Original Article

Predictors of central line-associated bloodstream infections in cancer patients undergoing chemotherapy through implanted venous access ports: a retrospective, observational study

Hao Chen[#]^, Takamasa Yamane[#], Terunobu Haruyama, Masashi Ishihara, Hiroki Kazahari, Takahiko Sakamoto, Shigeru Tanzawa, Takeshi Honda, Yasuko Ichikawa, Kiyotaka Watanabe, Nobuhiko Seki

Department of Oncology, Teikyo University Hospital, Tokyo, Japan

Contributions: (I) Conception and design: H Chen; (II) Administrative support: H Chen, N Seki; (III) Provision of study materials or patients: T Yamane; (IV) Collection and assembly of data: T Yamane; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Nobuhiko Seki, MD, PhD. Department of Oncology, Teikyo University Hospital, 2-11-1 Kaga, Itahashi, Tokyo 173-8606, Japan. Email: nseki@med.teikyo-u.ac.jp.

Background: Central venous catheters (CVCs) are sometimes superior to peripheral vascular access for chemotherapy. Central line-associated bloodstream infections (CLABSIs) are an important complication of CVCs in chemotherapy.

Methods: A retrospective, observational study was conducted to investigate patients with implanted venous access ports (PORTs) from July 2010 to June 2021 in a teaching hospital. General conditions of the PORTs, backgrounds, and characteristics of patients were compared between CLABSI cases and uninfected cases to identify predictors of CLABSI.

Results: A total of 566 patients with PORTs who underwent chemotherapy were enrolled in this study, with CLABSI identified in 41 patients, for a total of 436,597 catheter-days. The median duration of PORT use was 26 *vs*. 494 days (P<0.001) in the CLABSI and uninfected groups, respectively. There were no significant differences in tumor classification, staging, white blood cell (WBC) count, neutrophil proportion, lymphocyte proportion, albumin, C-reactive protein (CRP), and performance status between the CLABSI and uninfected groups. Multivariable analysis showed that antibiotic usage within the previous week, total protein (TP), and immediate PORT use were independently associated with CLABSI, and their odds ratios (ORs) were 4.89 [95% confidence interval (CI): 1.67, 14.35], 1.95 (95% CI: 1.14, 3.53), and 3.13 (95% CI: 1.18, 8.30), respectively. The area under the curve (AUC) of the receiver-operating characteristic curve for TP was 0.63, and the cutoff value was 5.9 g/dL.

Conclusions: PORT implantation should be avoided in patients who had antibiotic treatment episodes within 1 week, especially for those with low serum TP levels.

Keywords: Central venous catheters (CVCs); central line-associated bloodstream infection (CLABSI); chemotherapy

Submitted Jul 13, 2023. Accepted for publication Oct 20, 2023. Published online Dec 05, 2023.
doi: 10.21037/tcr-23-1217
View this article at: https://dx.doi.org/10.21037/tcr-23-1217

^ ORCID: 0000-0003-3074-2235.

Introduction

Chemotherapy is a common treatment for cancer patients that can prolong the survival of those with metastases. Intravenous administration of chemotherapy is associated with potential complications of extravasation and phlebitis (1,2). Reliable and safe access to a central vein over a long period for the delivery of chemotherapy and collection of blood samples is of great importance in modern oncology practice (3). Even more, repeated venipuncture is an unpleasant experience for patients, which makes central venous catheters (CVCs) superior to peripheral vascular access (4).

Cancer patients frequently require CVCs for therapy and parenteral nutrition and are at high risk of CVC-related infections due to disease-related and treatment-related immunosuppression (5). Hickman, peripherally inserted central catheters (PICCs), and implanted venous access ports (PORTs) are three suitable catheterization methods as CVCs for intravenous chemotherapy (6-8). Several trials showed that PORTs were superior to PICCs in cancer patients (8-11). Based on clinical symptoms and laboratory findings, localized infections of CVCs such as exit-site infections, tunnel infections, and port-pocket infections are distinguished from central line-associated bloodstream infections (CLABSIs) or catheter-related blood stream infections (CRBSIs). However, the definitions of CLABSI or CRBSI are not interchangeable, since the criteria vary substantially between the two definitions (12,13).

