

Risk Factors for Unplanned Early Implantable Port Catheter Removal in Adult Hematology Cancer Patients Receiving Chemotherapy: A Propensity Score Matching Study

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Purpose: Implantable port catheter is a reliable vascular access for chemotherapy infusion in cancer patients. However, patients with hematology malignancies usually present with a myriad of blood cell abnormalities that put them at risk of infection and mechanical problems requiring catheter removal. This study aims to determine the risk factors associated with unplanned (catheter removal other than completion of treatment plan) early (within 90 days of catheter implantation) implantable port catheter removal.

Patients and Methods: A retrospective, propensity score-matched study of 386 patients with hematology malignancies who received implantable venous access ports between January 2015 and December 2022. We conducted a univariate analysis to select the variables for propensity score matching. Patients with unplanned early implantable port catheter removal (early group) were matched 1:1 to patients without unplanned early removal (non-early group).

Results: Univariate analysis demonstrated a statistically significant difference between early and non-early groups for age ($p = 0.048$), hemoglobin level ($p = 0.028$), thrombocytopenia ($p = 0.025$), and PG-SGA ($p < 0.001$). Thrombocytopenia was the only independent risk factor with a statistically significant difference in Cox proportional hazard analysis, HR 2.823, 95 CI 1.050–7.589, $p = 0.040$. The median catheter survival for patients with thrombocytopenia was 61 days (95% CI 28.58–93.42) compared to 150 days (95% CI 9.81–290.19) for patients without thrombocytopenia, $p = 0.015$. Patient survival is not affected by early catheter removal. The median survival for patients in the early group was 28.28 months (95% CI 27.43–29.15) compared to 32.39 months (95% CI 24.11–40.68), for the non-early group, $p = 0.709$.

Conclusion: Hematology malignancy patients with thrombocytopenia are at high risk for unplanned early port catheter removal without survival difference.

Keywords: hematology, malignancy, vascular port, risk factors, explanation

Introduction

Since the introduction of totally implantable port systems in the early 1980s,¹ these devices have provided reliable vascular access for the delivery of chemotherapy, fluids, medications, blood products, and parenteral nutrition solutions. However, implantable port systems are susceptible to infection and obstruction, as with all foreign materials. The reported infection rate for implantable port catheters is 0.1–1.5 per 1000 catheter days in oncology patients.² Patients needing port implantation often present with depressed immune function due to their disease or related to the treatment. Infection is the most common cause of premature port removal in adult patients with cancer, followed by mechanical complications and thrombosis.^{3,4} The risk for infection among patients with solid and hematology malignancies has conflicting results in the literature. Several authors have found hematology malignancy as a significant risk factor for port infection^{5,6}, while others found no higher risk.^{7,8} The reported increased risk of hematology malignancies could be related to the different degrees of cytopenia that are frequently found at presentation, as well as the consequence of chemotherapy regimens. Unplanned early implantable catheter removal causes treatment interruption and delay of the

treatment plan; knowing which risk factors are associated with this condition allows clinicians to correct those factors and avoid a futile surgical procedure. Most reports set the unplanned early catheter removal period at 30 days from implantation. Since most treatment schedules go beyond 30 days, we extended this period to 90 days from implantation and evaluated the potential factors related to unplanned early port removal through a propensity score matching in hematology malignancy patients.

Materials and Methods

Study Populations

A single-center retrospective study was conducted at Chang Gung Memorial Hospital, Chiayi branch, and included all patients older than 18 years old with a diagnosis of hematology malignancy who received permanent implantable port access from January 2015 to December 2022. The Institutional Review Board of Chang Gung Memorial Hospital approved this retrospective clinical study using anonymous personal information and waived individual informed consent (No. 202301171B0). For this study, we followed the principles of the Declaration of Helsinki.

