Original Article

Patterns of use and outcomes of peripherally inserted central catheters in hospitalized patients with solid tumors: A multicenter study

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BACKGROUND: The risk of peripherally inserted central catheter (PICC)-related complications in patients hospitalized with solid tumors remains unclear. Existing studies are limited by single-center, outpatient designs and include heterogenous patients. **METHODS:** A retrospective cohort study was designed and included adult patients with solid organ cancers who were admitted to a general medicine ward or intensive care unit and received a PICC. Data were collected from November 2013 to December 2019 at 50 Michigan hospitals. Major complications were defined as central line–associated bloodstream infection, deep vein thrombosis, pulmonary embolism, and catheter occlusion. Hospital variation in PICC use and outcomes was examined. **RESULTS:** Data included 3235 hospitalized patients with solid tumors who had PICCs placed for 51,047 catheter days. Most catheters were double-lumen devices (57.0%). Notably, 17.5% of patients had another central venous catheter at the time of PICC insertion. The most common indications for PICC use were antibiotics (34.5%) and difficult access or blood draws (21.6%); chemotherapy was the primary indication in only 15.7% of patients. A major PICC-related complication occurred in 491 patients (15.2%); catheter occlusion was the most prevalent complication ($n = 322$; 10.0%) followed by deep vein thrombosis ($n = 116$; 3.6%), central line–associated bloodstream infection ($n = 82$; 2.5%), and pulmonary embolism ($n = 20$; 0.6%). Significant variation in indications for PICC use, device characteristics, and frequency of major complications across hospitals was observed ($p < .001$). **CONCLUSIONS:** PICCs were associated with significant complications in hospitalized patients who had solid malignancies and were often used for reasons other than chemotherapy. Policies and guidance for the appropriate use of PICCs in oncologic patients appear necessary. ***Cancer* 2022;128:3681-3690**. © *2022 American Cancer Society.*

LAY SUMMARY:

- Peripherally inserted central catheters (PICCs) are devices placed in peripheral veins to deliver medication to large veins near the heart.
- PICCs are used frequently in oncology.
- The objective of this report was to describe PICC-associated complications in hospitalized patients with solid tumors.
- This study was performed across 50 Michigan hospitals and included 3235 patients with solid tumor cancers and who had a PICC.
- Overall, 15.2% of patients experienced a complication, including central line-associated bloodstream infections, deep vein thrombosis, pulmonary embolism, or catheter occlusion.
- Complication rates varied across hospitals.
- PICCs are associated with substantial complications in hospitalized patients with solid tumors.

KEYWORDS: central venous catheters, neoplasms, neoplasms, oncology, peripherally inserted central catheters, quality improvement, retrospective studies, venous thrombosis.

INTRODUCTION

Central venous catheters (CVCs) are devices in which the tips terminate in the great vessels of the chest. They are commonly used in oncology and play an essential role in the care of patients with cancer. CVCs include nontunneled devices, such as peripherally inserted central catheters (PICCs), percutaneous CVCs, and subcutaneously inserted devices, including tunneled catheters and ports.[1] Although they are vital to care, complications with CVCs are common and problematic. For example, insertion complications, such as arrhythmia and pneumothorax, are known to occur, as are delayed complications such as tip migration, infection, and thrombosis.[1]

Compared with the general population, oncology patients are at higher risk for complications from CVCs in the setting of immunosuppressive therapies, weakened host defenses, and a prothrombotic state secondary to malignancy. Prospective surveillance studies in adult patients with cancer have reported a central line bloodstream infection (CLABSI)

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incidence of 1.1–7.5 per 1000 CVC days, leading to increased morbidity and hospital costs.[2] Similarly, catheter-related thrombosis commonly affects patients with cancer who have CVCs,[1] and the risk of upper extremity deep venous thrombosis (DVT) is high.[3] Even if is subclinical, thrombosis of the catheterized vein may be an important risk factor for CLABSI in patients with cancer.[4] Furthermore, catheter occlusion, defined as temporary or permanent inability to aspirate blood or infuse through a lumen,[5,6] can interrupt and delay therapy, cause damage to the corresponding vein, and require device replacement.[5]

Despite these risks, limited data on PICC use and complications in hospitalized oncology patients are currently available. Existing studies suffer from small sample size or single-center designs. In addition, previous studies did not distinguish risks between hematologic and solid tumor malignancies and often pooled all cancer diagnoses in their analysis.

Therefore, we conducted a multicenter study to describe PICC use and outcomes among hospitalized patients with solid tumors. We hypothesized that patients with metastatic disease would have a higher frequency of overall PICC complications because of advanced disease burden and that those who had gastrointestinal and pancreatic cancers would have more thrombotic complications from PICCs given their association with a higher risk of venous thromboembolism (VTE).[7]

MATERIALS AND METHODS

Study setting and participants

We used data from the Michigan Hospital Medicine Safety (HMS) Consortium, a collaborative quality initiative funded by Blue Cross Blue Shield of Michigan and Blue Care Network. A core HMS initiative is measuring and improving PICC use and outcomes in participating hospitals across Michigan.[8] The design and setting of the HMS PICC initiative have been previously described.[9,10] We retrospectively examined data collected prospectively on PICCs inserted across 50 hospitals participating in the HMS initiative from November 2013 to December 2019. Adult patients who were admitted to a general medicine ward or an intensive care unit (ICU) and received a PICC for any reason were eligible. Patients who were younger than 18 years, pregnant, admitted to a nonmedical service (e.g., general surgery), or admitted under observation status were excluded. At each hospital, a dedicated medical record abstractor used a standardized protocol and template to collect data directly from the medical record. To ensure data accuracy, random audits are performed annually at each site (for full details on these processes, see Supporting Materials).