The frequency of CLABSIs in cancer patients is estimated at 0.5–10 per 1,000 CVC days (14). There are associations between CLABSI and hospital mortality rate, length of hospital stay, and 30-day re-admission outcomes (15), and many factors contribute to CLABSIs. Based on the route of entry of bacteria, CLABSIs are classified as extraluminal and intraluminal, with pathogens migrating along an external surface of the catheter from the skin entry site and migrating along an internal surface of the catheter, respectively (16,17). Patient characteristics, provider characteristics, and device characteristics are also potentially associated with CLABSIs.

PORTs are indispensable for cancer patients undergoing chemotherapy. There have been only a few studies investigating risk factors for CLABSI in cancer patients (18,19), but there was no consensus on predictors of infection. This study was designed to identify predictors contributing to CLABSI in cancer patients who underwent chemotherapy with PORT. The general conditions of patients before PORT implantation, according to background and characteristics, were collected and compared between CLABSI and non-CLABSI groups. We present this article in accordance with the STARD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1217/rc).

Highlight box

Key findings

- This study found that antibiotic usage within the previous week, total protein (TP) levels, and immediate usage were independently associated with implanted venous access port (PORT) infections.

What is known and what is new?

- Hypoalbuminemia, the timing of port placement, and steroid use were previously reported as risk factors for PORT infections.
- PORT implantation should be avoided in patients who have received antibiotic treatment within 1 week, especially those with serum TP levels below 5.9 g/dL.

What is the implication, and what should change now?

- Establishing a schedule for PORT implantation may be necessary for patients undergoing chemotherapy.

Methods

This was a retrospective, observational study of patients admitted to a Teikyo University Hospital in Japan from July 1, 2010, to June 30, 2021. This study was approved by the Institutional Review Board of Teikyo University Hospital (No. 21-116) and conformed to the provisions of the Declaration of Helsinki (as revised in Brazil, 2013). Written informed consent was obtained from participants before starting the study.

Definition

The US Centers for Disease Control and Prevention (CDC) defines CLABSI as a laboratory-confirmed bloodstream infection not related to an infection at another site that develops within 48 hours of central line placement (20).

PORT procedure

All operations for PORT insertion were performed by the section of Interventional Radiology in the Department of Radiology under strict aseptic conditions with standard sterile precautions in coordination with the insertion bundle procedure suggested by the CDC (21). Blood tests,

including a blood count, were performed to assess the basic information of the patient who underwent PORT insertion. Catheter site dressings were used as recommended by Disease Control and Prevention guidelines to prevent intravascular catheter infection. A prophylactic antibiotic (cefazolin) was administered before the procedure to prevent surgical-site infection (22). Ultrasound and radiographic guidance techniques for catheter insertion were used in all cases. Generally, the subclavian approach was chosen for venous access. PORTs were implanted subcutaneously under local anesthesia. A single-lumen catheter was inserted through the guide wire at the puncture site, and the tip was placed at the level of the cavoatrial junction, confirmed under fluoroscopy. The pouch for the port reservoir was dissected into the subcutaneous tissue of the chest wall. The catheter was tunneled under the skin from the pouch to the venous entry site and subsequently inserted into the superior vena cava. The port reservoir was then immobilized with sutures in the subcutaneous tissue. First, the catheter's length was precisely measured on fluoroscopy and cut to the correct length in the pouch. Various port systems were used, including a titanium reservoir with 8-Fr MRI ports (Bard Inc., Salt Lake City, UT, USA), 6-Fr Orphis CV kit (Sumitomo Bakelite Company Limited, Tokyo, Japan), and 5-Fr IV catheters and Septum ports from Orca CV kits (Sumitomo Bakelite Co., Tokyo). The choice of devices for each case was based on the underlying disease, patient anatomy, availability of the device, and the type of chemotherapy. Protocols for appropriate care and maintenance of PORTs were established by the Infection Control Doctor panel.

Antibiotic usage

Blood cultures were collected if patients had a fever over 38 ℃. The blood culture procedure was performed according to the guidebook published by the Infectious Diseases Society of America and the American Society for Microbiology (23), and it was usually conducted by medical interns. In patients with a positive culture result, PORT replacement would be delayed until a confirmed negative culture after antibiotic treatment. A negative blood culture was not normally confirmed before PORT insertion. The selection of antibiotics was according to the symptoms and/or suspected diseases of patients according to The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2020 (24).

