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ORIGINAL ARTICLE

Supraclavicular catheterization of the brachiocephalic vein: a way to prevent or reduce catheter maintenance-related complications in children

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Abstract
Placement of a central venous catheter (CVC) in the brachiocephalic vein (BCV) via the ultrasound (US)-guided supraclavicular approach was recently described in children. We aimed to determine the CVC maintenance-related complications at this site compared to the others (i.e., the femoral, the subclavian, and the jugular). We performed a retrospective data collection of prospectively registered data on CVC in young children hospitalized in a pediatric intensive care unit (PICU) during a 4-year period (May 2011 to May 2015). The primary outcome was a composite of central line-associated bloodstream infection (CLABSI) and deep-vein thrombosis (CLAT) according to the CVC site. Two hundred and twenty-five children, with respective age and weight of 7.1 (1.3–40.1) months and 7.7 (3.6–16) kg, required 257 CVCs, including 147 (57.2%) inserted in the BCV. The risk of the primary outcome was lower in the BCV than in the other sites (5.4 vs 16.4%; OR: 0.29; 95% CI: 0.12–0.70; $p =$ 0.006). CLABSI incidence density rate (2.8 vs 8.96 per 1000 catheter days, $p < 0.001$) and CLAT incidence rate (2.7 vs 10%, $p =$ 0.016) were also lower at this site.

Conclusion: BCV catheterization via the US-guided supraclavicular approach may decrease CVC maintenance-related complications in children hospitalized in a PICU.

What is Known:
- *Placement of a central venous catheter (CVC) in children is associated with mechanical risks during insertion, and with infectious and thrombotic complications during its maintenance.*
- *Ultrasound (US)-guided supraclavicular catheterization of the brachiocephalic vein (BCV) is feasible in infants and children.*

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What is New:
- *This observational study suggested that BCV catheterization* via *the US-guided supraclavicular approach was associated with a lower risk of CVC insertion and maintenance-related complications, compared with the other catheterization sites.*

Keywords Brachiocephalic vein · Catheter-associated bloodstream infection · Catheter-associated deep-vein thrombosis · Children · Supraclavicular approach · Ultrasound guidance

Abbreviations

BCV	brachiocephalic vein
CDC	Centers for Disease Control and Prevention
CLABSI	central line-associated bloodstream infection
CLAT	central line-associated deep vein thrombosis
CVC	central venous catheter
NHSN	National Healthcare Safety Network
PICU	pediatric intensive care unit
PIM	pediatric index of mortality
US	ultrasound

Introduction

The placement of a central venous catheter (CVC) is a common procedure in pediatric intensive care units (PICUs) for the administration of parenteral nutrition and medication. The risks are mechanical complications, mainly during insertion, and infectious and thrombotic complications during its maintenance. Preventing these adverse events is a priority. CVC (i.e., central line)-associated bloodstream infection (CLABSI) in particular generates increased mortality, morbidity, and cost, and CVC-associated deep vein thrombosis (CLAT) has been associated with catheter malfunction, venous congestion, chylothorax, and pulmonary and systemic embolism [6, 30].

In children as in adults, increasing evidence argues for two-dimensional ultrasound (US) guidance of CVC insertion to improve the success rate and reduce mechanical complications [1]. Most of the studies have been conducted in the operating room by anesthesiologists, who targeted the internal jugular vein in randomized controlled trials [27]. Recently, the feasibility of a US-guided approach to reach the brachiocephalic vein (BCV) was described in children [25]. Indeed, the supraclavicular fossa leaves sufficient space to position the transducer for an in-plane approach, providing an excellent longitudinal view of the BCV before puncture, regardless of the hemodynamic or respiratory conditions. CVC placement using this technique was also reported to be safe and reliable in the context of a neonatal and/or pediatric ICU [12].

