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Risk factors for recurrent central line-associated bloodstream infections in a pediatric intensive care unit

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Background/aim: It is recommended that a central venous catheter (CVC) be removed if central line-associated bloodstream infection (CLABSI) has been diagnosed. The objective of this retrospective study was to evaluate the risk factors for recurrent CLABSI in reinserted catheters in a pediatric intensive care unit.

Materials and methods: Patients with recurrent and nonrecurrent CLABSI were compared in terms of the catheter exchange interval, the interval between negative blood culture and reinsertion of the CVC, and the pre-/reinsertion treatment duration.

Results: Thirty-one patients with initial CLABSI had reinserted CVCs, and 12 (38.7%) of these patients were diagnosed with recurrent CLABSI. In the recurrent group, the catheter exchange interval, the interval between negative blood culture and reinsertion of the second CVC, and pre-/reinsertion treatment duration were found to be shorter. Logistic regression analysis revealed that if the interval between negative blood culture and reinsertion of the second CVC was shorter than 4 days, recurrent CLABSI risk increased by 1.7-fold (P = 0.021). Sterile gauze-dressed patients had shorter cumulative catheter surveys than the polyurethane-dressed patients (P = 0.005). **Conclusion:** Using transparent polyurethane dressings instead of sterile gauze for maintaining the CVC and delaying the reinsertion procedure for at least 4 days after the negative culture might be helpful in preventing recurrent CLABSI.

Key words: Central line-associated bloodstream infections, risk factors for recurrence, pediatric intensive care unit

1. Introduction

Central venous catheters (CVCs) are essential for the management of children in intensive care units. CVCs are not only useful for the administration of medications, blood products, parenteral nutrition, and fluid therapy; they are also essential for invasive procedures such as hemodynamic monitorization and plasmapheresis. One of the most important complications of CVCs are central line-associated bloodstream infections (CLABSIs), which are associated with high morbidity and mortality in addition to increased medical costs due to longer hospital stays and the use of more expensive antimicrobial drugs (1–3).

Once a CLABSI is suspected, general recommendations include removal of the catheter for nontunneled CVCs (4,5). However, in practical clinical settings, a substantial number of patients with CLABSIs require reinsertion of their CVCs since these patients still require reliable persistent venous lines for their ongoing therapy. Data related to the risk factors associated with recurrent

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CLABSI following catheter removal and reinsertion are limited to a few studies, most of which focused on adult patients only (6–8).

In this study, we focused on the risk factors of the recurrence of CLABSI in a retrospective cohort of children in a pediatric intensive care unit (PICU) following catheter reinsertion.

2. Materials and methods

2.1. Study population, hospital setting, and inclusion/ exclusion criteria

In this retrospective study, the clinical data of patients between the ages of 1 month old and 18 years old and hospitalized at the PICU of Dr. Behçet Uz Children's Research and Training Hospital from July 2012 to July 2014 were collected. Dr. Behçet Uz Children's Hospital is a tertiary-care pediatric teaching hospital. At the time of the study, the PICU had 24 beds and 772 patients were hospitalized annually there. The study was approved by the institutional research board. A retrospective cohort of patients with CLABSIs was formed by using clinical data. Among the patients with CLABSI, those who had had a reinserted, nontunneled CVC formed the study group. Clinical findings and microbiological data were analyzed for the risk of recurrent CLABSI in this group.

Patients who had more than one CVC at the same time or whose CVC duration was shorter than 48 h were excluded from the study. Patients with persistent CLABSI were also not enrolled in this study.

2.2. Central venous catheter insertion technique

For the catheterization process, 1, 2, or 3 lumen polyurethane nontunneled temporary catheters (B. Braun, Melsungen, Germany) were chosen. None of them were antimicrobial-impregnated catheters. Before the implementation process and according to the guidelines of the Centers for Disease Control and Prevention (CDC), hand hygiene was ensured and powder-free sterile gloves, a mask, a cap, and a sterile scrub suit were worn (4). For skin antisepsis, 10% povidone iodine or 2% chlorhexidine solutions were used. The entire body of the patient, with the exception of the intervention site, was covered with sterile drapes. Catheters were inserted using the Seldinger technique. For the dressing of the catheter site, the first choice was a transparent polyurethane cover (Tegaderm, 3M Medical, St Paul, MN, USA) and whenever that was not possible sterile gauze was used instead. The transparent polyurethane cover was changed every 7 to 10 days, and sterile gauzes were changed every 2 days.

