



CHILDREN WITH ACUTE LYMPHOBLASTIC AND MYELOID LEUKEMIA AND CENTRAL LINE-ASSOCIATED INFECTIONS: IMPACT OF PERIOPERATIVE ABSOLUTE NEUTROPHIL COUNT

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ABSTRACT

The safety of using tunneled central venous catheters for pediatric neutropenic or acute leukemic patients is unknown at the present time. Children with lymphoblastic (ALL) or myeloid leukaemia or myeloid leukemia are investigated for the relationship between the absolute neutrophil count (ANC) and the risk of CLABSI after TCVC placement. Specifically, we look at patients who are between the ages of five and fourteen (AML). In terms of the Materials as well as the Methods: Children who had been admitted to a tertiary referral hospital for the purpose of receiving a TCVC placement anytime between January 2000 and December 2015 were included in a retrospective observational study. A study was conducted for this purpose. The competing-risk regression model and traditional regression model were both considered utilised by the researchers in order to arrive at an accurate estimation of the impact that perioperative ANC has on the progression of CLABSI. Results: Over the course of 498 consecutive TCVC implants, 350 children received TCVCs. Three hundred and twenty-two of these children were affected by neutrophilic conditions, while 326 of these children were affected by non-neutrophilic conditions (65.5%). An interquartile range of 3.1–10.9 years was found in the age distribution of these children, averaging 6.4 years old. Overall, 99,681 catheter days were observed for each TCVC; the interquartile range for observation time was 116.1–265.9. The median observation time for each TCVC was 217.1 days. Neutropenic and nonneutropenic patients did not differ significantly in their rates of early TCVC-related CLABSI within 30 days of TCVC placement (hazard ratio = 1.250, $p = 0.502$; Hazard ratio = 1.633, $p = 0.143$). The cause of early CLABSI was found to be female genital morphology (hazard ratio 2.640, $p = 0.006$) and the use of TCVC to treat relapsed leukemia. Also, we discovered that TCVC use during relapse of leukemia (hazard ratio 2.004, $p = 0.003$) and use of double-lumen catheters (hazard ratio 2.607, $p = 0.003$) both increased the risk of leukemia. In children undergoing treatment for acute leukemia who have neutropenia, the TCVC is safe to insert, and there is no increased risk of CLABSI associated with this procedure.

Keywords: - Neutropenia, Absolute Neutrophil Count, Catheter-Related Bloodstream Infection, Tunnelled Central Venous Catheters, Acute Lymphoblastic Leukaemia, Acute Myeloid Leukaemia.

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INTRODUCTION

Acute lymphoblastic leukaemia, also known as Two of the most common types of acute childhood leukemia are acute lymphoblastic leukaemia (ALL) and

acute myeloid leukaemia leukaemia (AML). These two subtypes of leukaemia are responsible for approximately 30 percent of all cases of cancer diagnosed in children and adolescents (1). The intensive treatment of both ALL and

AML requires continuous access to the central veins for an extended period of time, which can be accomplished with a tunnelled central venous catheter, for example (TCVC). As a direct result of this, the process of administering Fluids, blood products, and parenteral nutrition included in chemotherapy, antibiotics, and parenteral nutrition is simplified. Despite this, TCVCs are frequently associated with infectious occurrences such as central line-associated bloodstream infections (CLABSI) and local catheter exit-site infections (CESI) (CLABSI). Both of these factors have the potential to impede or halt cancer treatment, which can result in a significant rise in morbidity and mortality (2–4). Moreover, healthcare-associated infections involving CLABSI are the most costly (7,8). Several studies have examined the impact of neutrophil levels at the time of catheter insertion on the development of CESI and CLABSI in pediatric patients with hematological diseases, as these patients are a priori at a higher risk of infection. It has been proposed that a low perioperative absolute neutrophil count (ANC) could be a risk factor for CESI/CLABSI in paediatric patients with hematological medical conditions, after several studies discovered a negative correlation between neutropenia and CLABSI in paediatric cancer patients. This hypothesis is based on the fact that a low ANC has been shown to increase the risk of both CESI and CLABSI. Because of this, some hospitals and other medical facilities will only recommend TCVC placement in patients whose absolute neutrophil count (ANC) is greater than 0.5 10⁹/L or even 1.0 10⁹/L. However, there is a lack of consensus in the scientific literature regarding the connection between CESI and CLABSI risk are increased during perioperative neutropenia. It has been shown that neutropenic children and non-neutropenic children are equally likely to develop CESI and CLABSI at the time of catheter placement, suggesting that even with neutropenia, a TCVC can be used safely (9-11). Several early studies investigated perioperative ANC and TCVC-associated infective complications in various patient groups. There are differences in risk for CLABSI between these patient populations at the start of the study (12). In addition, we investigated the impact of perioperative neutropenia on the development of both CESI (Child-Ending Surgery Infection) and CLABSI (Child Ending Blood Clot Infection) in a large and well-defined cohort of children with ALL and AML receiving a TCVC.

