Pediatric Radiology (2021) 51:1481–1486
https://doi.org/10.1007/s00247-021-05019-6

ORIGINAL ARTICLE

Line days as a determinant of central line-associated bloodstream infections in pediatric patients with tunneled femoral peripherally inserted central catheters

Kevin S. H. Koo[1] · Andrew B. Cooper[2] · Eric J. Monroe[1] · Joseph Reis[1] · Giridhar M. Shivaram[1] · Danielle M. Zerr[3]

Received: 12 November 2020 / Revised: 31 December 2020 / Accepted: 11 February 2021 / Published online: 6 March 2021

Abstract

Background Ultrasound (US)-guided tunneled femoral peripherally inserted central catheters (PICCs) are a safe central venous access option in infants and neonates. Studies have shown, however, that femoral central venous access has the potential for high central line-associated bloodstream infection (CLABSI) rates with a significant increase in risk around line day 30, though no studies have evaluated these risks exclusively for tunneled femoral PICCs.

Objective The primary purpose of this study was to evaluate the relationship between line duration and the risk of CLABSI in tunneled femoral PICCs in children.

Materials and methods Four hundred forty-five patients (196 females, 249 males; median age: 49.4 days; median weight: 3.7 kg) who underwent 573 tunneled femoral PICC placements or exchanges from Jan. 1, 2017, to Jan. 31, 2020, were included in the study. All tunneled femoral PICCs were placed using US technique and catheter specifications, including catheter size (French) and length (cm), were retrieved from the electronic medical record. The location of the PICC placement, the number of lumens, the laterality of placement, and the patient's age and weight were also recorded. Only non-mucosal barrier injury CLABSIs, according to the Centers for Disease Control and Prevention (CDC) definitions, were counted as CLABSI for this study. The number of central line days until a CLABSI event was analyzed with an accelerated failure time model using the exponential, Weibull, and log-normal distributions to determine the probability of a CLABSI over time, taking into consideration the recorded covariates.

Results Tunneled femoral PICC placements accounted for 14,855 line days, during which 20 non-mucosal barrier injury CLABSIs (CLABSI rate of 1.35 per 1,000 line days) occurred during the study period. The highest CLABSI rate occurred in PICCs placed in the neonatal intensive care unit (NICU) at 2.01 per 1,000 line days and the lowest occurred in PICCs placed in interventional radiology at 0.26 per 1,000 line days. Overall, PICCs placed outside of interventional radiology had a CLABSI rate of 1.72 per 1,000 line days. The CLABSI rate during the first 30 days a line was in situ was lower than the rate after 30 days (0.51 per 1,000 line days vs. 3.06 per 1,000 line days, respectively). Statistical modeling and hazard estimation using the Akaike information criterion corrected for small sample size (AICc)-average of log-normal, Weibull and exponential distributions demonstrate the daily risk of CLABSI rapidly increases from day 1 to day 30, with the risk remaining high for the duration of line days.

Conclusion While tunneled femoral PICCs are a relatively safe and effective central venous access alternative, the rate of CLABSI appears to rapidly increase with increasing line days until around day 30 and then remains high thereafter.

Keywords Central line-associated bloodstream infection · Infants · Interventional radiology · Line days · Neonates · Peripherally inserted central catheters · Ultrasound

✉ Kevin S. H. Koo
kevin.koo@seattlechildrens.org

[1] Section of Interventional Radiology, Department of Radiology, Seattle Children's Hospital, University of Washington, 4800 Sand Point Way NE, Seattle, WA 98105, USA

[2] Enterprise Analytics, Seattle Children's Hospital, Seattle, WA, USA

[3] Division of Infectious Diseases, Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, WA, USA

Introduction

Ultrasound (US)-guided tunneled femoral peripherally inserted central catheters (PICCs) are a technically feasible and safe central venous access option in infants and neonates [1–3]. Studies have shown that femoral PICCs have the potential for high infection risk with reported central line-associated bloodstream infection (CLABSI) rates between 0.78 and 4.4 per 1,000 line days [4, 5].

While a short subcutaneous tunnel has been shown to confer some protection against central line bacterial colonization, little is known as to how long these effects protect against CLABSI [6, 7]. Some studies have suggested that the risk of CLABSI increases after line day 35 of PICCs in the neonatal intensive care unit (NICU), but no studies have evaluated these risks exclusively for tunneled femoral PICCs [8].