From the electronic medical record at the time of catheter implantation, we extracted the following data: age, sex, body weight, and height, body mass index, cancer type (leukemia, lymphoma, multiple myeloma, and myelodysplastic syndrome), smoking status, Charlson comorbidity index,⁹ laboratory values (CBC/DC, albumin level, creatinine), catheter implantation day, catheter removal day, and the reason for catheter removal. We use the Scored Patient-Generated Subjective Global Assessment of Nutritional Record score (PG-SGA score) for nutrition status evaluation.¹⁰ Trained onco-nutritionist evaluated all cancer patients within 72 hours of admission. The result of the PGSGA classified patients into normal nutrition (score 0–1), mild malnutrition (score 2–3), moderate malnutrition (score 4–8), and severe malnutrition grade C (score >9). The catheter survival (catheter age in days) was calculated as catheter removal day (last follow-up or death) minus catheter implantation day. We recorded the record till the removal of the implantable catheter, patient loss to follow-up, or the patient's death. The cancer case manager contacted those patients who lost their follow-up appointments for a status update. Patients not reachable by telephone and withdrawn from the National Taiwan Health Insurance scheme were presumed dead. Missing data was found for albumin (N = 15, 3.88%) and PGSGA score (N = 12, 3.11%). Analysis of the missing data revealed a missing at-random pattern, and a multiple-imputation technique (number of imputations: 5) was used to replace these missing values.

We defined bacteremia as the presence of a positive in blood culture. Catheter-related bloodstream infection requires at least 1 of the following: (i) positive culture of the catheter tip or port reservoir associated with a positive peripheral blood culture with the same microorganism or the difference in time to positivity of blood culture drawn from the catheter versus that from a peripheral vein (positivity of the catheter blood sample was at least 2 hours before that of the peripheral blood sample) (ii) local or general sign of infection, such as fever and chills, positive culture from the vascular port (catheter tip or the port reservoir), and regression of clinical signs of infection after port removal, despite a negative peripheral blood culture.¹¹ We use ultrasound or computed tomography to diagnose catheter venous thrombosis. Pocket infection is confirmed when there are local signs of infection, such as local heat, erythema, and purulent discharge. Pocket exposure is confirmed when there is skin disruption and direct visualization of the port reservoir.

Surgical Procedure

We implanted all ports in the operating room by attending or senior surgical residents under fluoroscopic control to confirm the final catheter's tip position (distal superior vena cava and right atrium junction). Most of the catheter implantation was under local anesthesia (10 to 20 mL of 2% mepivacaine hydrochloride) with a single dose of prophylactic antibiotic with cephalosporin. The surgical approach usually consisted of a subclavian incision that uses the cephalic vein for venotomy. In case of a cephalic vein that is too small, tortuous, or unavailable, the surgeon could puncture the subclavian or internal jugular. The catheter was passed through the venotomy site to the superior vena cava-right atrium junction under fluoroscopic guidance. Upon confirmation of the catheter tip's position, the catheter was cut and assembled with the injecting port. Upon creating a small subcutaneous, we fixed the injection port to the underlying pectoralis muscle fascia, and the surgical incision closed in layers. At the end of the procedure, we filled the injecting

port and catheter with diluted heparin saline solution. We use a non-coring Huber needle to deliver all injections through the implantable port system. The implantable port system was flushed at the end of each infusion or routinely once every 4–12 weeks by trained oncology nurses. Removal of the implantable catheter is usually recommended after the completion of the chemotherapy plan with a disease-free of at least 24 months, by the patient's request, or the presentation of any catheter-related complication.