METHODS

The Individuals Being Studied and the Data That Are Collected

The study included all paediatric patients diagnosed with ALL or AML who underwent sequential placement of tunnelled central venous catheters. The study was conducted between January 1, 2000 and December 1, 2015. Patients had to be under the age of 18 to participate in the study. Patients who had never had a catheter inserted

before were included in the study alongside patients who had prior experience with catheters. The purpose of the study was to compare the outcomes of patients who had never had a catheter inserted before. We were able to retrieve the information with the assistance of the Patient Data Management System (PDMS), which contained patient and device characteristics (such as the patient's age at the time of TCVC placement, sex, and the presence of an underlying malignancy), laboratory (absolute neutrophil count), and microbiological tests. Evaluation of the Device, Its Characteristics, and the Method of Placement Conducted Before Surgery

Laboratory examinations, such as a complete blood count and tests of coagulation, were typically a part of the preoperative workup in the majority of cases. We did not consider the presence of an ANC that was less than 0.5 x 10⁹/L to be an indication that the TCVC should not be inserted. A single dose of a prophylactic antibiotic, given during surgery, such as cefuroxime, was administered to each patient in order to act as a preventative measure. This was done regardless of the patient's ANC status. While the patient was under the influence of general anaesthesia, the TCVC was inserted into their body in the operating room. Attending surgeons were accountable for either personally carrying out or directly supervising each and every procedure. We did not use any in-line filters or anti-infective lock prophylaxis while we were inserting the TCVC because we wanted to avoid the risk of spreading infection. We were able to successfully cannulate the catheter by using anatomical landmarks in conjunction with a modified version of the Seldinger technique (13). A tunnel was made under the patient's skin, and each catheter was inserted through that tunnel. At the end of the subcutaneous tunnel that was the furthest away from the patient, the tissue ingrowth cuff was positioned there. The right internal jugular vein was accessed in virtually all of the patients in order to perform the cannulation procedure. When determining which size catheter would be most suitable for the patient, their age as well as their weight were taken into account. The utilisation of fluoroscopy made it possible to accurately verify that the distal catheter tip had been correctly positioned between the junction of the superior vena cava and the right atrium. Throughout the entirety of the time that this investigation was conducted, not a single adjustment was made to any of the standard operating procedures or methods that were carried out. The postoperative maintenance procedures for the TCVC were carried out in accordance with the standard operating procedure manual that was utilised at our establishment. This was done in order to ensure that the procedures were carried out correctly.

Definitions

As per the criteria established by the Centers for Disease Control and Prevention (LCBI 1 criteria, [laboratory confirmed bloodstream infection]) and the

National Healthcare Safety Network (NHSN), a patient was considered to have contracted CLABSI when he or she developed bacteremia or fungemia that originated from one or both lumens of the implanted device at least 48 hours after insertion. This infection was not related to (14, 15). As a direct consequence of this, the researchers did not take into account as an event of interest for the primary endpoint any cases of CLABSI that occurred in children within the first 48 hours after TCVC placement. It is considered to be a recurrent case of catheter-associated infection if it has been more than 14 days since the patient was last treated for a catheter-related bloodstream infection (CLABSI). As a result, positive blood cultures obtained within two weeks after an earlier episode of CLABSI were not considered new instances of the infection because they occurred within the first two weeks of the prior CLABSI case. Neutropenia was defined as having an absolute neutrophil count (ANC) of less than 0.5×10^9 cells/L.