Data extraction

To ensure that all eligible cases were enrolled, the study investigators screened the hospital database for cases including any implantation or removal of central catheters or patient lists with results of catheter cultures.

Inclusion and exclusion criteria

All enrolled cases had been diagnosed as having malignancy with pathological findings or clinical diagnoses. Inclusion criteria were as follows: (I) PORTs were used for chemotherapy; and (II) clinical information and laboratory findings from before implantation were available. The exclusion criteria were as follows: (I) duration of PORT use was unclear, since catheters removed outside of the hospital were placed at other institutions; and (II) other reasons (e.g., informed consent not obtained).

Variables and definitions

The primary objective of the present study was to identify the predictors of CLABSI. To identify potential factors related to CLABSI, patients' characteristics including vital signs, laboratory data, performance status (PS), and classification of tumors were collected. White blood cell (WBC), total protein (TP), albumin, and C-reactive protein (CRP) were included as predictors of CLBASI according to the previous study (25). Data were collected the nearest day before implantation, usually 1 day before the surgery. Operation sites of PORTs were also checked between groups. Information about prior chemotherapy and antibiotic usage was also collected 1 week before PORT implantation (26). Whether there was immediate use of the PORT within 1 week after implantation for chemotherapy was also noted. PS was identified according to the Eastern Cooperative Oncology Group PS (27). Complications of venous port systems are divided into periprocedural early (≤30 days after implantation) and delayed (>30 days) complications (28). Early CLABSI was defined as infection that occurred within 30 days.

Statistical analyses

The results are presented as numbers and percentages or medians and interquartile ranges (IQRs) unless otherwise indicated. Groups were compared using Wilcoxon rank-

Table 1 General information related to PORT implantation in patients

Variables	CLABSI	Uninfected	P value
Duration (days)	26 [17, 30]	494 [297, 895]	<0.001
Site			0.851
Left subclavian vein	7 (17.1)	92 (17.5)	
Right subclavian vein	34 (82.9)	433 (82.5)	
Prior chemotherapy			0.938
Yes	22 (53.7)	285 (54.3)	
No	19 (46.3)	240 (45.7)	
Antibiotic within 1 week			<0.001
Yes	21 (51.2)	108 (20.6)	
No	20 (48.8)	417 (79.4)	
Prior fever within 1 week			0.006
Yes	15 (36.6)	98 (18.7)	
No	26 (63.4)	427 (81.3)	
Immediate use of CVC			0.039
Yes	29 (70.7)	284 (54.1)	
No	12 (29.3)	241 (45.9)	

Data are presented as median [interquartile range] or n (%). PORT, implanted venous access port; CLABSI, central line-associated bloodstream infection; CVC, central venous catheter.

sum tests. Candidate risk factors for early CLABSI were selected as those showing values of P<0.2 for differences between groups. Variables for inclusion in the multivariable regression analysis were determined by stepwise regression analysis using modeling with the minimum corrected Akaike's information criterion (AIC) in the forward direction. In all instances, two-tailed values of P<0.05 were considered significant. Data analysis was performed using JMP software (version 15.0; SAS Institute, Cary, NC, USA).

Results

A total of 566 patients with PORTs who underwent chemotherapy for a total of 436,597 catheter-days were enrolled in this study, with 41 cases of CLABSI. CLABSI occurred within 1 month in 34 cases. The number of CLABSIs per 1,000 catheter days was 0.94. PORTs were removed in all patients and re-inserted in 38 patients after treatment of the infection (*Table 1*). The median PORT duration was 26 days (IQR, 17, 30 days) *vs.* 494 days (IQR, 297, 895 days) (P<0.001) in the CLABSI and uninfected groups, respectively. The mean PORT duration (standard error) was 42.4 (56.2) days. The right subclavian vein was the most frequent site selected for PORTs, and there were no significant differences between the groups in PORT placement sites (P=0.851). More than half of the patients underwent chemotherapy before PORT implantation. The frequency of antibiotic usage and an episode of fever in the 1 week prior to PORT insertion was higher in the CLABSI group, 51.2% *vs.* 20.6% (P<0.001) and 36.6% *vs.* 18.7% (P=0.006), respectively. The frequency of immediate PORT use, with chemotherapy conducted within 1 week, was higher in the CLABSI group (70.7% *vs.* 54.1%; P=0.039).