In our clinic, the infection control committee performs regular education sessions about catheter insertion, followup processes, disinfection during the maintenance of catheters, and hand hygiene for all employees. We did not use the guidewire exchange technique for implementation of new catheters in our PICU.

2.3. Microbiologic criteria

The definition of CLABSI was based on the new CDC definitions (9).

2.3.1. Definition of CLABSI

CLABSI is defined as a laboratory-confirmed bloodstream infection (LCBI) for which the central line (CL) has been in place for >2 calendar days from the date of the event, with the day of device placement being day 1 and the CL having been in place on the date of the event or the day before. If the CL was in place for >2 calendar days and was then removed, the LCBI criteria must be fully met on the day of discontinuation or the next day. If the patient is admitted or transferred to a facility with a CL in place (e.g., tunneled or implanted central line), and that is the patient's only central line, the day of first access as an inpatient is considered day 1. "Access" is defined as line placement, infusion, or withdrawal through the line.

2.3.2. Definition of recurrent CLABSI

Recurrent CLABSI is defined as a new CLABSI development occurring after catheter removal and three negative blood cultures on consecutive days.

2.4. Data collection, study design, and statistics

Patient demographics, comorbid diseases, and PRISM 3 (Pediatric Risk of Mortality 3) scores (10) were recorded. Type and duration of the first catheter, the isolated microorganism, time of reproduction, and the name, duration, and initiation day of the antibiotic or antifungal agent and the day of the negative blood culture were all recorded.

Type and insertion site of the second catheter, disinfection material, catheter site dressing type used during insertion, and the number of punctures performed were recorded. The presence of blood transfusion or total parenteral nutrition therapy via this catheter, the presence of mechanical ventilation support, and the presence of neutropenia were also noted. The isolated microorganism thought to be the causative agent for CLABSI and the day on which the positivity of the culture occurred were recorded.

"Early initiation of appropriate antimicrobial treatment" was accepted if the appropriate antimicrobial treatment had been started within 48 h of the initial CLABSI diagnosis. "Appropriate antimicrobial treatment" was defined if the cultured microorganism was susceptible to at least one of the antimicrobial agents and the therapy was given for 10–14 days (5,7).

We defined four parameters related to catheter reinsertion to identify the risk factors contributing to recurrent CLABSI:

1. First CVC removal time: interval between initial CLABSI and the removal of the first catheter.

2. Interval between negative blood culture and the second CVC: the interval between the negative culture obtained after the treatment of initial CLABSI and the reinsertion of the second CVC.

3. Catheter exchange interval: the interval between the removal of the first catheter and the implementation of the second one.

4. Pre-/reinsertion treatment duration: the duration of appropriate antimicrobial treatment before the reinsertion of the second catheter.

All of the data were primarily evaluated by descriptive statistical methods. For numeric data, the mean and median as the measures of central tendency and the standard deviation (SD) and interquartile range (IQR) as measures of spread were used. The Kolmogorov–Smirnov test and the coefficient of variation were used to assess the distribution of the data and a histogram, stem and leaf diagrams, and box-plot graphs were used, as well. Numeric data were compared with the Mann–Whitney U-test and Student's t-test. Categorical data were compared by using the chi-square test and Fisher's exact test between the generated groups. Kaplan–Meier survival analysis was performed to investigate the effect of the variables that had statistically significant differences for the recurrence risk in the catheter survey.

Variables with significant differences were analyzed by multivariate logistic regression analysis using a backward stepwise procedure to predict risk of recurrence. The Hosmer–Lemeshow test was used to assess the goodness of fit of the models. The cutoff value of numeric data showing a significant difference was determined by using receiver operating characteristic (ROC) curve analysis. The sensitivity, specificity, positive predictive, and negative predictive values of the limits were calculated in the presence of a significant limit value. P < 0.05 was considered statistically significant. SPSS 15.0 (SPSS Inc., Chicago, IL, USA) was used for the corresponding procedures.