Endpoints

Among patients with perioperative ANC below 0.5×10^9 cells/L, we aimed to determine the impact of predicting CLABSI (censored at premature catheter removal, death, or the last follow-up) within the first 30 days after TCVC placement. The comparison was completed by comparing two levels of ANC: those with ANCs 0.5×10^9 cells/L and those with ANCs greater than 0.5×10^9 cells/L. This was conducted by comparing patients with ANCs of 0.5×10^9 cells/L and those with ANCs greater than 0.5×10^9 cells/L. The qualitative differences in the primary outcome were analyzed using the univariable (unadjusted) and multivariable survival models (including the patient's age and underlying malignancy, sex, procedures used for TCVC implantation, type of TCVC, and number and size of lumens in the catheter) survival models. The secondary outcome measures of this study were the incidence of CLABSI across the whole study period, the incidence of CESI within 30 days following TCVC implantation, and the description of the microorganisms detected during the first CLABSI stratified by children's neutropenic status preoperatively and at the time of infection onset after surgery. Our primary outcomes were the number of CLABSI occurring during the overall study period as well as the number of CESIs occurring within 30 days after TCVC implantation.

Statistics

The use of frequencies and percentages was necessary in order to adequately describe categorical variables such as gender and the type of catheter that was inserted into the patient. For continuous variables such as age and the amount of time a catheter was in use, the median as well as the corresponding interquartile range was reported (IQR). Analyzing categorical variables was done using Fisher's exact test, and analyzing continuous variables was done using the Mann-Whitney U test. The collected data was subjected to both tests. For each case,

the total number of catheter days (CD) could be calculated by adding up all of the days between the time of the insertion of the TCVC and when the follow-up procedure was completed (e.g., elective catheter removal, premature catheter explantation, and death). We calculated the complication rate (CR) per 1,000 CDs by multiplying the number of CDs experiencing complications by 1,000 and then dividing this number by the total number of CDs experiencing complications (16, 17). To estimate the risk of developing CLABSI during short-term (within the first 30 days after TCVC placement) and overall follow-up periods, the traditional Kaplan–Meier method (a univariate/unadjusted analysis, crude HR) and Cox regression survival analysis (a multivariate/adjusted analysis) were used. It was done to assess whether the short-term and overall follow-up periods were associated with a greater risk for CLABSI. A competing-risks regression model (Fine and Gray [cumulative incidence function [CIF]]) was used to estimate the risk of developing CLABSI during the short-term period as well as the overall follow-up period in order to account for the competing risks (elective or non-elective catheter removal). In the survival analysis, the endpoint of interest was determined to be the time at which the patient experienced their very first CLABSI. The analysis did not take into account any CLABSI incidents that occurred consecutively to one another. Every statistical test was carried out in two separate ways, and in order for a result to be regarded as significant, a p-value of less than 0.05 had to be achieved.

Results

Conduct Studies on the People

Throughout the course of the research, our department cared for a total of 350 patients who were diagnosed with either ALL ($n = 284$, 81.1 percent) or AML ($n = 66$, 18.9 percent). At the time of catheter implantation, the median age of the patients was 6.4 (56.6 percent were male, 43.4 percent were female) (interquartile range: 3.1–10.9 years). The patients' ages ranged from 3.1 to 10.9 years, with 10.9 being the median age. There were a total of 498 tunnelled central venous catheters inserted into these patients. Of those, Groshong catheters made up 68.3 percent of the total ($n = 340$), Hickman-Broviac catheters made up 25.9 percent ($n = 129$), and port catheters made up 5.8 percent ($n = 29$). 399 of these devices were used for the primary treatment of the disease, 75 (15.1%) were used for the first relapse of the disease, 12 (2.4%) were used for the second relapse of the disease, and one (0.2%) was used for the third relapse of the disease. TCVCs were used to treat 11 primary and relapsed cases of leukemia, or 2.2% of the total number. TCVCs contained a total of 99,681 CDs, ranging from 116.4 to 260.5 per case. This variable had an interquartile range of 116.4–260.5. Out of 172 patients, 34.5 percent were observed to suffer from perioperative neutropenia. In neutropenic children, TCVC insertion was done when they were 5.2 years old (IQR: 2.7 to 8.1), and their catheters

tended to be smaller (66.3 percent of 7 French catheters, $p = 0.0006$) and smaller (61.6 percent, $p = 0.00266$). Furthermore, patients with perioperative neutropenia were significantly more likely to have Hickman-Broviac catheters (34.9 percent, $p = 0.0038$), and also had a far higher frequency of primary disease (90.7 percent, $p = 0.0001$) compared to patients without perioperative neutropenia. Patients who did not have perioperative neutropenia did not have either of these factors. Table 1 provides a summary of the detailed characteristics of children who had or did not have neutropenia at the time that they had their TCVC inserted. The table compares the characteristics of children who had neutropenia to those who did not.

