Peripherally Inserted Central Venous Catheter for Pediatric Hematologic Diseases; A Retrospective 11-year Single-center Experience.

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Abstract

Purpose. Peripherally-inserted central catheters (PICCs) are successfully increasingly used in children in onco-hematologic setting. PICC insertion, especially in oncologic patients, can be associated with adverse events (thrombosis, obstruction and infections). Data regarding the use of PICC, as long-term access in pediatric patients with severe hematologic diseases, are still limited.

Methods. We retrospectively evaluated the safety and efficacy of 218 PICC, inserted in 154 pediatric patients diagnosed and treated at Pediatric Hematology Unit, Sapienza University of Rome, for severe hematologic disease in a 11-year period (98 acute lymphoblastic leukemias, 20 acute myeloid leukemias, 20 Hodgkin lymphomas, 6 non-Hodgkin lymphomas, 8 severe aplastic anemias, 2 acquired thrombotic thrombocytopenias).

Results. The 218 PICC analyzed were in situ for a median dwell time of 160 days (range 12–898). In 38 children, PICC was inserted twice and in 10, three times or more due to hematopoietic stem cell transplant, disease recurrence or PICC-related complications. The overall complication rate was 32%: central-line associated bloodstream infections (CLABSI) occurred in 21% of cases after a median time of 105 days; a catheter-related thrombosis (CRT) in 3% and mechanical complications in 8% of cases. Premature removal for complications occurred in 36.7% of PICC. No death related to PICC complications was observed.

Conclusion. In our experience, PICC was a cheap, safe and reliable device for long-term intravenous access in children with severe hematologic illnesses. This has been possible with the help of dedicated PICC team.

Introduction

The management of patients with severe hematologic disease is complex and requires a collaborative program involving phisicians, patients, nurses and all other members of the health care team[1, 2]. In pediatric age, the frequent limitation in peripheral venous access, together with the discomfort of the continuous venipunctures, a long-lasting venous access has become mandatory to safely administer treatments and improve quality of life[3]. A reliable intravenous access is required for the safe administration of chemotherapeutic agents, in order to avoid peripheral extravasation of ulcerative drugs, and to infuse blood products, anti-infective drugs and parenteral nutrition. Furthermore, it allows to easily perform blood samples, necessary for the management of the complex hematologic patient. Peripherally-inserted central catheters (PICCs) are increasingly used in onco-hematological setting, both for adults and children[4–7]. PICC insertion is an easy and not-expensive procedure that can be performed by trained nurses at the bedside, whereas catherer removal is quick and simple. PICC line is inserted percutaneously into a peripheral vein with its tip residing in a central vein, mostly near the junction between the superior vena cava and the right atrium. Compared with other surgically placed central venous catheters (CVC), PICC allows to prevent, at insertion, complications such as pneumothorax and hemothorax, to reduce the

risk of arterial punctures and hemorrhage, that could be particularly severe in children with leukemia-induced thrombocytopenia and/or coagulopathy. However, as in the case of traditional CVC, PICC insertion, especially in oncologic patients, can be associated with adverse events (thrombosis, obstruction and infections) that could potentially result in catheter removal and delayed intravenous treatment, besides an increase of costs for the replacement of the device[3–6]. It has been reported that the latest polyurethane devices involve a lower incidence of infectious and thrombotic complications[5]. The information regarding the use of PICC, as long-term access in pediatric patients with severe hematologic diseases, are still limited.

In our Institute, since January 2010, PICCs have been inserted to all pediatric patients with hematologic (neoplastic and non-neoplastic) diseases requiring a long-term venous access devices for diagnostic procedures and treatments. We report here our experience over a 11-year use of PICC in pediatric patients with a severe hematologic illness.

Patients And Methods

Study design

This is a monocentric retrospective study including pediatric patients (age 1–19 years) with severe hematologic diseases diagnosed and treated at the Institute of Hematology, Sapienza University of Rome, Policlinico Umberto I, who received an ultrasound-guided PICC line from February 2010 to August 2021. Pediatric acute promyelocytic leukemia at disease onset and children with PICC primary placed outside our Institute were excluded.