The primary purpose of this study was to evaluate the relationship between line duration and the risk of CLABSI in tunneled femoral PICCs in children. Our hypothesis is that increased tunneled femoral PICC duration is associated with an increased rate of CLABSI.

Materials and methods

This single-center retrospective cohort study was conducted with institutional review board approval and in compliance with the Health Insurance Portability and Accountability Act. Informed consent was not required for this retrospective study. This study was assessed using the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines [9].

All pediatric patients <18 years of age who underwent US-guided single-access tunneled femoral PICC placements and exchanges by interventional radiology, inclusive of bedside procedures and those in the interventional radiology suite, from Jan. 1, 2017, to Jan. 31, 2020, (1,126 days) were included. Patients >18 years of age and those who underwent PICC placement at other anatomical locations were excluded.

Four hundred and forty-five patients (196 females, 249 males) who underwent 573 tunneled femoral PICC placements were included in the study. All tunneled femoral PICCs were placed using sterile surgical techniques as previously described with tip confirmation using US or fluoroscopy depending on procedural location [1, 3, 5]. Bedside procedures were performed with the same sterile surgical patient prep techniques as in the interventional radiology suite except for removing the patient's existing linens, if the patient was unable to be moved. Exchange procedures were performed if additonal lumens were required in a patient with an existing tunneled femoral PICC (i.e. single lumen to double lumen) or if there was clinical evidence of PICC dysfunction. An exchange procedure was performed by removing the existing PICC over a 0.018-in. or a 0.010-in. guidewire (depending on existing PICC size) and reinserting a new tunneled femoral PICC, cut to the same length as the previous PICC, via the same insertion site.

Catheter specifications were retrieved from the electronic medical record. Catheter size was recorded in French (Fr) and single or dual lumens was specified. The length of the catheter and the laterality of the tunneled femoral PICC were collected along with patient age, weight, gender and indication for central access. Central line days were calculated counting one central line day for each day a patient had one or more central lines in place. Bloodstream infection organisms were also recorded. Only non-mucosal barrier injury CLABSIs, according to the Centers for Disease Control and Prevention (CDC) definitions, were counted as CLABSIs for this study [10]. The CLABSI rate was calculated by dividing the total number of non-mucosal barrier injury CLABSIs by the number of central line days and multiplying by 1,000 [11].

The number of central line days preceding a CLABSI event was analyzed with an accelerated failure time model [12]. These models can be used to estimate the potential effects of covariates while also allowing the probability of a CLABSI event to change over time. Exponential, Weibull and log-normal distributions were tested to determine the probability of a CLABSI over time, with the exponential model assuming no change over time and the Weibull and log-normal distributions allowing for different patterns for the change. Focusing on the relationship between line duration and the risk of CLABSI, covariates were analyzed to ensure counfounders were neither hiding nor accentuating the relationship. These covariates included the location of PICC placement, the length of PICC, the number of lumens, Fr size, the laterality of placement, along with the patient's gender, weight, age, race/ethnicity and use of interpretive services. Separate models were fit for each distribution, and the most parsimonious model under each assumed distribution was selected based on a combination of likelihood ratio tests for nested models and Akaike information criterion corrected for small sample size (AICc) for non-nested models [13, 14]. These final models were then compared based on AICc. The relationship between line duration and the risk of CLABSI was then estimated based on AICc model-averaging over all the models that were examined. With AICc model-averaging, the model with the best balance between goodness of fit and complexity receives the highest weight and subsequent models are downweighted based on how their AICc value compares with the best model [14]. Due to the low CLABSI rate of lines placed in interventional radiology, the high CLABSI rate for exchange procedures, as well as their respective low sample sizes, data from line placements in interventional radiology and exchange procedures were excluded from further analyses. The exclusion of these instances was performed post hoc after identifying the impact of these confounders on the final

model. All models were built using the R statistical programming language (v3.6.2; The R Foundation for Statistical Computing, Vienna, Austria).

