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Original Article

Port-catheter complications in children with malignancy

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ABSTRACT

Objective: Central venous access catheters (CVC) are crucial for chronically ill patients, especially in pediatric cancer patients. The aim of this study was to determine subcutaneous implanted port-catheter-related early and late complications and outcomes of catheters in children with malignancy.

Material and Methods: This retrospective study evaluated complications related to subcutaneous implanted port catheters in children with malignancies who were hospitalized in the Pediatric Hematology and Oncology clinics.

Results: The mean age of 69 patients (M/F,37/32) at diagnosis were 6.4±4.85 years (6 months-17 years). During the study period, 89 port catheters were inserted and 141 complications were detected in 54 (60%) of 89 port catheters in a total of 19226 catheter days. Infectious, thrombotic, and mechanical complications were noted in 98 (69.5%), 29 (20.5%), and 14 (10%) port catheters, respectively. Six different complications were identified in one port catheter, while seven complications were found in three different port catheters of a patient with acute myeloid leukemia (AML). The patients who had severe neutropenia (neutrophil count $<0.5x10^9$) on the day of insertion showed more complications than non-neutropenic patients (63.6%, p <0.001). Fifty-seven early (40.4%) and 84 late (59.6%) complications were noted. The most catheterized vein was the right external jugular vein (n=45), with 32 of these cases resulting in complications. The complication rate for the catheters in right external jugular vein was significantly higher than the others (p= 0.024). Infectious complications were most prevalent both in the early and in the late periods (p<0.001). Gram-positive bacteria, gram-negative bacteria and fungi were identified in 61.6%, 34.9%, and 3.5% catheter cultures, respectively. An antibiotic lock therapy with systemic antibiotics was used in 20 infection episodes; and the antibiotic lock failed only in two infection episodes.

Conclusion: Our study highlighted a high rate of complication-related port catheter removal, with skin flora infections. The choice of vein for insertion and the positioning of the port-catheter tip are also key factors contributing to complications. Ensuring proper implantation, usage, maintenance is essential to minimize both early and late complications.

Keywords: Children, Complication, Malignancy, Port catheter

INTRODUCTION

Central venous access catheters (CVCs) are essential for chronically ill patients, particularly pediatric cancer patients, as they provide a long-term route for administering medications, blood products, nutritional supplements, and fluids. These catheters are typically inserted into a large vessel, with the tip extending to the heart or major vessels like the superior vena cava (1). Implantable port catheters are often the most suitable choice for cancer patients due to their lower risk of infection and extravasation (2). However, both the nature of the malignancy and the irritative effects of vesicant antineoplastic drugs can increase the risk of catheter-related complications (3). Early complications, which occur within 30 days of central line insertion, primarily include cardiac, vascular, pulmonary, and catheter placement issues. Late complications are mainly associated with infections and device dysfunction (3, 4).

This study aimed to determine the early and late complications related to subcutaneous implanted port catheters, as well as the outcomes of catheter use, in children with malignancies hospitalized in pediatric hematology and oncology clinics.

MATERIALS and METHODS

This retrospective study evaluated complications related to subcutaneous implanted port catheters in 69 children with

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malignancies who were hospitalized in the Pediatric Hematology and Oncology clinics of Ankara Children's Health and Diseases Hematology and Oncology Training and Research Hospital between January 2014 and June 2015. The patient's age, diagnosis, port-catheter insertion date, the vein in the catheter placed, the position of the tip of the catheter, neutrophil count and presence of fever at the time of port insertion, port catheter, and peripheral blood culture results and if present, the treatment characteristics with antibiotics or antibiotic lock therapy were recorded. Port-catheter complications of patients who underwent hematopoietic stem cell transplantation were not included. If a port catheter was removed and a new one was inserted in a subsequent session, the new port was considered a distinct catheter.

Port catheters were inserted by pediatric surgeons under general anesthesia in the operating room of our hospital, 7-10 days after the diagnosis of leukemia or solid tumors. Different brands and sizes were used based on the patient's age and weight. The catheters were inserted into the vein deemed appropriate by the surgeon, without the use of ultrasound guidance. After obtaining a blood culture from the catheter, heparinized saline (100 international units/ml, 2-3 ml) was administered, and the catheter was used the following day. The catheter tip was verified using chest radiographs and echocardiography for all patients.

