

Mitbander Urvashi B (Orcid ID: 0000-0001-8443-4970)
Taxbro Knut (Orcid ID: 0000-0001-8711-9044)
Zhang Qisu (Orcid ID: 0000-0001-6098-517X)
Chopra Vineet (Orcid ID: 0000-0001-8670-9376)

Title

Patterns of Use and Outcomes of Peripherally Inserted Central Catheters in Hospitalized
Patients with Solid Tumors: A Multi-Center Study

Running Title

PICC Use and Outcomes in Solid Tumors

Authors

Urvashi B. Mitbander MD¹, Marcus J. Geer MD¹, Knut Taxbro MD PhD^{2,3}, Jennifer K. Horowitz
MA¹, Qisu Zhang MPH^{1*}, Megan E. O'Malley PhD¹, Nithya Ramnath MBBS^{1,4}, and Vineet Chopra
MD MSc⁵

From: ¹Department of Internal Medicine, University of Michigan Health System, Ann Arbor, MI,
USA; ²Department of Anaesthesia and Intensive Care Medicine, Ryhov County Hospital,
Jönköping, Sweden; ³Department of Biomedical and Clinical Sciences, Linköping University,
Linköping, Sweden; ⁴Medical Oncology, Veterans Affairs, Ann Arbor Healthcare System, Ann
Arbor, MI, USA; ⁵Department of Medicine, University of Colorado, Denver, Aurora, CO, USA.

*Employee at the time of the study

Author Contribution Statement:

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1002/cncr.34410](https://doi.org/10.1002/cncr.34410)

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Urvashi B. Mitbander MD: Conceptualization, data interpretation, literature review, writing-original draft, writing – reviewing and editing

Marcus J. Geer MD, Conceptualization, writing – reviewing and editing

Knut Taxbro MD PhD, Writing – reviewing and editing

Jennifer K. Horowitz MA, Project administration, writing – review and editing.

Qisu Zhang MPH, Project administration, writing – review and editing

Megan E. O’Malley PhD, Conceptualization, data curation, data analysis, methodology

Nithya Ramnath MBBS, Conceptualization, data interpretation, writing – reviewing and editing

Vineet Chopra MD MSc, Conceptualization, data interpretation, writing – reviewing and editing, funding acquisition

Funding Statement:

This work was funded by the Blue Cross and Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships Program.

The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript, and decision to submit the manuscript for publication.

Conflict of Interest Statement:

The authors report no conflict of interest.

ACKNOWLEDGEMENT:

Conflict of Interest Statement:

Urvashi B. Mitbander MD: no conflict of interest

Marcus J. Geer MD,

Knut Taxbro MD PhD,

Jennifer K. Horowitz MA,

Qisu Zhang MPH,

Megan E. O'Malley PhD,

Nithya Ramnath MBBS,

Vineet Chopra MD MSc

Word Count – 2,991

Corresponding Author

Vineet Chopra, MD MSc

Robert W. Schrier Chair of Medicine

Professor of Medicine

Department of Medicine

University of Colorado Anschutz Medical Campus

12631 E 17th Avenue, Aurora, CO 80045 | Mail Stop B178

E: vineet.chopra@cuanschutz.edu

P: 303-724-1783

Precis

PICCs are associated with significant complications in hospitalized patients with solid malignancies and are often used for reasons other than chemotherapy. Policies and guidance for appropriate use of PICCs in oncologic patients appear necessary.

Lay Summary

Peripherally inserted central catheters (PICC) are devices placed in peripheral veins to deliver medication to large veins near the heart. PICCs are used frequently in oncology. We aim to describe PICC associated complications in hospitalized patients with solid tumors. This study was performed across 50 Michigan hospitals and includes 3,235 patients with a solid tumor cancer and a PICC. We found 15.2% of patients experienced a complication including central line-associated bloodstream infection, deep vein thrombosis, pulmonary embolism, or catheter occlusion. Complication rates varied across hospitals. In conclusion, PICCs are associated with substantial complications in hospitalized patients with solid tumors.

Keywords:

Peripherally inserted central catheters; central venous catheters; oncology; neoplasms, retrospective studies; venous thrombosis; quality improvement

Structured Abstract

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 admitted to a general medicine ward or intensive care unit who received a PICC. Data was collected from 11/2013-12/2019 at 50 Michigan hospitals. Major complications were defined as central line-associated bloodstream infection (CLABSI), deep vein thrombosis (DVT), pulmonary embolism (PE), and catheter occlusion. Hospital variation in PICC use and outcomes was examined.

Results

Data included 3,235 hospitalized patients with solid tumors with 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 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 DVT (n=116, 3.6%), CLABSI (n=82, 2.5%), and PE (n=20, 0.6%).