3. Results

A total of 168 patients were catheterized 265 times, and 39 were diagnosed with initial CLABSI. A CVC was then reinserted in 31 of these 39 patients (79%), and 12 patients (12/31; 38.7%) were diagnosed as having recurrent CLABSI. The study group consisted of 17 females (54.8%) and 14 males (45.2%). Their median age was 22 months (minimum 1, maximum 166 months), and the median hospitalization day was 195 days (minimum 19, maximum 977 days). The median PRISM 3 score was 4.19 (minimum 0, maximum 8). The most common comorbidities were neuromuscular diseases (45.2%), cardiovascular diseases (25.8%), metabolic diseases (22.6%), and genetic syndromes (6.5%), respectively. The median initial CLABSI development time was 27 days (minimum 4, maximum 119 days). Antimicrobial therapy had been initiated within 1.77 days (ranging from the first day to 5 days) and had been continued for 16.92 ± 4.87 days (minimum 8, maximum 21 days). *Candida parapsilosis* was the most common cause of recurrent (33.4%) and nonrecurrent (52.6%) CLABSIs (Table 1). Nineteen of the reinserted CVCs were subclavian (61.3%), 8 of them were femoral (25.8%), and 4 of them were jugular (12.9%).

There was no statistically significant difference between recurrent and nonrecurrent CLABSIs in terms of age, sex, PRISM 3 score, hospitalization duration, and comorbid diseases (P > 0.05). Initial CLABSI development duration, antimicrobial treatment initiation time, and the duration of antimicrobial therapy showed no significant difference (P > 0.05). There was no significant difference between the two groups in terms of means of early initiation of antimicrobial treatment (<48 h) and duration until removal of the first CVC (P > 0.05). No significant statistical differences between the recurrent and nonrecurrent groups according to the causative microorganism (fungi vs. bacteria) were present (P > 0.05) (Table 1).

Table 1. Distribution of the microorganisms isolated at the initial CLABSI diagnosis and the reinsertion of the central venous catheters.

Isolated microorganisms	Initial CLARSIa	Cases of catheter reinsertion (n = 31)				
	(n = 39)	Recurrent CLABSI (n = 12)	Nonrecurrent CLABSI (n = 19)	P-value		
Fungi (n = 26; 66.7%)		Fungi (n = 21; 67.8%)				
Candida parapsilosis	11 (28.2%)	4 (33.4%)	10 (52.6%)	0.293		
Candida albicans	9 (23.1%)	2 (16.8%)	3 (15.8%)	0.65		
Candida lustensia	4 (10.3%)	1 (8.3%)	0	-		
Candida tropicalis	2 (5.1%)	1 (8.3%)	0	-		
Total		8 (66.8%)	13 (68.4%)			
Bacteria (n = 13; 33.3%)		Bacteria (n = 10; 32.2%				
Staphylococcus epidermidis	7 (18%)	1 (8.3%)	1 (5.3%)	0.63		
Pseudomonas aeruginosa	3 (7.5%)	1 (8.3%)	2 (10.5%)	0.67		
Serratia marcescens	1 (2.6%)	1 (8.3%)	0	-		
Acinetobacter baumannii	1 (2.6%)	1 (8.3%)	0	-		
Klebsiella pneumonia	1 (2.6%)	0	3 (15.8%)			
Total	39 (100%)	4 (33.2%)	6 (31.6%)	0.9		

^a: Central line-associated blood stream infection.

In the recurrent CLABSI group, "catheter exchange interval", "interval between negative blood culture and the second CVC", and "pre-/reinsertion treatment duration" were found to be significantly shorter compared to the nonrecurrent group (P = 0.001; P = 0.001; P = 0.008). The incidence of sterile gauze use as catheter site dressing instead of a transparent polyurethane cover was found to be higher in the recurrent group compared to the nonrecurrent group (P = 0.012) (Table 2).