Data collection

The following information were collected: a) patients' clinical and laboratory characteristics (age, gender, underlying disease, peripheral blood count with platelets and WBC at time of PICC insertion, coagulation profile, including known predisposing factors of venous thrombosis); b) PICC insertion data and site, dwell time (calculated from insertion to removal), PICC line type (open or valved); c) data and reasons of PICC removal and PICC-related adverse events (AEs: occlusion, exit-site infection, PICC-related bacteremia or fungemia, thrombosis), or other reasons (accidental removal, end of intensive therapy, PICC damage, patient's death).

PICC insertion and maintenance

A "PICC Team" including phisicians, nurses and health personnel active in the daily PICC care, is present at our centre[6, 7]. The guidelines for CVC management of the Italian Association of Pediatric Hematology and Oncology Group (AIEOP), were followed by our PICC Team[3].

In our pediatric patients, we used the Groshong PICC produced by Bard (Bard, Inc), with a diameter of 4Fr, an average length of 25/55cm, in silicone material, with a valve placed on the tip. Alternatively, Bard's

Power PICC was used; this is a non-valved device made up of polyurethane material that allows the transit of liquids at high flows.

Details about PICC insertion and maintenance are provided in Supplementary Information.

Study endpoints and definition of PICC-related complications

The aim of the study was to assess the reability and safety of PICC in pediatric patients who needed prolonged appropriate vascular access for management and treatment of hematologic diseases and to evaluate the catheter life, the incidence of PICC-related AEs and PICC removal causes.

Overall PICC-related complications were defined as the presence of at least one of the abovedescribed AEs.

Mechanical complications included complete or partial occlusions (inability to flush, infuse or aspirate and resistance with flushing and aspiration), malfunction, dislocation, and rupture. Temporarily occlusions resolved with recanalization using flushing solutions (heparin and/or plasminogen activators-urokinase), were not included.

PICC-associated bloodstream infections were defined as those occurring in patients who developed fever without another identificable infectious source and with positive blood cultures (2 or more) from catheter, described, according to the National Healthcare Safety Network's criteria, as central line-associated bloodstream infections (CLABSI)[8, 9]. Exit-site infection was defined as the presence of purulent lesion with erythema and/or tenderness close to the PICC exit, confirmed by the positive swab culture and absence of concomitant positive blood culture.

Catheter-related thrombosis (CRT) was suspected by edema, erythema of the cannulated arm, associated with lack of flow, and confirmed by ultrasound.

Accidental removal was defined as an unplanned PICC removal by the child.

We divided our patients' cohort into the following subgroups based on age: early childhood (1–5 years), middle childhood (6–12 years), and adolescents (12–19 years)[9].

Data and statistical analysis

Clinical data were retrospectively recorded for all patients in a database managed by the PICC Team and all the investigators directly involved in the patients' care. An informed consent for the use of the data for scientific purposes was requested from each patient's parents.

The statistical analysis was carried out at the GIMEMA (Gruppo Italiano Malattie EMatologiche dell'Adulto) Data Center in Rome, Italy. Follow-up was updated on January 1, 2022.

Details are given in Supplementary Information.

Results

Patients profile and PICC characteristics

From February 2010 to August 2021, 218 PICC-lines were inserted in 154 patients aged less than 19 years with severe hematologic diseases attending our Hematology Pediatric Unit; 38 of these patients underwent PICC insertion twice, and 10 patients three times or more, because of disease recurrence or need of reinsertion after accidental removal or due to PICC-related complications.

The demographic characteristics of the study subjects (gender, age, type of hematologic disease and thrombofilic screening) are shown in Table 1. In 144 patients (94%) the underlying diagnoses was an oncohematologic disease, whom 98 cases (64%) were acute lymphoblastic leukemias (ALL); 10 patients had a non-neoplastic hematologic illness. In 79 (51%) children a complete thrombophilic screening was available at diagnosis and it was positive in 29 (37%) of them (Table 1).