Significant variation in indication for PICC use, device characteristics, and frequency of major complications across hospitals was observed ($p < 0.001$).

Conclusions

PICCs are associated with significant complications in hospitalized patients with solid malignancies and are often used for reasons other than chemotherapy. Policies and guidance for appropriate use of PICCs in oncologic patients appear necessary.

Background

Central venous catheters (CVC) are devices whose 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 non-tunneled devices such as peripherally inserted central catheters (PICCs), percutaneous CVCs, and subcutaneously inserted devices including tunneled catheters and ports.¹ Although 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) incidence of 1.1 to 7.5 per 1,000 CVC days, leading to increased morbidity and hospital costs.² Similarly, catheter-related thrombosis commonly affects cancer patients with CVCs¹ and risk of upper-extremity deep venous thrombosis (DVT) is high.³ Even if 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 is currently available. Existing studies suffer from small sample size or single center

designs. Additionally, previous studies do not distinguish risks between hematologic and solid tumor malignancies and often pool all cancer diagnoses in their analyses.

Therefore, we conducted a multi-center 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 due to advanced disease burden, and that gastrointestinal and pancreatic cancers would have more thrombotic complications from PICCs given their association with higher risk of VTE.⁷

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 HMS from November 2013 to December 2019. Adult patients admitted to a general medicine ward or intensive care unit (ICU) who received a PICC for any reason were eligible. Patients who are under 18, 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 uses 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. See appendix for full detail on these processes.

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, hormonal therapy, surgery, radiation therapy, or bone marrow transplant for a cancer diagnosis in the six months prior to PICC placement; or (3) patients hospitalized (>24 hours) with a primary cancer admission diagnosis in the six months prior to PICC placement. Only patients with a solid tumor diagnosis at time of PICC insertion were included (see Appendix); 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. Burden of comorbid conditions was expressed using the Charlson Comorbidity Index (CCI).¹¹ Provider characteristics, including attending specialty at time of PICC insertion and type of operator who placed the PICC were recorded. Information on hospital characteristics, such as number of beds, teaching status, and location were obtained from publicly-reported hospital data.¹² Device characteristics, including number of lumens, gauge, presence or absence of anti-infective or anti-thrombotic 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, venous thromboembolism (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 where 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 time of PICC placement and subsequently confirmed via imaging (ultrasonography or venogram for DVT; computed tomography, high-probability ventilation-perfusion scan, or pulmonary angiogram for PE). Because we have previously shown that PICCs are associated with 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 chi-square tests for categorical variables. All statistical tests were two-sided with a P value <0.05 considered statistically significant. Hospital variation was examined using the

Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables. To ensure stable estimates, analysis of complications across hospitals was restricted to those with ≥ 25 solid tumor patients. While 50 hospitals reported data for solid tumor patients during the study period, only 34 hospitals reported data for ≥ 25 patients; therefore, these hospitals (with lower volumes) were excluded when comparing variation across sites. SAS version 9.4 (SAS Institute) was used for all analyses.

Results

Demographics

A total of 3,235 solid tumor patients 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 ($n=1,477$) and 37,402 catheter days among patients with non-metastatic disease ($n=1,758$). The median age was 67.3 years (IQR 58.6-75.6), and most patients were overweight ($n=840$, 26.0%) or obese ($n=1,040$, 32.1%). The most common primary cancer diagnoses were non-small 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 ($n=2,318$, 71.7%) but 24.5% ($n=794$) were admitted directly to an intensive care unit (ICU); almost one-third (31.0%, $n=1,003$) received care in an ICU at any time during hospitalization. During hospitalization, 61.0% ($n=1,972$) of patients received pharmacologic VTE prophylaxis, and 23.2% ($n=749$) received treatment dose anticoagulation.

PICC Characteristics

Most PICCs (n=2,817, 87.1%) were placed following one insertion attempt, were double-lumen (n=1,845, 57.0%), followed by single-lumen (n=1,109, 34.3%), and triple-lumen (n=270, 8.3%) devices. PICCs were 5 to 7 French in 66.4% (n=2,147) of cases and 2 to 4.5 French in 30.6% (n=989) of cases. The median PICC dwell time was 13 days (IQR 6-30); 2.8% (n=89) were coated or impregnated with an anti-thrombotic material, while 5.5% (n=177) were anti-microbial 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 time of PICC placement, 17.5% (n=566) of patients had a concurrent CVC, including a non-dialysis CVC (e.g., tunneled CVC, non-tunneled CVC or port) in 474 patients, 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 (IV) antibiotics (n=1,115, 34.5%), followed by difficult access/blood draws (n=699, 21.6%), parenteral nutrition (n=578, 17.9%), chemotherapy (n=509, 15.7%), and medications requiring central access (n=413, 12.8%). Among the 509 PICCs 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 1,000-device days. DVT in either the upper or lower-extremity occurred in 3.6% (n=116) of patients and PE in 0.6% (n=20) of patients. VTE prophylaxis was administered prior to a DVT in 62.1% (n=82) of cases whereas treatment dose anticoagulation was administered prior to an event in 18.1% (n=21) and 20.0% (n=4) of DVT and PE cases, respectively (Table 2).

