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Catheter-related complications in onco-hematologic children: A retrospective clinical study on 227 central venous access devices

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Abstract

Background: The use of central venous access devices (CVADs) is of paramount importance to safely deliver antiblastic and support therapies in children with cancer. Though, in pediatric patients, as much as in adults, CVADs are potentially associated with severe complications which may result in unscheduled interruption of therapy, hospitalization, increased morbidity/mortality, and increased cost of care.

Methods: We have reviewed retrospectively our experience with CVADs in children with solid tumors and hematologic diseases, with the purpose of verifying if the adoption of well-defined insertion and maintenance bundles might be effective in reducing catheter-related complications, and in particular catheter-related thrombosis.

Results: A total of 227 CVADs were analyzed: 175 peripherally inserted central catheters (PICCs), 50 centrally inserted central catheters (CICCs), and 2 femorally inserted central catheters. All CVADs were non-valved, non-cuffed power injectable polyurethane catheters; 81% were tunneled. Median dwelling time of CVADs was 172 days, for a total number of 39,044 catheter days. A very low incidence of both symptomatic catheter-related thrombosis (0.9%) and catheter-related blood stream infection (0.56 episodes per 1000 catheter days) was found. Unscheduled removal or guidewire replacement because of mechanic complications occurred in 15.7% of CVADs. There was no difference in terms of complications between PICCs and CICCs or between tunneled and non-tunneled catheters.

Conclusions: Our experience with CVADs in oncologic and hematologic children suggests that catheter-related complications may be minimized by the adoption of appropriate insertion and maintenance bundles.

Keywords

Central venous catheterization, PICC, pediatric oncology, catheter-related thrombosis, catheter-related complications, CRBSI, pediatric cancer patients

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Introduction

The most frequent types of cancer in the pediatric population are hematologic neoplasms (leukemia and lymphoma), tumors of the nervous central system and neuroblastomas.[1] Cancer treatment implies a multidisciplinary approach which includes the combined use of surgery, antiblastic chemotherapy, radiotherapy, immuno-therapy, and/or bone marrow transplantation. Such approach has dramatically improved the overall 5-year survival rate in children with cancer (about 80%).[2] In this clinical context, central venous

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access devices (CVADs) have become of paramount importance to ensure the feasibility of repeated blood sampling and the safe delivery of oncologic therapies (chemotherapy, immunotherapy) as well as of support therapies (parenteral nutrition, blood and platelet transfusions, stem cell infusion).[3,4]

Although essential for the treatment of any onco-hematologic patient, CVADs are potentially associated with complications which may result in unscheduled hospitalization, prolongation of hospital stay, increased morbidity/mortality and increased cost of care.[3] In the last decade, peripheral inserted central catheters (PICCs) have been increasingly used in adult cancer patients as an alternative option to centrally inserted central catheters (CICCs),[5,6] since PICC insertion is minimally invasive and is not associated with the risk of immediate severe complications (pneumothorax, hemothorax, hematomas, etc.) potentially associated with CICC insertion. Also, PICCs can be safely inserted even in cancer patients with bleeding disorders or receiving antithrombotic therapy.[7]

The use of PICCs in onco-hematologic children has been questioned by some authors, because of the fear of catheter-related thrombosis (CRT).[8,9] Though, other authors[10] have noted that the apparent high risk of CRT reported in some studies is due to a confusion between two different devices, the ultrasound guided PICCs (inserted in children) and the epicutaneo-cava catheters (inserted in neonates), the latter being notoriously characterized by a high incidence of local thrombosis. Also, the actual risk of CRT for ultrasound guided PICCs in adult patients—according to recent reviews and meta-analyses—is mainly dependent on the technique of PICC insertion,[5,6] and this may be true also in pediatric patients.

In this retrospective study, we have analyzed the clinical performance of different types of CVADs (all inserted according to a well-defined insertion protocol) in a cohort of onco-hematologic pediatric patients, during a period of 4 years, focusing on the risk of catheter-related complications (and mainly on the risk of CRT).