When nominal data were analyzed between the recurrent and nonrecurrent groups, only catheter site dressing material was found to be statistically significantly different (P = 0.012). Catheter surveys of the groups with catheter site dressed with sterile gauze and with catheter site dressed with transparent polyurethane were compared via Kaplan–Meier survival analysis, and the cumulative results for the group with the catheter site dressed with sterile gauze were found to be lower (P = 0.005) (Figure 1).

ROC analysis was performed for the "catheter exchange interval", "interval between negative blood culture and the second CVC", and "pre-/reinsertion treatment duration". These were found to be statistically different between the recurrent and the nonrecurrent group in order to determine cutoff values. The cutoff values for the catheter exchange interval, the interval between negative blood culture and the second CVC, and the pre-/reinsertion treatment duration was 11.5, 4, and 10.5 days, respectively (Table 3; Figure 2).

3.1. Comparisons between fungi and bacteria and between recurrent and nonrecurrent CLABSI

ROC analysis was performed for 3 numerical datasets in order to determine separate cutoff values for groups with either bacteria cultured or fungi cultured at the time of the first CVC. The bacteria-cultured group and the fungicultured group had cutoff values similar to each other and similar to the general cutoff value, as well. The cutoff value for the catheter exchange interval was found to be 11 days (AUC: 0.91, P: 0.03, 95% CI: 0.7-0.98) for the bacteriacultured group, whereas the cutoff value for the fungicultured group was 11.5 days (AUC: 0.79, P: 0.02, 95% CI: 0.6-0.99). The interval between the negative blood culture and the second CVC was found to be 4.5 days (AUC: 0.87, P: 0.01, 95% CI: 0.6-0.97) in the bacteria-cultured group whereas the same interval was found to be 4 days (AUC: 0.85, P: 0.007, 95% CI: 0.69-0.94) in the fungi-cultured group. Cutoff values for the pre-/reinsertion treatment period for the bacteria- and the fungi-cultured groups were 10 days (AUC: 0.78, P: 0.003, 95% CI: 0.69-0.96) and 10.5 days (AUC: 0.79, P: 0.002, 95% CI: 0.7-0.98), respectively.

Independent variables that had statistically significant differences were used to perform multivariate logistic regression analyses for prediction of recurrence risk, and only "interval between negative blood culture and the second CVC" was found to be statistically significantly different (P: 0.021, RR: 1.7, 95% CI: 1.4–5.96). In other words, if the second CVC was reinserted in the first 4 days after the negative blood culture was obtained, the risk of recurrence of CLABSI increased 1.7 times.

4. Discussion

The importance of CLABSIs has remained constant in PICUs despite improved techniques and ongoing preventive strategies (1,11). Although the risk factors for developing CLABSIs have been studied before (12– 16), studies focusing on the risk factors for developing recurrent CLABSI after reinsertion of a CVC have been limited, especially in children (6–8). In this study, we aimed to investigate possible risk factors for the reoccurrence of CLABSI.

Generally, the most dominant microorganisms cultured in CLABSI cases were coagulase-negative staphylococci; however, the incidence of Candida species is reported to have increased in the last decade (4). In our study, Candida species predominated in recurrent CLABSI cases, supporting previous reports (7). Candida parapsilosis was the most common cause of recurrent (33.4%) and nonrecurrent (52.6 %) CLABSI, which could be due its being the second causative agent among Candida species in our PICU (17). Other reasons include the organism's growth capacity and its affinity for intravascular devices and prosthetic materials (18,19). Chin et al. reported that fungal CLABSIs, in contrast to bacterial infections, were independently associated with recurrent CLABSI (7); however, in our study we could not find such a tendency with Candida infections compared to bacterial infections.

Once CLABSI is diagnosed, the general suggestion is to remove the catheter, especially nontunneled ones (4,5). However, in clinical practice, these patients are in need of catheter reinsertion during their follow-up visits. In our study, the recurrence of CLABSI was observed in 38.7% of patients who had catheters reinserted. Previous studies were limited to mostly adults.

Chin et al. conducted a study in an adult population receiving nontunneled catheters and observed a 41.5% recurrence rate of CLABSI (7). Erbay et al. also found a similar rate (34%) with many catheter types in an adult population (8). Flynn et al. reported that the recurrence rate was as high as 44% for totally implantable CVCs, while it was reported as 8% for tunneled catheters in their pediatric study population (6).