Patients' background characteristics are summarized in *Table 2*. There were no significant differences in tumor classification, staging, WBC count, neutrophil proportion, lymphocyte proportion, albumin, CRP, and PS between the CLABSI and uninfected groups. The proportion of females was higher in the CLABSI group (P=0.036), and the median age was also lower in the CLABSI group (61 *vs.* 69 years; P=0.048). TP was lower in the CLABSI group (5.9 *vs.* 6.3 g/dL, P=0.007).

Multivariable regression analysis was performed to investigate the factors contributing to early CLABSI. The final model included TP, prior infection with antibiotic usage within 1 week, immediate PORT use within 1 week, sex, and fever in the previous week (*Table 3*). The results showed that prior infection with antibiotic usage within 1 week, TP, and immediate PORT use were independently associated with CLABSI; their odds ratios (ORs) were 4.89 [95% confidence interval (CI): 1.67, 14.35], 1.95 (95% CI: 1.14, 3.53), and 3.13 (95% CI: 1.18, 8.30), respectively. The relationship between TP and CLABSI is shown in *Figure 1*. The area under the curve (AUC) of the receiver-operating characteristic (ROC) curve for TP was 0.63, and the cutoff value was 5.9 g/dL.

The distribution of causative microorganisms in cultures from patients with CLABSI is shown in *Table 4*. *Staphylococcus aureus* was detected in 13 cases (32%), including five cases of methicillin-resistant *Staphylococcus aureus* (MRSA), as the most frequent microorganisms identified in CLABSI, followed by *Staphylococcus epidermidis* in 9 (22%) cases. *Candida albicans* (12%) was the most frequent fungal infection in CLABSI. Staphylococcal and candidal infections accounted for 29/41 (71%) and 8/41 (20%) of all infections, respectively.

Table 2 Background characteristics of enrolled patients with CLABSI

Characteristics	CLABSI	Uninfected	P value
Sex (F/M)	20/21	183/342	0.036
Age (years)	61 [52, 73]	69 [60, 74]	0.048
Tumor classification			0.602
Gastrointestinal cancer	16 (39.0)	218 (41.5)	
Lung cancer	7 (17.1)	101 (19.2)	
Breast cancer	3 (7.3)	52 (9.9)	
Gynecological tumor	2 (4.9)	42 (8.0)	
Others	13 (31.7)	112 (21.3)	
Staging			0.067
II	0 (0)	36 (6.9)	
III	6 (14.6)	123 (23.4)	
IV	35 (85.4)	366 (69.7)	
WBC	5,800 [4,100, 7,550]	6,000 [4,500, 8,500]	0.702
Neu (%)	69 [59, 82]	71 [61, 79]	0.841
Lym (%)	18 [8, 29]	19 [11, 24]	0.632
TP (g/dL)	5.9 [5.4, 6.5]	6.3 [5.9, 6.8]	0.007
Alb (g/dL)	3.1 [2.6, 3.7]	3.4 [2.7, 3.8]	0.117
CRP (mg/dL)	1.2 [0.2, 4.6]	0.8 [0.2, 4.2]	0.757
PS[†]			0.818
0	16 (39.0)	238 (45.9)	
1	19 (46.3)	208 (40.1)	
2	5 (12.2)	65 (12.5)	
3	1 (2.4)	8 (1.5)	

Data are presented as median [interquartile range] or n (%). [†], six patients in the uninfected group lost information of PS. CLABSI, central line-associated bloodstream infection; F, female; M, male; WBC, white blood cell; Neu, neutrophil; Lym, lymphocyte; TP, total protein; Alb, albumin; CRP, C-reactive protein; PS, performance status.

Discussion

This study compared 41 cases of CLABSI with a median duration of 26 days and 525 cases of uninfected patients with PORTs who underwent chemotherapy. On multivariate analysis, TP, antibiotic therapy within 1 week before PORT insertion, and chemotherapy within 1 week after PORT insertion were independently associated with CLABSI.