Methods

This retrospective analysis was designed to investigate the clinical performance and the complication rate of CVADs in onco-hematologic pediatric patients, for the purpose of quantifying the risk of symptomatic CRT and of all other catheter-related complications when proper insertion and maintenance bundles are consistently adopted.

We reviewed the charts of all children with cancer who had a central venous access device (CVAD) inserted for chemotherapy or other supportive intravenous treatment in a 4-year period. This single-center study was conducted on patients admitted to the department of pediatric oncology of a large university hospital in the metropolitan area of Rome, Italy ("A. Gemelli" University Hospital, Catholic University School of Medicine). The study protocol was approved by the local Ethics Committee, and the review was conducted according to the STROBE recommendations for retrospective studies. The parents (or guardians) were informed about the objective of the study and signed an informed consent form.

We included in the study all children (age ranging from birth to 17-year-old) candidate to central venous catheterization in a 4-year period. Totally implanted venous access devices (chest-ports, PICC-ports, femoral ports) and peripheral venous access devices (short peripheral catheters, long peripheral catheters, midline catheters) were not included in this analysis. Other exclusion criteria were the following: age >17 years, denial of parental consent, and CVADs placed in emergency. The CVADs included in the analysis were peripheral inserted central venous catheters (PICCs), centrally inserted central catheters (CICCs), and femorally inserted central venous catheters (FICCs), all of them inserted according to an insertion bundle described in a previous study.[11]

This bundle includes seven evidence-based strategies:

(1) Ultrasound preprocedural evaluation of all deep veins using previously described protocols: the Rapid Central Vein Assessment (RaCeVA),[12] the Rapid Peripheral Vein Assessment (RaPeVA),[13,14] the Rapid Femoral Vein Assessment (RaFeVA).[15] An ideal vein/catheter ratio of at least 3:1 was considered acceptable.[16]
(2) Aseptic technique (hand hygiene, maximum barrier protections, skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol).
(3) Real-time ultrasound guided venipuncture with different techniques in terms of vein view (short axis, long axis, oblique axis) and needle approach (in-plane, out-of-plane), depending on the vein considered and on the clinical situation.[17] Ultrasound was also used to assess the proper direction of the guidewire and of the catheter (ultrasound-based tip navigation), according to the ECHOTIP-Ped protocol.[18] In case of CICC insertion, ultrasound was used to assess the absence of pneumothorax, immediately after venipuncture, as currently recommended.[17]
(4) Intra-procedural verification of tip location by non-invasive methods such as intracavitary ECG,[19] and/or ultrasound-based tip location according to the ECHOTIP-Ped protocol.[18] Post-procedural X-ray was taken into consideration as an option only in case of failure (not feasibility or not applicability) of both intracavitary ECG and ultrasound-based tip location.
(5) Appropriate planning of the exit site of the CVAD adopting tunneling whenever needed, so to move the exit site away from areas at high risk of

bacterial contamination or dislodgment. Tunneling options were decided according to the RAVESTO protocol.[20]

(6) Sutureless securement of the venous catheter, as currently recommended.[21] Securement was achieved either by skin adhesive sutureless devices (StatLock, BD; GripLok, Zevon) or by subcutaneous anchorage (SecurAcath, Interrad).
(7) Protection of the exit site using cyanoacrylate glue[22] and semipermeable transparent membranes with high permeability (high MVTR = high Moisture Vapor Transfer Rate) (Tegaderm Advance, 3M; IV3000, Smith & Nephew; SorbaView, Centurion); a value of MVTR > 1500[23] was considered acceptable.

All insertion procedures were performed in a dedicated procedure room of the local pediatric intensive care unit. Sedation, analgesia and local or general anesthesia were used in all patients, in different combinations, depending on the age of the patient and his/her compliance and clinical status. Further details about our CVAD insertion protocol, including the ECG monitors and the ultrasound devices we used, have been described in the study quoted above.[11]

The choice of CVAD was based on the vein availability. If deep veins of appropriate caliber were available at the upper arm, PICC was preferred over CICC. FICCs were used only in selected cased of documented obstruction/compression of the superior vena cava. Non-valved, non-cuffed power injectable polyurethane VADs of many different brands were used (Healthline, DeltaMed, MedComp, Plan-1-Health, Cook Medical, Vygon). Both in infants and in children, 3–4 Fr single or 4–5 Fr double lumen catheters were used: catheters currently marketed as PICCs were used "off label" also as CICCs or FICCs, as previously described.[13,24,25] This allowed us to use micro-introduction kits with 21G echogenic needle and soft straight tip 0.018″ guidewire for all procedures.