Table 1
Demographic characteristics for distinct patient

Variables	**N. patients 154 (%)**
Gender: Male/Female	87/67 (56/44)
Age (years): median	11.5
Range	1.7–18.5
≤ 5	36 (23%)
6–12	45 (29%)
> 12	73 (47%)
Type of hematologic disease:	98 (64)
Acute lymphoblastic leukemia	20 (13)
Acute myeloid leukemia	20 (13)
Hodgkin lymphoma	6 (3.9)
Non-Hodgkin lymphoma	8 (5.2)
Severe aplastic anemia	2 (1.3)
Thrombotic thrombocytopenic purpura	144 (94)
Oncologic disease	10 (6)
Other hematologic disease	
Thrombophilic screening	79
Total number available	29 (37)
Positive:	12
- Protein C deficiency	3
- Protein S deficiency	4
- Factor V leiden	6
- LAC*	2
- Protein C deficiency + LAC*	2
- Factor II	50 (63)
Negative	
*LAC: lupus anticoagulant	

PICC lines were inserted in operating room, with moderate sedation in 70 (45%) patients; all of them aged less than 11 years and were in phase of acute illness and in state of psychological stress.

The characteristics of the 218 PICCs included in our case series and the details about PICC insertion are reported in Table 2. Two-hundred-seven/218 (95%) PICC lines were placed on a single attempt. The majority of PICCs was inserted in the right arm (68%). No children developed PICC-related bleeding after insertion. The tip of the PICC was confirmed to be in central circulation by plain radiography in all patients. At the time of PICC insertion, 12 (5.5%) patients presented less than $20x10^9$/L platelet count, 37 (17%) had platelet count ranging from $20x10^9$/L to $50x10^9$/L, and 169 (78%) children more than $50x10^9$/L. In children with low platelet count (< $20x10^9$/L), platelets transfusions were administered immediately before the catheter insertion. Severe neutropenia (PMN < $0.5x10^9$/L) at the time of PICC insertion was present in 37 (17%) children: 25 ALL, 5 acute myeloid leukemia (AML), 5 severe aplastic anemia (SAA), 1 Hodgkin lymphoma (HL), 1 non-Hodgkin lymphoma (NHL).

Table 2
Characteristics of the 218 PICCs

Characteristics	Number 218 (%)
PICC site:	149 (68)
right	69 (32)
left	
PICC position	186 (85)
Basilic vein	29 (13.4)
Brachial vein	3 (1.4)
Other vein	
PICC type	211 (97)
Groshong	1 (0.5)
Power PICC	5 (2.3)
Bilume	1
NR°	
Type of disease	207 (95)
Oncologic	11 (5)
Non-oncologic	
Phase of hematologic disease	118 (54)
Onset	60 (28)
Complete Remission	23 (11)
Relapse	17 (7.8)
Pre-HSCT*	
Platelets (x10^9/L) at time of PICC insertion	1 (0.5)
< 10.0	11 (5)
10.0–20.0	37 (17)
20.0–50.0	169 (78)
> 50.0	

°NR: not reported; *HSCT: hematopoietic stem cell transplant

Characteristics	Number 218 (%)
Neutrophils (x10^9/L) at time of PICC insertion	37 (17)
< 0.5	39 (18)
0.5–1.0	142 (65)
> 1.0	
°NR: not reported; *HSCT: hematopoietic stem cell transplant	

The 218 PICC analyzed were in situ for a median dwell time of 160 days (range 12–898); the median duration of PICC is shorter for patients undergoing heamatopoietic stem cell transplantation (HSCT) compared to those who inserted PICC in the other disease's phases (disease onset 199 days; relapse 139 days; remission 132 days; HSCT 100 days; $p < 0.001$).

PICC-related complications

In our case series, a total of 75 PICC-related complications occurred in 69/218 PICCs, with an overall PICC-related complications rate of 32% (1.77/1,000 PICC days).

