are essential for patient management, single-lumen catheters should be preferred as they may be less likely to induce complications.⁶ PICCs with antimicrobial coating have been developed. However, evidence is inconsistent regarding their preventive effect on catheter-related infections, and their use cannot currently be recommended.²⁸

Insertion procedure

PICCs should be inserted by use of maximal barrier precautions using antiseptic hand wash, sterile gown, gloves and a large sterile drape. The area of insertion is cleaned with 2% chlorhexidine in 70% isopropyl alcohol. The appropriate vein is cannulated with an IV catheter or the supplied needle (Fig. 3A). After removing the tourniquet, a guide wire is inserted into the vein (Seldinger technique – Fig. 3B). The PICC is prepared by filling it with isotonic saline and cutting the catheter to the appropriate length. The length is determined by measurement along the course of the vein to the SVC using the tape included in the pre-packed PICC set. A small incision of the skin and subcutaneous tissue is made, and a dilator and peel-away introducer are threaded cautiously into the vein (Fig. 3C). The wire and dilator are removed, and the PICC is inserted via the peel-away sheath. Difficulties in advancing the guide wire or the catheter centrally can often be overcome by abducting the arm up to 90 degrees. Flexion of the patient's head forward and towards the ipsilateral shoulder reduces the risk of advancing the catheter into the jugular veins. Before removing the peel-away introducer, the catheter tip placement is controlled

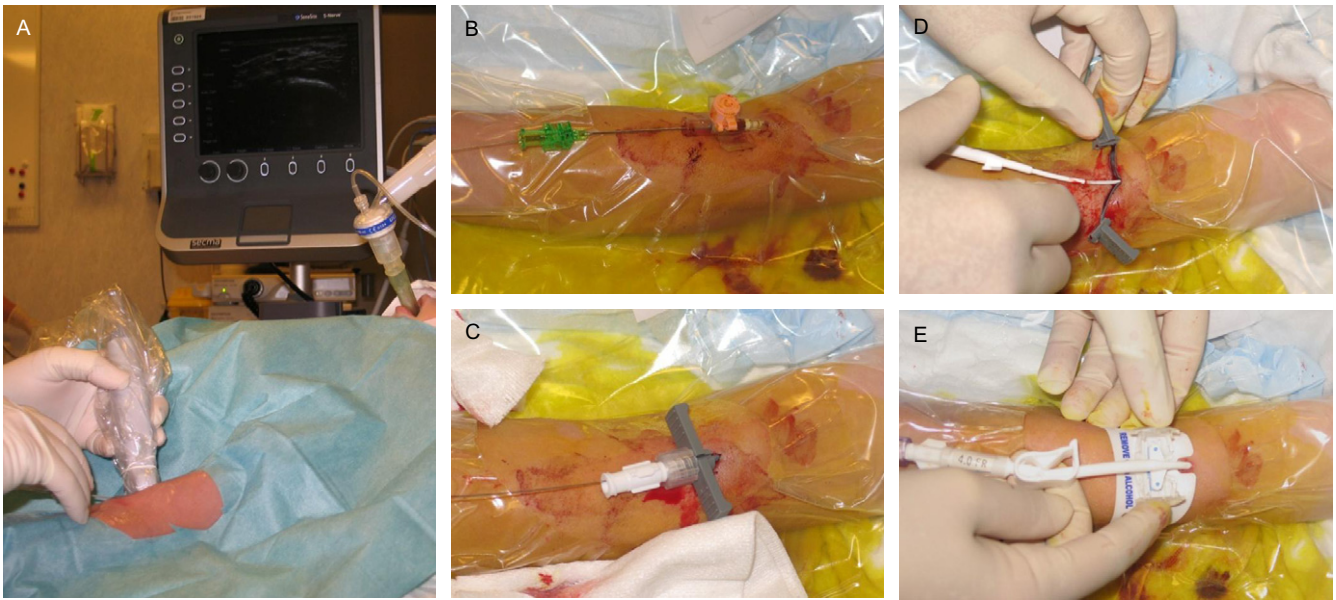


Fig. 3. Peripherally inserted central catheter placement.