CVAD maintenance was adherent to the local hospital policies and to the current international recommendations[21]: dressing change every 7 days (unless dirty, soiled or partially detached), skin antisepsis with chlorhexidine 2% in alcohol, change of skin-adhesive sutureless devices every 7 days, use of chlorhexidine-releasing sponge dressings only in non-tunneled catheters, adoption of needle free connectors with neutral displacement (changed every 7 days), disinfecting caps, flush and lock with saline only, daily surveillance of the exit site (to rule out edema, erythema, tenderness, etc.).

Endpoints

The primary endpoint was to evaluate the incidence of symptomatic catheter-related thrombosis (CRT) in the first 6 months after insertion.

Secondary end-point was the incidence of other CVAD-related complications occurring in the first 6 months: immediate complications at insertion, early complications (within 48 h from insertion) and late complications (after 48 h and within 6 months), the latter including infections (exit site infection, infection of the tunnel, or catheter-related blood stream infection) and mechanical complications (catheter rupture, tip migration, accidental dislodgment, irreversible malfunction due to lumen occlusion).

Symptomatic catheter-related thrombosis (CRT) was diagnosed by ultrasound examination, performed only if suspected because of suggestive clinical signs and symptoms (swelling of the ipsilateral arm, pain, erythema, etc.). Local skin infection was defined by the presence of erythema and tenderness over the exit site or the tunnel, regardless of the presence of fever or purulent discharge. The diagnosis of catheter-related blood stream infection (CRBSI) was based on the method of Differential Time to Positivity (DTP).[26,27] Catheter malfunction was defined as persistent inability to infuse normal saline solution despite the manual pressure performed on the piston of a 10 ml syringe, or as ability to infuse but with persistent difficulty in blood withdrawal. Dislodgment was defined as catheter movement of more than 2 cm from the original position at the exit site.

Statistical analysis

The natural history of each CVAD (insertion related complications, late complications, cause of removal, etc.) was analyzed for a 6-month period after insertion, reviewing the patients' clinical records.

An electronic database was created, including relevant clinical data concerning the patients (age, weight, sex, type of cancer, type of therapy, duration of therapy), CVAD insertion (type of catheter, tunneled or not, caliber of vein vs catheter caliber, type of sedation/anesthesia) and CVAD-related complications (early, i.e. withing 48 h, vs late, i.e. from 48 h to 6 months). Reasons for CVAD removal (completion of treatment, death, or complication requiring removal) and duration of catheterization were also recorded.

The statistical analysis of the anamnestic characteristics of the sample and of the incidence of complications was performed using Excel files. The incidence of complications was compared with the figures reported in the literature. Data were normalized considering the different characteristics of the individual devices used and the other characteristics shown on the data collection sheet.

Results

In this retrospective analysis, we studied 115 onco-hematologic pediatric patients: 64 males (55.7%) and 51 females (44.3%). Mean age was 8 years (range 2 months–17 years): 26 infants between 2 months and 3 years old (22.6%), 67

Table 1. Diagnosis of neoplastic disease in the patients' population.

Diagnosis	Total = 115 children
Acute Lymphoblastic Leukemia	23
Glioma	14
Lymphoma	12
Astrocytoma	12
Ewing sarcoma	10
Neuroblastoma	10
Rhabdomyosarcoma	8
Germinal cells tumor	7
Medulloblastoma	7
Osteosarcoma	3
Ovarian cancer	2
Wilms tumor	1
Neuroectodermal tumor	1
Retinoblastoma	1
Medullo-epithelioma	1
Ependymoma	1
Nasopharynx tumor	1
Hepatic sarcoma	1

children between 4 and 14 years old (58.2%), and 22 adolescents between 15 and 17 years old (19.1%). The types of cancer are shown in Table 1.