We attempted to identify the possible risk factors for recurrent CLABSIs after the first CLABSI; however, we could not find a meaningful relationship between age, sex, PRISM 3 scores, hospitalization duration, or comorbid diseases and CLABSI recurrence. Previous studies

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Table 2. Comparison between the recurrent and the nonrecurrent CLABSI groups.

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	Recurrent CLABSIª	Nonrecurrent CLABSI	P-value		
Age (months) [median (IQR ^b ; min-max)]	25 (34; 1–90)	20 (14; 1–166)	0.64		
Sex (n; %)					
Female	4 (33.3)	13 (68.4)	0.050		
Male	8 (66.7)	6 (31.6)	0.056		
PRISM 3 ^c score [median (IQR; min-max)]	4.17 (3; 2-6)	4.21 (4; 0-8)	0.96		
Hospitalization day (days) [median (IQR; min-max)]	281 (434; 22–977)	140 (110; 19–484)	0.509		
Comorbid diseases (n; %)					
Neuromuscular	6 (50)	8 (42.1)			
Cardiovascular	2 (16.7)	6 (31.6)			
Metabolic	3 (2.5)	4 (21.1)	0.00		
Genetic	1 (8.3)	1 (5.2)]		
1st CVC ^d					
Initial CLABSI development time (days) [median (IQR; min-max)]	23 (21; 6-84)	29.6 (19; 4–119)	0.164		
Initiation of the therapy after the 1st CLABSI (days) [median (IQR; min-max)]	1.67 (2; 0-4)	1.84 (1; 0-5)	0.92		
Early initiation of antimicrobial treatment (<48 h) (n, %)	10 (83.3)	15 (78.9)	0.76		
Antimicrobial treatment duration (days) [median (IQR; min-max)]	16.9 (7; 8–21)	19.5 (7; 10–40)	0.82		
1st CVC removal time (days) [median (IQR; min-max)]	2 (3; 0–7)	2 (1; 0-4)	0.66		
Catheter exchange interval (days) [median (IQR; min-max)]	7.58 (7; 3–12)	23.3 (28; 5–54)	0.001*		
Interval between negative blood culture and the second CVC (days) [median (IQR; min-max)]	2.67 (4; 0-8)	16.1 (19; 0-48)	0.001*		
Pre-/reinsertion treatment period (days) [median (IQR; min-max)]	8.08 (7; 3–15)	14.95 (11; 5–35)	0.008*		
Cultured microorganism at the 1st CLABSI (n; %)					
Bacteria	4 (33.3)	6 (31.6)			
Fungus	8 (66.7)	13 (68.4)	0.9		
2nd CVC					
Total parenteral nutrition (n; %)					
Yes	4 (33.3)	7 (36.8)			
No	8 (66.7)	12 (63.2)	0.84		
Blood transfusion (n; %)					
Yes	5 (41.7)	9 (47.4)			
No	7 (58.3)	10 (52.6)	0.75		
Mechanical ventilation support (n; %)					
Yes	9 (75)	15 (78.9)			
No	3 (25)	4 (21.1)	0.79		
Neutropenia (n; %)					
Yes	1 (8.3) 1 (5.3)				
No	11 (91.7)	18 (94.7)	0./3		
Catheter site (n; %)		1			
Subclavian	7 (58.3)	12 (63.2)			
Jugular	2 (16.7)	2 (10.5)	0.93		
Femoral	3 (25)	5 (26.3)	7		

Table 2. Continued).

Number of catheter lumens (n; %)				
1	7 (58.3)	16 (84.2)	- 0.2	
≥2	5 (41.7)	3 (15.8)		
Number of punctures (n; %)				
1	9 (75)	11 (57.9)	0.45	
≥2	3 (25)	8 (42.1)		
Disinfection material (n; %)				
10% povidone iodine	8 (66.7)	14 (73.7)	0.7	
2% chlorhexidine	4 (33.3)	5 (26.3)		
Catheter dressing (n; %)				
Transparent polyurethane	5 (41.7)	17 (89.5)	- 0.012*	
Sterile gauze	7 (58.3)	2 (10.5)		

^a: Central line-associated blood stream infection.