Results

Of the 573 tunneled femoral PICCs placed, 550 were performed as new placements while the remaining 23 were performed as exchange procedures (12 of which were performed at the bedside). PICC Fr size ranged from 1.9 Fr to 6 Fr with 3 Fr (*n*=264, 46.1%), 1.9 Fr (*n*=197, 34.4%) and 4 Fr (*n*=105, 18.3%) being the most common. Single lumen PICCs (*n*=463, 80.8%) were more common than dual lumen PICCs (*n*=110, 19.2%). The median length of the PICC was 17.0 cm (range: 7–41 cm). Three hundred and fifty-seven (62.3%) PICCs were placed in the right femoral vein while 216 (37.7%) were placed in the left femoral vein.

The median age of the patient at the time of PICC placement was 49.4 days (range: 0.5–5,294.7 days) while median weight was 3.7 kg (range: 0.6–128.4 kg) (Table 1). The most common indication for central venous access was a preexisting cardiac anomaly (*n*=243), followed by unspecified central access needs (*n*=116), total parenteral nutrition dependence (*n*=69) and respiratory distress (*n*=67).

During the 3-year study period, tunneled femoral PICC placements accounted for 14,855 line days, during which 20 non-mucosal barrier injury CLABSIs were recorded, yielding a CLABSI rate of 1.35 per 1,000 line days. The most common CLABSI organism was *Enterococcus* sp. (*n*=4) followed by methicillin-susceptible *Staphylococcus aureus* (MSSA) (*n*=4) and *Serratia* sp. (*n*=3). A complete list of the identified CLABSI organisms are listed in Table 2.

Non-mucosal barrier injury CLABSI, total line days and CLABSI rate by tunneled femoral PICC location of placement are listed in Table 3 with the highest CLABSI rate occurring in PICCs placed in the NICU at 2.01 per 1,000 line days and the lowest occurring in PICCs placed in interventional radiology at 0.26 per 1,000 line days. Overall, PICCs placed outside of interventional radiology had a CLABSI rate of 1.72 per 1,000 line days and accounted for 74.3% of the total line days and 95% of the CLABSIs. Four non-mucosal barrier injury CLABSIs (20% of the total CLABSIs) were identified in patients who underwent an exchange procedure totaling 1,352 line days (9.1% of the total line days) with a CLABSI rate of 2.96 per 1,000 line days. The overall CLABSI rate for those who did not undergo an exchange was 1.18 per 1,000 line days. The CLABSI rate, inclusive of exchange procedures, for the first 30 line days was lower than the CLABSI rate for patients with more than 30 line days (0.51 per 1,000 line days vs. 3.06 per 1,000 line days).

Further analysis of PICCs placed at the bedside was performed using accelerated failure time models with log-normal, Weibull and exponential distributions. For the most

Table 1 Patient demographics and PICC characteristics of patients with tunneled femoral PICCs from 2017 to 2020

	CLABSI (*n*=20)	Non-CLABSI (*n*=553)
Gender		
Male	12	298
Female	8	255
Age		
Median (days)	53.5	49.0
Range	6.6–3,970.0	0.5–5,300.0
Weight		
Median (kg)	3.3	3.7
Range	0.8–50.0	0.6–128.4
PICC French size		
1.9	7	190
2.6	0	1
3	8	256
4	3	102
5	0	2
6	2	2
Number of lumens		
Single	15	448
Dual	5	105
PICC length (cm)		
Median	16.2	17
Range	9–41	7–37

CLABSI central line-associated bloodstream infection, *PICC* peripherally inserted central catheter

Table 2 Organisms accounting for CLABSI in tunneled femoral PICCs from 2017 to 2020

Organism	Count (*n*=20)
Enterococcus species	4
Methicillin-susceptible *Staphylococcus aureus* (MSSA)	4
Serratia species	3
Enterobacter species	1
Pseudomonas species	1
Klebsiella pneumoniae	1
Staphylococcus epidermidis	1
E. coli species	1
Candida species	1
Methicillin-resistant *Staphylococcus aureus* (MRSA)	1
Acinetobacter species	1
Janibacter species	1

CLABSI central line-associated bloodstream infection, *PICC* peripherally inserted central catheter

Table 3 Number of CLABSIs and CLABSI rate of tunneled femoral PICC by location of placement

Location	Number of catheters placed	Number of CLABSIs	Line days	CLABSI rate (#/1,000 line days)
IR	142	1	3,813	0.26
Bedside		19	11,043	1.72
CICU	196	9	5,204	1.73
NICU	158	8	3,980	2.01
PICU	77	2	1,859	1.08