Hospitalized patients who received PICCs and had cancer were identified in three ways: (1) the documented indication for PICC placement was chemotherapy in a patient with a known malignancy; (2) receipt of chemotherapy, hormone therapy, surgery, radiation therapy, or bone marrow transplantation for a cancer diagnosis in the 6 months before PICC placement; or (3) a patient was hospitalized (>24 hours) with a primary cancer admission diagnosis in the 6 months before PICC placement. Only patients with a solid tumor diagnosis at the time of PICC insertion were included (see Supporting Materials); patients with a primary hematologic malignancy were excluded.

Clinical covariates

Data, including patient demographics, clinical history, laboratory values, documented indication for PICC placement, and information on PICC removal, were abstracted from patient medical records. The burden of comorbid conditions was expressed using the Charlson Comorbidity Index (CCI).[11] Provider characteristics, including attending specialty at the time of PICC insertion and type of operator who placed the PICC, were recorded. Information on hospital characteristics, such as the number of beds, teaching status, and location, was obtained from publicly reported hospital data.[12] Device characteristics, including the number of lumens, gauge, presence or absence of an anti-infective or antithrombotic coating, number of insertion attempts, and catheter tip confirmation, were collected from PICC insertion notes. With respect to oncologic history, details, including history of past or present cancer, cancer type, and presence or absence of malignancy, were recorded.

Outcomes

The primary outcome of interest was PICC-related adverse events, including CLABSI, VTE (i.e., upper and lower extremity DVT and pulmonary embolism [PE]), and catheter occlusion. CLABSI was defined in accordance with the National Healthcare Safety Network criteria as a laboratory-confirmed bloodstream infection (not present on admission) with identification of an eligible organism in the presence of a CVC on the day of or before the event.[13] We also recorded suspected CLABSI as instances in which a PICC was removed without confirmatory cultures, with the reason for removal documented as *line sepsis*, *catheter-bacteremia*, or *suspected infection*. Catheter occlusion was recorded when one of

two criteria were met: a medical provider documented catheter occlusion in the medical record or tissue plasminogen activator was administered to treat signs compatible with occlusion (e.g., poor blood return, sluggish flow).[5] VTE was defined as clinically suspected DVT and/or PE not present at the time of PICC placement and subsequently confirmed on imaging (ultrasonography or venogram for DVT; computed tomography, high-probability ventilation-perfusion scan, or pulmonary angiogram for PE). Because we previously demonstrated that PICCs are associated with a risk of both upper and lower extremity thrombosis,[14,15] we included both types of events.

Statistical analysis

Pairwise comparisons were performed using *t*-tests for continuous variables and Pearson χ^2 tests for categorical variables. All statistical tests were two-sided, with a p value $< .05$ considered statistically significant. Hospital variation was examined using the Kruskal–Wallis test for continuous variables and the Pearson χ^2 test for categorical variables. To ensure stable estimates, analyses of complications across hospitals were restricted to hospitals that had ≥25 patients with solid tumors. Although 50 hospitals reported data for patients with solid tumors during the study period, only 34 hospitals reported data for ≥25 patients; therefore, these hospitals (with lower volumes) were excluded when comparing variations across sites. SAS version 9.4 (SAS Institute Inc.) was used for all analyses.

RESULTS

Demographics

In total, 3235 patients with solid tumors who had PICCs placed for a total of 51,047 catheter days were included in this analysis. There were 27,510 catheter days among patients with metastatic disease (n = 1477) and 37,402 catheter days among patients with nonmetastatic disease (n = 1758). The median patient age was 67.3 years (interquartile range [IQR], 58.6–75.6 years), and most patients were either overweight (n = 840; 26.0%) or obese (n = 1040; 32.1%). The most common primary cancer diagnoses were nonsmall cell lung cancer, colon cancer, and breast cancer (Table 1).

The median CCI was 6 (IQR, 3–8). Most patients were initially admitted to inpatient medical floors (n = 2318; 71.7%), but 794 (24.5%) were admitted directly to an ICU, and almost one third (31.0%, n = 1003) received care in an ICU at any time during hospitalization. During hospitalization, 1972 patients (61.0%) received pharmacologic VTE prophylaxis, and 749 (23.2%) received treatment dose anticoagulation.

PICC characteristics

Most PICCs (n = 2817; 87.1%) were placed after one insertion attempt and were double-lumen (n = 1845; 57.0%), followed by single-lumen (n = 1109; 34.3%), and triple-lumen (n = 270; 8.3%) devices. PICCs were from 5-French to 7-French in 66.4% (n = 2147) of cases and from 2-French to 4.5-French in 30.6% (n = 989) of cases. The median PICC dwell time was 13 days (IQR, 6–30 days); 2.8% (n = 89) of devices were coated or impregnated with an antithrombotic material, and 5.5% (n = 177) were antimicrobial-coated. Accidental dislodgement or removal of a PICC was documented in 2.8% (n = 91) of all patients, and catheter tip migration occurred in 3.5% (n = 112) of all patients. At the time of PICC placement, 17.5% (n = 566) of patients had a concurrent CVC, including a nondialysis CVC (e.g., tunneled CVC, nontunneled CVC, or port) in 474 patients, a dialysis catheter in 51 patients, and an additional PICC in 45 patients.

Documented indications for PICC use

The most common indication for PICC placement was intravenous antibiotics (n = 1115; 34.5%), followed by difficult access/blood draws (n = 699; 21.6%), parenteral nutrition (TPN; n = 578; 17.9%), chemotherapy (n = 509; 15.7%), and medications requiring central access (n = 413; 12.8%). Among the 509 PICCs that were placed for chemotherapy, 72% (n = 369) were documented to have been used for this reason. Chemotherapies delivered through PICCs included irritants (n = 201; 54.5%,), vesicants (n = 28; 7.6%), both (n = 94; 25.5%), or other (n = 162; 43.9%).

