Investigation of Complications Following Port Insertion in a Cancer Patient Population: A Retrospective Analysis

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ABSTRACT: Central venous access devices, specifically implantable ports, play an essential role in the care of oncology patients; however, complications are prevalent. This retrospective single-institutional review was performed to identify rates of complications from port placement and potential factors associated with these events. A retrospective analysis of 539 cancer patients who underwent port insertion between March 2016 and March 2017 at our institution was conducted. Data examining 18 potentially predictive factors were collected, and multivariate analysis was conducted using logistic regression and odds ratios (ORs) with standard errors to determine predictive factors. Out of 539 patients, 100 patients (19%) experienced 1 complication, and 12 patients (2%) experienced 2 or more complications. An overall lower rate of complications was seen in patients on therapeutic anticoagulation (OR: 0.17, $P < .001$) or on antiplatelet agents (OR: 0.47, $P = .02$). No patients on therapeutic anticoagulation developed venous thromboembolism (VTE; 0%). Right-sided port insertion was associated with decreased rates of infection (OR: 0.44, $P = .04$). Insertion as inpatient was associated with an increased risk for mechanical failure (OR: 4.60, $P < .01$). This analysis identified multiple predictive factors that can potentially put patients at a higher risk of experiencing complications following port insertion. Our data show lower rates of VTE for patients on anticoagulation or antiplatelet therapy. Further analysis is also necessary to determine why port insertion as an inpatient places patients at a higher risk of complications. This study highlights the risks associated with port placement and prompts the clinician to have an informed discussion with the patient weighing the risks and benefits.

KEYWORDS: adjuvant therapy, complementary medicine, epidemiology, metastasis, prognostic biomarker

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Introduction

Subcutaneous venous access devices, more commonly known as ports, provide long-term intermittent venous access and are used for the administration of chemotherapy, parenteral nutrition, frequent infusions (ie, intravenous immunoglobulin [IVIG], blood transfusions), and frequent blood draws. Ports are commonly used in oncology for the administration of chemotherapy, specifically when chemotherapeutic agents are potential vesicants (capable of causing tissue damage on extravasation) or irritants (capable of injuring the venous lumen) and/or when prolonged infusions (ie, 5-fluorouracil continuous venous infusion) are required. Ports are also placed for patient comfort when repetitive venous access is anticipated.[1] Placement of these devices commonly involves a minor surgical procedure under imaging guidance by interventional radiology, in either the inpatient or the outpatient setting.

Numerous studies investigating complications associated with ports and the associated risk factors have been performed, with reported overall complication rates ranging from 7.2% to 32.1%.[2-4] Such complications are often divided into procedural, early complications (<30 days) and late complications (≥30 days).[5]complications include catheter malposition or migration, arterial rupture, pneumothorax, wound dehiscence, and infection, with complication rates of 0.7% to 4.6%.[6] Late complications, including infection, venous thromboembolism (VTE), extravasation, and mechanical failure, have higher reported incidence rates of 1.9% to 17.0%.[3,6,7] Of these, infection and VTE have the highest reported incidence rates, ranging from 2.3% to 22.0% and 0.1% to 18.0%, respectively.[7] The rate of complications necessitating device removal is reported to be 6% to 7%.[8]

Studies have identified age < 50, increased body mass index (BMI) (>28), decreased time to first use (<6 days), left-sided placement, and intermediate- and high-risk chemotherapy regimens (ie, those including vesicants and more likely to cause neutropenia) as risk factors for port-related complications. In addition, certain malignancies, such as pancreatic and gastric cancers, are associated with increased risk developing port-related complications.[4,5,9]

The aim of our study was to document port-associated complications in oncologic patients at our institution and to identify potential predictive factors for developing such complications.

Methods

A retrospective study was conducted to identify all patients in a 1-year span (from March 2016 to March 2017) with a diagnosis of cancer who had a port inserted on an inpatient or outpatient basis at our institution. This study was reviewed and approved by our Institutional Review Board. Patients were identified through our institution's Tumor Registry. Multiple data points were

collected as potential predictive factors, including age, sex, BMI, white blood cell (WBC) count, hemoglobin, hematocrit, platelet count, type of cancer, stage of cancer, Khorana score (components of which include cancer type, platelet count, hemoglobin, leukocyte count, and BMI), surgery within prior 6 months, current use of anticoagulation or antiplatelet agents, history of prior VTE (deep venous thrombosis and/or pulmonary embolism [PE]), insertion on an inpatient or outpatient basis, port site (left or right), initial planned duration of chemotherapy, and initial planned cycles of chemotherapy.