Table 3 Multivariable analysis of factors contributing to early CLABSI

Risk factors	OR	95% CI	P value
Antibiotic usage	4.89	1.67–14.35	0.005
TP	1.95	1.14–3.53	0.011
Immediate PORT use[†]	3.13	1.18–8.30	0.014
Sex	–	–	0.720
Prior fever within 1 week	–	–	0.893

[†], chemotherapy was conducted within 1 week by PORTs. CLABSI, central line-associated bloodstream infection; OR, odds ratio; CI, confidence interval; TP, total protein; PORT, implanted venous access port.

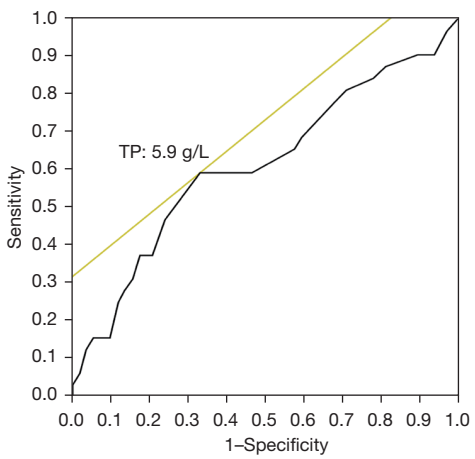

Figure 1 ROC curve for the relationship between total protein and CLABSI. The area under the curve of the ROC curve for total protein is 0.63, and the cutoff value is 5.9 g/dL. TP, total protein; ROC, receiver operating characteristic; CLABSI, central line-associated bloodstream infection.

Previous studies showed that low WBC count, low platelet count, inpatient, hypoalbuminemia, and combined with other operations were the risk factors associated with CLABSI (18,29-31). Due to the different settings of the studies, there was no consensus regarding the risk factors for CLABSI. The present study focused on factors predicting CLABSI in cancer patients and added three potential risk factors that may be useful in the prevention of CLABSI in clinical practice.

Prior infection before insertion was reported as an independent risk factor in a previous study (32). However, there is no robust evidence to indicate the effectiveness of antimicrobial prophylaxis at the time of central venous

Table 4 Distribution of causative microorganisms in cultures from patients with CLABSI

Microorganisms	Number of cases	Frequency
Staphylococcus epidermidis	9	22%
Staphylococcus aureus	8	20%
Staphylococcus aureus (MRSA)	5	12%
Staphylococcus hominis	3	7%
Staphylococcus capitis	2	5%
Staphylococcus simulans	1	2%
Streptococcus constellatus	1	2%
Achromobacter xylosoxidans	1	2%
Enterococcus faecium	1	2%
Klebsiella pneumoniae	1	2%
Serratia marcescens	1	2%
Candida albicans	5	12%
Candida glabrata	2	5%
Candida tropicalis	1	2%

CLABSI, central line-associated bloodstream infection; MRSA, methicillin-resistant Staphylococcus aureus.

port placement. Considering the increased risks of allergic reactions caused by aimless antimicrobial drug usage and the development of resistant microorganisms, the use of antimicrobial prophylaxis is not recommended (33). Cefazolin was routinely administered for the prevention of surgical site infection. Nevertheless, when compared with previous studies, the incidence of PORT infections was not decreased. The incidence of early infectious complications (within 30 days) was low, ranging from 0% to 3% in the group without antimicrobials (34,35). Prior infection with antibiotic usage within 1 week is independently associated with an increased risk of PORT infections. Therefore, it might be useful to avoid PORT infections by constructing a PORT after the infection has subsided.

Nutritional status was considered a risk factor for CLABSI, and body mass index, albumin, and TP were identified in previous studies (18,19). There was no consistent conclusion on which parameter was the most useful predictor for CLABSI. In the present study, TP was an independent risk factor for CLABSI, but the AUC of TP was 0.63, which was a "fair" predictor of CLABSI, with a cutoff value of 5.9 g/dL (36). Proteins play a crucial role in the process of tissue repair and regeneration. Insufficient protein levels in the body can hinder its ability to effectively mend damaged tissues, including those affected by infections (37). Moreover, low protein levels are frequently associated with malnutrition, which significantly impacts an individual's overall health. Malnourished individuals often have compromised immune systems, making them more susceptible to infections (38). Malnutrition or antibiotic usage before insertion suggested an impaired immune status in cancer patients. Patients could be at higher risk of CLABSI when undergoing PORT insertion if they were previously treated with antibiotics with a low TP.