PICC-related complications

A PICC-related major complication (CLABSI, DVT, PE, or catheter occlusion) occurred in 15.2% (n = 491) of patients. Catheter occlusion was the most common major complication, occurring in 10.0% (n = 322) of patients. CLABSI occurred in 2.5% (n = 82) of patients, or 1.6 events per 1000 device-days. DVT in either the upper or lower extremity occurred in 3.6% (n = 116) of patients, and PE occurred in 0.6% (n = 20) of patients. VTE prophylaxis was administered before a DVT in 62.1% (n = 82) of patients, whereas treatment dose anticoagulation was administered before an event in 18.1% (n = 21) and 20.0% (n = 4) of patients with DVT and PE, respectively (Table 2).

TABLE 1. Patient, Device, and Provider Characteristics Among Hospitalized Patients with Solid Tumors Who Received Peripherally Inserted Central Catheters (Stratified By Metastatic vs. Nonmetastatic Disease)

Variable	No. (%)		p	Total no. (%), $n = 3235$
	Metastatic, $n = 1477$	Nonmetastatic, $n = 1758$		
Age, years				
18–49	156 (10.6)	147 (8.4)	< .001	303 (9.4)
50–69	733 (49.6)	758 (43.1)		1491 (46.1)
≥70	541 (36.6)	801 (45.6)		1342 (41.5)
Sex				
Male	735 (49.8)	939 (53.4)	.04	1674 (51.7)
Female	742 (50.2)	819 (46.6)		1561 (48.3)
Race				
White	1073 (72.6)	1306 (74.3)	.47	2379 (73.5)
Black	327 (22.1)	344 (19.6)		671 (20.7)
Other	38 (2.6)	50 (2.8)		88 (2.7)
Unknown	39 (2.6)	58 (3.3)		97 (3.0)
Body mass index				
Underweight: <18.5 kg/m^2	107 (7.2)	123 (7.0)	.003	230 (7.1)
Normal: 18.5–24.9 kg/m^2	521 (35.3)	522 (29.7)		1043 (32.2)
Overweight: 25.0–29.9 kg/m^2	384 (26.0)	456 (25.9)		840 (26.0)
Obese: >30.0 kg/m^2	434 (29.4)	606 (34.5)		1040 (32.1)
Charlson Comorbidity Index: Median [IQR]	8.0 [7.0–10.0]	4.0 [2.0–5.0]	< .001	6.0 [3.0–8.0]
Documented indication				
Antibiotics	466 (31.6)	649 (36.9)	.001	1115 (34.5)
Blood transfusion or blood products	15 (1.0)	12 (0.7)	.30	27 (0.8)
Chemotherapy	307 (20.8)	202 (11.5)	< .001	509 (15.7)
Chemotherapy only	226 (73.6)	166 (82.2)	.02	392 (77.0)
Chemotherapy and additional indication	81 (26.4)	36 (17.8)	.02	117 (23.0)
Difficult access/blood draws	363 (24.6)	336 (19.1)	< .001	699 (21.6)
Medications requiring central access	197 (13.3)	216 (12.3)	.37	413 (12.8)
Multiple incompatible fluids	40 (2.7)	44 (2.5)	.71	84 (2.6)
Parenteral nutrition	300 (20.3)	278 (15.8)	.001	578 (17.9)
Medications requiring central access per hospital policy	2 (0.1)	3 (0.2)	.8	5 (0.2)
Unknown	140 (9.5)	175 (10.0)	.65	315 (9.7)
Attending physician specialty				
Hematologist/oncologist	188 (12.7)	180 (10.2)	< .001	368 (11.4)
Nonhematologist/oncologist	1289 (87.3)	1578 (89.8)		2867 (88.6)
No. of insertion attempts				
1	1284 (86.9)	1533 (87.2)	.66	2817 (87.1)
≥2	142 (9.6)	164 (9.3)		306 (9.5)
Unknown	51 (3.5)	61 (3.5)		112 (3.5)
Level of care at time of PICC placement				
Outpatient	2 (0.1)	3 (0.2)	< .001	5 (0.2)
Emergency room	22 (1.5)	15 (0.9)		37 (1.1)
Intensive care unit	370 (25.1)	424 (24.1)		794 (24.5)
Inpatient medical floor	1077 (72.9)	1241 (70.6)		2318 (71.7)
Ever treated in intensive care unit	490 (33.2)	513 (29.2)	.01	1003 (31.0)
Hospital characteristics				
Metropolitan	1356 (91.8)	1610 (91.6)	.82	2966 (91.7)
Nonprofit	1264 (85.6)	1538 (87.5)	.11	2802 (86.6)
Teaching	834 (56.5)	1081 (61.5)	.004	1915 (59.2)
Bed size				
1–249 beds	238 (16.1)	305 (17.3)	.42	543 (16.8)
250–374 beds	480 (32.5)	538 (30.6)		1018 (31.5)
≥375 beds	759 (51.4)	915 (52.0)		1674 (51.7)
Line thickness				
2.0–4.5 French	413 (28.0)	576 (32.8)	.003	989 (30.6)
5.0–7.0 French	1021 (69.1)	1126 (64.1)	.002	2147 (66.4)
No. of lumens				
Single	455 (30.8)	654 (37.2)	< .001	1109 (34.3)
Double	893 (60.5)	952 (54.2)		1845 (57.0)
Triple	122 (8.3)	148 (8.4)		270 (8.3)
Antimicrobial-coated	46 (3.1)	131 (7.5)	< .001	177 (5.5)
Antithrombotic-coated	45 (3.0)	44 (2.5)	.35	89 (2.8)
Line duration: Median [IQR], days	11.0 [5.0–30.0]	14.0 [6.0–30.0]	< .001	13.0 [6.0–30.0]