PICC-related infections were documented in 50/218 (23%) cases. CLABSI occurred in 46/218 cases (21%); exit-site infection in 4/218 (1.8%) cases. The median time interval between PICC insertion and CLABSI onset was 112 days (range 16–898). The incidence of CLABSIs was 1.28/1,000 PICC days. Gram-positive (+) bacteria were documented in 27 (54%) cases and the most frequent isolated agent was coagulase-negative *Staphylococcus*. Gram-negative bacteria (-) were involved in 15 cases (30%) and one case of mixed gram-positive and gram-negative bacteremia was documented. Seven catether-related fungemias were observed (6 *Candida glabrata* and 1 *Roduturela glutinis*) (Table 3). CLABSI occurred during severe neutropenia (PMN < 0.5x10^9/L) in 17 (37%) out of 46 cases. Appropriate therapy with systemic antibiotics and/or antifungal drugs was administered to all children. PICC was removed in 45 of 46 cases of CLABSI and in 2/4 of the exit-site infections. No patient died from infections (Table 4).

Table 3
PICC-related adverse events

Adverse Event	Number (%)
Infections	50 (100)
CLABSI*	46 (92)
Exit-site infections	4 (8)
Gram-positive bacteria	27 (54)
Gram-negative bacteria	15 (30)
Mixed (Gram+/Gram-)	1 (2)
Fungemia	7 (14)
CRT**	7 (100)
Age (years) ≤ 5	3 (42.8)
6–12	2 (28.6)
>12	2 (28.6)
Disease: Acute lymphoblastic leukemia	4 (57.1)
Acute myeloid leukemia	2 (28.6)
Thrombotic thrombocytopenic purpura	1 (14.3)
Mechanical complications	18 (100)
Age (years) ≤ 5	8 (44.4)
6–12	6 (33.3)
> 12	4 (22.2)
Type of mechanical complication	1 (5.5)
Occlusion	10 (55.5)
Malfunctioning	3 (16.6)
Breakage	4 (22.2)
Malpositioning	16 (89)
PICC type:	2 (11)
Groshong	
Bilumen	

*CLABSI: central line associated bloodstream infection; **CRT: catheter-related thrombosis

Table 4
Causes of PICC removal

Event	Number (%)
Chemotherapy completion	119 (55)
Infections	61 (28)
- PICC-related infections	47 (21.5)
• CLABSI*	45 (21)
• Exit-site infections	2 (0.9)
- Other systemic infections°	14 (6.4)
CRT**	2 (0.9)
Other reasons:	17 (7.8)
- Breakage	3 (1.4)
- Malpositioning	4 (1.8)
- Malfunctioning	5 (2.3)
- Occlusion	1 (0.5)
- Accidental removal	4 (1.8)

*CLABSI: central line associated bloodstream infection; **CRT: catheter-related thrombosis; °Suspected but unconfirmed catheter-related infections

A CRT was recorded in 7/218 (3.2%) cases (2 AML, 4 ALL, 1 Thrombotic thrombocytopenic purpura-TTP) (Table 3). Time between PICC insertion and thrombosis spanned between 15 to 399 days (median 165). The incidence of CRT was 0.18/1,000 PICC days. At time of CRT, platelet count was > $50x10^9$/L in 6 patients and between 25 and $50x10^9$/L in the other child. All 4 children with ALL who developed CRT had previously received Peg-Asparaginase, as part of induction therapy (incidence rate of CRT in ALL children who had received asparaginase was 5% [4/78]), while no CRT event was observed in the ALL patients not treated with asparaginase. In 4/7 CRT cases, the thrombophilic screening was positive (2 Lupus Anticoagulant positivities and 2 protein C deficiency). All patients, not previously receiving thromboprophylaxis, underwent low-molecular-weight heparin (LMWH) therapy while the catheters remained in place; PICC was removed in 2 of 7 CRT after 15 and 165 days, for treating physician decision (Table 4). No fatal event related to CRT was observed.

Mechanical complications occurred in 18 of 218 (8.3%) PICCs: malfunctioning in 10 cases, complete obstruction in 1, ruptures in 3 and malpositioning in 4 cases. Mechanical complications were documented at a median time interval of 186 days (range 24–399) from PICC insertion, with an incidence of 0.46/1,000 PICC days. In 13/18 (72%) cases, PICC was immediately removed.

Accidental removal occurred in 4 children (Table 4).