The Most Important Outcome

It was discovered that a total of 165 CLABSI episodes had taken place over the course of the entire study (the CR was calculated to be 1.65 for every 1,000 CD [99,681 days]). It was determined that 127 (76.9 percent) of these were first CLABSI episodes, 29 (17.6 percent) were first recurrent episodes, 7 (4.2 percent) were second recurrent episodes, and 2 (1.2 percent) were third recurrent episodes. In the neutropenic at implantation cohort, we found 47/165 cases of CLABSI, which is a prevalence rate of 28.5%. Out of these, 35 (74.4 percent) were first episodes of CLABSI, 8 (17.0 percent) were first recurrent episodes of CLABSI, 3 (6.4 percent) were second recurrent episodes of CLABSI, and 1 (2.1 percent) was a third recurrent episode of CLABSI. There were 118/165 (69.2 percent) CLABSI episodes in non-neutropenic patients, of which 92 (77.9 percent) were first CLABSI episodes, 21 (17.8 percent) were first recurrent episodes, 4 (3.4 percent) were second recurrent episodes, and 1 (0.8 percent) was a third recurrent episode. There was one patient who experienced a third recurrent episode. After the insertion of a TCVC, there were a total of 37 (first) cases of CLABSI and 4 CESI in the first thirty days after the procedure. Fifteen of the 37 cases of CLABSI occurred in patients who were neutropenic, which accounts for 40.5 percent of the total, while the remaining 22 cases occurred in patients who were not neutropenic at the time of implantation, which accounts for 59.5 percent of the total (all in non-neutropenic at implantation patients). CLABSI cases were all successfully managed conservatively with antibiotics, whereas CESI cases required early removal of the patient's catheter as the only solution. In contrast, all CESI cases required early removal of the patient's catheter as the only solution. Perioperative neutropenia did not influence the development of early CLABSI (HR 1.533, 95 percent confidence interval 0.846–3.152, $p = 0.13$) in univariable and multivariable competing-risks regression models (HR 1.250, 95 percent confidence interval 0.650–2.402, $p = 0.502$). Despite the presence of neutropenia during the surgery, this result still occurred. Univariable models revealed an association between higher rates of CLABSI and female sex (hazard ratio [HR] 2.640, 95

percent confidence interval [CI] 1.328–5.250, $p = 0.006$), as well as patients who received TCVC after relapsed leukemia (hazard ratio [HR] 4.347, 95 percent confidence interval [CI] 2.283–8.264, $p = 0.0001$). A multivariable regression model also showed that both of these variables contribute to CLABSI, including female sex (HR 2.444, 95 percent confidence interval [CI] 1.227–4.865, $p = 0.011$); treatment with TCVC for relapsed leukemia (HR 4.032, CI 1.519–10.638, $p = 0.005$). (Table 2) Confidence intervals are ranges corresponding to a certain level of confidence.

The Consequences of the Secondary Effects

During the course of the overall study, there was an incidence of CLABSI

Throughout the entirety of the study, it was estimated that the CLABSI-free TCVC survival rate was 76 percent within the cohort of patients who were neutropenic at the time of implantation, and 71 percent within the cohort of patients who were not neutropenic at the time of implantation. One hundred and ten of the one hundred and twenty-seven first CLABSI events were successfully managed with conservative treatment, while seventeen (13.4 percent) required removal of the catheter earlier than planned. Patients who had perioperative neutropenia had a lower risk of CLABSI than patients who did not have it (hazard ratio The HR of 0.698 was in the range of 0.472–1.024 ($p = 0.066$); and the HR of 0.895 ranged from 0.596–1.344 ($p = 0.594$). CLABSI was more likely to occur in patients who did not have perioperative neutropenia (hazard ratio [HR]. 2.214, 95 percent confidence interval [CI] 2.207–4.694, $p = 0.0001$), and the use of Groshong catheters (hazard ratio [HR]. \$–6,864, 95% confidence interval \$–1,055–2,500, $p = 0.028$), and the use of double-lumen catheters (hazard ratio [HR] 3\$. 432, 95 percent confidence interval Although the effect of TCVCs was still seen in the multivariable regression model (hazard ratio [HR] 2.004, 95 percent confidence interval [CI]: 1. These variables were also significant (hazard ratio: 2.607, 95 percent confidence interval: 1.392–4.880, $p = 0.003$), as was the use of double-lumen catheters (hazard ratio: 2.608, 95 percent confidence interval: 1.392–4.880, $p = 0.003$).