Statistical Analysis

We first conducted a univariate analysis of the entire cohort to determine the factors associated with unplanned early catheter removal. These factors were used later on for propensity score matching between patients with and without unplanned early catheter removal (matching 1:1). We calculated the propensity score using logistic regression with unplanned early catheter removal as the dependent variable with a caliper width of 0.2 times the standard deviation of the propensity score without replacement to pair-match patients “with and without” unplanned early catheter removal. Because of the no normal distribution, we presented continuous variables as median \pm standard deviation and categorical variables as percentages. According to the variable cell size, we used Chi-square or Fisher's exact tests to analyze categorical variables, the Mann–Whitney *U*-test to analyze continuous variables, and the Kruskal–Wallis test to analyze ordinary variables. By using standard definitions, we converted continuous variables into categorical variables. Leukopenia: white cell counts of less than $3.5 \times 1000/\mu\text{L}$, Neutropenia: absolute neutrophil counts of less than $1.5 \times 1000/\mu\text{L}$, Lymphopenia: absolute lymphocyte counts of less than $1.5 \times 1000/\mu\text{L}$, thrombocytopenia: platelet counts of less than $100 \times 1000/\mu\text{L}$. Hypoalbuminemia: albumin level of less than 3.5 g/dL. We divided the PGSGA score into normal nutrition (score 0–1) and malnutrition (score 2–8) for multivariate analysis. We use the Cox proportional hazard analysis to estimate the significance level and relative risks with a 95% confidence interval (CI). A *P* value of <0.05 indicated a statistically significant difference. The clinical data was analyzed using SPSS statistical software version 29.0 (SPSS Inc., Chicago, IL, USA).

Results

Our cancer registry identified 408 patients with hematology malignancies during the study period. After excluding 22 patients, we included 386 patients in the final analysis. We registered 31 cases of unplanned early implantable port catheter removal. The total duration of follow-up was 261,534 catheter days, and the incidence of unplanned early catheter removal was 0.12/1000 catheter days. The indication for catheter removal was bacteremia ($n = 3$), catheter-related bloodstream infection ($n = 21$), fever of unknown cause ($n = 5$), pocket infection ($n = 1$), pocket exposure ($n = 1$), and severe cardiac arrhythmia ($n = 1$). On univariate analysis of the un-matched cohort, we found a statistically significant difference for the following factors: cancer type, hemoglobin level, leukopenia, neutropenia, thrombocytopenia, and PG-SGA. We used these factors as the dependent variables for the propensity score matching process to match patients with (the early group) and without unplanned early implantable catheter removal (non-early group). [Figure 1](#) shows the patient selection and matching process.

Following the matching process, there was no statistically significant difference between early group and non-early group for sex, smoking history, cancer type, body mass index, Charlson comorbidity score, creatinine, hypoalbuminemia, neutropenia, and lymphopenia. Univariate analysis of the matched cohort demonstrated a statistically significant difference between the early and non-early groups for age ($p = 0.048$), hemoglobin level ($p = 0.028$), thrombocytopenia ($p = 0.025$), and PG-SGA ($p < 0.001$). [Table 1](#) shows the cohort and matched cohort demographic characteristics.

Risk factors for early unplanned catheter removal:

Cox proportional hazard analysis shows no statistically significant differences for age ($p = 0.441$), hemoglobin level ($p = 0.396$), and malnutrition (PS-SGA score 2–8) ($p = 0.075$). Patients with thrombocytopenia have nearly three times higher risk for unplanned early implantable catheter removal than those without thrombocytopenia (HR 2.823, 95 CI 1.050–7.589, $p = 0.040$). [Table 2](#) presents the adjusted Cox proportional hazard analysis for unplanned early catheter removal.

Catheter survival analysis using the Kaplan–Meier method showed significant differences for the early and non-early groups. The median catheter survival for the early group was 65 days (95% CI 50.02–79.99) compared to 156 days (95% CI 42.92–269.09) for the non-early group, $p = 0.021$. ([Figure 2](#)) Thrombocytopenia has a significant effect on catheter