CICU cardiac intensive care unit, *CLABSI* central line-associated bloodstream infection, *IR* interventional radiology, *NICU* neonatal intensive care unit, *PICC* peripherally inserted central catheter, *PICU* pediatric intensive care unit

parsimonious model under each distribution (the model with the lowest AICc), the exponential distribution had the most support, though the models with log-normal and Weibull distributions had AICc values within two points of the exponential, indicating substantial support for these other distributions as well. All models within 10 AICc points of the most parsimonious model for each distribution were then selected. The hazard function across the total set of models with covariates set to their median (for continuous variables) or modal value (for categorical variables) was then averaged, weighted by their AICc. The resulting model-averaged hazard function demonstrates that daily risk rapidly increases from day 1 through day 30, with the risk remaining relatively stable for the duration of line days (Fig. 1). Applying the same approach to patients who underwent a PICC exchange demonstrated that the risk of developing a CLABSI is highest on the first day, and then levels off to a risk that is nearly three times the maximum risk of patients who did not have their PICCs exchanged (Fig. 2).

Discussion

In this study of 573 tunneled femoral PICCs, an increased duration of central venous access was associated with a higher rate of CLABSI even after controlling for other factors. As patients who require tunneled femoral PICCs are often critically ill, it is important to consider how this observation may more reasonably inform the optimal duration of such devices and guide clinicians to consider alternative central venous access when nearing the 30-day mark.

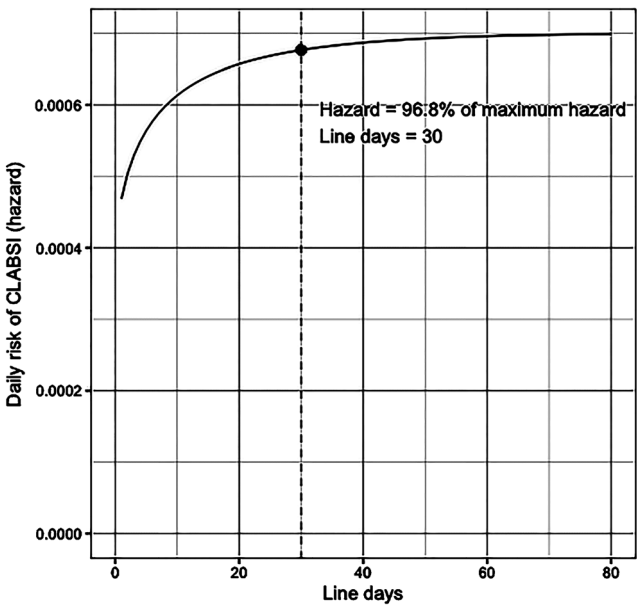

Fig. 1 Daily risk of central line-associated bloodstream infection (CLABSI) as a function of line duration, excluding non-bedside and peripherally inserted central catheter (PICC) exchange procedures. All other covariates are set at their median (for continuous variables) or their mode (for categorical variables). The hazard rapidly increases with increasing duration until around day 30 and then remains at this high level

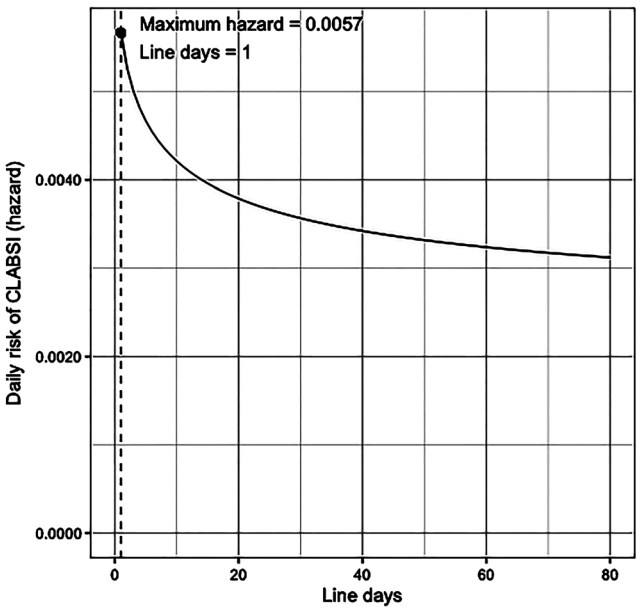

Fig. 2 Daily risk of central line-associated bloodstream infection (CLABSI) as a function of line duration for PICC exchange procedures performed at the bedside. All other covariates are set at their median (for continuous variables) or their mode (for categorical variables). The hazard is at its maximum of 0.0057 on the first day and then decreases over time to reach an asymptote at around 0.003

While the overall CLABSI rate reported in this study (1.35 per 1,000 line days) is consistent with rates reported in the literature (0.78 and 4.4 per 1,000 line days), tunneled femoral PICCs left in place for longer than 30 days had a significantly higher rate of CLABSI in our series [4, 5]. This is consistent with existing literature that suggests PICCs left in for longer than 35 days in the perinatal period have a higher rate of infection [8].