In patients who were neutropenic and patients who were not neutropenic, different organisms were isolated during the initial clabsi. From a total of 127 blood cultures and 140 individual specimens, a total of 28 unique bacterial and fungal strains were isolated. These strains were found to be present in the blood. There were 116 cases of monomicrobial CLABSI, and there were 11 cases of polymicrobial CLABSI, which accounted for 8.7 percent of the total. *E. coli* was the most widely isolated organism (16 out of 214), followed by coagulase-negative staphylococci (14 out of 11%) and viridans streptococci (30 out of 214%). There was no difference between neutropenic and nonneutropenic patients in the distribution of bacteria or fungi in CLABSIs occurring within the first 30 days after TCVC placement. Both at OP and at

CLABSI, this is the conclusion of the study. In contrast to non-neutropenic patients, neutropenic patients had a significant difference in numbers of Gram-positive bacteria between all study periods (predominance of V.

streptococci [n = 30, 27.0 percent] in the neutropenic group, p = 0.009; see also: Neutropenic patients had a higher incidence of V. streptococci than non-neutropenic patients).

Table 1: Study population characteristics such as clinical and device characteristics.

Characteristics	Number of cohorts: 498	Neutropenics when TCVC is implanted		
		Yes, 172 out of 344 (34.5%)	were negative, and 326 (65.5%) were positive	statistically
According to age and years (IQR).	6.5 (3.1–11.3)	5.2 (2.7–8.0)	7.6 (3.4–12.4)	<0.0002
Men (%)	274 (54)	93 (54.0)	181 (55.4)	0.7767
Conclusion				
- PERFECT	409 (82.0)	140 (81.3)	269 (82.4)	0.8058
0.79	89 (17.8)	32 (18.5)	57 (17.4)	
The use of TCVC				
for initial treatment	399 (80.0)	156 (90.8)	243 (74.4)	< 0.0002
1st regression	75 (15.0)	13 (7.5)	62 (19.1)	
The second relapse	12 (2.3)	–	12 (3.6)	
3rd relapse	1 (0.1)	1 (0.5)	–	
Stages of multiple diseases	11 (2.1)	–	–	
TCV				
and Groshong	340 (68.2)	104 (60.4)	236 (72.3)	0.0037
Hickman	129 (25.8)	60 (34.8)	69 (21.1)	
(Local)	29 (5.7)	8 (4.6)	21 (6.3)	
Diameter of the catheter (French)				
- ≤7	278 (55.7)	114 (66.2)	164 (50.2)	0.0005
- >7	220 (44.1)	58 (33.8)	162 (49.6)	
Lumens of catheters				
- Individual lumens	273 (54.7)	106 (61.5)	167 (51.1)	0.0265
(Dual lumen)	225 (45.1)	66 (38.3)	159 (48.7)	
Days of catheterization, Total	99,682	35,171	64,510	–

Table 2: Univariable and multivariable regression analysis for primary outcome.

	30 days early (early CLABSI)			
	Probability of incident (95% CI), p-value			
	based on model one		incorporating multiple variables	
	Conventional	index	Traditionally	known as "CFT"
retirement	1.040 (0.975–1.109), 0.236	1.039 (0.973–1.110), 0.244	1.035 (0.955–1.121), 0.404	1.0355 (0.962–1.114), 0.352