Port catheter complications were classified as early or late. Early complications were defined as those occurring within the first 30 days after catheter insertion, while late complications were those that developed after this period. Both early and late complications were further examined in three categories.

Mechanical complications included fractures, migration, catheter kinking, leakage, extravasation, reservoir rotation, catheter failure, pneumothorax, and bleeding. Thrombotic complications were classified as partial catheter lumen occlusion (suspected when there is an inability to aspirate blood but the ability to infuse) or complete venous thrombus (suspected when there is an inability to both aspirate and infuse), confirmed by Doppler ultrasound or echocardiogram.

Infectious complications were defined as catheter-related local infections (indicated by symptoms such as tenderness, erythema, induration, and purulent discharge at the catheter reservoir), microbiologically documented catheter infections (where a bacterium was identified in the port-catheter culture but not in peripheral blood), or catheter-related bloodstream infections (where the same microorganism was detected in both catheter and peripheral blood cultures in cases with clinical signs of suspected infection). Coagulase-negative Staphylococci (CoNS) and other skin contaminants were considered infection-related agents if two blood cultures were positive, or if one culture was positive along with clinical signs of active infection.

Statistical analysis

Statistical analysis was performed using SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, Ill., USA). Descriptive statistics were presented as numbers and percentages for categorical variables, and as mean values with standard deviations for numerical variables. Chi-square and Fisher's Exact tests were employed to compare categorical variables. A significance level of $p<0.050$ was considered statistically significant.

RESULTS

In this study, 89 port catheters of 69 patients were analyzed. The mean age of the patients were 6.4±4.85 years (6 months- 17 years) (Figure 1). Male female ratio was 37/32. Port catheters were mostly used in patients with hematologic malignancies (n=60, 86.9%), followed by (n=9, 13.1%) patients with solid tumors. Forty-six of these patients (66.6%) were diagnosed with acute lymphoblastic leukemia (ALL), 14 (20.2%) had acute myeloid leukemia (AML) and nine patients had different oncologic malignancies (Neuroblastoma (n=4), rhabdomyosarcoma (n=2), Wilms tumor (n=1), Ewing sarcoma (n=1), and desmoplastic small round cell tumor (DSRCT) (n = 1).

A total of 141 complications were detected in 54 (60%) of the 89 port catheters during the study period, which included an analysis of 19 226 catheter days. The time between port insertion and detection of complications was 19 to 546 days. Six different complications were detected in one port catheter, while seven complications were detected in three different port catheters of a patient with AML.

Infectious, thrombotic, and mechanical complications were noted in 98 (69.5%), 29 (20.5%), and 14 (10%) port catheters, respectively. Nine patients (5%) were febrile on the day of port-catheter insertion and seven of them developed infectious complications, however the complication rates weren't different in patients with and without fever (p=0.150). All complications

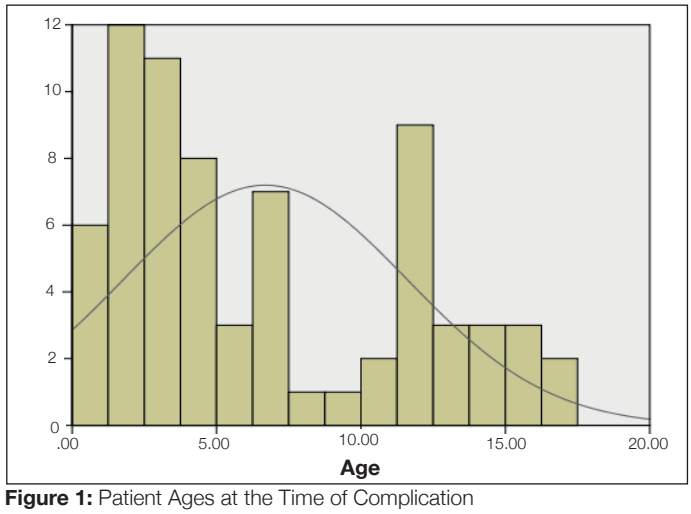

Figure 1: Patient Ages at the Time of Complication

Table I: Types of complications

Complication	n (%)	per 1000 days
Infection (n=98)		
Microbiologically documented catheter infection	70 (71.4)	5
Catheter related blood stream infections	16 (16.4)	
Local infections	12 (12.2)	
Mechanical (n=14)		
Leakage	4 (28.5)	0.8
Reservoir rotation	1 (7.1)	
Extravasation	3 (21.5)	
Catheter fracture	2 (14.3)	
Bleeding in catheter site	1 (7.1)	
Catheter failure	3 (21.5)	
Trombotic (n=29)		
Partial catheter occlusion	25 (86.3)	1.5
Venous thrombosis	4 (13.7)	