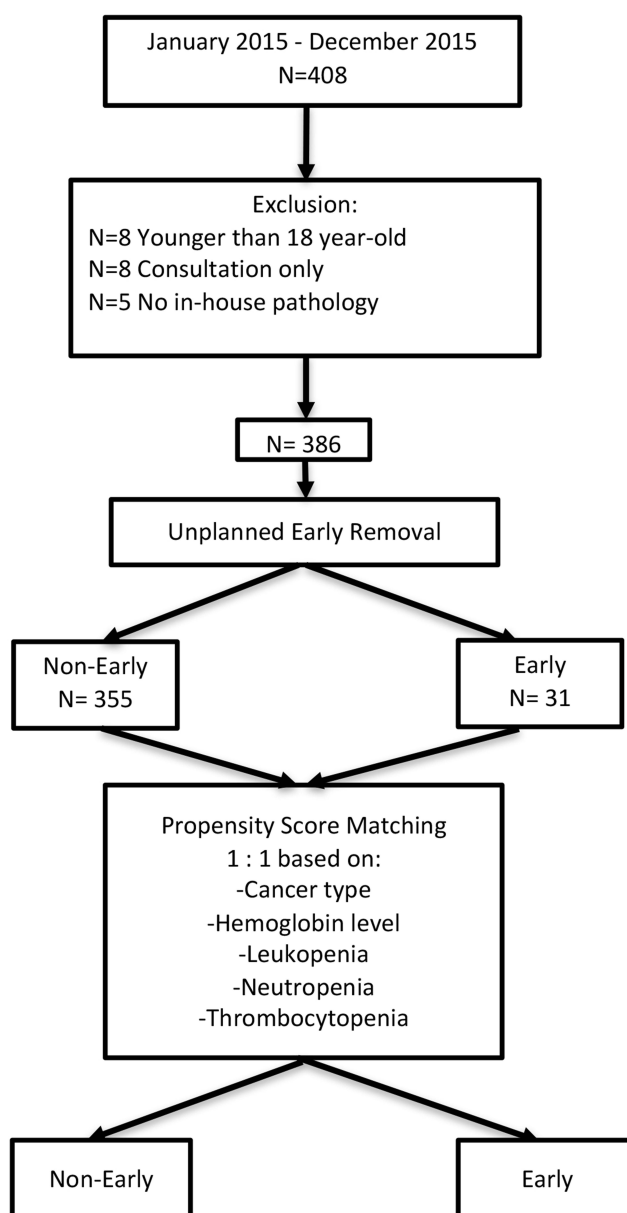


Figure 1 Patient recruitment and matching process.

survival. The median catheter survival for patients with thrombocytopenia was 61 days (95% CI 28.58–93.42) compared to 150 days (95% CI 9.81–290.19) for patients without thrombocytopenia, $p = 0.015$. (Figure 3) The median patient survival is not affected by early catheter removal. The median survival for the early group was 28.28 months (95% CI 27.43–29.15) compared to 32.39 months (95% CI 24.11–40.68) for the non-early group, $p = 0.709$. (Figure 4)

Discussion

This propensity score matching study of hematology malignancies demonstrated that thrombocytopenia is an independent risk factor for unplanned early port catheter removal. The median catheter survival for the early group was 65 days (95% CI 50.02–79.99) compared to 156 days (95% CI 42.92–269.09) for the non-early group, $p = 0.021$.

Cancer patients usually require central line catheters for chemotherapy, antibiotics, and intravenous fluid infusion, as well as blood product transfusion and repeated blood draws. Although several types of central line catheters could serve these purposes, totally implantable port catheters have a lower risk of infections.^{12,13} Nonetheless, infectious conditions and