Thus far, no study has assessed the infectious and thrombotic complications occurring after US-guided CVC placement in the BCV of children. Given the anatomical characteristics of this type of catheterization—that is, placement in a large vessel more distant from oral secretions than the internal jugular vein—we hypothesized that this technique would be associated with fewer complications, not only during insertion but also during maintenance. The primary objective of this study was to assess a composite of CLABSI and CLAT, according to the CVC site, in the PICU of a university hospital.

Materials and methods

Setting

This single-center cohort study was conducted from 1 May 2011 to 1 May 2015. The 8-bed unit is the sole referral center for a region of nearly 3 million inhabitants. Children from 1 month to 18 years are admitted for medical or surgical pathologies; surgical correction of the congenital cardiac malformations, however, is not performed in the institution. Term neonates may be hospitalized in the PICU, particularly in the case of congenital malformation or an evaluation made in the pediatric emergency department. The study was approved by the local ethics committee.

Study design

The patients were selected from a prospective database that collects demographics, diagnoses, procedures, and morbidities for all patients admitted to the PICU. Eligible patients were those requiring the placement of a CVC since 2011.

The criteria for noninclusion were (i) a CVC for hemodialysis or hemofiltration, (ii) an umbilical vein or epicutaneocava catheter, and (iii) catheters not placed in the department.

CVC placement and maintenance

CVC placement did not require airway intubation. However, sedation-analgesia (i.e., IV ketamine 1–5 mg/kg), sometimes associated with local anesthesia (i.e., lidocaine 5 mg/kg), was systematic.

The selection of the site was made by the physician in charge of the patient, including junior residents. The decision therefore depended on the operator's experience and the patient specificities (emergent situation, bleeding diathesis, skin lesions on a CVC placement site).

The maximal sterile barrier during insertion included surgical hand antisepsis, a surgical mask and cap, sterile gloves, and a long-sleeved gown.

The antiseptic procedures were in accordance with the institutional recommendations for skin preparation before CVC placement. For infants under 30 months of age, the four steps are as follows: skin scrubbing with Biseptine®, a combination of 0.25% chlorhexidine, 0.025% benzalkonium chloride, and 4% benzylic alcohol-drying with sterile gauze-a second application of Biseptine®-spontaneous drying. In infants over 30 months of age, the steps are as follows: skin scrubbing with 4% chlorhexidine-rinsing with sterile water-drying with sterile gauze-application of 0.5% chlorhexidine in 70% ethanol-spontaneous drying.

CVC placement was carried out bedside using the Seldinger technique. Since 2011, the supraclavicular approach to the BCV has systematically been US-guided, with a Philips CX50 (Philips Healthcare, the Netherlands) equipped with wide-band linear probes L15-7io (7 to 15 MHz) and L12-3 (3 to 12 MHz). We used real-time US needle guidance with an in-plane technique, with the operator holding the US probe in one hand and manipulating the needle with the other. The US probes and cables were protected by a sterile sheath, and a sterile gel was used for the US guidance procedure. US guidance was left to the clinician's initiative for the other catheterization sites—that is, femoral, subclavian, or jugular.

The CVCs were standard polyurethane catheters. Heparin-bonded and antibiotic- or antiseptic-impregnated CVCs were not used. Prophylactic anticoagulation with unfractionated heparin was not systematic but could be used in cases of high risk of thrombosis, usually at a dose of 0.5–1 units/kg per hour. Written protocols for the measures concerning CVC maintenance were strictly followed, notably for CVC dressing and changes and the installation, use and replacement of the administration set (Octopus with Bionector, Vygon, France), and tubing.

CLABSI was systematically considered in cases of hyperthermia, unexplained clinical deterioration, CLAT, inflammatory biological reaction, or unexpected biological abnormality [6].

CLAT was systematically considered in cases of catheter dysfunction (e.g., increase in perfusion pressure or absence of venous return), CLABSI, sepsis, edema in the CVC drainage territory, vena cava syndrome, chylothorax, or pulmonary or systemic embolism [6].

Data collection

Information on the CVC recorded in the database included its characteristics (length, diameter, number of lumens), the operator (junior or senior), the site, number of attempts, duration of the procedure, use of US guidance, and complications occurring at insertion (arterial puncture, massive bleeding, pneumothorax) and during maintenance—that is, CLABSI and/or CLAT.