Table II: Complications of port catheters based on the time of occurrence

Complication	Mechanical*	Infectious*	Thrombotic*
Early (<30 days) (n=57)	10 (17.5)	42 (73.7)	5 (8.8)
Late (>30 days) (n=84)	4 (4.8)	56 (66.7)	24 (28.5)
Total (n=141)	14 (10)	98 (69.5)	29 (20.5)

***:** *n(%)*

Table III: Microorganisms identified in port catheter cultures

Microorganisms	n (%)
Gram positive bacteria	68 (61.8)
Coagulase negative *staphylococcus*	60 (54.6)
Others	8 (7.2)
Gram negative bacteria	36 (32.7)
Klebsiella	17 (15.4)
E. coli	5 (4.5)
Pseudomonas	4 (3.6)
Enterobacter	4 (3.6)
Others	6 (5.5)
Candida	6 (5.5)

were more frequently observed in the patient group that was neutropenic at the time of port insertion (63.6%, p <0.001), while a platelet count below 50 000/mm³ did not influence the frequency of complications (%53.4 vs 46.6%, p=0.880).

Total complications were noted at 7.3 per 1000 catheter days. Infectious, thrombotic, and mechanic complications were noted at 5, 1.5, and 0.8 per 1000 catheter days, respectively. Fifty-seven early (40.4%) and 84 late (59.6%) complications were noted. Complication types and periods were shown in Table I and Table II. Infectious complications were most prevalent in both the early and the late periods (p<0.001). Although early mechanical and late infectious complications were more common, no statistically significant difference was detected

Table IV: Port catheters after complications and outcome

	Continuation*	Revision*	Removal*
Mechanical (n=14)	8 (57)	4 (28.5)	2 (4.5)
Infectious (n=98)	77 (78.5)	0	21 (21.5)
Thrombotic (n=29)	25 (86)	3 (10.5)	1 (3.5)

***:** *n(%)*

between the type of complications (p=0.090). Most thrombotic complications occurred in the late period (p<0.001).

The vein used for port insertion and the types of complications were evaluated. The most used veins were the right external jugular vein (n=45; 32 of them complicated) and the left external jugular vein (n=25; 12 of them complicated). The complication rates of the external jugular vein and internal jugular vein were similar, however, the complication rate in the right external jugular vein was significantly higher compared to the left external jugular vein (50.6% vs 49.4%, p=0.010). All port-catheter tips were evaluated using echocardiography, and the frequency of complications was significantly higher in patients with catheter tips located in the right atrium (RA) (44.9%, p=0.011).

Infectious complications accounted for 98 (69.5%) of the 141 total complications. Among these, local infections were noted in 12 cases (12.2%). Microbiologically documented catheter infections and catheter-related bloodstream infections were detected in 70 (71.4%) and 16 (16.4%), respectively. Gram-positive bacteria, gram-negative bacteria and fungi were identified in 61.8%, 32.7%, and 5.5% catheter cultures, respectively. The most identified microorganisms were coagulase-negative *Staphylococci* (CoNS) and *Klebsiella species* (Table III). Port catheters were removed in 21 infection episodes due to infectious complications. Antibiotic lock therapy, in conjunction with systemic antibiotics, was used in 20 episodes of infection. Vancomycin was administered in 17 episodes for CoNS and *Enterococci*, while ciprofloxacin was used in two episodes for *E. coli* and one episode for *K. kingae*. Antibiotic lock therapy was ineffective in only two episodes.