Data regarding numerous potential complications of port insertion were collected via review of the electronic medical record (EMR). All ports were inserted by Interventional Radiology using real-time ultrasound guidance. This included immediate complications such as pneumothorax and arterial rupture, in addition to delayed complications including infection (both systemic and port pocket site), VTE, mechanical failure (refractory to tissue plasminogen activator [tPA] through port), extravasation, or catheter migration.

Statistical Analysis

Normally distributed data are presented as proportions (mean ± SD) and for variables not conforming to a normal distribution as median and interquartile range (IQR). Two-sample comparisons were performed by Fisher exact and χ^2 tests as appropriate. For proportions, Student *t* test was used for normally distributed variables and Mann-Whitney *U* test for other variables. Shapiro-Wilk test was used to determine the normality of continuous variables. A 2-sided *P* value $< .05$ was used to indicate statistical significance in all analyses. Multivariate analysis was conducted using logistic regression and odds ratios (ORs) were calculated with robust standard errors. The multivariate model included all relevant clinical and baseline characteristics thought by the investigators to be related to the likelihood of patients developing complications, and this was favored over models using forward or backward stepwise regression. All patients with missing values were excluded from the analysis. Stata version 15.0 (StataCorp, College Station, TX, USA) was used for statistical analysis.

Results

Baseline characteristics

Overall, 539 patients met the inclusion criteria. Of them, 100 patients (18.6%) developed a complication during 1 year of follow-up. Mean age was 59.3 ± 13.4, 285 were female (52.9%), mean BMI was 27.7 ± 6.8, and there were no statistically significant differences in age, sex, or BMI in the complication group compared with the group that did not experience a complication (Table 1).

Laboratory values

Mean WBC count was 7.8 ± 5.3, mean hemoglobin was 11.9 ± 2.1, and mean platelet count was 280 ± 126, with no statistically significant differences in complication rates between groups.

Incidence of complications

Out of 539 patients, 100 patients (18.6%) experienced 1 complication and 12 patients (2.2%) experienced 2 or more complications. In total, 39 patients (7.2%) developed VTE (mean time to development: 123 days, range: 4-450 days, median: 97 days), 37 patients (6.9%) developed infection (mean time to development: 95 days, range: 1-455 days, median: 49 days), 20 patients (3.7%) experienced mechanical failure (mean time to development: 127 days, range: 2-393 days, median: 108 days), 11 patients (2.0%) experienced catheter migration (mean time to development: 133 days, range: 2-293 days, median: 113 days), and 5 patients (0.9%) experienced extravasation (mean time to development: 47 days, range: 25-97 days, median: 34 days). One patient developed a pneumothorax (the same day), and no patients experienced arterial rupture (Table 2).

Predictors of complications

On univariate analysis, a higher percentage of patients in the no-complication group were on anticoagulation as compared with the complication group (12.8% vs 5.0%, respectively, $P = .03$), suggesting a protective effect for anticoagulants against overall complications. In addition, antiplatelet use was also associated with a lower incidence of overall complications (OR: 0.47, $P = -.02$). A higher proportion of patients who did not develop complications were using antiplatelet agents (25.9% in the no-complication group vs 15% in the complication group, $P = .02$), again suggesting a protective effect for antiplatelet agents against overall complications (Table 3).

On multivariate analysis, anticoagulation use was associated with a lower incidence of overall complications (OR: 0.17, $P < .01$).

Patients were also less likely to develop VTE if they were on an antiplatelet agent (OR: 0.28, $P = .03$). Of note, no patients on anticoagulation developed VTE. Port insertion as inpatient was associated with an increased risk for mechanical failure (OR: 4.33, $P < .01$) and catheter migration (OR: 4.33, $P < .01$). Higher BMI was also associated with an increased risk for catheter migration (OR: 1.08, $P = .02$). On multivariate analysis, right-sided port insertion was associated with decreased rates of infectious complications (OR: 0.44, $P = .04$).