Most patients ($n=55$) had only one CVAD inserted (47.9%), 28 patients had two CVADs (24.3%), 19 patients had three CVADs (16.5%), 13 patients had four CVADs or more (11.3%).

A total of 227 CVADs were included in the analysis, most of them being PICCs ($n=175$; 77%); CICCs were used in 22% of cases ($n=50$), and mainly inserted by a supraclavicular approach to the brachio-cephalic vein (only in a minority of patients they were inserted by an infraclavicular approach to the axillary vein). FICCs were used in two patients (1%). Most CVADs ($n=184$; 81%) were tunneled: 140 PICCs (puncture site in the proximal third of the upper arm and exit site in the middle third), 42 CICCs (puncture site in the supraclavicular area and exit site in the infraclavicular area), and 2 FICCs (puncture site at the groin and exit site at mid-thigh).

Median dwelling time of all CVADs was 172 days (range 1–655 days), for a total number of 39,044 catheter days. Adhesive sutureless devices were used for 163 CVADs (71.8%) while only 64 (28.19%) were secured with subcutaneous anchorage.

The incidence of symptomatic catheter related thrombosis (CRT) was 0.9% (i.e. two cases: one PICC-related and one CICC-related). CRT did not require CVAD removal; both cases were managed by anti-thrombotic treatment, and the CVADs were used for chemotherapy without interruptions.

There were no immediate/early insertion-related complications. Post-procedural X-ray was never used, as tip location was always verified successfully during the procedure.

As regards infective complications, we recorded five cases (2.2%; 0.12 episodes/1000 catheter days) of documented exit site infection (positive culture of the skin at the exit site), all of them in tunneled CVADs, and all successful managed by conservative treatment (systemic antibiotics and local antisepsis). There was no case of tunnel infection. Catheter colonization without bacteremia was diagnosed by DTP in 20 cases (8.8%; 0.51 episodes/1000 catheter days): 14 cases were successfully managed by conservative treatment with 2% taurolidine lock, while six cases required CVAD removal. CRBSI was diagnosed by DTP in 22 cases (9.7%; 0.56 episodes/1000 catheter days): 6 cases were successfully managed by conservative treatment (antibiotic lock therapy + systemic antibiotics), while 16 cases required CVAD removal. There was no difference in infective complications comparing PICCs and CICCs or comparing tunneled versus non-tunneled catheters or comparing children with hematologic diseases versus children with solid tumors.

As regards mechanical complications, we recorded 12 cases (5.2%) of tip migration (secondary malposition), four catheter ruptures (1.7%), and 20 cases (8.8%) of accidental dislodgment. Most of these complications were treated—whenever possible—by guidewire replacement of the CVAD. Interestingly, the incidence of accidental dislodgment was 10.4% in CVADs secured with skin adhesive sutureless securement (17 out of 163 CVADs), but only 4.6% in CVADs secured with subcutaneous anchorage (3 out of 64 CVADs). Catheter malfunction due to lumen occlusion occurred in 20 cases (8.8%), but there was no case of irreversible occlusion requiring removal. There was no difference in mechanical complications between PICCs and CICCs or between tunneled versus non-tunneled catheters.

Table 2 reports the incidence of each catheter-related complication.

In summary, reasons for unscheduled CVAD removal (or guidewire replacement) were either infection/colonization ($n=22$; 9.7%) or mechanical complications ($n=36$; 15.7%). In most patients ($n=126$; 56%), CVADs were removed because of completion of treatment. Follow up was not completed for 11 CVADs (4.8%), due to referral of the patients to another hospital. Ten CVADs (4.4%) were still being used for chemotherapy at 6-month follow up. Death during the 6-month follow up occurred in 22 patients (9.7%).

As no cuffed CVAD was used, all catheter removals were easily performed bedside, without requirement of sedation or anesthesia, and without any reported complication.