Twenty-five (86.3%) of the thrombotic complications were classified as partial catheter occlusions. In cases of catheter occlusion, a heparin lock was attempted first; if recanalization was not achieved, a tissue plasminogen activator (tPA) was administered into the catheter lumen. Venous thrombosis was detected with doppler USG in four of 29 (13.7%) thrombotic complications. The locations of thrombosis were the right external jugular vein (n=2), superior vena cava (n=1), and left external jugular vein (n=1). Two of the four thromboses were acute, and these ports continued to be used with low molecule weight heparin therapy. Port catheters that were not recanalized with either heparin or tPA were revised or removed, respectively.

Mechanical complications were 10% (n=14) of all complications. These were leakage (n=4), reservoir rotation (n=1), extravasation (n=3), catheter fracture (n=2), bleeding in the catheter site (n=1), and catheter failure (n=3). Pneumothorax, arterial injury, air embolism, and arrhythmia did not occur in any patient.

In all complications, 78% of the port catheters continued to be used, 5% were revised, and 17% were removed. The outcome of catheters are shown on Table IV. The most common cause of catheter removal was an infection. Coagulase-negative *Staphylococci*, which is the main element of skin flora, are the most common infectious agent.

DISCUSSION

The use of port catheters provides significant convenience for both patients receiving chemotherapy and healthcare workers (5-7). Reported incidence rates of catheter-related complications in children with malignancies range from 6% to 41% (8-10). During our study period, the incidence of port-catheter-related complications was higher, with complications detected in 75% of port catheters, and early complications accounting for 40.4% of these. Although our study found a higher rate of port catheter-related complications compared to the literature, most of the affected ports remained usable, as most complications were microbiologically documented catheter infections with CoNS. The infection-related catheter removal rate has been reported as 9.3% to 26.8% (11).

The overall complication rate was found to be 7.3 per 1.000 catheter days. In a study including all types of central venous catheters, infection, thrombosis, and mechanical complications were reported at rates of 3.7, 0.2, and 0.4 per 1.000 catheter days, respectively, in patients with hematologic diseases (12). Port catheter-related infection rates were reported as 2.5 and 7.4 per 1.000 catheter days in two different studies from our country, which are consistent with our findings (13,14). In another study, port catheter-associated venous thrombosis, and infections were noted at 0.67 events and 0.84 events per 1000 catheter days, respectively (15). The higher incidence of complications in our study compared to the literature may be attributed to factors such as the variety of underlying diseases and treatments, differing criteria for classifying complications, variations in catheter care protocols, the type of vein used for catheter insertion, and the experience of both the insertion and management teams. Infectious complications were the most prevalent in both the early and late periods, while mechanical complications were more common in the early period. The early period is representative of the induction phases of leukemia treatment in which the patients are not in remission, have neutropenia or thrombocytopenia, and are most susceptible to infection. A high rate of mechanical complications might have been caused due to not using USG or fluoroscopic guidance at the time of catheter insertion.

In our study, thrombotic complications were common in the late period. Catheters are artificial surfaces and lack vascular endothelial function such as inhibition of platelet adhesion or inflammatory response. Thrombotic complications in the late period can be clarified by the duration of use is extended, the risk of both fibrin sheath formation and thrombosis increases due to the precipitation of the medical drugs, blood components, and handling errors (2,16). Neutropenia is another risk factor for leading port catheters to infectious complications (17). In the mechanical, infectious and thrombotic complication groups, early complications were seen statistically significantly in cases with neutrophil count <1500/mm^3 at the time of port insertion.

Efforts are ongoing to identify effective flushing and locking solutions to prevent both infectious and mechanical complications associated with port catheter devices (18). The use of antibiotic prophylaxis before placement is also controversial (19,20). A single dose of antibiotics targeted to skin flora is still given to immunocompromised patients before the insertion of CVC in some centers. Disinfection of the hub, needleless connector, or injection port with alcohol or chlorhexidine is also recommended (21). Consistent with the literature, we did not use routine antibiotic prophylaxis in pediatric cancer patients with port catheters during the study period. Studies have shown that implementing a catheter care bundle can prolong catheter life and reduce treatment costs by decreasing the frequency of infections. The key components of the catheter care bundle identified in these studies include skin cleansing with chlorhexidine, ensuring sterility during catheter insertion, selecting non-femoral veins for insertion, and adhering to strict sterility protocols in daily care (22). Devrim et al. (23) inserted split-septum catheters and utilized pre-filled syringes as part of their catheter care bundle. They demonstrated that the use of central line bundles not only decreased the risk of catheter-related infections but also prolonged the time to develop infections, resulting in cost-effectiveness (24).