Discussion

Central venous access remains a basic and essential component of care for oncology patients. However, the placement of a foreign body in the vascular system carries multiple risks and potential complications which have been well described in the literature ranging from infections to thromboembolic events. These complications are responsible for significant morbidity and mortality in an already vulnerable population.

Table 1. Baseline characteristics for overall patients as well as comparing patients with and without complications.

	OVERALL (N = 539)	COMPLICATION (N = 100)	NO COMPLICATION (N = 439)	*P* VALUE
Age, mean ± SD	59.3 ± 13.4	58.3 ± 13.4	59.6 ± 13.4	.38
Female, n (%)	285 (53)	57 (57)	228 (52)	.36
BMI, mean ± SD	27.7 ± 6.8	27.9 ± 7.7	27.6 ± 6.6	.69
WBC	7.8 ± 5.3	8.3 ± 9.8	7.6 ± 3.5	.23
Hemoglobin	11.9 ± 2.1	11.8 ± 2.2	12 ± 2.1	.30
Platelets	280 ± 126	287 ± 159	278 ± 118	.49
Metastatic cancer	236 (43.8%)	47 (47%)	189 (43%)	.47
Khorana score, median (IQR)	1 (0-2)	1 (0-2)	1 (0-2)	.58
Surgery in the last 6 months	172 (32%)	34 (34%)	138 (31.5%)	.63
On anticoagulation	61 (11.3%)	5 (5%)	56 (12.8%)	**.03**
On antiplatelets	129 (24%)	15 (15%)	114 (25.9%)	**.02**
History of prior DVT/PE	51 (9.6%)	9 (9%)	42 (9.6%)	.89
Inpatient port insertion	77 (14.3%)	15 (15%)	62 (14.2%)	.83
Right-sided port site	451 (84%)	82 (82%)	369 (84%)	.55
Planned duration for insertion (if not indefinitely), median (IQR)	16 (8-20)	16 (7-20)	16 (8-20)	.81
Port placed for long-term use (ie, >3 months)	62 (11.5%)	15 (15%)	47 (10.7%)	.23

BMI, body mass index; DVT, deep venous thrombosis; IQR, interquartile range; PE, pulmonary embolism; WBC, white blood cell.
Bold *P* values are statistically significant.

Table 2. Distribution of complications.

	NUMBER	PERCENT INCIDENCE IN COHORT
Overall complications	100	18.6
Leading to hospitalization	51	
Leading to death	8	
Infection	37	6.9
VTE	39	7.2
Mechanical failure	20	3.7
Catheter migration	11	2
Extravasation	5	1
Pneumothorax	1	0.2

VTE, venous thromboembolism.

Multiple devices exist to access the central venous system, including peripherally inserted central catheters (PICCs), tunneled catheters, and central venous ports. Infection remains one of the most common complications with placement of these devices, with an incidence as high as 2.7 per 1000 catheter days for all types of central venous catheters as a whole.[10] Most of these events stem from the colonization of skin flora at the catheter's external surface, most commonly coagulase-negative *Staphylococcus* species such as *Staphylococcus epidermidis*.

The literature shows that PICC lines and ports have lower rates of complications as compared with tunneled catheters (19% vs 32%, $P < .05$).[11] Our data corroborate those findings with an overall complication rate of 18.6% in our population of patients. When comparing ports and PICC lines, there is a slight decrease in complication rates with ports (0.142 vs 0.414 complications/100 catheter days, $P = .011$).[12,13]

Our data have shown that patients on existing anticoagulation or antiplatelet therapy benefited from decreased thromboembolic complications, and right-sided port placement led to decreased rates of infectious complications. A higher BMI was also associated with increased complication, specifically catheter migration. Inpatient insertion also led to higher rates of catheter migration as well as mechanical failure. It is unclear if a higher rate of complications with inpatient insertion represents an opportunity for process improvement at our institution or if there are inherent differences in patients selected to have ports inserted on an inpatient basis. Such factors should be taken into account by the clinician in light of the overall patient profile to determine the optimal timing, positioning, and setting of port placement.