TABLE 1. *Continued*

Variable	No. (%)			
	Metastatic, $n = 1477$	Nonmetastatic, $n = 1758$	p	Total no. (%), $n = 3235$
Catheter days, total	27,510	37,402	—	51,407
Current central venous catheter in place	324 (21.9)	242 (13.8)	< .001	566 (17.5)
PICC	25 (7.7)	20 (8.3)	.81	45 (8.0)
Central venous catheter, nondialysis	275 (84.9)	199 (82.2)	.40	474 (83.7)
Central venous catheter for renal dialysis	27 (8.3)	24 (9.9)	.51	51 (9.0)
Chemotherapy delivered through PICC	204 (13.8)	165 (9.4)	< .001	369 (11.4)
Irritant	119 (58.3)	82 (49.7)	< .001	201 (54.5)
Vesicant	6 (2.9)	22 (13.3)	.01	28 (7.6)
Irritant/vesicant	50 (24.5)	44 (26.6)	.14	94 (25.5)
Other chemotherapy drug	93 (45.6)	69 (41.8)	.002	162 (43.9)
Accidental dislodgement or removal of PICC	45 (3.1)	46 (2.6)	.461	91 (2.8)
Catheter tip migration	62 (4.2)	50 (2.8)	.036	112 (3.5)
Laboratory values at time of PICC placement: Median [IQR]				
Creatinine, mg/dL	0.8 [0.6–1.2]	0.9 [0.7–1.3]	.44	0.9 [0.6–1.2]
Hemoglobin, g/dL	9.6 [8.4–11.1]	9.8 [8.6–11.4]	.73	9.7 [8.5–11.3]
Platelet count, $\times 10^9$/L	229.0 [142.0–329.0]	236.0 [160.0–326.0]	.52	234.0 [153.0–328.0]
WBC, $\times 10^9$/L	9.8 [6.5–14.6]	9.1 [6.3–13.2]	.32	9.4 [6.3–13.9]
INR	1.2 [1.1–1.3]	1.1 [1.0–1.3]	98	1.2 [1.1–1.3]
eGFR, mL per minute/m^2	79.0 [60.0–119.0]	66.0 [51.6–108.0]	.57	73.0 [55.0–113.0]
Type of cancer				
Lung nonsmall cell	248 (16.8)	181 (10.3)	< .001	429 (13.3)
Colon	192 (13.0)	185 (10.5)	0.03	377 (11.7)
Breast	165 (11.2)	181 (10.3)	.42	346 (10.7)
Prostate	143 (9.7)	169 (9.6)	.95	312 (9.6)
Lung small cell	127 (8.6)	88 (5.0)	< .001	215 (6.6)
Bladder	74 (5.0)	118 (6.7)	.04	192 (5.9)
Pancreas	109 (7.4)	70 (4.0)	< .001	179 (5.5)
Stomach	75 (5.1)	66 (3.8)	.07	141 (4.4)
Uterine	57 (3.9)	68 (3.9)	.99	125 (3.9)
Liver	62 (4.2)	54 (3.1)	.09	116 (3.6)
Kidney	60 (4.1)	39 (2.2)	.002	99 (3.1)
Brain	24 (1.6)	71 (4.0)	< .001	95 (2.9)
Ovarian	62 (4.2)	28 (1.6)	< .001	90 (2.8)
Rectal	30 (2.0)	50 (2.8)	.14	80 (2.5)
Metastatic with unknown origin	49 (3.3)	0 (0.0)	< .001	49 (1.5)
Unknown	5 (0.3)	11 (0.6)	.25	16 (0.5)
Other[a]	272 (18.4)	328 (18.7)	.86	600 (18.5)

Abbreviations: eGFR, estimated glomerular filtration rate; INR, international normalized ratio; IQR, interquartile range, PICC, peripherally inserted central catheter; WBC, white blood cells.

[a]"Other" tumor types include appendiceal cancer, esophageal cancer, esthesioneuroblastoma, fibrosarcoma, histiocytoma, Kaposi sarcoma, malignant pleural effusion without unspecified cancer, squamous cell carcinoma (nonlung–derived), testicular cancer, and tonsillar cancer.

In catheters with an antimicrobial coating, catheter occlusion occurred less frequently ($n = 40$ vs. $n = 282$; $p < .001$); however, differences in rates of CLABSI were not significant probably because of the small number of cases ($n = 6$ vs. $n = 76$; $p = .457$) (see Table S1). In catheters with an antithrombotic coating, CLABSI and catheter occlusion rates did not differ significantly (see Table S2).

Major complications occurred more frequently in patients with ovarian ($n = 23$; 25.6%), uterine ($n = 24$; 19.2%), pancreatic ($n = 33$; 18.4%), and brain ($n = 16$; 16.8%) cancer. VTE was more common in patients with pancreatic, uterine, bladder, nonsmall cell lung, and brain cancer (Table 3).

Differences in outcomes between metastatic versus nonmetastatic disease

Compared with patients who had nonmetastatic disease, those with metastatic disease had greater comorbidity burden (median CCI, 8 [IQR, 7–10] vs. 4 [IQR, 2–5]; $p < .001$) and were more likely to be ever treated in the ICU (33.2% vs. 29.2%; $p = .01$). Patients who had metastatic disease more frequently received double-lumen rather than single-lumen catheters (60.5% vs. 54.2% and 30.8% vs. 37.2% [$p < .001$] for both comparisons, respectively). Patients with metastatic disease were also more likely to have a concurrent CVC (21.9% vs. 13.8%; $p < .001$) at the time of PICC placement and more often