In conclusion, port catheter complications remain a significant concern for children with cancer, presenting challenges despite the availability of standardized practice guidelines. Our study highlighted a high rate of complication-related port catheter removal, with infections—especially those caused by CoNS, a common element of skin flora—being the leading cause. The choice of vein for insertion and the positioning of the port-catheter tip are also key factors contributing to complications. Ensuring proper implantation, usage, and maintenance is essential to minimize both early and late complications. Furthermore, comprehensive training for clinicians, patients, and caregivers, including simulations, hand hygiene education, and the use of ultrasound guidance during catheter placement, is essential for improving outcomes and preventing complications.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital (2014-246).

Contribution of the authors

Bağcı MS: Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical

interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Yazal Erdem A:*** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study. ***Özbek NY:*** Constructing the hypothesis or idea of research and/or article. ***Yaralı N:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Ullman AJ, Bernstein SJ, Brown E, Aiyagari R, Doellman D, Faustino EVS, et al. The Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics: miniMAGIC. Pediatrics 2020;145:S269-S284. https://doi.org/10.1542/peds.2019-3474I
2. Bawazir O, Banoon E. Efficacy and clinical outcome of the port-a-cath in children: a tertiary care-center experience. World J Surg Oncol 2020;18:134. https://doi.org/10.1186/s12957-020-01912-w
3. Machat S, Eisenhuber E, Pfarl G, Stübler J, Koelblinger C, Zacherl J, Schima W. Complications of central venous port systems: a pictorial review. Insights Imaging 2019;10:86. https://doi.org/10.1186/s13244-019-0770-2
4. Ross AB, Rouanet E, Murphy AJ, Weldon CB, Weil BR. Complications associated with totally implantable access ports in children less than 1 year of age. J Pediatr Surg 2022;57:463-8. https://doi.org/10.1016/j.jpedsurg.2021.12.004
5. Kılıç S, Soyer T, Karnak İ, Çiftçi AÖ, Tanyel FC, Şenocak ME. Evaluation of the removal reasons of totally implantable venous devices in children: a retrospective study. Turk J Pediatr 2016;58:187-94. https://doi.org/10.24953/turkjped.2016.02.010
6. Zhang H, Li Y, Zhu N, Li Y, Fu J, Liu J. Comparison of peripherally inserted central catheters (PICCs) versus totally implantable venous-access ports in pediatric oncology patients, a single center study. Sci Rep 2022;12:3510. https://doi.org/10.1038/s41598-022-07584-8
7. van den Bosch CH, Spijkerman J, Wijnen MHWA, Hovinga ICLK, Meyer-Wentrup FAG, van der Steeg AFW, et al. Central venous catheter-associated complications in pediatric patients diagnosed with Hodgkin lymphoma: implications for catheter choice. Support Care Cancer 2022;30:8069-79. https://doi.org/10.1007/s00520-022-07256-3
8. Jan HC, Chou SJ, Chen TH, Lee CI, Chen TK, Lou MA. Management and prevention of complications of subcutaneous intravenous infusion port. Surg Oncol 2012;21:7-13. https://doi.org/10.1016/j.suronc.2010.07.001
9. Cesaro S, Cavaliere M, Pegoraro A, Gamba P, Zadra N, Tridello G. A comprehensive approach to the prevention of central venous catheter complications: results of 10-year prospective surveillance in pediatric hematology-oncology patients. Ann Hematol 2016;95:817-25. https://doi.org/10.1007/s00277-016-2634-x
10. Sosnowska-Sienkiewicz P, Moryciński S, Januszkiewicz-Lewandowska D, Michalik K, Madziar K, Kukfisz A, et al. Totally implantable venous ports in infants and children: a single-center retrospective study of indications and safety. Front Oncol 2024;14:1351630. https://doi.org/10.3389/fonc.2024.1351630
11. Kugler E, Levi A, Goldberg E, Zaig E, Raanani P, Paul M. The association of central venous catheter placement timing with infection rates in patients with acute leukemia. Leuk Res 2015;39:311-3. https://doi.org/10.1016/j.leukres.2014.12.017
12. Pektaş A, Kara A, Gurgey A. Cohort Study: Central Venous Catheter-Related Complications in Children with Hematologic Diseases at a Single Center. Turk J Haematol 2015;32:144-51.https://doi.org/10.4274/Tjh.2013.0403
13. Sarper N, Zengin E, Corapçioglu F, Tugay M. Totally implantable central venous access devices in children with hemato-oncologic malignancies: evaluation of complications and comparison of incidence of febrile episodes with similar patients without central venous access devices. Pediatr Hematol Oncol 2006;23:459-70. https://doi.org/10.1080/08880010600712514
14. Celebi S, Sezgin ME, Cakır D, Baytan B, Demirkaya M, Sevinir B, et al. Catheter-associated bloodstream infections in pediatric hematology-oncology patients. Pediatr Hematol Oncol 2013;30:187-94. https://doi.org/10.3109/08880018.2013.772683
15. Beckers MM, Ruven HJ, Seldenrijk CA, Prins MH, Biesma DH. Risk of thrombosis and infections of central venous catheters and totally implanted access ports in patients treated for cancer. Thromb Res 2010;125:318-21. https://doi.org/10.1016/j.thromres.2009.06.008
16. Onyeama SN, Hanson SJ, Dasgupta M, Baker K, Simpson PM, Punzalan RC. Central Venous Catheter-associated