In addition, the medical files of all CVC patients were reviewed to assess risk factors of thrombosis, whether medical (e.g., age, cardiac disease, trauma, burns, hematologic disease, chylothorax, dehydration) or biological (e.g., hyperleukocytosis, congenital or acquired thrombophilia, disseminated intravascular coagulation).

CLABSI was confirmed following a protocol for monitoring nosocomial infections (NI) implemented in the Department of Neonatology and the PICU in 2009 [8]. Briefly, potential NIs were tracked from alerts generated by a computerized physician order entry system and were then individually reviewed weekly by an expert group to consensually confirm or withdraw the diagnosis and validate the type of NI, the site, the causal microorganism, and the antibiotic resistance profile. The group used the definitions of the Centers for Disease Control and Prevention (CDC) and the National Healthcare Safety Network (NHSN) for healthcare-associated infections [17].

The diagnosis of CLAT was validated only after confirmation of the diagnosis by a Doppler-US examination, performed by a pediatric radiologist.

Outcomes

The primary outcome was the incidence of CVC maintenance-related complications, from the time of catheter insertion to 48 h after catheter removal. Maintenance-related complications were defined as a composite of CLABSI and CLAT, regardless of which occurred first [23].

Secondary outcomes included the incidence of immediate mechanical complications, the risk factors of immediate and maintenance complications, and the time to occurrence of maintenance-related complications during CVC use.

Statistical analysis

For categorical variables, the comparisons were made using Chi^2 or Fischer's exact test if Chi^2 was not a valid test. For continuous variables, the distributions were tested with the Shapiro-Wilk method and not all were found to be normal. Thus, results are shown as medians and ranges, and comparisons were made using nonparametric tests (Mann-Whitney Wilcoxon or Kruskal-Wallis tests). The occurrence of CVC maintenance-related complications was estimated by the Kaplan-Meier product-limit estimator. Risk factors of CLABSI and CLAT were assessed by testing the interaction term between each pairwise comparison and the characteristics of the population, including demographics, admission pattern, biological data, and treatments; the characteristics of the CVC, including placement procedure and site; and the presence of another CVC maintenance-related complications. A multiple logistic regression model with stepwise forward variable selection was performed to identify significant

Table 1 Characteristics of the population according to the catheterization site

	Supraclavicular CVC (*n* = 147)	Other CVC sites (*n* = 110)	*p*
Demographics			
Age (months)	4.6 (0.7–38.7)	12.5 (2.4–41.6)	0.014
Weight (kg)	6.4 (3.2–16.0)	10.1 (4.0–17.0)	0.063
Female	72 (49)	44 (40)	0.165
PIM 2	6.2 (1.8–17.8)	7.2 (2.1–25.9)	0.209
Admission pattern			
Post-surgery	23 (15.6)	14 (12.7)	0.592
Organ disease or failure			
neurological	56 (38.1)	27 (24.5)	0.023
respiratory	22 (15)	33 (30)	0.005
severe sepsis	19 (12.9)	13 (11.8)	0.850
gastrointestinal/hepatic	17 (11.6)	8 (7.3)	0.292
cardiac	12 (8.2)	9 (8.2)	1.000
renal/metabolic	10 (6.8)	8 (7.3)	1.000
trauma and burns	8 (5.4)	10 (9.1)	0.324
hematologic	3 (2)	2 (1.8)	1.000
Biology			
platelet count (10^9/L)[a]	295.5 (221.5–394.0)	340.0 (192.0–429.0)	0.440
fibrinogen (g/L)[b]	3.0 (2.1–4)	2.7 (1.7–3.6)	0.076
PTT (%)[c]	77 (62–90)	74 (53–86)	0.160
prothrombin time (P/C ratio)[d]	1.05 (0.92–1.30)	1.06 (0.90–1.30)	0.780
Treatment			
Antithrombotic	18 (12.2)	20 (18.2)	0.215
preventive	12 (8.2)	14 (12.7)	0.296
curative	6 (4.1)	6 (5.4)	0.767
Antibiotic	103 (70)	73 (66.4)	0.588
Risk factors of thrombosis			
Clinical risk factors[e]	108 (73)	72 (65)	0.171
Biological risk factors[f]	0 (0)	3 (2.7)	0.077