Chemotherapy was started on the first day of PORT catheter insertion in 67–74% of patients in previous study (39). The present study showed that chemotherapy conducted within 1 week was more common in the CLABSI group. To avoid immediate PORT use, a schedule for PORT implantation might be useful to prevent CLABSI. Chemotherapy was usually scheduled according to tumor molecular characteristics and staging, and there could be a delay between pathological diagnosis and treatment. Cancer patients with the following conditions might need an immediate schedule for PORT implantation: intravenous (IV) injection needed many times over 6 months or longer; small veins and need for multiple pokes to place an IV; or IV treatment must be given through a port (for example, when chemotherapy requires multiple days).

In the present study, most patients were diagnosed with CLABSI within 30 days, which implies that the risk factors identified in this paper mainly represent predictors of early complications. The incidence of early PORT infections was higher than in the previous study (6.0% *vs.* 1.2%) (40). Besides the limitation of being a single-center study, a higher ratio of gastrointestinal cancer patients may also play an important role in the high incidence of PORT infections due to malnutrition. Most PORT infections originate from the skin flora (65%), catheter or catheter joints (30%), or other pathways (5%) (41). Various microorganisms are responsible for CLABSI infections but are essentially bacteria and fungi. As bacteria, coagulase-negative staphylococci were frequently encountered, followed by *Staphylococcus aureus*, whereas *Candida* species are the most common fungal pathogens (42). In this study, a similar result for causative microorganisms was obtained, though *Staphylococcus aureus* including (MRSA) was more frequent than *Staphylococcus epidermidis*, and *Candida* also played an important role in CLABSI.

Limitations

Some limitations of this study need to be considered when interpreting the results. First, this study was carried out at one medical facility, so there is possible selection bias in the classification of tumors, regimens of chemotherapy, the procedure of PORT implantation, and the care provided to patients. There were only a few cases of hematological malignancies enrolled in this study, which have an important role in contributing to CLABSI. Second, due to the rare occurrence of CLABSI, only a few patients were included in this study. Third, other factors, such as daily PORT care, the average usage of PORTs, and the medications used in chemotherapy, which could affect CLABSI, were not included in this study due to limited information or the small number of cases. Fourth, while the history of previous bacteremia or infections might be useful as a predictor of CLABSI, but such information was not collected because it was difficult to determine an appropriate period between previous bacteremia or infection and CLABSI.

Conclusions

TP, prior antibiotic usage, and immediate PORT use were independently associated with an increased risk of CLABSI. PORT implantation should be avoided in patients who have received antibiotic treatment or had antibiotic treatment episodes within 1 week, especially for those with serum TP below 5.9 g/dL. A schedule for PORT implantation might be necessary for patients considering chemotherapy.

Acknowledgments

The authors would like to thank Ms. Ikigami Sayaka for her cooperation in data collection.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1217/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1217/dss

Peer Review File: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1217/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1217/coif). N.S. obtained research grants from Eli Lilly, Chugai Pharmaceutical, Taiho Pharmaceutical, Pfizer, Ono Pharmaceutical, Nippon Kayaku, Takeda Pharmaceutical, and Boehringer Ingelheim and received speaking honoraria from Eli Lilly, AstraZeneca, MSD, Chugai Pharmaceutical, Taiho Pharmaceutical, Pfizer, Ono Pharmaceutical, Nippon Kayaku, Takeda Pharmaceutical, Daiichi Sankyo, Boehringer Ingelheim, and Bristol Myers Squibb. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Institutional Review Board of Teikyo University Hospital (No. 21-116) and conformed to the provisions of the Declaration of Helsinki (as revised in Brazil, 2013). Written informed consent was obtained from participants before starting the study.