^b: Interquartile range.

^c: Pediatric Risk of Mortality Score 3.

^d: Central venous catheter.

*: P-values found to be statistically significant (P < 0.05).



Figure 1. Kaplan–Meier survival analysis of catheter survival between the group with catheter site dressed with a sterile sponge and the group with catheter site dressed with transparent polyurethane.

Table 3. Results of rece	eiver operating	characteristic a	nalysis.
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	Cutoff value (days)	Sensitivity (%)	Specificity (%)	+ Predictivity (%)	- Predictivity (%)	AUC ^b	Р	95% CI ^c
Catheter exchange interval	11.5	91	73	69	93	0.842	0.002	0.7-0.98
Interval between negative blood culture and the second CVC ^a	4	75	84	75	84	0.844	0.01	0.6-0.95
Pre-/reinsertion treatment duration	10.5	75	68	60	81	0.779	0.001	0.7-0.98

^a: Central venous catheter.

^b: Area under the curve.

^c: Confidence interval.



Figure 2. In this receiver operating characteristics diagram, the cutoff values, sensitivity, specificity, and area under the curve are marked with arrows and observed to be high.

reported more recurrence in burn patients (8), in males, and in patients with high APACHE II scores (7), but no linkage could be shown in multivariable models. Another study also reported that there was no difference between the two groups when the same variables as in our study were used (6).

It is important to initiate antibiotic therapy as soon as possible once CLABSI has been diagnosed (4). The current Infectious Diseases Society of America guidelines recommend at least 10 to 14 days of therapy for CLABSI (5). In our center, appropriate antibiotic therapy was initiated in the early stages of initial CLABSI (1.77 days; IQR: 1, minimum 0, maximum 5) and continued for approximately 17 days on average; however, no difference was observed between the recurrent and nonrecurrent groups. Our findings are supported by previous reports presented by Flynn et al., in which no difference between the recurrent and the nonrecurrent group was found by

means of appropriate antimicrobial therapy (6). Moreover, Chin et al. reported that delayed administration of appropriate antibiotics (>48 h after diagnosis of a catheterrelated bloodstream infection) was not associated with recurrent catheter-related infections (7). These findings suggest that appropriate therapy might be effective for current CLABSIs; however, it does not prevent possible recurrent CLABSIs in the future.

Current guidelines recommend the removal of the catheter at early stages after CLABSI has been detected (4,5). Many studies reported that the removal of the catheter at the early stage of blood stream infection had positive effects on mortality, especially within 72 h in the case of *Candida* spp. blood stream infections (19,20). Conflicting studies have been published since 2002 (21–23); however, in our clinic we perform catheter removal as soon as possible. In our study the median removal time of the CVC was 2 days and removal time was not significantly different between the recurrent and nonrecurrent groups.

Many risk factors have been reported for initial CLABSI development. The site, number of lumens, type of catheter, catheterization technique, total parenteral nutrition administration, blood or blood products administration, and hemodialysis via catheter were the most common risk factors reported (12,14). Young patient age, treatment with immunosuppressives, the presence of neutropenia, and the presence of mechanical ventilation support were also found to be definite risk factors for initial CLABSI development (24,25). We hypothesized that the risk factors of recurrent CLABSI might be the same as the risk factors of initial CLABSI. However, we could not find a link between the second CVC site, number of lumens, puncture numbers during insertion, or the disinfection material and recurrent CLABSI. The exact insertion site that will lower the risk of infection is still being debated (4); however, in our study, we observed that the site of insertion did not differ between the groups.

In our study, we attempted to determine the modifiable risk factors, but we found no statistically significant differences between the recurrent and the nonrecurrent groups in terms of total parenteral nutrition support, mechanical ventilation support, blood or blood products admission via catheter, and patients being neutropenic. Our findings supported previous reports. Flynn et al. studied whether catheter type, presence of sepsis, or recent bone marrow transplantation affected recurrence risk and found that only totally implantable catheters increased this risk (6). Different risk factors associated with recurrent CLABSI were defined before. Chin et al. investigated total parenteral nutrition support, blood transfusion, the presence of neutropenia, catheter site, and the department in which the insertion was performed. A high risk of recurrence was reported to be associated with procedures performed in intensive care units (7). On the other hand, Erbay et al.

reported that blood transfusions were associated with a higher risk of recurrence (8).