TABLE 2. Device-Related Complications

Variable	No. (%)		*p*	Total, No. (%)
	Metastatic	Nonmetastatic		
Complications				
Any major complication	211 (14.3)	280 (15.9)	.19	491 (15.2)
CLABSI, confirmed and suspected	33 (2.2)	49 (2.8)	.32	82 (2.5)
DVT	59 (4.0)	57 (3.2)	.25	116 (3.6)
PE	9 (0.6)	11 (0.6)	.95	20 (0.6)
VTE, includes PE, LEDVT, and UEDVT	65 (4.4)	67 (3.8)	.40	132 (4.1)
Catheter occlusion	131 (8.9)	191 (10.9)	.06	322 (10.0)
Death	298 (20.2)	188 (10.7)	< .001	486 (15.0)
Treatment anticoagulant before major event (% of patients with positive event)				
DVT	9 (15.3)	12 (21.1)	.42	21 (18.1)
PE	2 (22.2)	2 (18.2)	.82	4 (20.0)
VTE	11 (16.9)	14 (20.9)	.34	25 (18.9)
VTE prophylaxis before major event (% of patients with positive event)				
DVT	39 (66.1)	32 (56.1)	.27	71 (61.2)
PE	5 (55.6)	9 (81.8)	.56	14 (70.0)
VTE	41 (63.1)	41 (61.2)	.82	82 (62.1)
Any treatment anticoagulant	346 (23.4)	403 (22.9)	.74	749 (23.2)
Any VTE prophylaxis	907 (61.4)	1065 (60.6)	.63	1972 (61.0)

Abbreviations: CLABSI, central line-associated bloodstream infection; DVT, deep vein thrombosis; LEDVT, lower extremity deep vein thrombosis; PE, pulmonary embolism; UEDVT, upper extremity deep vein thrombosis; VTE, venous thromboembolism.

TABLE 3. Peripherally Inserted Central Catheter Complications (by Tumor Type)

Variable	No. (%)							
	Any major complication	CLABSI	DVT: UEDVT and LEDVT	PE	VTE	Catheter occlusion	Death	Total
Solid tumor population[a]	491 (15.2)	82 (2.5)	116 (3.6)	20 (0.6)	132 (4.1)	322 (10.0)	486 (15.0)	3235 (100.0)
Lung nonsmall cell	61 (14.2)	8 (1.9)	18 (4.2)	3 (0.7)	20 (4.7)	41 (9.6)	95 (22.1)	429 (13.3)
Colon	55 (14.6)	11 (2.9)	11 (2.9)	5 (1.3)	15 (4.0)	35 (9.3)	31 (8.2)	377 (11.7)
Breast	48 (13.9)	5 (1.4)	10 (2.9)	3 (0.9)	13 (3.8)	31 (9.0)	54 (15.6)	346 (10.7)
Prostate	27 (8.7)	4 (1.3)	10 (3.2)	—	10 (3.2)	17 (5.4)	42 (13.5)	312 (9.6)
Lung small cell	24 (11.2)	2 (0.9)	5 (2.3)	1 (0.5)	6 (2.8)	18 (8.4)	38 (17.7)	215 (6.6)
Bladder	28 (14.6)	6 (3.1)	9 (4.7)	1 (0.5)	9 (4.7)	14 (7.3)	24 (12.5)	192 (5.9)
Pancreas	33 (18.4)	8 (4.5)	11 (6.1)	3 (1.7)	12 (6.7)	13 (7.3)	35 (19.6)	179 (5.5)
Stomach	22 (15.6)	4 (2.8)	4 (2.8)	1 (0.7)	5 (3.5)	15 (10.6)	21 (14.9)	141 (4.4)
Uterine	24 (19.2)	4 (3.2)	8 (6.4)	1 (0.8)	9 (7.2)	17 (13.6)	16 (12.8)	125 (3.9)
Liver	12 (10.3)	2 (1.7)	3 (2.6)	—	3 (2.6)	7 (6.0)	19 (16.4)	116 (3.6)
Kidney	10 (10.1)	2 (2.0)	2 (2.0)	—	2 (2.0)	7 (7.1)	15 (15.2)	99 (3.1)
Brain	16 (16.8)	1 (1.1)	4 (4.2)	2 (2.1)	6 (6.3)	11 (11.6)	23 (24.2)	95 (2.9)
Ovarian	23 (25.6)	3 (3.3)	3 (3.3)	1 (1.1)	4 (4.4)	18 (20.0)	12 (13.3)	90 (2.8)
Rectal	11 (13.8)	1 (1.3)	2 (2.5)	—	2 (2.5)	9 (11.3)	3 (3.8)	80 (2.5)
Other[b]	98 (16.3)	16 (2.7)	22 (3.7)	—	22 (3.7)	65 (10.8)	79 (13.2)	600 (18.5)
Metastatic of unknown origin	6 (12.2)	—	—	—	—	6 (12.2)	14 (28.6)	49 (1.5)
Unknown	4 (25.0)	1 (6.3)	2 (12.5)	—	2 (12.5)	2 (12.5)	2 (12.5)	16 (0.5)

Abbreviations: CLABSI, central line-associated bloodstream infection; DVT, deep vein thrombosis; DVT, deep vein thrombosis; LEDVT, lower extremity deep vein thrombosis; PE, pulmonary embolism; UEDVT, upper extremity deep vein thrombosis; VTE, venous thromboembolism.

[a]Because of the data-collection process, types of cancer are collected through positive patient histories of cancer. Patients with multiple positive histories of cancer (n = 437) are counted in each category row.

[b]"Other" tumor types include appendiceal cancer, esophageal cancer, esthesioneuroblastoma, fibrosarcoma, histiocytoma, Kaposi sarcoma, malignant pleural effusion without unspecified cancer, squamous cell carcinoma (nonlung–derived), testicular cancer, and tonsillar cancer.

had a PICC placed for difficult venous access (24.6% vs. 19.1%; $p < .001$) or TPN (20.3% vs. 15.8%; $p = .001$). The rates of CLABSI, DVT, PE, and catheter occlusion did not differ significantly according to the presence or absence of metastases.

Hospital variation in PICC use and outcomes

Among the 50 hospitals in this study, 34 submitted data for ≥25 patients who had solid tumors and were included for our analysis of hospital variation in PICC-related outcomes. The documented indications for PICCs use, the

number of catheter lumens, and PICC dwell times varied significantly across sites ($p < .001$ for all comparisons; Table 4). For example, placement indication for chemotherapy ranged from 0.0% to 44.0% ($p < .001$) of all hospitals, the use of single-lumen PICCs ranged from 10.2% to 73.2% ($p < .001$), and median catheter dwell times ranged from 8 to 30 days ($p < .001$). The frequency of major complications also varied among hospitals ($p < .001$): rates of DVT ranged from 0% to 10.6% ($p = .01$), whereas catheter occlusion rates ranged from 1.1% to 25.4% ($p < .001$). Variations in the rates of PE and CLABSI were observed but did not reach statistical significance ($p = .34$ for both).