Table I Cohort and Matched Cohort Demographic Characteristics

Parameter	Cohort				Matched Cohort			
	All	Non-early group	Early group	P value	All	Non-early group	Early group	P value
Number of patients n (%)	386 (100)	355 (92)	31 (8)		62 (100)	31 (50)	31 (50)	
Age (median±SD in years)	63.00±15.54	63.00±15.34	60.00±17.02	0.060	63.00 ±15.81	67.00±13.50	60.00±17.02	0.048
Sex n (%)				0.532				0.798
Female	154 (39.90)	140 (39.40)	14 (45.20)		27 (43.50)	13 (41.90)	14 (45.20)	
Male	232 (60.10)	215 (60.60)	17 (54.80)		35 (56.50)	18 (58.10)	17 (54.80)	
Smoking history n (%)				0.931				0.755
No	309 (80.10)	284 (80.00)	25 (80.60)		49 (79.00)	24 (77.40)	25 (80.60)	
Yes	77 (19.90)	71 (20.00)	6 (19.40)		13 (21.00)	7 (22.60)	6 (19.40)	
Cancer type				<0.001				0.434
Leukemia	133 (34.50)	109 (30.70)	24 (77.40)		48 (74.20)	22 (71.00)	24 (77.40)	
Lymphoma	235 (60.90)	229 (64.50)	6 (19.40)		11 (17.70)	5 (16.10)	6 (19.40)	
Multiple myeloma	9 (2.30)	8 (2.30)	1 (3.20)		1 (1.60)	0 (0)	1 (3.20)	
Myelodysplastic syndrome	9 (2.30)	9 (2.50)	0 (0)		4 (6.50)	4 (12.90)	0 (0)	
Body Mass Index				0.050				0.058
Underweight	17 (4.40)	16 (4.50)	1 (3.20)		2 (3.20)	1 (3.20)	1 (3.20)	
Normal weight	227 (58.80)	213 (60.00)	14 (45.20)		35 (56.50)	21 (67.70)	14 (45.20)	
Overweight	114 (29.50)	103 (29.00)	11 (35.50)		19 (30.60)	8 (25.80)	11 (35.50)	
Obesity	28 (7.30)	23 (6.50)	5 (16.10)		6 (9.70)	1 (3.20)	5 (16.10)	
Charlson comorbidity score (median±SD)	3.00±1.96	3.00±1.98	3.00±1.68	0.196	3.00±2.21	3.00±2.59	3.00±1.68	0.198
Creatinine (median±SD in mg/dl)	0.83±0.60	0.83±0.60	0.83±0.59	0.552	0.82±0.77	0.76±0.91	0.83±0.59	0.451
Hypoalbuminemia				0.856				1.000
No	332 (86.00)	305 (86.90)	27 (87.10)		54 (87.10)	27 (87.10)	27 (87.10)	
Yes	54 (14.00)	50 (14.10)	4 (12.90)		8 (12.90)	4 (12.90)	4 (12.90)	
Hemoglobin	10.85±2.51	11.00±2.51	9.50±1.90	<0.001	8.60±2.05	8.20±2.11	9.50±1.90	0.028
Leukopenia n (%)				<0.001				0.442
No	321 (83.20)	302 (85.10)	19 (61.30)		35 (56.50)	16 (51.60)	19 (61.30)	
Yes	65 (16.80)	53 (14.90)	12 (38.70)		27 (43.50)	15 (48.40)	12 (38.70)	
Neutropenia n (%)				<0.001				0.610
No	315 (81.60)	297 (83.70)	18 (58.10)		34 (54.80)	16 (51.60)	18 (58.10)	
Yes	71 (18.40)	58 (16.30)	13 (41.90)		28 (45.20)	15 (48.40)	13 (41.90)	
Lymphopenia n (%)				0.414				1.000
No	151 (39.10)	141 (39.70)	10 (32.30)		20 (32.30)	10 (32.30)	10 (32.30)	
Yes	235 (60.90)	214 (60.30)	21 (67.70)		42 (67.70)	21 (67.70)	21 (67.70)	

(Continued)

Table 1 (Continued).

Parameter	Cohort				Matched Cohort			
	All	Non-early group	Early group	P value	All	Non-early group	Early group	P value
Thrombocytopenia n (%)				<0.001				0.025
No	274 (71.00)	261 (73.50)	13 (41.90)		18 (29.00)	5 (16.10)	13 (41.90)	
Yes	112 (29.00)	94 (26.50)	18 (58.10)		44 (71.00)	26 (83.90)	18 (58.10)	
PG-SGA (Scored Patient Generated Subjective Global Assessment) n (%)								
Total PG-SGA Score				0.006				<0.001
0–1 point	114 (29.50)	100 (28.20)	14 (45.20)		18 (29.00)	4 (12.90)	14 (45.20)	
2–3 points	171 (44.30)	156 (43.90)	15 (48.40)		25 (40.30)	10 (32.30)	15 (48.40)	
4–8 points	101 (26.20)	99 (27.90)	2 (6.50)		19 (30.60)	17 (54.80)	2 (6.50)	

Table 2 Adjusted Cox Proportional Hazard Analysis for Unplanned Early Catheter Removal

Unplanned Early Catheter removal			
Parameter	Adjusted hazard ratio	95% CI	P value
Age	0.990	0.963–1.016	0.441
Hemoglobin	0.913	0.739–1.127	0.396
Thrombocytopenia			
No	Ref		
Yes	2.823	1.050–7.589	0.040
PG-SGA			
Normal nutrition	Ref		
Malnutrition	2.264	0.921–5.565	0.075

Notes: PG-SGA: Scored Patient Generated Subjective Global Assessment.