Univariate analyses for all categorical data in our study revealed that only the sterile gauze usage rate for catheter site dressing was statistically higher in the recurrent group. Moreover, the cumulative catheter survey results of the sterile gauze group were found to be lower than those for transparent polyurethane dressings (Tegaderm). An analysis of six studies reported a 4-fold increase in the rate of catheter-related blood stream infection when polyurethane dressing was used to secure the CVC (26). However, the authors acknowledged that this research was at risk of bias and associated with wide confidence intervals, due to the small study population. In our relatively large-scale study, transparent polyurethane dressing was found to be protective against recurrent CLABSI, suggesting that more large-scale studies are required to support our findings.

In our study, "catheter exchange interval", "interval between negative blood culture and the second CVC", and "pre-/reinsertion treatment duration" were found to be shorter in cases of recurrent CLABSI; however, Chin et al. reported that there was no significant difference between these three datasets (7). On the other hand, Erbay et al. compared the groups by catheter removal time only and found no difference (8). In our ROC analysis, we found that the cutoff values for "catheter exchange interval", "interval between negative blood culture and the second CVC", and "pre-/reinsertion treatment duration" were 11.5 days, 4 days, and 10.5 days, respectively. According to these results, we postulated that if these time periods were shorter than the determined cutoff values, the recurrence risk would increase. However, only "interval between negative blood culture and the second CVC" was found to be effective in the prediction of risk of recurrence. Moreover, if a second CVC insertion is done earlier than 4 days after the negative blood culture has been obtained, the recurrence risk will increase 1.7 times. Thus, we recommend that the reinsertion of the catheter be delayed at least 4 days after the negative culture.

Our study has several limitations due to its retrospective design and heterogeneous patient characteristics. However, since studies focusing on the recurrence of CLABSI in children are limited, this particular study has provided additional data to the literature concerning recurrence risks (6).

In conclusion, a considerable number of children whose catheters have been removed due to CLABSI will experience recurrent CLABSI. According to our study, using transparent polyurethane dressings instead of sterile gauze for maintaining the CVC, coupled with delaying the reinsertion procedure for at least 4 days after the negative culture, might be helpful in preventing recurrent CLABSI. Further studies are required to determine additional risk factors and possible interventions to prevent recurrent CLABSI.

References

- 1. Hatler C, Buckwald L, Salas-Allison Z, Murphy-Taylor C. Evaluating central venous catheter care in a pediatric intensive care unit. Am J Crit Care 2009; 18: 514-520.
- 2. Randolph AG, Brun-Buisson C, Goldmann D. Identification of central venous catheter-related infections in infants and children. Pediatr Crit Care Med 2005; 6: 19-24.
- Tomlinson D, Mermel LA, Ethier MC, Matlow A, Gillmeister B, Sung L. Defining bloodstream infections related to central venous catheters in patients with cancer: a systematic review. Clin Infect Dis 2011; 53: 697-710.
- O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control 2011; 39: 1-34.
- Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. 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: 1-45.
- Flynn PM, Willis B, Gaur AH, Shenep JL. Catheter design influences recurrence of catheter-related bloodstream infection in children with cancer. J Clin Oncol 2003; 21: 35.
- Chin BS, Han SH, Lee HS, Jeong SJ, Choi H, Kim CO, Choi JY, Song YG, Kim JM. Risk factors for recurrent catheter-related infections after catheter-related bloodstream infections. Int J Infect Dis 2010;14: 16-21.
- Erbay A, Ergönül O, Stoddard GJ, Samore MH. Recurrent catheter-related bloodstream infections: risk factors and outcome. Int J Infect Dis. 2006; 10: 396-400.
- 9. Centers for Disease Control and Prevention. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-Central Line-Associated Bloodstream Infection. Atlanta, GA, USA: CDC; 2017.
- Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. Crit Care Med 1996; 24: 743-752.
- 11. Thomas D, Parameswaran N, Harish BN. Catheter related blood stream infections in the paediatric intensive care unit: a descriptive study. Indian J Crit Care Med 2013; 17: 135-139.
- 12. Hammarskjöld F, Berg S, Hanberger H, Taxbro K, Malmvall BE. Sustained low incidence of central venous catheter-related infections over six years in a Swedish hospital with an active central venous catheter team. Am J Infect Control 2014; 42: 122-128.
- Krishnaiah A, Soothill J, Wade A, Mok QQ, Ramnarayan P. Central venous catheter-associated bloodstream infections in a pediatric intensive care unit: effect of the location of catheter insertion. Pediatr Crit Care Med 2012; 13: 176-180.
- 14. Rey C, Alvarez F, De-La-Rua V, Concha A, Medina A, Díaz JJ, Menéndez S, Los-Arcos M, Mayordomo-Colunga J. Intervention to reduce catheter-related bloodstream infections in a pediatric intensive care unit. Intensive Care Med 2011; 37: 678-685