References

1. Kim JT, Park JY, Lee HJ, et al. Guidelines for the management of extravasation. J Educ Eval Health Prof 2020;17:21.
2. Manrique-Rodríguez S, Heras-Hidalgo I, Pernia-López MS, et al. Standardization and Chemical Characterization of Intravenous Therapy in Adult Patients: A Step Further in Medication Safety. Drugs R D 2021;21:39-64.
3. Mielke D, Wittig A, Teichgräber U. Peripherally inserted central venous catheter (PICC) in outpatient and inpatient oncological treatment. Support Care Cancer 2020;28:4753-60.
4. Pu YL, Li ZS, Zhi XX, et al. Complications and Costs of

Peripherally Inserted Central Venous Catheters Compared With Implantable Port Catheters for Cancer Patients: A Meta-analysis. Cancer Nurs 2020;43:455-67.
5. Böll B, Schalk E, Buchheidt D, et al. Central venous catheter-related infections in hematology and oncology: 2020 updated guidelines on diagnosis, management, and prevention by the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). Ann Hematol 2021;100:239-59.
6. Hinojosa W, Cruz A, Cruz-Utrilla A, et al. Complications associated with peripherally inserted central catheters and Hickman™ in patients with advanced pulmonary hypertension treated with intravenous prostanoids. Respir Med 2021;189:106649.
7. He E, Ye K, Zheng H. Clinical effect and safety of venous access ports and peripherally inserted central catheters in patients receiving tumor chemotherapy: a systematic review and meta-analysis. Ann Palliat Med 2021;10:9105-13.
8. Moss JG, Wu O, Bodenham AR, et al. Central venous access devices for the delivery of systemic anticancer therapy (CAVA): a randomised controlled trial. Lancet 2021;398:403-15.
9. Clatot F, Fontanilles M, Lefebvre L, et al. Randomised phase II trial evaluating the safety of peripherally inserted catheters versus implanted port catheters during adjuvant chemotherapy in patients with early breast cancer. Eur J Cancer 2020;126:116-24.
10. Taxbro K, Hammarskjöld F, Thelin B, et al. Clinical impact of peripherally inserted central catheters vs implanted port catheters in patients with cancer: an open-label, randomised, two-centre trial. Br J Anaesth 2019;122:734-41.
11. Patel GS, Jain K, Kumar R, et al. Comparison of peripherally inserted central venous catheters (PICC) versus subcutaneously implanted port-chamber catheters by complication and cost for patients receiving chemotherapy for non-haematological malignancies. Support Care Cancer 2014;22:121-8.
12. See I, Iwamoto M, Allen-Bridson K, et al. Mucosal barrier injury laboratory-confirmed bloodstream infection: results from a field test of a new National Healthcare Safety Network definition. Infect Control Hosp Epidemiol 2013;34:769-76.
13. Mermel LA, Allon M, Bouza E, et al. 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.
14. Buetti N, Timsit JF. Management and Prevention of Central Venous Catheter-Related Infections in the ICU. Semin Respir Crit Care Med 2019;40:508-23.
15. Chovanec K, Arsene C, Gomez C, et al. Association of CLABSI With Hospital Length of Stay, Readmission Rates, and Mortality: A Retrospective Review. Worldviews Evid Based Nurs 2021;18:332-8.
16. Neoh KG , Li M , Kang ET , et al. Surface modification strategies for combating catheter-related complications: recent advances and challenges. J Mater Chem B 2017;5:2045-67.
17. Janum S, Zingg W, Classen V, et al. Bench-to-bedside review: Challenges of diagnosis, care and prevention of central catheter-related bloodstream infections in children. Crit Care 2013;17:238.
18. Zhang S, Kobayashi K, Faridnia M, et al. Clinical Predictors of Port Infections in Adult Patients with Hematologic Malignancies. J Vasc Interv Radiol 2018;29:1148-55.
19. Becker F, Wurche LA, Darscht M, et al. Totally implantable venous access port insertion via open Seldinger approach of the internal jugular vein-a retrospective risk stratification of 500 consecutive patients. Langenbecks Arch Surg 2021;406:903-10.
20. Haddadin Y, Annamaraju P, Regunath H. Central Line–Associated Blood Stream Infections. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
21. Centers for Disease Control and Prevention (CDC). [access on Jan 2022]. Available online: https://www.cdc.gov/infectioncontrol/pdf/strive/CLABSI101-508.pdf
22. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013;14:73-156.
23. Miller JM, Binnicker MJ, Campbell S, et al. A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology. Clin Infect Dis 2018;67:e1-e94.
24. Egi M, Ogura H, Yatabe T, et al. The Japanese Clinical Practice Guidelines for Management of Sepsis and Septic Shock 2020 (J-SSCG 2020). Acute Med Surg 2021;8:e659.
25. Furuhashi S, Morita Y, Ida S, et al. Risk Factors for Totally Implantable Central Venous Access Port-related Infection in Patients With Malignancy. Anticancer Res 2021;41:1547-53.
26. Viana Taveira MR, Lima LS, de Araújo CC, et al. Risk factors for central line-associated bloodstream infection