Abbreviations: CI, confidence interval; Ref, reference.

mechanical obstruction may prompt the unplanned early removal of these implantable catheters. This later condition is problematic in cancer patients because of treatment interruption, prolonged hospital stays, and increases in medical costs. Patients with hematology malignancies present frequently with different degrees of cytopenia that put them at risk of infection. Leukopenia and its subset neutropenia is an indicator of underlying immunosuppression. The literature is conflicting regarding the significance of neutropenia as a risk factor for port infection. While some studies have reported a higher risk for port infections in prospective and retrospective studies,^{5,14,15} others have found no association.^{16,17} In this study, we found no increased risk for unplanned early removal of implantable catheters with patients with leukopenia or neutropenia.

According to the cancer type, patients with leukemia reported a higher risk for catheter-related infections as compared to patients with lymphoma or myeloma.¹² In the analysis of the risk for unplanned early catheter removal according to the cancer type in this study, we found a higher prevalence of leukemia patients in the early group on univariate analysis of the entire cohort with significant statistical significance; however, after propensity score matching there was no difference.

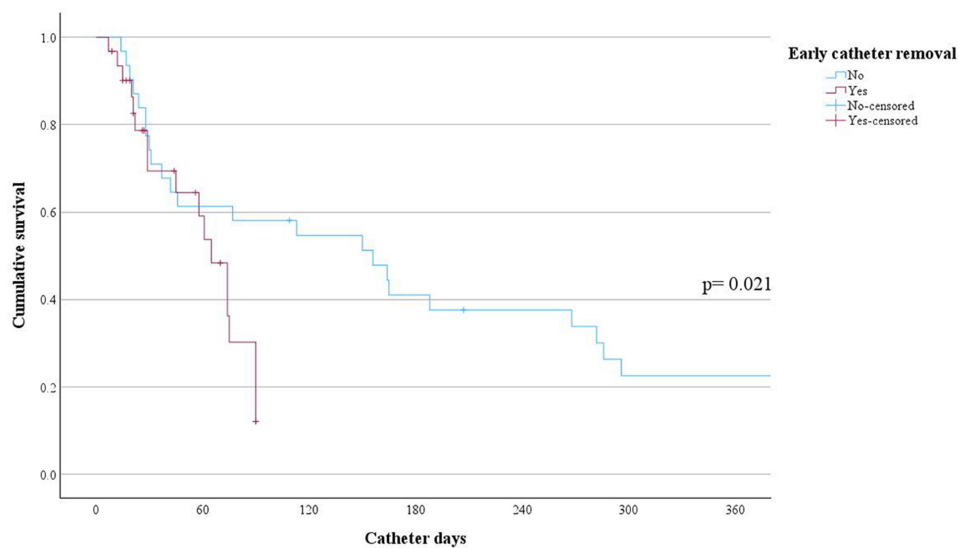


Figure 2 Kaplan-Meier catheter survival analysis. The median catheter survival for the early group was 65 days (95% CI 50.02–79.99) compared to 156 days (95% CI 42.92–269.09) for the non-early group, $p = 0.021$.

Abbreviations: CI, confidence interval.