Discussion

This retrospective study suggests that use of CVADs in the onco-hematologic pediatric patients is safe, being associated with a very low incidence of complications, if well-defined insertion and maintenance bundles are consistently adopted.

In particular, the use of PICCs (175 in this analysis) appears to be particularly safe in oncologic and hematologic pediatric patients.

Table 2. Incidence of catheter-related complications (6-month follow up).

	n	%	n/1000 cath.days	Removal
Symptomatic catheter-related thrombosis (CRT)	2/227	0.9		-
Exit site infection	5/227	2.2	0.12	-
Catheter colonization	20/227	8.8	0.51	6
Catheter-related blood stream infection (CRBSI)	22/227	9.7	0.56	16
Tip migration	12/227	5.2		12
Catheter rupture	4/227	1.7		4
Accidental dislodgment:	20/227	8.8		
- skin-adhesive device	17/163	10.4		17
- subcutaneous anchorage	3/64	4.6		3
Lumen occlusion	20/227	8.8		-

In a previous study on 36 PICCs inserted by a radiology team under fluoroscopic guidance in 32 pediatric oncologic patients,[28] the overall incidence of complications was 5.29 per 1000 catheters days. Lumen occlusion was reported as the most frequent complication (2.98/1000 catheter days), followed by CRBSI (1.98/1000 catheter days) and accidental removal (0.3/1000 catheter days). The authors used 4 Fr single lumen PICCs, but no measurement of the veins was reported.

Symptomatic CVAD-related thrombosis has been reported to very high (30%–68%) in children with lymphoma.[29] In a recent study in children with leukemia,[30] the incidence of CRT was 10.2% in children with PICCs but only 1.5% in children with tunneled-cuffed CICCs. In the mentioned study, the caliber of the catheter had been chosen according to the age and weight of the patients, without any mention of the caliber of the veins; also, the final position of the catheter tip had been verified by a post-procedural chest X-ray (contrary to the recommendations of the current guidelines).[21]

In another prospective multicenter study in children aged 6 months–18 years,[9] the incidence of CVAD-related thrombosis was reported to be 5.9%. The incidence of PICC-related thrombosis was 9%, higher than the incidence observed with tunneled CICCs or ports. The choice of the type of device had been done randomly in a 1:1 fashion, with no consideration of the venous patrimony of the child or of the caliber of the vein.

On the contrary, in our study the incidence of symptomatic CRT was very low (0.9%), although many children (35 out of 115) had hematologic neoplastic diseases (acute lymphoblastic leukemia or lymphoma) (see Table 1). Also, there was no significant difference of incidence of CRT between PICCs and CICCs. The very low incidence of CRT reported in our study is probably explained by the adoption of a well-defined insertion bundle[11] which includes all the evidence-based strategies which are known to be effective in preventing CRT: use of ultrasound for the systematic examination of the veins before the procedure, so to ensure a proper catheter/vein ratio of 1:3 or lower[16]; use of ultrasound guided venipuncture with micro-introduction kit, so to minimize the endothelial trauma[17,31]; accurate intraprocedural methods of tip location, such as intracavitary ECG and echocardiography[18,19]; appropriate sutureless securement so to stabilize the catheter.

As regards CRBSI, its incidence in oncologic and hematologic pediatric patients has been reported to be 3.5/1000 catheter days for tunneled-cuffed CICCs and 3/1000 catheter days for PICCs.[32] The risk of CRBSI has been reported to be particularly high in children with acute myeloid leukemia (AML) and aged 1 year or less.[33] In a population of 560 pediatric patients with AML and neutropenia, the incidence of CRBSI was 11 episodes per 1000 neutropenic days for tunneled CICCs, 13.7 for PICCs and 10.7 for ports.[34]

The increasing use of insertion and maintenance bundle has certainly reduced the incidence of catheter related infection.[35,36] Implementing bundles of maintenance and care of central venous catheters have shown a 28% reduction in CRBSIs also among pediatric onco-hematologic patients.[37,38]