DISCUSSION

In this retrospective, multicenter cohort study of 3235 patients who had a solid tumor diagnosis, we observed that PICCs were most often placed for intravenous antibiotics or difficult access; the placement of PICCs for the primary indication of chemotherapy was infrequent. At the time of PICC placement, 17.5% ($n = 566$) of patients had a concurrent CVC. Four hundred ninety-one (15.2%) patients experienced a major PICC-related complication, with catheter occlusion being the most prevalent of these harms. Although rates of CLABSI, DVT, and PE did not differ significantly by the presence of metastatic disease, the frequency of PICC complications did vary by primary tumor diagnosis. In addition, significant hospital variations in PICC indication, characteristics, and complications were observed. Taken together, these findings suggest that an opportunity exists to improve and streamline PICC use, patient safety, and catheter outcomes in patients with solid tumors.

Within each cancer type in our cohort, a higher percentage of patients had metastatic disease than nonmetastatic disease. As expected, patients with metastases had more comorbidities and more often needed ICU care. Notably, these patients also were more likely to have a PICC placed for TPN or difficult access and were more likely to have an existing CVC at the time of PICC insertion. Although our study design precludes an understanding of the appropriateness of these decisions, the use of PICCs in this context is problematic. Patients with advanced disease may be more likely to be malnourished[16] or unable to receive enteral nutrition and may be more likely to have poor vascular access because of a history of frequent venipuncture and vein exhaustion.[17] Whether the insertion of an additional central catheter in these patients is helpful and is associated with better outcomes is unclear and worthy of further exploration.

TABLE 4. Hospital Variation in Peripherally Inserted Central Catheter Characteristics and Complications

Variable	Range across hospitals, %							p[a]
	Min	10th Pctl	25th Pctl	Med	75th Pctl	90th Pctl	Max	
Placement indication								
Antibiotics	11.1	21.3	25.4	35.7	47.2	49.0	55.3	< .001
Blood transfusion or blood products	0.0	0.0	0.0	0.0	1.4	2.4	7.3	.002
Chemotherapy	0.0	4.2	6.3	14.4	21.4	26.8	44.0	< .001
Difficult access/blood draws	0.0	7.3	11.6	17.4	24.0	51.0	75.8	< .001
Medications requiring central access	0.0	1.6	4.2	7.8	19.5	29.1	48.9	< .001
Multiple incompatible fluids	0.0	0.0	0.0	1.4	3.8	6.3	10.6	< .001
Parenteral nutrition	2.5	6.9	9.6	17.2	24.8	31.3	40.5	< .001
Medications requiring central access per hospital policy	0.0	0.0	0.0	0.0	0.0	0.0	4.3	< .001
Unknown	0.0	0.0	2.7	6.9	15.3	18.7	29.2	< .001
No. of lumens								
Single	10.2	16.7	27.7	33.5	43.0	48.6	73.2	< .001
Double	24.4	41.7	48.6	54.4	66.9	76.0	85.4	< .001
Triple	0.0	0.0	0.0	5.7	13.8	21.3	36.7	< .001
Line duration, days	8	10	11	13	15	20	30	< .001
Complications								
Major complication	2.4	7.3	9.5	12.5	18.4	26.1	30.2	< .001
CLABSI, any	0.0	0.0	0.0	2.2	3.8	4.3	6.3	.34
DVT: UEDVT and LEDVT	0.0	0.0	1.7	3.1	4.2	7.1	10.6	.01
PE	0.0	0.0	0.0	0.0	1.3	2.1	2.9	.34
VTE	0.0	0.0	2.0	3.8	5.2	7.9	10.6	.01
Catheter occlusion	1.1	2.4	3.9	8.8	12.9	18.2	25.4	< .001
Death	4.9	7.6	11.8	15.3	18.4	19.8	34.3	.01
Any VTE prophylaxis	40.0	48.0	54.3	60.4	67.9	74.0	77.8	< .001
Any treatment anticoagulation	7.3	13.9	17.9	24.0	27.8	31.9	35.9	< .001

Abbreviations: CLABSI, central line-associated bloodstream infection; DVT, deep vein thrombosis; LEDVT, lower extremity deep vein thrombosis; Max, maximum; Med, median; Min, minimum; Pctl, percentile; PE, pulmonary embolism; UEDVT, upper extremity deep vein thrombosis; VTE, venous thromboembolism.

In contrast to PICC use in outpatient settings, in which the most common indication for insertion is chemotherapy, the most common indication for PICC placement in our hospitalized cohort was intravenous antibiotics.[18,19] One possible explanation for this difference is that hospitalized patients are sicker and more likely to need antimicrobials than relatively healthier outpatients. We also noted that, when PICCs were placed for the primary indication of chemotherapy, infusions of vesicants or irritant chemotherapeutic drugs did not always occur. Furthermore, our data show that about one half of chemotherapy agents infused through PICCs were not irritants or vesicants, suggesting that these agents could be safely administered peripherally without the use of PICCs.[20]