	30 days early (early CLABSI)			
	Probability of incident (95% CI), p-value			
	based on model one		incorporating multiple variables	
	Conventional	index	Traditionally	known as "CFI"
Gender (male vs. female)	2.638 (1.326–5.263), 0.006	2.640 (1.328–5.250), 0.006	2.427 (1.199–4.926), 0.014	2.444 (1.227–4.865), 0.011
Conclusion Between AML and ALL	1.519 (0.717–3.218), 0.276	1.518 (0.716–3.217), 0.276	1.336 (0.614–2.915), 0.464	1.343 (0.579–3.116), 0.492
TCV between relapse treatment and initial treatment	4.339 (2.276–8.270), < 0.0001	4.347 (2.283–8.264), < 0.0001	4.045 (1.765–9.270), 0.001	4.032 (1.519–10.638), 0.005
This type of TCVC includes Groshong, Hickman-Broviac, and Port catheters	1. Ref. 1.366 (0.607–2.942), 0.471 0.885 (0.210–3.721), 0.867	1. Ref. 1.307 (0.609–2.801), 0.492 1.063 (0.7508–2.221), 0.871	1. Ref. 0.552 (0.102–2.988), 0.491 0.642 (0.072–5.732), 0.691	1. Ref. 0.728 (0.358–1.481), 0.382 0.931 (0.448–1.936), 0.849
Diameter of the catheter (French) (≤7 vs. >7)	2.232 (1.148–4.329), 0.018	2.230 (1.150–4.323), 0.018	1.460 (0.284–7.498), 0.651	1.317 (0.366–4.739), 0.673
Lumens of DL catheters compared with SL catheters	2.681 (1.346–5.319), 0.005	2.677 (1.348–5.318), 0.005	1.838 (0.514–6.578), 0.349	1.720 (0.540–5.473), 0.358
ADC after TCVC placement (<0.5 vs. >0.5)	1.250 (0.648–2.409), 0.504	1.250 (0.650–2.402), 0.502	1.642 (0.830–3.246), 0.154	1.633 (0.846–3.152), 0.143

Table 3: The secondary outcome can be analyzed both with univariate and multivariate regression.

	CLABSI as a whole			
	(probability ratio, 95% confidence interval)			
	Single-variable models		Multiple-variable models	
	Conventional	Regression	Analysis	Coefficients of variability
Regarding age	1.053 (1.017–1.091), 0.004	1.053 (1.016–1.091), 0.004	1.019 (0.977–1.064), 0.377	1.019 (0.976–1.064), 0.376
Gender Men vs. Women	1.094 (0.771–1.550), 0.615	1.093 (0.770–1.552), 0.617	1.039 (0.726–1.485), 0.833	0.727 (0.696–1.497), 0.816
Conclusion between AML and ALL	1.636 (1.072–2.493), 0.022	1.636 (1.070–2.501), 0.023	1.319 (0.845–2.057), 0.223	1.324 (0.845–2.074), 0.219
Use of the TCVC compared with first therapy.	3.214 (2.221–4.651), < 0.0001	3.215 (2.207–4.694), < 0.0001	2.007 (1.289–3.123), 0.002	2.004 (1.240–3.326), 0.005
Types (Groshong, Hickman-Broviac, Port catheter) of TCVC	1. Ref. 1.638 (1.053–2.547), 0.029 1.280 (0.560–2.926), 0.558	1. Ref. 1.626 (1.055–2.500), 0.028 1.132 (0.732–1.751), 0.579	1. Ref. 0.698 (0.261–1.868), 0.474 0.760 (0.215–2.688), 0.670	1. Ref. 0.792 (0.414–1.516), 0.483 1.502 (0.904–2.497), 0.116
Catheter diameter (French) (≤7 vs. >7)	2.824 (1.964–4.065), <0.0001	2.825 (1.973–4.041), <0.0001	1.139 (0.452–2.865), 0.782	1.061 (0.535–2.109), 0.865

	CLABSI as a whole			
	(probability ratio, 95% confidence interval)			
	Single-variable models		Multiple-variable models	
	Conventional	Regression	Analysis	Coefficients of variability
Lumens in catheters (DL vs. SL)	3.333 (2.304–4.830), <0.0001	3.335 (2.316–4.801), <0.0001	2.739 (1.288–5.847), 0.009	2.607 (1.392–4.880), 0.003
AAN at CVC placement (<0.5 vs. >0.5)	0.698 (0.467–1.018), 0.062	0.698 (0.472–1.024), 0.066	0.898 (0.595–1.355), 0.609	0.895 (0.596–1.344), 0.594