Venous Thromboembolism in Children With Hematologic Malignancy. J Pediatr Hematol Oncol 2018;40:e519-e524. https://doi.org/10.1097/MPH.0000000000001229

17. Planas Díaz I, Molina Mata M, Casal Beloy I, Cabello Laureano R. Indwelling-tunneled-central-venous-catheter-related early bacteremia and preoperative prophylaxis: a case and control study. Cir Pediatr 2024;37:99-103. https://doi.org/10.54847/cp.2024.03.10
18. Rickard CM, Ullman AJ. Bloodstream infection and occlusion of central venous catheters in children. Lancet Infect Dis 2018;18:815-7. https://doi.org/10.1016/S1473-3099(18)30267-6
19. Johnson E, Babb J, Sridhar D. Routine Antibiotic Prophylaxis for Totally Implantable Venous Access Device Placement: Meta-Analysis of 2,154 Patients. J Vasc Interv Radiol 2016;27:339-43. https://doi.org/10.1016/j.jvir.2015.11.051
20. Akbar SA, Qudsia ZF, Ashraf MN, Tarar MA, Qazi AQ. Prophylactic Antibiotics for Reducing Central Line-associated Blood Stream Infection in Children with Totally Implantable Venous Access Devices. J Coll Physicians Surg Pak 2020;30:304-8. https://doi.org/10.29271/jcpsp.2020.03.304
21. Chesshyre E, Goff Z, Bowen A, Carapetis J. The prevention, diagnosis and management of central venous line infections in children. J Infect 2015;71:S59-75. https://doi.org/10.1016/j.jinf.2015.04.029
22. Rabelo BS, de Alvarenga KAF, Miranda JWFB, Fagundes TP, Cancela CSP, de Castro Romanelli RM, et al. Risk factors for catheter-related infection in children with cancer: A systematic review and meta-analysis. Am J Infect Control 2023;51:99-106. https://doi.org/10.1016/j.ajic.2022.05.005
23. Devrim İ, Özkul MT, Çağlar İ, Oruç Y, Demiray N, Tahta N, Vergin C. Central line bundle including split-septum device and single-use prefilled flushing syringes to prevent port-associated bloodstream infections: a cost and resource-utilization analysis. BMC Health Serv Res 2020;20:336. https://doi.org/10.1186/s12913-020-05221-6
24. Devrim İ, Sandal OS, Çelebi MY, Hepduman P, Gönüllü A, Atakul G, et al. The impact of central line bundles on the timing of catheter-associated bloodstream infections and their microbiological distribution in critically ill children. Eur J Pediatr 2023;182:4625-32. https://doi.org/10.1007/s00431-023-05141-7