Values are expressed as medians (Q25-75) or numbers (%)

CVC central venous catheter, *PIM* pediatric index of mortality, *PTT* partial thromboplastin time, *P/C ratio* patient/control time ratio

For the biological tests, the respective numbers for supraclavicular CVCs and other site CVCs were [a] 143 and 109, [b] 95 and 78, [c] 98 and 84, [d] 97 and 82

[e] Including age < 1 year or > 14 years, dehydration > 10% of body weight, cardiac disease, trauma, burns, hematologic diseases, and chylothorax

[f] Including hyperleukocytosis > 100,000/mm^3 , congenital or acquired thrombophilia, and disseminated intravascular coagulation

independent risk factors for the primary outcome. The significance level for entering a variable in the model was $p < 0.2$. A p value < 0.05 was considered statistically significant. SAS software was used for all statistical analyses (Cary, NC, USA).

Results

One thousand five hundred and fifty-eight patients were admitted to the PICU during the study period, corresponding to 8478 hospitalization days. Among them, 225 (14.5%) required CVC placement, including 24 patients requiring 2 successive CVCs and 4 requiring 3, giving a total of 257 CVCs and 2967 catheter days. The CVC utilization ratio was 0.36 (0.34–0.40).

Characteristics of the population according to the catheterization site (Table 1)

The supraclavicular approach to the BCV was performed in 147 (57.2%) patients. The other CVC insertion sites were the

Table 2 Characteristics of the CVC placement procedure according to the catheterization site

	Supraclavicular CVC ($n = 147$)	Other CVC sites ($n = 110$)	p
Awake patient	57 (38.8)	35 (31.8)	0.293
Urgent placement[a]	131 (89.1)	84 (76.4)	0.010
Senior operator	85/140 (60.7)	73/99 (73.7)	0.039
Ultrasound guidance	147 (100)	60 (54.6)	< 0.001
CVC/CBW ratio	0.584 (0.281–0.961)	0.458 (0.292–0.869)	0.429
Procedure duration (min)	30 (16–50)	40 (30–60)	0.018
Success at first puncture	87/133 (65.4)	38/74 (51.4)	0.073

Values are expressed as medians (Q25-75) or numbers (%)

CVC/CBW: ratio of the central venous catheter external diameter to the child's body weight

[a] Placement within the first 2 h following admission or for sudden severe clinical worsening

femoral (29.2%), the jugular (2.3%), and the subclavian (11.3%), using the infraclavicular approach.

Children with supraclavicular CVC were younger and differences were observed in their admission pattern, with respiratory distress being less frequent and neurological symptoms (mainly status epilepticus and non-traumatic coma) more frequent compared with children with CVCs placed in other sites. The pediatric index of mortality (PIM), risk factors of thrombosis, laboratory coagulation tests, and antithrombotic and antibiotic treatments were comparable between groups.

Characteristics of the CVC placement procedure according to the catheterization site (Table 2)

Supraclavicular catheterization of the BCV was more frequent in a context of emergency and less frequently performed by a senior operator. US guidance was systematic, and the duration of the procedure—from preparation of the operative field to the end of the sterile occlusive dressing—was shorter with this technique. The ratio of the CVC's external diameter to the child's body weight was comparable between groups.

CVC-related complications according to the catheterization site

Arterial puncture was less frequent with the supraclavicular catheterization procedure. No other difference was observed for immediate mechanical complications (Table 3).

CVC maintenance-related complications occurred in 26 cases (10.12%) out of the entire cohort, including 15 cases of CLABSI, 15 cases of CLAT, and 4 cases of associated CVC infection and thrombosis.