The existing literature on CLABSI has produced varying conclusions on the appropriate duration of PICCs with some concluding that 25 days is an optimal cutoff to avoid CLABSI while others have suggested an indefinite duration may be appropriate [15, 16]. This is understandable given the many potentially confounding factors that contribute to CLABSI. Greenberg et al. [17] reported that increased dwell time of PICCs was not associated with increased risk of CLABSI in a retrospective cohort of 13,327 patients. PICCs in their cohort were not specific to tunneled femoral PICCs, however. As our study reports, this may be an important distinction and may provide an additional layer for risk stratification of PICCs with respect to CLABSI.

The decision to eliminate PICCs placed in interventional radiology and PICC exchange procedures from the final model was based on the low sample size of both instances and the low rate of CLABSI in lines placed in interventional radiology and the conversely high rate of CLABSI in PICC exchange procedures. Eliminating these two occurrences allowed the model to focus more narrowly on similar procedural conditions without further increasing the number of confounders. Indeed, our modeling analysis demonstrates that the risk of CLABSI for these central venous catheters rises precipitously over the first 30 days and remains high for the duration of line days in our patient population. This risk seems to persist despite the possible protective effects of the subcutaneous tunnel [6, 7]. Given that most of the infections seen in our series are enteric based, the subcutaneous tunnel may only offer limited protection in the post-procedure period.

The CLABSI rate in our study also differed significantly by procedural location, with all bedside procedures having a higher CLABSI rate when compared to tunneled femoral PICCs placed in interventional radiology, counter to the experience of Chau and colleagues [5]. The potential for transmitting microorganisms is well described in the hospital environment, particularly when considering high-touch patient areas such as patient beds, curtains and telephones [18, 19]. As such, the higher infection rates of bedside procedures despite perioperative precautions, sterile technique and proper draping may be explained by lapses in sterile technique involving the environment, which likely differs from that found in a procedural suite. Alternative explanations for the higher CLABSI rate in lines placed at the bedside is the underlying severity of illness of the patient driving the need for bedside procedures, multiple unsuccessful vascular access attempts prompting interventional radiology consultation and difficulty maintaining femoral catheter exit site sterility over the duration of vascular access.

Exchange procedures of existing tunneled femoral PICCs in our series also accounted for significantly higher CLABSI rates. It is well documented in the literature that line exchange procedures have a higher rate of infection, with McCoy et al. [20] citing a 25-fold increase in insertion-related CLABSI with PICC exchanges [20–22]. Coupling this risk with the fact that the majority of the exchange procedures (12/23) were done at the bedside likely compounded the risk for CLABSI in our series. Prophylactic antibiotics could be utilized during line exchange procedures to mitigate this risk, but the lack of data to support or refute its use has led to sporadic applications in clinical practice. Interestingly, the risk of CLABSI appeared highest in the immediate days following a PICC exchange with the risk falling with increasing line day duration. This may be an argument for antibiotic use during the exchange of these lines though further research will be needed to validate this claim. Similarly, future work may address any benefit of antibiotic impregnated PICCs in these specific circumstances. Lastly, while our experience suggests that establishing de novo access would likely decrease CLABSI rates compared to PICC exchange procedures, that potential benefit must be weighed against long-term vascular access preservation.

Limitations of the study include its single-institution setting and its retrospective design. In addition, we were unable to control for all potential confounders, such as different underlying diagnoses. Despite utilizing regression analysis to control for these factors, contributing factors to CLABSI are multifaceted and some of these factors are likely not captured in this study.

Conclusion

While tunneled femoral PICCs are a relatively safe and effective central venous access alternative in some children, the rate of CLABSI in these catheters increases with increasing line days. Similarly, the guidewire exchange of tunneled femoral PICCs and the placement of these catheters at the bedside are also associated with higher CLABSI rates. The duration of use of tunneled femoral PICCs and the location in which they are placed should therefore be closely monitored.