in pediatric oncology patients with a totally implantable venous access port: A cohort study. Pediatr Blood Cancer 2017;64:336-42.
27. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5:649-55.
28. Machat S, Eisenhuber E, Pfarl G, et al. Complications of central venous port systems: a pictorial review. Insights Imaging 2019;10:86.
29. Bamba R, Lorenz JM, Lale AJ, et al. Clinical predictors of port infections within the first 30 days of placement. J Vasc Interv Radiol 2014;25:419-23.
30. Tang L, Kim CY, Martin JG, et al. Length of Stay Predicts Risk of Early Infection for Hospitalized Patients Undergoing Central Venous Port Placement. J Vasc Interv Radiol 2020;31:454-61.
31. Chang TC, Yen MH, Kiu KT. Incidence and risk factor for infection of totally implantable venous access port. Langenbecks Arch Surg 2022;407:343-51.
32. Chen IC, Hsu C, Chen YC, et al. Predictors of bloodstream infection associated with permanently implantable venous port in solid cancer patients. Ann Oncol 2013;24:463-8.
33. Sugawara S, Sone M, Sakamoto N, et al. Guidelines for Central Venous Port Placement and Management (Abridged Translation of the Japanese Version). Interv Radiol (Higashimatsuyama) 2023;8:105-17.
34. Di Carlo I, Toro A, Pulvirenti E, et al. Could antibiotic prophylaxis be not necessary to implant totally implantable venous access devices? Randomized prospective study. Surg Oncol 2011;20:20-5.
35. Karanlik H, Kurul S, Saip P, et al. The role of antibiotic prophylaxis in totally implantable venous access device placement: results of a single-center prospective randomized trial. Am J Surg 2011;202:10-5.
36. Jones CM, Athanasiou T. Summary receiver operating characteristic curve analysis techniques in the evaluation of diagnostic tests. Ann Thorac Surg 2005;79:16-20.
37. Yue Z, Yu Y, Gao B, et al. Advances in protein glycosylation and its role in tissue repair and regeneration. Glycoconj J 2023;40:355-73.
38. Sasaki H, Nagano S, Taniguchi N, et al. Risk Factors for Surgical Site Infection after Soft-Tissue Sarcoma Resection, Including the Preoperative Geriatric Nutritional Risk Index. Nutrients 2018;10:1900.
39. Madabhavi I, Patel A, Sarkar M, et al. A Study of Use of "PORT" Catheter in Patients with Cancer: A Single-Center Experience. Clin Med Insights Oncol 2017;11:1179554917691031.
40. Skummer P, Kobayashi K, DeRaddo JS, et al. Risk Factors for Early Port Infections in Adult Oncologic Patients. J Vasc Interv Radiol 2020;31:1427-36.
41. Kubeček O, Paterová P, Novosadová M. Risk Factors for Infections, Antibiotic Therapy, and Its Impact on Cancer Therapy Outcomes for Patients with Solid Tumors. Life (Basel) 2021;11:1387.
42. Pinelli F, Cecero E, Degl'Innocenti D, et al. Infection of totally implantable venous access devices: A review of the literature. J Vasc Access 2018;19:230-42.

Cite this article as: Chen H, Yamane T, Haruyama T, Ishihara M, Kazahari H, Sakamoto T, Tanzawa S, Honda T, Ichikawa Y, Watanabe K, Seki N. Predictors of central line-associated bloodstream infections in cancer patients undergoing chemotherapy through implanted venous access ports: a retrospective, observational study. Transl Cancer Res 2023;12(12):3538-3546. doi: 10.21037/tcr-23-1217