A total of 199/218 (91%) PICCs were removed; 119/218 (54.5%) PICCs were electively removed at the end of the scheduled treatment. Anticipate PICC removal for complications occurred in 80/218 (36.7%) cases: in 45/218 (21%), PICC was removed for CLABSI, in 2/218 (0.9%) for exit-site infections, in 2/218 (0.9%) for thrombosis, and in 17/218 (7.8%) cases for mechanical problems or accidental removal. In the remaining 14/218 (6.4%) cases, PICC was prematurely removed for suspected but unconfirmed catheter-related infections (non-PICC-related reasons) (Table 4).

All PICCs were successfully removed without surgical intervention.

Regarding the remaining 19/218 (9%) cases, 3 patients were transferred to another hospital before PICC removal, 7 children still had PICC in situ at the time of analysis, and 9 children died with PICC still in situ.

Factors affecting the PICC-related complications and dwell

The influence of patients' characteristics on the frequency of PICC-related complications are reported in Table 5.

Table 5
Logistic regression model for complications

Characteristics	OR*	95%CI§	p-value
Gender: Female/Male	0.86	0.48–1.53	0.61
Age	0.90	0.84–0.95	< 0.001
Age classes (years): >10/≤10	0.39	0.21–0.70	0.004
Diagnosis: acute leukemias/others diseases	4.8	1.81–16.6	0.004
Phase of disease:	0.48	0.13–1.39	0.21
Onset	1.63	0.85–3.11	0.14
Relapse	0.70	0.19–2.14	0.56
Complete remission			
Pre-HSCT°			
Platelets ($x10^9$/L) at PICC insertion:	0.74	0.38–1.47	0.39
< 50.0			
> 50.0			
neutrophils ($x10^9$/L) at PICC insertion:	0.83	0.40–1.78	0.62
< 0.5			
> 0.5			
Thrombofilic screening	1.86	0.89–3.94	0.10
Normal	0.93	0.47–1.84	0.83
Altered			
Not performed			
Site of PICC: left/right	0.68	0.35–1.26	0.23
PICC time: ≥ 2 times/once	0.88	0.46–1.64	0.69

*OR: odds ratio; §CI: confidence interval; °HSCT: hematopoietic stem cell transplant

The incidence of complications was influenced by patients' age (odds ratio-OR 0.90–95%CI 0.84–0.95; p < 0.001). Median age of children who developed PICC-related AEs was 6.3 years (range 1.7–18.0) compared with 11.8 years (range 2.3–18.5) for those who did not showed AEs (p < 0.001). According to age subgroups, the cumulative complications rate was 33%, 38% and 29% (p 0.010), respectively for early, middle childhood and adolescents. There were differences in the incidence of complications between

patients with acute leukemia and those with other neoplastic/non-neoplastic hematological diseases (94% vs 6%; p 0.002; OR 4.80, 95%CI: 1.81–16.6; p 0.004); in particular, incidence of infections was higher in acute leukemia compared with other hematological illnesses (94% vs 6%; p 0.018; OR 4.12, 95%CI: 1.4–17.7; p 0.023) (Table 6). Furthermore, ALL was statistically associated with higher incidence of PICC-related AEs ($p < 0.001$), especially CLABSI (1.44/1,000 PICC days). There was not a significant difference in PICC-related complication incidence between the 17 patients who received HSCT and those treated with chemotherapy alone. The neutrophil count (< 0.5 and > $0.5x10^9$/L) at time of PICC insertion and previous PICC placement did not influenced the incidence of complications (p 0.70) and PICC-related infections ($p > 0.99$ and p 0.86).

Table 6
Univariate analysis of PICC-related infections

Characteristics	OR*	95%CI§	p-value
Gender: Female/Male	0.48	0.24–0.93	0.035
Age	0.95	0.89–1.01	0.10
Age classes (years): >10/≤10	0.56	0.29–1.06	0.076
Diagnosis: acute leukemias/other diseases	4.12	1.4–17.7	0.023
Non-oncologic/oncologic disease	1.28	0.27–4.61	0.73
Phase of disease:	0.59	0.13–1.90	0.42
Onset	2.11	1.05–4.24	0.035
Relapse	0.52	0.08–2.02	0.41
Complete remission			
Pre-HSCT°			
Platelets ($x10^9$/L) at PICC insertion:	1.04	0.50–2.30	0.93
< 50.0			
> 50.0			
Neutrophils ($x10^9$/L) at PICC insertion:	1.10	0.48–2.73	0.83
< 0.5			
> 0.5			
PICC site: left/right	0.46	0.21–0.96	0.047
PICC time: ≥ 2 times/once	0.92	0.44–1.82	0.81