In the cases of CLABSI, a single microorganism was isolated in the blood cultures. The most common microorganism was coagulase-negative *Staphylococci* (9 cases), but we also found *Staphylococcus aureus* in 3 cases, gram-negative bacteria in 2 cases (*Escherichia coli* and *Klebsiella pneumoniae*), and *Candida tropicalis* in 1 case. As 2902 catheter days were free of infection, the CLABSI incidence density rate was 5.17 per 1000 catheter days.

CVC maintenance-related complications occurred less frequently with the supraclavicular catheterization procedure (5.4 vs 16.4%; OR: 0.29; 95% CI: 0.12–0.70; $p = 0.006$). While the CLABSI incidence rate was not significantly different, CLABSI incidence density rate and CLAT incidence rate were also lower with this technique (Table 4).

The rates of CLABSI and CLAT occurring with or without the supraclavicular catheterization procedure are shown on Fig. 1a, b. The median time to onset of CLABSI was 14 (6–16) days for the supraclavicular site and 11 (9–15) days for the others sites ($p = 0.771$). For CLAT, these delays were, respectively, 15.5 (9–25.5) and 7 (6–21) days ($p = 0.157$).

Subgroup analysis

Logistic regression analysis for the occurrence of CLABSI revealed a higher risk associated with the presence of CLAT

Table 3 Immediate mechanical complications during catheterization

	Supraclavicular CVC ($n = 147$)	Other CVC sites ($n = 110$)	p
Multiple punctures (≥ 3)	24/133 (18)	19/74 (25.7)	0.21
Arterial puncture	2 (1.4)	8 (7.3)	0.006
Pneumothorax	0 (0)	1 (0.91)	0.428
CVC misplacement[a]	8 (5.4)	5 (4.5)	1.00

Values are expressed as numbers (%)

[a] Abnormal route and/or tip position of the central venous catheter (CVC)

Table 4 CVC maintenance-related complications according to the catheterization site

	Supraclavicular CVC ($n = 147$)	Other CVC sites ($n =$ 110)	p
CLABSI and/or CLAT	8 (5.4)	18 (16.4)	0.006
CLAT	4 (2.7)	11 (10)	0.016
CLABSI	5 (3.4)	10 (9.1)	0.063
CVC length of use (days)	10 (6–17)	8 (4–14)	0.036
CVC days free of infection	1786 (99.50%)	1116 (95.22%)	< 0.001
CLABSI incidence density rate (per 1000 catheter days)	2.8	8.96	< 0.001

Values are expressed as medians (Q25-75) or numbers (%)

CVC central venous catheter, *CLABSI* central line-associated bloodstream infection, *CLAT* central line-associated deep vein thrombosis

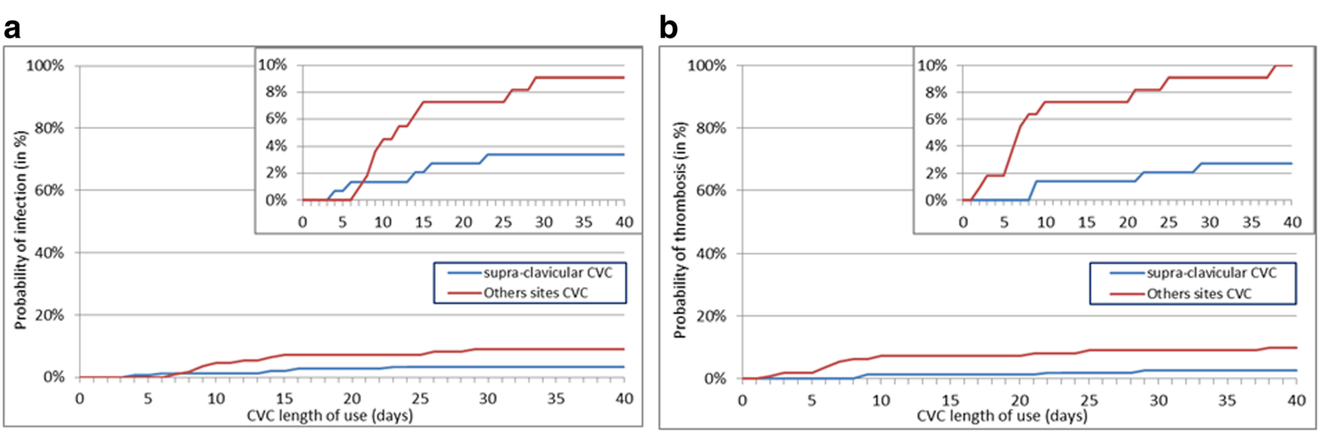
(OR = 12.8 [95% CI, 2.29 to 62.9], $p = 0.0018$). For the occurrence of CLAT, logistic regression analysis revealed higher risks associated with catheterization of the femoral vein (OR = 6.11 [95% CI, 1.77 to 25.6], $p = 0.0064$) and CLABSI (OR, 9.8 [95% CI, 2.08 to 43.25], $p = 0.026$).