Discussion

In this observational study, we retrospectively evaluated the association between perioperative neutropenia and other potential risk factors on the development of CLABSI among a large and homogenous cohort of paediatric patients with ALL and AML who were undergoing placement of TCVC. The patients all had leukaemia at the time of the study. Every one of the patients was found to be suffering from either of the two types of leukaemia. We were able to demonstrate that an absolute neutrophil count (ANC) of less than $0.5 \times 10^9/L$ at the time a catheter was being inserted did not correlate with an increased risk of CLABSI in either the short-term or the overall study follow-up periods. This was the conclusion we reached after analysing the results of the study. In addition, we demonstrated that the presence of In the overall cohort of neutropenic and non-neutropenic patients that were undergoing TCVC implantation at the same time, the sex of the female child and the use of TCVCs led to the development of CLABSI during the first 30 days after insertion. Patient population as a whole was shown to be affected by this. The use of double-lumen catheters and TCVC during relapses of leukaemia was found to be risk factors contributing to CLABSI over the entire study period increases the risk for CLABSI. This was discovered during the investigation of risk factors that contribute to CLABSI. This was uncovered in the course of research into the factors that increase the likelihood of CLABSI occurring.

According to this study, periprocedural neutropenia was not associated with CLABSI risk, which is in agreement with the findings of a significant number of other studies (10–22). Some studies, however, have found that catheter-associated infections are more likely when the patient is perioperatively neutropenic of catheter-associated bloodstream infection (CLABSI) episodes in neutropenic children. [CLABSI] stands for catheter-associated bloodstream infection. As a consequence of this, it was proposed that these patients not be eligible for placement of TCVCs and that An alternative way of bridging the venous system would be to use a peripherally inserted central venous catheter (PICC) or percutaneous central

venous catheter (CVC) instead of the endovascular approach. This was done in order to maintain access to the patient's veins (7, 8, 23). Our findings, on the other hand, cannot be directly compared to those of other research that has already been published because there is a great deal of variation among the populations that were studied. This is due to the fact that our study was conducted in a different country.

A preliminary analysis showed that 7.4 percent (37/498) of TCVC were affected by CLABSI events in the early stages, while 33.1 percent (165/498) of TCVC were affected by CLABSI in the later stages. Similar results were found in a previous study that measured the incidence rate of late CLABSI among children who had undergone cancer therapy. According to the findings of that study, the overall rate of infectious episodes was 29 percent (24). During the entirety of the research project, there were a total of 99,681 days, and the incidence rate of CLABSI was 1.65 cases per 1,000 CD. This is in line with the findings of earlier studies, which reported pooled CR rates for a variety of haematological Solid tumors and malignancies range from 1.6 to 3.1 per 1,000 CD (25–29). Previous studies have found similar results. Additionally, American National Healthcare Safety Network published the safety rate for the years 2006–2008, which was 2.3, was even lower than what was found with these results, which were even lower (30). Specifically, it was discovered that children who were given a diagnosis of acute leukaemia had a risk for catheter infections that was anywhere from 3.7 to 14.9 times higher than patients who were given a diagnosis of solid malignancies. This finding was made in comparison to patients who were given a diagnosis of other types of cancer (12, 25). As a result of this, while conducting our research, we came to the conclusion that the CLABSI rate among children with acute leukaemia was astonishingly low.

We also examined alternative factors involved in the occurrence of CLABSI and found high odds of TCVC-associated infection were associated with the gender of the patient (hazard ratio = 2.640, 95 percent confidence interval = 1.328–5.250, $p = 0.006$) and the use of TCVC in the treatment of relapsed leukaemia (hazard ratio = 4.347,

95 percent confidence interval = 2.283–8.264, $p = 0.0001$). There were no studies indicating a correlation between females and early CLABSI before this study. It was the first study to demonstrate this correlation. An observation that children with relapsed malignancies are more likely to suffer CLABSI is consistent with findings of a prospective multicenter study involving paediatric cancer patients. A total of 32 children participated in the study. Antineoplastic therapy and increased risk of side effects have been linked to patients who receive intense treatment because organ toxicity accumulates after receiving the first-line treatment. Antineoplastic therapy is known to cause side effects in patients who are more susceptible to them. Patients who have been diagnosed with advanced cancer are among those who are most at risk for experiencing adverse effects as a result of anticancer treatment (33, 34).

Furthermore, there was an increased risk of developing CLABSI when using dual-lumen TCVCs for the entirety of the study period (hazard ratio = 2.607, 95 percent confidence interval = 1.392–4.880, $p = 0.003$). This was one of the primary reasons we decided against using dual-lumen TCVCs. Those findings are aligned with those obtained from the literature, which found a range of HRs for double-lumen catheters, ranging from 2.4 (95 percent confidence interval [CI], 1.6–3.5) to 3.13 (95 percent confidence interval [CI], 2.11–4.65) (35, 36).