- Wylie MC, Graham DA, Potter-Bynoe G, Kleinman ME, Randolph AG, Costello JM, Sandora TJ. Risk factors for central line-associated bloodstream infection in pediatric intensive care units. Infect Cont Hosp Ep 2010; 31: 1049-1056.
- Pinon M, Bezzio S, Tovo PA, Fagioli F, Farinasso L, Calabrese R, Marengo M, Giacchino M. A prospective 7-year survey on central venous catheter-related complications at a single pediatric hospital. Eur J Pediatr 2009; 168: 1505-1512.
- 17. Ağın H, Devrim I, İşgüder R, Karaarslan U, Kanık E, Günay İ, Kışla M, Aydın S, Gülfidan G. Risk factors for candidemia in pediatric intensive care unit patients. Indian J Pediatr 2014; 81: 1158-1162.
- Hirai Y, Asahata S, Ainoda Y, Goto A, Fujita T, Totsuka K. Nosocomial *Candida parapsilosis* candidaemia: risk factors, antifungal susceptibility and outcome. J Hosp Infect 2014; 87: 54-58.
- Holland LM, Schröder MS, Turner SA, Taff H, Andes D, Grózer Z, Gácser A, Ames L, Haynes K, Higgins DG et al. Comparative phenotypic analysis of the major fungal pathogens *Candida parapsilosis* and *Candida albicans*. PLoS Pathog 2014; 10: e1004365.
- 20. Garnacho-Montero J, Díaz-Martín A, García-Cabrera E, Ruiz Pérez de Pipaón M, Hernández-Caballero C, Lepe-Jiménez JA. Impact on hospital mortality of catheter removal and adequate antifungal therapy in *Candida* spp. bloodstream infections. J Antimicrob Chemoth 2013; 68: 206-213.
- 21. Nucci M, Anaissie E. Should vascular catheters be removed from all patients with candidemia? An evidence-based review. Clin Infect Dis 2002; 34: 591-599.
- 22. Nucci M, Anaissie E, Betts RF, Dupont BF, Wu C, Buell DN, Kovanda L, Lortholary O. Early removal of central venous catheter in patients with candidemia does not improve outcome: analysis of 842 patients from 2 randomized clinical trials. Clin Infect Dis 2010; 51: 295-303.
- 23. Velasco E, Portugal RD. Factors prompting early central venous catheter removal from cancer patients with candidaemia. Scand J Infect Dis 2011; 43: 27-31.
- 24. Downes KJ, Metlay JP, Bell LM, McGowan KL, Elliott MR, Shah SS. Polymicrobial bloodstream infections among children and adolescents with central venous catheters evaluated in ambulatory care. Clin Infect Dis 2008; 46: 387-394.
- 25. Perlman SE, Saiman L, Larson EL. Risk factors for late-onset health care-associated bloodstream infections in patients in neonatal intensive care units. Am J Infect Control 2007; 35: 177-182.
- Webster J, Gillies D, O'Riordan E, Sherriff KL, Rickard CM. Gauze and tape and transparent polyurethane dressings for central venous catheters. Cochrane Database Syst Rev 2011; 11: CD003827.