with fluoroscopy. This allows correction of non-central catheter placement or inappropriate catheter length. PICC placement without fluoroscopic guidance requires manipulation in up to 85% of insertions in order to achieve correct central tip placement.²³ Once the PICC is in place, the peel-away sheath can be removed, and the catheter fixed in place (Fig. 3D–E). The use of a suture-free securing device (StatLock, C.R. BARD, Inc., Covington, GA, USA) with a transparent dressing is preferred over tape or sutures. A review by Frey and Schears cites randomised evidence showing a significant reduction in dislodgement and unplanned removals compared with taped securement.²⁹

Catheter tip placement

Acceptable catheter tip placement has been debated intensively. However, several observational studies suggest that non-centrally placed PICCs have shorter patency and higher complication rates.^{10,30,31} Thus, PICC insertion should aim to place the tip of the PICC in the distal part of the SVC or in the right atrium. Tip location in the right ventricle must be avoided because of the risk of tachyarrhythmias and myocardial lesion.²³ The carina can be used as a simple landmark for appropriate positioning. Studies on cadavers have demonstrated that the carina is located approximately 0.5 cm above the pericardial duplication as it transveres the SVC.³² The position of the arm during insertion and subsequent chest radiographs influences the tip loca-

tion.³³ During control of the tip position, the arm should be positioned in the 'natural' position by the side with flexion of the elbow.

PICC care and maintenance

Careful post-operative management is vital to maintain PICC patency and prevent complications. Aseptic technique and proper hand hygiene should be observed during handling and the dressing and administration sets replaced at regular intervals or when soiled. Continual education of health-care workers and parents has been shown to decrease the incidence of catheter-related blood stream infection (CRBSI) in CVCs.³⁴ Several consensus guidelines from national or international societies provide detailed recommendations for the care of central venous devices.^{35–37} However, because few studies deal specifically with PICCs in the paediatric population, these recommendations are largely based on adult studies and studies dealing with different types of CVCs.

Complications

The most common PICC-related complications include mechanical problems (occlusions, accidental dislodgement, breakage or leakage of the catheter), infections (local or systemic), phlebitis and venous thrombosis. The overall rates of complications in paediatric populations are generally low but have been reported in a number of studies ranging

from 1.11 to 19.3 per 1000 catheter days, varying with the type of population studied and the clinical setting.^{6-12,38-40} Comparisons between individual studies are further complicated by dissimilar registration of complications, as well as varying standards of catheter care and maintenance. While some studies focus on complications resulting in catheter removal,^{9,10,12,39,40} Barrier et al. registered all complications in 1290 PICCs inserted for prolonged antimicrobial therapy in previously healthy, hospitalised children. The overall complication rate was as high as 19.3/1000 days, but only one-third was classified as serious, requiring antimicrobial treatment, removal or replacement of the PICC.⁶ Patient age < 5 years, double-lumen catheters and multiple daily uses were associated with a higher rate of complications. However, no individual risk factors have been consistently correlated to PICC complications.

Thiagarajan et al. found that completion of IV therapy was significantly more likely when PICCs were used in an outpatient setting compared with the hospital setting (77% vs. 69%).²⁷

The number of studies directly comparing PICCs with other central venous devices is limited. Furthermore, comparison of unrelated studies may be difficult because of the same heterogeneity in study populations, context and methods that account for the great variability in the complication rates seen between individual PICC studies. Compared with traditional CVCs, the few available non-randomised studies suggest that while PICCs may be associated with a higher frequency of mechanical problems such as occlusion or accidental displacement,^{7,8} serious complications such as deep venous thrombosis (DVT) or CRBSI seem to be no more frequent^{41,42} or even less so.⁴³ When compared with long-term central venous devices (TCVCs and implantable ports), one observational study in children with cancer suggests that the use of PICCs may be associated with a significantly higher risk of DVT despite a lower occurrence of catheter occlusion.¹⁶

The most common complications are discussed as follows.