*OR: odds ratio; §CI: confidence interval; °HSCT: hematopoietic stem cell transplant;

CRT occurred in 7 cases, 4 of them after L-Asparaginase treatment. Age, site of PICC insertion and PICC type, type and phase of disease, platelet count at insertion, positive thrombophilic screening did not affect the incidence of CRT ($p > 0.99$).

In our series, the median age of patients who developed mechanical complications was younger compared with the others (5.8 vs 10.6 years; p 0.007; OR 0.87, 95%CI: 0.76–0.96; p 0.013); no other characteristics significantly influenced the occurrence of this complication. The median duration of catheterization was 186 days and 159 days for those with and without mechanical complication, respectively.

Discussion

Central-line is mandatory for pediatric patients requiring prolonged venous access and in our experience PICC provides a reliable access for long-term treatments in children with severe hematologic diseases. In our patients, PICC has been used to administer fluid, blood products, therapeutic plasma exchange, anticancer agents, antibiotics and for blood sampling. This device resulted also in reduction of physical pain and psychological stress of children/adolescents with improvement of quality of life during intensive treatments. PICC has been beneficial for medical staff engaged in frequent blood sampling and drug administrations.

Consistent with the literature[4, 5, 10–18], in our experience, the basilic vein was generally the first choice vein for PICC insertion (85%). The cephalic and brachial veins were cannulated in only 15% of patients. The basilic vein has larger diameter than the brachial or cephalic and follows a straight trajectory, so the passage of the catheter into axillary, subclavian, anonymous vein and therefore into the superior vena cava is easier. Therefore, the procedure is more likely to be successful and there are fewer AEs[15]. Furthermore, the basilic vein covers a greater distance from arterial and nervous structures compared with the brachial vein, thus reducing the likelihood of involuntary injury.

Besides the obvious advantages, PICC is associated with complications, particularly in children with active cancers[12, 16–25]. Rate of PICC-related complications are reportedly high in the pediatric population, ranging from 34 to 56%[14, 19–25]. In our series, PICC-related complications occurred in 32% of cases, requiring PICC removal in 26.6%. Age and type of disease substantially influenced the incidence of complications; in our case series, median age of patients who developed AEs was significantly lower than those who not developed AEs (median age 6.3 vs 11.8; $p < 0.001$). This result, in line with what reported in literature, could be related to the grater difficulties in the home-management of the central-line for the younger children, due to their low awareness of the device utility and their behaviour that can increase infectious risk. Patients with ALL showed a significantly higher risk of AEs, in particular CLABSI (1.44/1,000 PICC days). ALL is the most common neoplasm in pediatric age and its prognosis has improved with the employment of more intensive chemotherapy regimens. The infectious risk is associated with compromised patient’s immune status, steroid use, frequent hospitalizations, together with the large number of venous accesses for the administration of chemotherapy and supportive