In our cohort of patients, the incidence of CRBSI was very low: 0.56 episodes per 1000 catheter days. This very low incidence of CRBSI is probably explained by the adoption of well-defined insertion and maintenance bundles which include all the evidence-based strategies which are known to be effective in preventing CRBSI: a strict policy of hand hygiene; consistent adoption of maximal barrier precautions; skin antisepsis with 2% chlorhexidine in 70% isopropyl alcohol; choice of an appropriate exit site with extensive adoption of the tunneling technique; sutureless securement of the catheters, as recommended by the current guidelines; protection of the exit site using cyanoacrylate glue and semipermeable transparent dressings; use of chlorhexidine-releasing sponge dressings in non-tunneled catheters; adoption of needle free connectors with neutral displacement protected by disinfecting caps; flush and lock with saline only; daily surveillance of the exit site.

As regards the mechanical complications, we had no case of irreversible lumen occlusion, which had been

reported as a frequent complication in previous studies.[28] This might be explained by the consistent use of needle-free connectors with neutral displacement and by a proper policy of catheter flushing with saline only. Also, the adoption of non-valved power injectable polyurethane CVADs played an important role in this regard: when lumen occlusion occurs, disobstruction of power injectable catheters is easy and effective, since it is possible to use small syringes (2 ml or 5 ml) which exert high pressure but do not harm these catheters. All lumen occlusions were successfully managed by hydraulic maneuvers, with no need for alteplase or urokinase.

The consistent use of power injectable polyurethane catheters may also explain the low rate of catheter rupture (1.76%).

Accidental dislodgment was somehow higher than expected. In a recent pediatric study on 311 tunneled catheters, both cuffed and non-cuffed, all secured by subcutaneous anchorage, the incidence of dislodgement was 2.6%.[39] In our study, the rate of dislodgment of subcutaneously anchored CVADs was 4.6%, and even higher in CVADs secured by skin adhesive sutureless device. This reflects our experience of a 4-year period, but our future clinical results are expected to improve, since we are now adopting subcutaneous anchorage in 100% of pediatric CVADs inserted in non-emergency situations; also, the staff has become more expert in the placement and in the management of the subcutaneous anchoring device, leading to its higher effectiveness in terms of risk of dislodgment.[40,41]

Conclusions

Our experience with CVADs in oncologic and hematologic children shows that the catheter-related complications may be minimized if a proper insertion bundle and a proper maintenance bundle are adopted.

Using appropriate prevention strategies, we have achieved a very low incidence of symptomatic CRT (0.9%) and CRBSI (0.56/1000 catheter days), both in PICCs and in CICCs.