There are several limitations to this study and analysis inherent to the study design as a single-institutional retrospective

Table 3. Multivariate analysis for risk of developing complications overall.

	ODDS RATIO (OR)	ROBUST STANDARD ERROR	*P* VALUE
Age (years)	1.00	0.01	.90
Sex—male	0.82	0.20	.42
BMI (kg/m^2)	1.00	0.02	.67
WBC (10^3/μL)	1.02	0.02	.26
Hemoglobin (g/dL)	0.95	0.05	.35
Platelets (10^9/L)	1.00	0.00	.72
Metastatic cancer	1.24	0.31	.38
Surgery in the last 6 months	1.12	0.28	.64
On anticoagulation	0.17	0.09	<.01
On antiplatelet agent	0.47	0.15	.02
History of prior VTE	2.27	0.97	.06
Inpatient port insertion	1.06	0.36	.86
Right-sided port site	0.84	0.26	.57
Port placed for long-term use (ie, >3 months)	1.38	0.49	.36

BMI, body mass index; VTE, venous thromboembolism; WBC, white blood cell.

review. Variables such as operator technique or other procedural aspects are difficult to ascertain and can be potential confounders (although perhaps practice techniques in a single institution may be less heterogeneous than if this were a multi-center study). In addition, regarding generalizability, despite a large sample size of 539 patients, our rates of complications (and deaths) following port insertion are limited as a single-institutional review. As can be seen in the medical literature with the heterogeneity of complication rates following port insertion (from 6% to 30%),[2,4] the same can be posited for death rates. With such heterogeneity among complication rates (and perhaps the way that complications/deaths are attributed), this could potentially explain the disparities among such data.

There is a 4% to 6% risk of VTE in the ambulatory cancer population and this risk increases over time. Routine prophylactic anticoagulation is not currently recommended in the general cancer population; however, special consideration for anticoagulation should be made in higher risk populations (ie, gastric, pancreatic, lung cancers).[14] In 1 study, the rate of VTE in patients with port devices was found to be 4.5% per year.[15] A previous meta-analysis found that anticoagulation prophylaxis was effective in preventing thromboembolic events[16]; however, they were not able to characterize the effectiveness of anticoagulation in preventing symptomatic VTE events; however, with the broad confidence intervals in the meta-analysis, clinical benefit was not excluded. Furthermore, other studies have failed to determine a beneficial effect with prophylactic use of heparin or warfarin products for catheter VTE prevention.[17] Our study has identified those patients taking anticoagulation and antiplatelet agents indeed benefited from overall decreased rate of complications, but whether this was due to some effect of these medications or other factors is unclear. Further studies would be needed to fully characterize this effect.

In this study, we demonstrated that the administration of anticoagulation and antiplatelet agents was associated decreased rates of VTE, and left-sided port insertion was associated with increased infectious complications. Our finding that left-sided port insertion is associated with increased infectious complications is particularly relevant given the rate of central-line-associated blood stream infections (CLABSIs) in hospitals. Furthermore, left-sided catheters have already been found to carry a higher thrombotic risk than right-sided catheters, theorized due to the increased length of the left-sided catheters.[10,18] However, these studies did not find a significant difference in infectious complications from right vs left placement. As left-sided catheters are typically about 1 to 2 cm longer than the right-sided catheters, the increase in foreign body surface area could be the cause associating increased rates of both thromboembolic events and infections.

Conclusions

In conclusion, we were able to identify the complications as well as complication rates of ports being placed in our oncology patient population. The study is important because it is crucial to continually identify the best practices and advocate on behalf of our patients to prevent them from untoward harm. Although ports offer significant convenience, they are not without risk as highlighted by this review and others. The possible risks should be discussed with all patients during the informed consent process. In addition, educating patients on signs and symptoms of potential complications could lead to decreased rates of morbidity and mortality. Our results suggest that anticoagulation prophylaxis, right-sided placement, and outpatient insertion may possibly lead to decreased complication rates in patients with subcutaneous venous access devices.

Author Contributions

All authors participated in the conceptualization, methodology, investigation, analysis, and writing of the manuscript.

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