measures. Moreover, the intensive chemotherapeutic regimens are associated with long periods of severe neutropenia that highly increase infectious risk. In our study, CLABSI occurred in 21% of cases with incidence rate of 1.28/1,000 PICC days. Our results are in line with other reports. Jaffray et al. found a comparable PICC-associated CLABSI prevalence (22%±2.8%) in a large multicenter study that included 1257 PICCs inserted in children (age 6–18 years); only 41% of them had a neoplastic disease[26]. A slightly lower overall CLABSI incidence rate (1.19/1,000 PICC days) was reported in a retrospective multicentre study of four pediatric intensive care units, where only 85/715 (11.9%) PICCs were inserted in oncologic/immunocompromised children[27]. The lower CLABSI incidence could be associated to the different immune status of the study populations. In another monocentric retrospective study conducted at our Institute, in 144 adults with AML, the CLABSI incidence rate was 22% (1.8/1,000 PICC days) with a median interval from PICC insertion to CLABSI of 56 days (range 7-365)[13]; in this study, despite less prolonged chemotherapeutic regimens and a shorter median catherer-dwell time (83 days; range 41–175), a moderately higher CLABSI incidence has been reported. Baier et al. found a higher CLABSI incidence rate of 10.6/1,000 CVC days and a CLABSI prevalence of 18.2%, in 610 hematologic/oncologic patients[28]. These variations in CLABSI incidence and prevalence rates are due to heterogeneity in the baseline hematologic patients' characteristics, to the presence of individual risk factors, comorbidities and distribution of underlying diseases, type of chemotherapy, proportion of neutropenic patients and lastly to the expertise in cather lines management and care.

Previous PICC placement is also reported as a risk factor for CLABSI[29]; in our series, the 48 children who underwent ≥ 2 PICC installations, did not showed an increased risk of infections (72% vs 28% for one PICC and ≥ 2, respectively; p 0.94). Other factors including platelet and neutrophil count at PICC insertion, type of PICC line, PICC site and altered thrombophilic screening, did not influenced the incidence of PICC-related complications and dwell.

In our study, the incidence rate of symptomatic CRT was lower than most published data (3.2%)[2, 4, 5, 10, 16–18]. In literature, it is estimated that over one third of deep venous thrombosis in the upper extremity is caused by PICCs[17]. In critically ill children, the reported prevalence of CRT varies from 1–9% [19], and, among different cancer centers, the venous thromboembolism rates, in patients with acute leukemia, range from < 1–81%[17–20, 30]. Jaffray et al. found a CRT incidence rate of 9%±1.4%[26], while a higher incidence (16.2%) was observed in 117 adults with hematologic malignancies[31]. The CRT incidence rate was quite similar (2.6%; 0.2/1,000 PICC days) in a monocentris retrospective study, including 612 PICCs/483 adults, treated in our institute[10]. The employment of ultrasound-guided PICC insertion has remarkably reduced the risk of insertion failure and consequently avoided the vascular endothelial damage. Thrombophilic genetic abnormalities are also an important risk factors for CRT[32]; in our patients' cohort, the thrombophilic screening documented a high thrombophilic predisposition in 4/7 patients. Finally, the CRT risk increases with age. In our group, only 2/7 patients who developed CRT were adolescents (age > 12 years). Despite the well known prothrombotic effects of some chemotherapeutic drugs, such as asparaginase[17, 18, 33], we did not observe an increased incidence of PICC-related thrombosis in the ALL subgroup who had received asparaginase (p = 0.26). In this regard, recent studies have suggested thromboprophylaxis in these children[34–36]; our patients, according to

current guidelines, did not received any antithrombotic therapy[29]. Furthermore, the careful evaluation between the vein caliber and catheter lumen, probably contributed to the reduction of the occurrence of CRT.

Accidental dislodgement is a typical PICC complication in children with reported rates ranging from 0.12 to 3.0/1,000 catheter days. Although PICC fixation with suture may decrease these rates[37, 38], in our pediatric series, the absence of suture fixation did not increase the risk of PICC dislocation. Only 4 young children had an accidental PICC removal.

Our study presents some limitations, above all its retrospective nature with problems of some incomplete documentation. Relevant factors that may contribute to PICC-related CLABSIs, such as median length of PICC line outside and length of hospitalization, were not collected. However, this was a single-center study where all children (both inpatients and outpatients) were followed by the same PICC-Team. Data were collected by doctors/nurses that have followed the patients. Our findings were consistent with other published data for patients, both adult and children, with severe hematologic/oncologic diseases. Despite these limitations, our results suggest that PICC line is a safe device that can be maintained for a long period of time, even in children with profound disease- and therapy-related immunosuppression.

Declarations

Ethics approval and consent to partecipate: Compliance with Italian ethical standards; Informed consent was obtained from all individual participants included in the study

Consent for publication: not applicable

Availability of data and materials: Data may be made available upon reasonable request.

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