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References

1. AIRTUM Working Group; CCM; AIEOP Working Group. Italian cancer figures, report 2012: Cancer in children and adolescents. *Epidemiol Prev* 2013; 37(1 Suppl 1): 1–225.
2. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. *J Clin Oncol* 2010; 28(15): 2625–2634.
3. Giordano P, Saracco P, Grassi M, et al. Recommendations for the use of long-term central venous catheter (CVC) in children with hemato-oncological disorders: management of CVC-related occlusion and CVC-related thrombosis. On behalf of the coagulation defects working group and the supportive therapy working group of the Italian Association of Pediatric Hematology and Oncology (AIEOP). *Ann Hematol* 2015; 94(11): 1765–1776.
4. Cellini M, Bergadano A, Crocoli A, et al. Guidelines of the Italian Association of Pediatric Hematology and Oncology for the management of the central venous access devices in pediatric patients with onco-hematological disease. *J Vasc Access* 2022; 23(1): 3–17.
5. Balsorano P, Virgili G, Villa G, et al. Peripherally inserted central catheter-related thrombosis rate in modern vascular access era-when insertion technique matters: a systematic review and meta-analysis. *J Vasc Access* 2020; 21(1): 45–54.
6. Schears GJ, Ferko N, Syed I, et al. Peripherally inserted central catheters inserted with current best practices have low deep vein thrombosis and central line-associated bloodstream infection risk compared with centrally inserted central catheters: a contemporary meta-analysis. *J Vasc Access* 2021; 22(1): 9–25.
7. Annetta MG, Bertoglio S, Biffi R, et al. Management of antithrombotic treatment and bleeding disorders in patients requiring venous access devices: a systematic review and a GAVeCeLT consensus statement. *J Vasc Access* 2022; 23: 660–671.
8. Badheka A, Bloxham J, Schmitz A, et al. Outcomes associated with peripherally inserted central catheters in hospitalised children: a retrospective 7-year single-centre experience. *BMJ Open* 2019; 9(8): e026031.
9. Jaffray J, Witmer C, O'Brien SH, et al. Peripherally inserted central catheters lead to a high risk of venous thromboembolism in children. *Blood* 2020; 135(3): 220–226.
10. Crocoli A, Cesaro S, Cellini M, et al. In defense of the use of peripherally inserted central catheters in pediatric patients. *J Vasc Access* 2021; 22(3): 333–336.
11. Pittiruti M, Celentano D, Barone G, et al. A GAVeCeLT bundle for central venous catheterization in neonates and children: a prospective clinical study on 729 cases. *J Vasc Access*. Epub ahead of print 9 May 2022. doi:10.1177/11297298221074472. PMID: 35533085.
12. Spencer TR and Pittiruti M. Rapid Central Vein Assessment (RaCeVA): a systematic, standardized approach for ultrasound assessment before central venous catheterization. *J Vasc Access* 2019; 20(3): 239–249.
13. Pittiruti, M and Scoppettuolo, G (eds). *Manuale GAVeCeLT dei PICC e dei midline*. 1st ed. Milan, IT: Edra SpA, 2016.
14. Brescia F, Pittiruti M, Spencer TR, et al. The SIP protocol update: Eight strategies, incorporating rapid peripheral vein assessment (RaPeVA), to minimize complications associated with peripherally inserted central catheter insertion. *J Vasc Access*. Epub ahead of print 27 May 2022. doi: 10.1177/11297298221099838. PMID: 35633065.