Our observed CLABSI rate of 1.6 per 1000 device-days is consistent with previously reported data in adult oncology patients.[2] However, we observed that CLABSI rates did not differ by the presence of metastatic disease, although more patients with metastatic disease were documented to receive a PICC for the indication of TPN, which is a reported independent risk factor for CLABSI.[21] DVT and PE occurred in 3.6% ($n = 116$) and 0.6% ($n = 20$) of patients in our cohort, respectively, which are lower than previously described rates of catheter-related thrombosis. The 2013 American Society of Clinical Oncology clinical practice guideline on CVC use in patients with cancer describes a variable incidence of catheter-related thrombosis from 4% to 8% in recent years, compared with rates from 27% to 66% before 2000.[22] Improvement in placement techniques, including the use of micro-introducer kits, ultrasound and electrocardiogram guidance,[23] and a greater awareness of the risks from PICCs, may explain this decline. The notably high rate of catheter occlusion observed in our study may relate to prolonged catheter dwell time, infusion of certain antibiotics or packed red blood cells, the use of multi-lumen PICCs, and malposition of the catheter tip.[5] Among tumor types, patients with gastrointestinal, pancreatic, and gynecologic cancers experienced the most PICC-related complications. CLABSI was more frequent in patients who had gastrointestinal, gynecologic, and genitourinary tumors, perhaps because of mucosal barrier damage in these tumors.[24] VTE was more common in those who had gastrointestinal, gynecologic, genitourinary, nonsmall cell lung, and brain tumors, all of which are known to be prothrombotic.[25]

Importantly, we observed that indication for PICC use, number of lumens, and catheter dwell time varied significantly among hospitals, as did rates of DVT, catheter occlusion, and overall complications. These findings demonstrate the marked variation in how PICCs are used in oncology populations and are unlikely to be related to disease characteristics alone.[26] Although our study was not designed to assess for reasons explaining this variation, differences in practice culture within hospitals, including knowledge of PICC benefits, ease of ability to obtain PICCs, and patient comfort, may explain these findings.[27] Importantly, discretionary use of PICCs can result in avoidable patient harm, which may be offset by earlier placement of ports in patients with solid timors.[28–32] Understanding the drivers of PICC use and the appropriateness of device choice in solid tumor oncology patients remains an important area for quality improvement in cancer care.

Our study has limitations. First, data on cancer type were missing for 8.8% of patients, and smaller sample sizes within specific cancer types limited comparisons across malignancies. Second, we were limited to data available in the medical record because they were used for abstraction; reasons for device choice can be complex and thus may not be well captured in electronic data. Third, despite substantial variation in PICC use across sites, we are unable to explain drivers of such variability. Fourth, although we have detailed data on PICCs, we lack an active comparator arm to compare incremental harms and benefits of these devices in this cohort. Finally, our data suggest associations between PICC use and adverse events but cannot define causality given the observational nature of our study.

Despite these weaknesses, our study has several strengths. First, to our knowledge, ours is among the largest retrospective cohort studies on patterns of PICC use in hospitalized patients with solid tumors. Through meticulous data collection and curation of patient-related and device characteristics, we present real-world data reflective of contemporary practice patterns in oncology. Finally, our study uniquely highlights significant variation in catheter choices and clinical outcomes across multiple hospitals, which raises questions regarding how PICCs are currently being used in oncology.

In conclusion, substantial variations in the use and outcomes of PICCs in patients with solid tumors during hospitalization suggest that it is time to evaluate and rethink our use of this device. Given that many PICCs placed for chemotherapy were not used for the same indication and that some patients had another CVC when PICCs were inserted, opportunities to improve quality of care exist. In addition, frequent use of PICCs in the ICU and placement of PICCs for TPN, especially in patients with metastatic disease, is problematic because these patients likely have incurable disease. Taken together, these findings have significant patient safety implications and support a research agenda aimed at improving catheter use and outcomes in

patients with solid tumors.[33] An evidence-based approach to inform the use of PICCs may help reduce morbidity and improve care and quality of life for patients with solid tumors.

AUTHOR CONTRIBUTIONS

Urvashi B. Mitbander: Conceptualization, data interpretation, literature review, writing–original draft, and writing–reviewing and editing. **Marcus J. Geer:** Conceptualization and writing–reviewing and editing. **Knut Taxbro:** Writing–reviewing and editing. **Jennifer K. Horowitz:** Project administration and writing–review and editing. **Qisu Zhang:** Project administration and writing–review and editing. **Megan E. O'Malley** Conceptualization, data curation, data analysis, and methodology. **Nithya Ramnath:** Conceptualization, data interpretation, and writing–reviewing and editing. **Vineet Chopra:** Conceptualization, data interpretation, writing–reviewing and editing, and funding acquisition.

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CONFLICTS OF INTEREST

The authors made no disclosures.