Declarations

Conflicts of interest None

References

1. Subramanian S, Moe DC, Vo JN (2013) Ultrasound-guided tunneled lower extremity peripherally inserted central catheter placement in infants. J Vasc Interv Radiol 24:1910–1913
2. Gaballah M, Krishnamurthy G, Keller MS et al (2014) US-guided placement and tip position confirmation for lower-extremity central venous access in neonates and infants with comparison versus conventional insertion. J Vasc Interv Radiol 25:548–555
3. Lungren MP, Pabon-Ramos WM (2013) Single-incision technique for placing femoral tunneled central venous catheters in infants. J Vasc Interv Radiol 24:755–756
4. Gaballah M, Krishnamurthy G, Berman JI et al (2015) Lower extremity vascular access in neonates and infants: a single institutional experience. J Vasc Interv Radiol 26:1660–1668
5. Chau A, Hernandez JA, Pimpalwar S et al (2018) Equivalent success and complication rates of tunneled common femoral venous catheter placed in the interventional suite vs. at patient bedside. Pediatr Radiol 48:889–894
6. Timsit JF, Bruneel F, Cheval C et al (1999) Use of tunneled femoral catheters to prevent catheter-related infection. Ann Intern Med 130: 729–735
7. Nahum E, Levy I, Katz J et al (2002) Efficacy of subcutaneous tunneling for prevention of bacterial colonization of femoral central venous catheters in critically ill children. Pediatr Infect Dis J 21: 1000–1004
8. Sengupta A, Lehmann C, Diener-West M et al (2010) Catheter duration and risk of CLA-BSI in neonates with PICCs. Pediatrics 125:648–653
9. von Elm E, Altman DG, Egger M et al (2007) The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 147:573–577
10. Torres D, González ML, Loera A et al (2016) The Centers for Disease Control and Prevention definition of mucosal barrier injury-associated bloodstream infection improves accurate detection of preventable bacteremia rates at a pediatric cancer center in a low- to middle-income country. Am J Infect Control 44:432–437
11. Centers for Disease Control and Prevention (2020) Bloodstream infection event (central line-associated bloodstream infection and non-central line associated bloodstream infection). https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf. Accessed 2 Sep 2020
12. Wei LJ (1992) The accelerated failure time model: a useful alternative to the cox regression model in survival analysis. Stat Med 11: 1871–1879
13. Harrell FE (2015) Regression modeling strategies: with applications to linear models, logistic and ordinal regression, and survival analysis, 2nd edn. Springer International Publishing, Switzerland
14. Burnham KP, Anderson DR (2002) Model selection and multimodel inference: a practical information-theoretic approach, 2nd edn. Springer-Verlag, New York
15. Park S, Moon S, Pai H, Kim B (2020) Appropriate duration of peripherally inserted central catheter maintenance to prevent central line-associated bloodstream infection. PLoS One 15:e0234966
16. Ullman AJ, Bernstein SJ, Brown E et al (2020) The Michigan appropriateness guide for intravenous catheters in pediatrics: miniMAGIC. Pediatrics 145:S269–S284
17. Greenberg RG, Cochran KM, Smith PB et al (2015) Effect of catheter dwell time on risk of central line-associated bloodstream infection in infants. Pediatrics 136:1080–1086
18. Dancer SJ, White L, Robertson C (2008) Monitoring environmental cleanliness on two surgical wards. Int J Environ Health Res 18: 357–364
19. Dancer SJ (2009) The role of environmental cleaning in the control of hospital-acquired infection. J Hosp Infect 73:378–385
20. McCoy M, Bedwell S, Noori S (2011) Exchange of peripherally inserted central catheters is associated with an increased risk for bloodstream infection. Am J Perinatol 28:419–424
21. Guttmann DM, Trerotola SO, Clark TW et al (2011) Malfunctioning and infected tunneled infusion catheters: over-the-wire catheter exchange versus catheter removal and replacement. J Vasc Interv Radiol 22:642–646
22. Gnannt R, Patel P, Temple M et al (2017) Peripherally inserted central catheters in pediatric patients: to repair or not repair. Cardiovasc Intervent Radiol 40:845–851