Among the 257 CVCs, 53 (20.6%) had been placed with the landmark technique and 204 (79.4%) with the US-guided technique. Immediate complications occurred in 9 patients (17%) in the first group vs 15 (7.4%) in the second ($p =$ 0.06). CVC maintenance-related complications, notably the occurrence of CLABSI and/or CLAT, were observed in 9 patients (17%) in the first group vs 17 (8.3%) in the second ($p =$ 0.07).

Discussion

This observational study of infants hospitalized in a PICU found that BCV catheterization via the US-guided supraclavicular approach was associated with a lower risk of CVC maintenance-related complications, compared with the other catheterization sites.

Studies on central line and ventilator bundles in pediatric patients are limited [3, 29], and their scientific basis is not as robust as in adults [28]. It has been suggested that the main drivers for reducing pediatric CLABSI are related to CVC maintenance rather than insertion [22]. In any case, some of the guidelines for insertion bundles, like avoiding the femoral vein, are debated with regard to infants and children, and this has resulted in a clear divergence between recommendations and practices [14]. In many adult ICUs, US guidance is now the standard of care for central venous access, but this practice is less widespread for pediatric CVC placement. In this study, visualization of the target vein with a real-time two-dimensional US technique was nearly systematic, used for the placement of 80% of the CVCs. According to our results, however, the use of the US-guided technique did not significantly reduce the complications associated with CVC insertion and maintenance. Senior physicians, especially the older ones, were more likely to select traditional sites, notably the femoral and the subclavian, and the landmark method of CVC



No.									
a SC	0	1	2	3	4	5	5	5	5
a OS	0	0	5	8	8	8	10	10	10
b SC	0	0	2	2	2	3	4	4	4
b OS	0	2	8	8	8	10	10	10	11

Fig. 1 Cumulative probability of CVC-related infection (**a**) and CVC-related thrombosis (**b**) with supraclavicular CVC (SC, blue, $n = 147$) and CVC inserted in other sites (OS, red, $n = 110$)

guidewire placement. Indeed, the current curriculum for PICU physicians in our institution now includes a systematic residency of 6 months in the pediatric operating room, where they are trained in real-time US needle guidance with an in-plane technique.

As in a recent meta-analysis including mainly adult patients, we found less risk of inadvertent arterial puncture using US for supraclavicular catheterization [1]. Consistent with previous reports, the BCV was successfully punctured on the first attempt in two thirds of our patients [2], and the entire placement procedure was shorter with this technique [4]. Moreover, we found a lower CLABSI incidence density rate, which may have resulted from decreased extraluminal colonization of the CVC from the cutaneous microbiota. In accordance with other studies carried out in children, most CLABSI in our cohort were caused by gram-positive organisms, particularly coagulase-negative *Staphylococci* [9, 11, 15]. However, two cases of CLABSI in young infants, one involving coagulase-negative *Staphylococci* and the other a *Staphylococcus aureus*, occurred, respectively, 4 and 6 days following supraclavicular catheterization of the BCV. These early CLABSI suggested that, despite the use of sterile US cover shields, the presence of the transducer in the puncture field may be a local source of contamination during CVC insertion. According to the recommendations of the French Society of Hospital Hygiene, the skin of infants less than 30 months old should be prepared with chlorhexidine and alcohol at low concentrations. The use of chlorhexidine in 70% alcohol, probably more effective in terms of antisepsis [5], is optional at this young age. This age group is nevertheless predominant in our PICU, and our policy now needs to be reviewed to ensure a procedure for US guidance in stringent aseptic conditions.