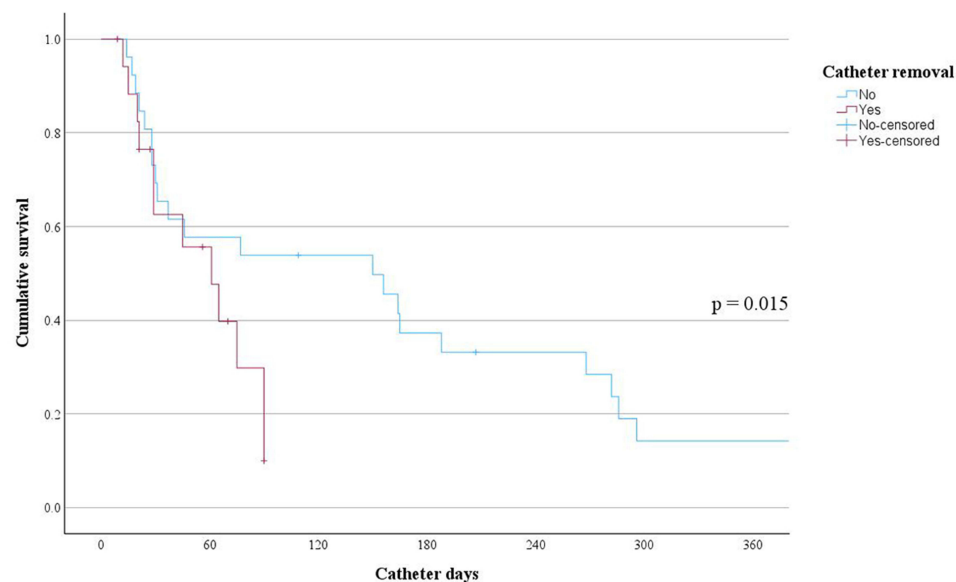


Figure 3 Effect of thrombocytopenia on catheter survival by Kaplan-Meier survival analysis. The median catheter survival for patients with thrombocytopenia was 61 days (95% CI 28.58–93.42) compared to 150 days (95% CI 9.81–290.19) for patients without thrombocytopenia, $p = 0.015$.

Abbreviations: CI, confidence interval.

This study found several factors associated with increased risk for unplanned early implantable catheter removal on univariate analysis: age, hemoglobin level, thrombocytopenia, and malnutrition, according to the PG-SGA. However, on multivariate analysis, only thrombocytopenia remained statistically significant.

Anemia (hemoglobin level less than 12g/dL for women and 13.5g/dL for men) is frequent in patients with hematology malignancies. In this study, the median hemoglobin level was 10.85 ± 2.51 mg/dL, indicating a high prevalence of anemia. None of the early and non-early group patients presented with a hemoglobin level of less than 7mg/dL, the level at which transfusion is recommended for hospitalized stable adult patients with hematologic and oncologic disorders by the Association for the Advancement of Blood and Biotherapies.¹⁷ Although there is a statistically

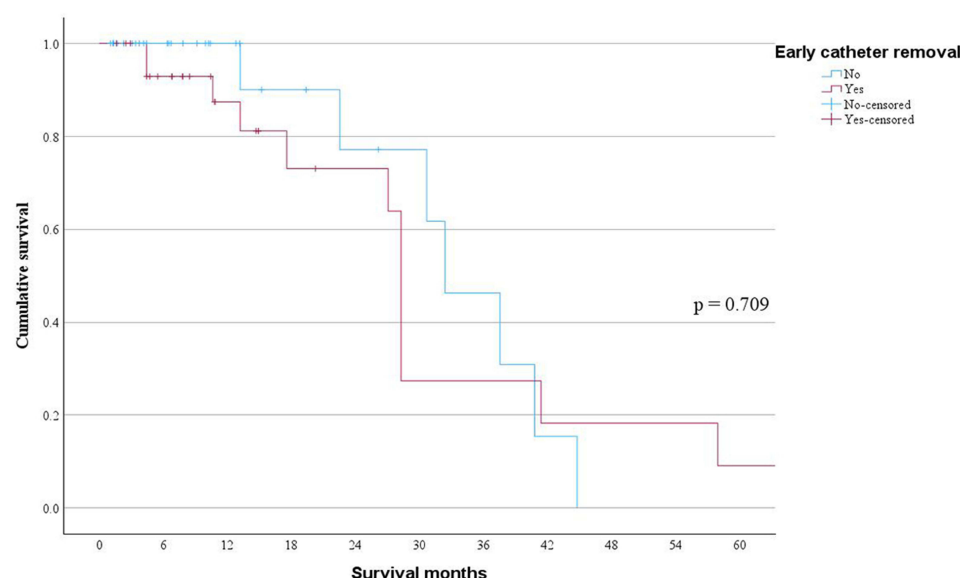


Figure 4 Effect of early unplanned catheter removal on patient survival. The median survival for the early group was 28.28 months (95% CI 27.43–29.15) compared to 32.39 (95% CI 24.11–40.68), for the non-early group, $p=0.709$.