Mechanical problems

Mechanical catheter complications are rarely life-threatening but may result in the interruption of treatment and the need for removal or replacement of the PICC. Occlusions of the inner lumen are not uncommon with rates of up to 10.6/1000 catheter days.^{6,7,17,18,38} They may be thrombotic or non-thrombotic in origin; the latter is caused by precipi-

tation of incompatible drugs and infusions inside the catheter. Furthermore, fibrin sheath formation on the outside of the catheter may form a pseudovalve, impairing aspiration from the catheter. Thiagarajan et al. found that the risk of catheter occlusion was significantly greater in PICCs with smaller lumina (2 French), while rates of accidental dislodgment were significantly greater in patients aged 30 days to 5 years than in neonates or older children.²⁷ Thrombotic occlusions and fibrin sheaths often respond to careful flushing with saline or to instillation of a fibrinolytic agent. In a mixed adult/paediatric population, urokinase 5000 IU/ml was highly successful in restoring catheter patency.⁴⁴ The solution was instilled in a dose corresponding to the internal volume of the catheter and left for 30 min before removal, and the process was repeated if necessary. Occlusions requiring removal or replacement of the catheter are rare at rates ranging from 0.06 to 2.47/1000 days.^{9-12,39} When used only rarely, the risk of occlusion may be reduced by daily flushing of the catheter with saline or a heparin solution (50–100 U/ml) corresponding to the catheter volume. The latter is preferably removed before reuse of the catheter. Breakage or leakage at the catheter exit site can often be repaired and only result in catheter removal at rates from 0 to 2.0/1000 days.^{9-12,38,39} Accidental dislodgement is more frequent in the paediatric population than in adult or neonatal populations possibly because of increased activity levels with less attention to the catheter. Rates are reported ranging from 0.12 to 3.0/1000 days.^{7,9,11,12,17,18,39}

A potentially serious complication has been reported in the form of catheter fracture with embolisation of a catheter fragment. Although long dwell time and a history of other catheter complications have been significantly associated with this complication, it is very rare.⁴⁵

Infection

PICC associated infections are potentially life-threatening and include local infections at the exit site and systemic infections. The overall rate of PICC-associated infections in children is reported as ranging from 0.2 to 6.4/1000 catheter days and seems to be higher in hospitalised compared with ambulatory patients.^{6,7,9-12,30,39,40,42,43,46} In addition to study heterogeneity, the large variation may also reflect varying definitions of CRBSI. The US Center for Disease Control and Prevention has published guidelines for the diagnosis of CRBSI, mainly involving matching peripheral blood cultures with

catheter blood or tip cultures.⁴⁷ However, few studies exist to validate these criteria in children, and many studies use less rigorous criteria. Special considerations in paediatric patients mean that it is not always possible to remove or replace PICCs for tip culture, and difficulties in obtaining peripheral blood samples may render paired culture with catheter blood unavailable. Randolph et al. have proposed a set of modified diagnostic criteria for practical purposes.⁴⁸

With these caveats, systemic infections have been reported at rates from 0.11 to 6.4/1000 days.^{6,7,9-12,30,39,40,42,46} Using broader criteria, Advani et al. surveyed 2592 PICCs in hospitalised children and found a systemic infection rate of 2.58/1000 days. Significant risk factors included a dwell time of over 21 days, catheter placement for parenteral nutrition, intensive care unit exposure and chronic metabolic conditions. Children who previously had a PICC complicated by infection were also at increased risk.⁴⁶

Levy et al. studied 279 PICCs placed in a tertiary-care paediatric hospital and reported a total rate of 4.4 infectious complications per 1000 catheter days requiring catheter removal. While this included cases of phlebitis (1.5/1000 days) and exit site infection (1.17/1000 days), CRBSI was only reported at a rate of 0.4/1000 days.³⁹

Exit site infection, usually defined as local erythema, tenderness or induration around the catheter exit site or purulent secretion from the catheter site, is reported at rates from 0.04 to 2.4/1000 days.^{7,10-12,39,40}

The pathogens most frequently identified in PICC-related infections are gram-positive cocci (coagulase-negative staphylococci, *Staphylococcus aureus*), while infections with gram-negative rods (*Klebsiella pneumoniae*) or fungi (*Candida* species) are also common.^{39,42,46}

Treatment of CRBSI requires appropriate systemic antibiotics and may necessitate removal of the catheter. However, the need for chronic catheterisation, multiple catheters or difficult venous access can make it necessary to preserve the catheter. In this case, systemic antibiotics should probably be supplemented with the use of a lock solution to counter biofilm formation in the indwelling catheter.⁴⁹⁻⁵¹ Although the evidence is sparse specifically regarding PICCs, the effect of antibiotic lock solutions is well documented for other types of IV devices. Vancomycin, gentamicin and cefazolin are commonly used,^{52,53} but no international consensus exists on the routine use of any antibiotic lock

solution.⁵⁴ Alternatively, disinfection with hydrochloric acid can be effective.^{55,56}