Although supraclavicular CVCs were used in younger patients and for longer periods, we observed markedly lower rates of CLAT following catheterization of this site compared with the others. Interestingly, our multivariate analyses also showed the strong relationship between the occurrences of CLAT and CLABSI. The fibrin sheath that develops inside and around the catheter promotes bacterial adherence and growth, particularly of coagulase negative *Staphylococci*, which produce a slime that protects the microorganism from the clearance mechanisms of the host defense [10]. Previous studies in children and a meta-analysis in adults have demonstrated a reduction in the incidence of both infection and thrombosis when heparin-bonded CVCs are used [18, 24].

It is likely that the systematic US guidance for supraclavicular catheterization of our patients helped reduce vessel wall injury, which is the first step in the process of thrombogenesis. Furthermore, a CVC inserted in the BCV follows a less marked curve and has shorter and more direct access to the heart than if it penetrates the subclavian vein between the clavicle and the first rib. This pathway may result in less adhesion to the vascular walls, less obstruction of the flow and, therefore, a lower risk of thrombosis [20]. The ratio of the size of the CVC to the size of the vessel is also an important factor to consider. It is particularly high in cases of femoral vein access in infants [13], and it appears more favorable when the BCV is catheterized. In neonates, the blood flow in the superior vena cava accounts for nearly 50% of cardiac output, increases to a maximum of 55% at the age of 2.5 years, and reaches the adult value of 35% by 6.6 years of age [26]. This maturational change, related to somatic growth, also explains the lower susceptibility to thrombosis in this territory in the presence of a CVC.

Our observational study has several limitations, including a short period of observation, a limited number of infants, and its monocentric nature. Information was sometimes missing in the CVC-specific files, which were only completed if the CVC had actually been placed. Thus, our database does not provide information on the failure rate of CVC placement in the PICU or the main causes for these failures. A randomized controlled trial would have reduced the sources of bias associated with observational studies. In children and neonates, the routine use of US guidance is now recommended for short- and long-term central venous access [19], which may complicate the initiation of such trials. Indeed, the populations most exposed to CLABSI and CLAT, such as burn, cardiovascular, and hematologic disease patients [7], were a minority in our cohort and equally distributed among groups. Last, the results from our PICU provide insight into how a specific bundle implementation—in the present study, the optimal catheter site selection—fits within a broader quality improvement strategy [21].

Conclusions

The CLABSI incidence density rate observed in our PICU was consistent with the rate calculated in 2012 for English PICUs [16], but still higher than those recently observed by other networks, notably in the USA [7]. Improvement of catheter maintenance-related complications in our unit will require more stringent compliance with CVC bundle policies. Our next step will be to reassess our antiseptics policy and increase education and training for vascular access placement in the aim of further reducing the risks occurring at CVC insertion.

Authors' Contributions Flora Habas Julien Baleine and Gilles Cambonie conceived and designed the study, contributed to the search of published work, data acquisition, data interpretation, drafted, and finalized the report.

Christophe Milési and Clémentine Combes performed data analysis, contributed to data interpretation, and critically revised the report.

Marie-Noëlle Didelot, Sara Romano-Bertrand, Delphine Grau, and Sylvie Aubas critically revised the report and made substantial contributions on the final manuscript.

Catherine Baud contributed to data acquisition and critically revised the report.

Compliance with ethical standards The study was approved by the local ethics committee.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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