15. Brescia F, Pittiruti M, Ostroff M, et al. The SIF protocol: a seven-step strategy to minimize complications potentially related to the insertion of femorally inserted central catheters. *J Vasc Access*. Epub ahead of print 29 August 2021. doi: 10.1177/11297298211041442. PMID: 34459295.
16. Nifong TP and McDevitt TJ. The effect of catheter to vein ratio on blood flow rates in a simulated model of peripherally inserted central venous catheters. *Chest* 2011; 140(1): 48–53.
17. Lamperti M, Biasucci DG, Disma N, et al. European Society of Anaesthesiology guidelines on peri-operative use of ultrasound-guided for vascular access (PERSEUS vascular access). *Eur J Anaesthesiol* 2020; 37(5): 344–376.
18. Zito Marinosci G, Biasucci DG, Barone G, et al. ECHOTIP-Ped: a structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in pediatric patients. *J Vasc Access*. Epub ahead of print 13 July 2021. doi: 10.1177/11297298211031391. PMID: 34256613.
19. Rossetti F, Pittiruti M, Lamperti M, et al. The intracavitary ECG method for positioning the tip of central venous access devices in pediatric patients: results of an Italian multicenter study. *J Vasc Access* 2015; 16(2): 137–143.
20. Ostroff MD, Moureau N and Pittiruti M. Rapid Assessment of vascular exit site and Tunneling Options (RAVESTO): a new decision tool in the management of the complex vascular access patients. *J Vasc Access*. Epub ahead of print 21 July 2021. doi: 10.1177/11297298211034306. PMID: 34289721.
21. Gorski LA, Hadaway L, Hagle ME, et al. Infusion therapy standards of practice, 8th edition. *J Infus Nurs* 2021; 44(1S Suppl 1): S1–S224.
22. Pittiruti M, Annetta MG, Marche B, et al. Ten years of clinical experience with cyanoacrylate glue for venous access in a 1300-bed university hospital. *Br J Nurs* 2022; 31(8): S4–S13.
23. Bainbridge P, Browning P, Bernatchez SF, et al. Comparing test methods for moisture-vapor transmission rate (MVTR) for vascular access transparent semipermeable dressings. *J Vasc Access*. Epub ahead of print 8 October 2021. doi: 10.1177/11297298211050485. PMID: 34622681.
24. Bernasconi F, Zanaboni C, Dato A, et al. Atypical use of PICC in infants and small children: a unicentric experience. *J Vasc Access* 2017; 18(6): 535–539.
25. Pittiruti M. The "off-label" use of PICCs. In: Andrucci S, Mussa B (eds) *Peripherally inserted central venous catheters*. Milan, IT: Springer/Verlag, 2014, pp.127–144.
26. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 49(1): 1–45.
27. Chaves F, Garnacho-Montero J, Del Pozo JL, et al. Diagnosis and treatment of catheter-related bloodstream infection: clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Spanish Society of intensive and Critical Care Medicine and Coronary Units (SEMICYUC). *Med Intensiva* 2018; 42(1): 5–36.
28. Fadoo Z, Nisar MI, Iftikhar R, et al. Peripherally inserted central venous catheters in pediatric hematology/oncology patients in tertiary care setting: a developing country experience. *J Pediatr Hematol Oncol* 2015; 37(7): e421–e423.
29. Piovesan D, Attard C, Monagle P, et al. Epidemiology of venous thrombosis in children with cancer. *Thromb Haemost* 2014; 111(6): 1015–1021.
30. Noailly Charny PA, Bleyzac N, Ohannessian R, et al. Increased risk of thrombosis associated with peripherally inserted central catheters compared with conventional central venous catheters in children with leukemia. *J Pediatr* 2018; 198: 46–52.
31. Lamperti M, Bodenham AR, Pittiruti M, et al. International evidence-based recommendations on ultrasound-guided vascular access. *Intensive Care Med* 2012; 38(7): 1105–1117.
32. Hord JD, Lawlor J, Werner E, et al. Central line associated blood stream infections in pediatric hematology/oncology patients with different types of central lines. *Pediatr Blood Cancer* 2016; 63(9): 1603–1607.
33. Kelada AS, Foster TB, Gagliano GC, et al. Central-line-associated bloodstream infections and central-line-associated non-CLABSI complications among pediatric oncology patients. *Infect Control Hosp Epidemiol*. Epub ahead of print 27 April 2022. 1–7. doi: 10.1017/ice.2022.91. PMID: 35475427.
34. Elgarten CW, Otto WR, Shenton L, et al. Risk of bacterial bloodstream infection does not vary by central-line type during neutropenic periods in pediatric acute myeloid leukemia. *Infect Control Hosp Epidemiol*. Epub ahead of print 25 April 2022. 1–8. doi: 10.1017/ice.2022.82. PMID: 35465865.
35. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU.[Erratum appears in N Engl J Med. 2007 Jun 21;356(25): 2660]. *New Engl J Med* 2006; 355(26): 2725–2732.
36. O'Grady NP, Alexander M, Burns LA, et al. Summary of recommendations: Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011; 52(9): 1087–1099.
37. Bundy DG, Gaur AH, Billett AL, et al. Preventing CLABSIs among pediatric hematology/oncology inpatients: national collaborative results. *Pediatrics* 2014; 134(6): e1678–e1685.
38. Rinke ML, Bundy DG, Chen AR, et al. Central line maintenance bundles and CLABSIs in ambulatory oncology patients. *Pediatrics* 2013; 132(5): e1403–e1412.
39. Crocoli A, Martucci C, Sidro L, et al. Safety and effectiveness of subcutaneously anchored securement for tunneled central catheters in oncological pediatric patients: a retrospective study. *J Vasc Access* 2021. Epub ahead of print 4 June 2021. doi: 10.1177/11297298211009364. PMID: 34088245.
40. Pinelli F, Pittiruti M, Van Boxtel T, et al. GAVeCeLT-WoCoVA consensus on subcutaneously anchored securement devices for the securement of venous catheters: current evidence and recommendations for future research. *J Vasc Access* 2021; 22(5): 716–725.
41. Pittiruti M, Scoppettuolo G, Dolcetti L, et al. Clinical experience of a subcutaneously anchored sutureless system for securing central venous catheters. *Br J Nurs* 2019; 28(2): S4–S14.