Our study found no effects of age, underlying type of leukaemia, or device types on the occurrence of early or overall CLABSI episodes. As a contrast, several studies reported a higher incidence of TCVC-associated infections in younger patients (22, 37), or in patients with acute myeloid leukemia (38) or who used tunnelled externalised catheters rather than ports (27, 39). No matter whether we looked at episodes from early CLABSI or those overall, this was the case. In addition to not performing any categorization or dichotomizing of the patients, we used age as continuous information in our regression models, hence the observed lack of a relationship between age and CLABSI risk. CLABSI risk is not dependent on age in our study, so this may explain why we observed no age dependency. Certainly, there are other possible explanations. In this case, the cutoff points would be arbitrary because they are not defined, causing a reduction in the information or an increase in bias (40, 41). Several biologically distinct subtypes of ALL and AML (42–44) receive treatment in radically different ways, likely contributing to the variation in complication rates within and between subtypes. This is significant given that CLABSI rates and underlying health conditions are not associated.

The vast majority of the organisms that were discovered in neutropenic patients who had CLABSI belonged to the group of streptococci known as Viridans (VGS). VGS are considered to be a normal component of

the flora that lives in the digestive tract. When neutropenia is present, the Due to compromised mucosal barriers, these organisms may be able to transit from the digestive tract into the bloodstream. VGS are the most common isolates within neutropenic adult and paediatric oncological study populations, and we confirmed this finding in our study of neutropenic patients with CLABSI. (45, 46)

We are completely conscious of the numerous drawbacks that are connected to this study. To begin, it is possible that the findings of the study cannot be generalised because it was a retrospective study and it was limited to a single centre. This means that the institution's particular treatment preferences and practises were not taken into account, which means that the results of the study cannot be generalised. Second, despite the fact that Unlike the LCBI 2 criteria, which considers patients' clinical characteristics, we used well-defined criteria for CLABSI (LCBI 1 criteria). This is because satisfying the requirements for LCBI 1 does not necessitate the presence of any sign or symptom, such as a high temperature. In addition to this, essential clinical information, such as the severity of the CLABSI, is not currently available. In spite of this, we are of the opinion that the CLABSI definition based on the criteria of LCBI 1 is more applicable and trustworthy in a scenario that involves the collection of retrospective data. Because the LCBI 1 criteria were applied During the first 48 hours after TCVC placement, none of the study participants were at risk for the study outcome (a central line that has been in place for more than two consecutive calendar days is considered an eligible central line). A central line that meets the eligibility criteria is one which has been in service for more than two continuous calendar days (immortal person-time). The study at hand might have underestimated the cumulative rate of the first CLABSI because of this. Third, because the frequency with which blood samples were drawn during the subsequent treatment course varied from patient to patient, we were not able to keep an accurate record of the ANC values from the point in time when the TCVC was inserted until the point in time when CLABSI occurred. This was due to the fact that the regularity of taking blood samples during the subsequent treatment course was not consistent. As a direct consequence of this, the CLABSI incidence could not be adjusted in accordance with the length of time that the neutropenia had been present. On the other hand, we recalculated the incidence of CLABSI to take into account 1,000 usage days for TCVC. Due to the fact that This investigation is primarily concerned with determining the factors that contribute to that increase the likelihood of developing CLABSI, the various treatment options for CLABSI were not taken into consideration by us. Because of the use of a stringent The inclusion of a large and homogeneous series of patients, as well as the application of univariate and multivariate analyses meant to minimize the interaction between clinical and device characteristics,

meant that our study provided strong evidence about CLABSI in male and female hematooncology patients. Our study provides robust evidence for each of these reasons. Although there are many factors that contribute to CLABSI in hematoon, we consider the results of our study to be credible.

We came to the conclusion that an absolute neutrophil count (ANC) of less than $0.5 \times 10^9/L$ during surgery does not have an effect on the CLABSI episodes in

paediatric patients with acute leukemia in the early or overall stages. According to our study. The use of double-lumen catheters versus TCVC for the treatment of relapsed leukemia has also been demonstrated to be independent risk factors for the progression of CLABSI. It is imperative that measures be taken to reduce the number of CLABSIs that occur through the implementation of catheter care programmes and increased levels of surveillance. It is also imperative that these measures be taken as soon as possible

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