significant difference in univariate analysis between the non-early group and early group (8.20 ± 2.11 vs 9.50 ± 1.90 , $p = 0.028$), the clinical significance of this difference is dismal because these patients were clinically stable and the procedure belonged to a low bleeding risk.

Thrombocytopenia could be related to decreased bone marrow production, increased destruction, splenic sequestration, or myelosuppressive chemotherapy effect. It is a common finding among hematologic malignancies and with higher frequency than those with solid tumors. According to a recent Danish study,¹⁸ the presence of thrombocytopenia was 18% among patients with hematologic malignancies compared to only 4% among patients with solid tumors. Among hematologic malignancies, thrombocytopenia was more common in patients diagnosed with leukemia. In a retrospective study, Bamba et al⁷ found thrombocytopenia to be a risk factor for early port infection. Keulers et al¹⁹ also found earlier infectious complications compared to those without thrombocytopenia, especially when associated with leukopenia or pancytopenia. Although the transfusion of platelets could correct the coagulopathy condition, it does not decrease the infectious risk. In line with the previous report, we found a higher risk for unplanned early catheter removal for patients with thrombocytopenia than those without thrombocytopenia, HR 2.823, (95% CI 1.050–7.589), $p = 0.040$. For the entire cohort, the catheter survival was significantly affected by thrombocytopenia. The median catheter survival for patients with thrombocytopenia was 61 days (95% CI 28.58–93.42) compared to 150 days (95% CI 9.81–290.19) for patients without thrombocytopenia, $p = 0.015$.

Malnutrition has detrimental effects, such as increasing the risk of complications, compromising the effectiveness of treatment, decreasing survival, and increasing health-care costs.²⁰ The prevalence of malnutrition depends on the tumor type, location, stage, and treatment.²¹ It is estimated that 40% to 80% of all cancer patients will be malnourished during the course of the disease.²² Malnutrition could be found at cancer presentation or as a consequence of the treatment. PG-SGA is a validated tool for nutritional screening, assessment, monitoring, and triaging adult oncology patients.^{10,23,24} In this report, 70% of patients at diagnosis were categorized as having any degree of malnutrition, according to the PG-SGA. A statistically significant difference was found in nutritional status between the early and non-early groups on univariate analysis (Table 2). However, on Cox Proportional Hazard analysis, the risk for unplanned early catheter removal in patients with malnutrition was not higher than those with normal nutrition, HR 2.264, 95% CI 0.921–5.565, $P = 0.075$.

Fortunately, the patient's median survival is not affected by early catheter removal. The median survival for the early group was 28.28 months (95% CI 27.43–29.15) compared to 32.39 (95% CI 24.11–40.68) for the non-early group, $p = 0.709$.

The present study presents with some shortcomings. Firstly, hematology malignancy comprises different types of cancers, such as leukemia, lymphoma, or multiple myeloma that present with distinct profiles for the various kinds of cytopenia that could have affected the outcome; secondly, since this study population is composed entirely of Chinese descent, to extrapolate the result to other ethnic group needs caution; thirdly, among the different hematology malignancies thrombocytopenia is more common in patients with leukemia; could be the disease rather than thrombocytopenia itself that affects the catheter survival and it deserves further examination, and finally, the retrospective recollection of data analysis and the relatively small number of patients. However, using propensity score matching allows us to reduce the bias due to confounding.

Conclusion

In our limited experience of patients with hematology malignancies presenting with thrombocytopenia, we found a higher risk of unplanned early catheter removal following port implantation. The median patient survival is not affected by unplanned early catheter removal.

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Disclosure

The authors declare no conflicts of interest in this work.

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