Venous thrombosis

A major concern in the use of all central venous lines is the risk of developing DVT. In children, more than 90% of DVT is risk-associated largely because of long-term indwelling central venous devices.⁵⁷ Even so, symptomatic PICC-related venous thrombosis is rare, reported at rates ranging from 0 to 0.19/1000 catheter days in paediatric patients.^{9,16,21,22,41,58} Risk factors include congenital thrombophilia and a history of catheter occlusion and catheter-related infection.^{16,58} In a study on long-term central venous devices including PICCs, Revel-Vilk et al. found that patients developing at least one episode of both catheter occlusion and infection had an increased risk of developing symptomatic catheter-related DVT (hazard ratio: 4.15; 95% confidence interval: 1.2-14.4).¹⁶ Other potential risk factors, including positive family history of thrombosis, underlying haematological or oncological diseases prior DVT, as well as the size of the catheter, number of lumina, a proximal tip location and long insertion time have in some cases been identified in relation to regular CVCs.⁵⁹ These findings have yet to be confirmed for PICCs in the paediatric population.

PICC-related DVT may lead to infection, post-thrombotic syndrome or pulmonary embolism. However, the majority of current observational studies register only clinically symptomatic DVT, which probably leads to underdiagnosis. In a study by Dubois et al., 214 children (age 0-18 years) with PICCs were screened systematically for venous thrombosis using US.⁵⁸ Twenty cases of DVT of varying severity were found (3.85/1000 days). Nevertheless, despite three cases of complete occlusion, only one patient presented with clinical symptoms. Conversely, Bui et al. screened 33 of 41 children with cystic fibrosis. All had PICCs placed for antibiotic therapy. However, using Doppler US, the team found no cases of DVT at the end of the therapy.⁶⁰ By comparison, the incidence of 'silent' venous thrombosis in traditional CVC is found to be as high as 50% when patients undergo systematic screening.⁶¹

The clinical significance of silent thrombosis remains unclear. Chance findings of tip or wall attached thrombi, or partial or total occlusions of peripheral and central veins may occur during routine computed tomography, magnetic resonance imaging or echocardiography. This leads to the dilemma of deciding whether treatment of these

findings is necessary or not. DVT in children is a serious complication, but the clinical practice regarding prevention, investigation and treatment of catheter-related occlusion/thrombosis varies greatly between paediatric centres.⁶² Treatment with low-molecular-weight heparin seems to be safe and effective in cases related to traditional CVCs.^{63–65} These findings have not yet been replicated with paediatric PICCs.

Therapy of silent thrombosis depends on several factors, such as the size and localisation of the thrombus, the degree of venous occlusion, intercurrent diseases and present coagulation status.

Summary

The literature contains a substantial number of studies concerning PICCs in the paediatric population. However, the majority of these are observational studies with few randomised, controlled trials, and comparison between studies is difficult because of marked heterogeneity in study populations, study design and end points. Child immunocompetence, clinical setting and patterns of use probably have a large impact on catheter patency and the incidence of complications.

Nevertheless, PICCs are emerging as a safe and valuable option for intermediate- to long-term central venous access in children. They can be used in both hospital and outpatient settings, and new types of PICC are being developed that may facilitate even broader indications and longer dwell times. PICC insertion is easy to learn, has very few serious perioperative risks, and can often be performed in local anaesthesia and/or light sedation. The incidence of serious long-term complications seems to be low and comparable with that of traditional CVCs, although tunnelled or implantable long-term devices may still be safer for long-term use.

Based on these considerations, PICCs may be indicated for:

- Short- to intermediate-term IV access in children requiring IV therapy for 4–5 days up to several weeks (antibiotics, total parenteral nutrition, frequent blood sampling)
- Long-term central venous access as an alternative to conventional long-term devices (TCVC or implantable port systems) in patients with significant coagulopathy or contraindications to GA, such as significant comorbidity
- Temporary central venous access for injection of toxic medications in oncology patients until a long-term device can be inserted (e.g., in children with cervical or mediastinal pathology)

Well-educated staff and the use of assisted visualisation improve insertion success and lower complication rates, US being the most promising modality for the future. Meanwhile, new methods are emerging to salvage infected or occluded catheters. Even so, further evaluation of PICCs in the care of infants and children by properly controlled and randomised clinical studies in the paediatric population is desirable.

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