REFERENCES

1. Kuter DJ. Thrombotic complications of central venous catheters in cancer patients. *Oncologist*. 2004;9(2):207-216. doi:10.1634/theoncologist.9-2-207
2. Hentrich M, Schalk E, Schmidt-Hieber M, et al. Central venous catheter-related infections in hematology and oncology: 2012 updated guidelines on diagnosis, management and prevention by the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology. *Ann Oncol*. 2014;25(5):936-947. doi:10.1093/annonc/mdt545
3. Verso M, Agnelli G. Venous thromboembolism associated with long-term use of central venous catheters in cancer patients. *J Clin Oncol*. 2003;21(19):3665-3675. doi:10.1200/JCO.2003.08.008
4. Wolf HH, Leithauser M, Maschmeyer G, et al. Central venous catheter-related infections in hematology and oncology : guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO). *Ann Hematol*. 2008;87(11):863-876. doi:10.1007/s00277-008-0509-5
5. Smith SN, Moureau N, Vaughn VM, et al. Patterns and predictors of peripherally inserted central catheter occlusion: the 3P-O study. *J Vasc Interv Radiol*. 2017;28(5):749-756.e2. doi:10.1016/j.jvir.2017.02.005
6. Baskin JL, Pui CH, Reiss U, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. *Lancet*. 2009;374(9684):159-169. doi:10.1016/S0140-6736(09)60220-8
7. Abdol Razak NB, Jones G, Bhandari M, Berndt MC, Metharom P. Cancer-associated thrombosis: an overview of mechanisms, risk factors, and treatment. *Cancers (Basel)*. 2018;10(10):380. doi:10.3390/cancers10100380
8. Michigan Hospital Medicine Safety Consortium. Peripherally Inserted Central Catheter (PICC) Use Initiative. Accessed June 6, 2021. https://www.mi-hms.org/quality-initiatives/peripherally-inserted-central-catheter-picc-use-initiative
9. Chopra V, Kaatz S, Conlon A, et al. The Michigan Risk Score to predict peripherally inserted central catheter-associated thrombosis. *J Thromb Haemost*. 2017;15(10):1951-1962. doi:10.1111/jth.13794
10. Herc E, Patel P, Washer LL, Conlon A, Flanders SA, Chopra V. A model to predict central-line-associated bloodstream infection among patients with peripherally inserted central catheters: the MPC Score. *Infect Control Hosp Epidemiol*. 2017;38(10):1155-1166. doi:10.1017/ice.2017.167
11. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. doi:10.1016/0021-9681(87)90171-8
12. The Leapfrog Group. Hospital and Surgery Center Ratings. Accessed June 6, 2021. https://ratings.leapfroggroup.org/
13. Centers for Disease Control and Prevention, National Healthcare Safety Network (NHSN). Chapter 4: Bloodstream infection event (central line-associated bloodstream infection and non-central line associated bloodstream infection). In: *The NHSN Patient Safety Component Manual*. NHSN; 2021. Accessed March 5, 2021. https://www.cdc.gov/nhsn/pdfs/validation/2021/pcsmanual_2021-508.pdf
14. Greene MT, Flanders SA, Woller SC, Bernstein SJ, Chopra V. The association between PICC use and venous thromboembolism in upper and lower extremities. *Am J Med*. 2015;128(9):986-993.e1. doi:10.1016/j.amjmed.2015.03.028
15. Barbar S, Noventa F, Rossetto V, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *J Thromb Haemost*. 2010;8(11):2450-2457. doi:10.1111/j.1538-7836.2010.04044.x
16. Arends J, Baracos V, Bertz H, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin Nutr*. 2017;36(5):1187-1196. doi:10.1016/j.clnu.2017.06.017
17. Larsen EN, Marsh N, O'Brien C, Monteagle E, Friese C, Rickard CM. Inherent and modifiable risk factors for peripheral venous catheter failure during cancer treatment: a prospective cohort study. *Support Care Cancer*. 2021;29(3):1487-1496. doi:10.1007/s00520-020-05643-2
18. Haider G, Kumar S, Salam B, Masood N, Jamal A, Rasheed YA. Determination of complication rate of PICC lines in oncological patients. *J Pak Med Assoc*. 2009;59(10):663-667.
19. Yap YS, Karapetis C, Lerose S, Iyer S, Koczwara B. Reducing the risk of peripherally inserted central catheter line complications in the oncology setting. *Eur J Cancer Care (Engl)*. 2006;15(4):342-347. doi:10.1111/j.1365-2354.2006.00664.x
20. Kreidieh FY, Moukadem HA, El Saghir NS. Overview, prevention and management of chemotherapy extravasation. *World J Clin Oncol*. 2016;7(1):87-97. doi:10.5306/wjco.v7.i1.87
21. Fonseca G, Burgermaster M, Larson E, Seres DS. The relationship between parenteral nutrition and central line-associated bloodstream infections: 2009–2014. *JPEN J Parenter Enteral Nutr*. 2018;42(1):171-175. doi:10.1177/0148607116688437
22. Schiffer CA, Mangu PB, Wade JC, et al. Central venous catheter care for the patient with cancer: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. 2013;31(10):1357-1370. doi:10.1200/JCO.2012.45.5733
23. Kleidon TM, Horowitz J, Rickard CM, et al. Peripherally inserted central catheter thrombosis after placement via electrocardiography vs. traditional methods. *Am J Med*. 2021;134(2):e79-e88. doi:10.1016/j.amjmed.2020.06.010
24. Wei Z, Tan B, Cao S, et al. The influence of neoadjuvant chemotherapy on gastric cancer patients' postoperative infectious complications: what is the negative role played by the intestinal barrier dysfunction? *Oncotarget*. 2017;8(26):43376-43388. doi:10.18632/oncotarget.14758
25. Mulder FI, Candeloro M, Kamphuisen PW, et al. The Khorana score for prediction of venous thromboembolism in cancer patients: a systematic review and meta-analysis. *Haematologica*. 2019;104(6):1277-1287. doi:10.3324/haematol.2018.209114
26. Chopra V, Flanders SA, Saint S, et al. The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): results from a multispecialty panel using the RAND/UCLA appropriateness method. *Ann Intern Med*. 2015;163(6 supp):S1-S40. doi:10.7326/M15-0744
27. Chopra V, Kuhn L, Coffey CE, et al. Hospitalist experiences, practice, opinions, and knowledge regarding peripherally inserted central catheters: a Michigan survey. *J Hosp Med*. 2013;8(6):309-314. doi:10.1002/jhm.2031

28. Taxbro K, Hammarskjold 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(6):734-741. doi:10.1016/j.bja.2019.01.038
29. 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(1):121-128. doi:10.1007/s00520-013-1941-1
30. Fang S, Yang J, Song L, Jiang Y, Liu Y. Comparison of three types of central venous catheters in patients with malignant tumor receiving chemotherapy. *Patient Prefer Adherence*. 2017;11:1197-1204. doi:10.2147/PPA.S142556
31. Coady K, Ali M, Sidloff D, Kenningham RR, Ahmed S. A comparison of infections and complications in central venous catheters in adults with solid tumours. *J Vasc Access*. 2015;16(1):38-41. doi:10.5301/jva.5000300
32. 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(10298):403-415. doi:10.1016/S0140-6736(21)00766-2
33. Byrnes MC, Schuerer DJE, Schallom ME, et al. Implementation of a mandatory checklist of protocols and objectives improves compliance with a wide range of evidence-based intensive care unit practices. *Crit Care Med*. 2009;37(10):2775-2781. doi:10.1097/ccm.0b013e3181a96379