In catheters with antimicrobial coating, catheter occlusion occurred less frequently (n=40 vs n=282, $p<0.001$); however, differences in rates of CLABSI were not significant likely owing to small numbers of cases (n=6 vs n=76, $p=0.457$) (Supplemental Table 1). In catheters with antithrombotic coating, CLABSI and catheter occlusion rates did not differ significantly (Supplemental Table 2).

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, non-small cell lung, or brain cancer (Table 3).

Differences in outcomes between metastatic vs. non-Metastatic Disease

Compared to patients with non-metastatic disease, those with metastatic disease had greater comorbidity burden (median CCI of 8 [IQR 7-10] vs. 4 [IQR 2-5], $p<0.001$) and were more likely to be ever treated in the ICU (33.2% vs 29.2%, $p=0.01$). Patients with metastatic disease more frequently received double than single lumen catheters (60.5% vs. 54.2% and 30.8% vs

37.2%, $p < 0.001$ for both comparisons respectively). Patients with metastatic disease were also more likely to have a concurrent CVC (21.9% vs 13.8%, $p < 0.001$) at the time of PICC placement and more often had a PICC placed for difficult venous access (24.6% vs 19.1%, $p < 0.001$) or parenteral nutrition (TPN) (20.3% vs 15.8%, $p = 0.001$). Rates of CLABSI, DVT, PE and catheter occlusion did not differ significantly by presence of metastases.

Hospital Variation in PICC Use and Outcomes

Among the 50 hospitals in this study, 34 submitted data for ≥ 25 solid tumor patients and were included for analysis of hospital variation in PICC-related outcomes. The documented indications for PICCs use, number of catheter lumens, and PICC dwell times varied significantly across sites ($p < 0.001$ for all comparisons) (Table 4). For example, placement indication for chemotherapy ranged from 0.0% to 44.0% ($p < 0.001$) of all hospitals, use of single lumen PICCs ranged from 10.2% to 73.2% ($p < 0.001$), and median catheter dwell times ranged from 8 to 30 days ($p < 0.001$). The frequency of major complications also varied among hospitals ($p < 0.001$): rates of DVT ranged from 0% to 10.6% ($p = 0.01$), whereas catheter occlusion rates ranged from 1.1% to 25.4% ($p < 0.001$). Variation in rates of PE and CLABSI were observed but did not reach statistical significance ($p = 0.34$ and $p = 0.34$, respectively).

Discussion

In this retrospective, multi-center cohort study of 3,235 patients with a solid tumor diagnosis, we observed that PICCs were most often placed for IV antibiotics or difficult access; 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 and ninety-one (15.2%) patients experienced a major PICC-related complication, with catheter occlusion being the most prevalent of these harms. While rates of CLABSI, DVT, and PE did not differ significantly by presence of metastatic disease, the frequency of PICC complications did vary by primary tumor diagnosis. Additionally, significant hospital variation in PICC indication, characteristics, and complications were observed. Taken together, these findings suggest 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 non-metastatic 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 understanding of appropriateness of these decisions, the use of PICCs in this context is problematic. Patients with advanced disease may be more likely to be malnourished¹⁶ or unable to receive enteral nutrition, as well as more likely to have poor vascular access due to history of frequent venipuncture and vein exhaustion.¹⁷ Whether insertion of an additional central catheter in these patients is helpful and associated with better outcomes is unclear and worthy of further exploration.

In contrast to PICC use in outpatient settings where the most common indication for insertion is chemotherapy, the most common indication for PICC placement in our hospitalized cohort was IV 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 shows that about half of chemotherapy agents infused through PICCs were not irritants or vesicants, suggesting these agents could be safely administered peripherally without use of PICCs.²⁰

Our observed CLABSI rate of 1.6 per 1,000 device days is consistent with previously reported data in adult oncology patients.² However, we found that CLABSI rates did not differ by presence of metastatic disease, even though more patients with metastatic disease were documented to receive a PICC for the indication of TPN, 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, 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 to 27% to 66% prior to 2000.²² Improvement in placement techniques, including use of micro-introducer kits, ultrasound and EKG guidance,²³ and 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, 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 gastrointestinal, gynecologic, and genitourinary tumors, perhaps due to mucosal barrier damage in these tumors²⁴. VTE was more

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common in gastrointestinal, gynecologic, genitourinary, non-small cell lung, and brain tumors, tumors which are known to be pro-thrombotic.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 on how PICCs are used in oncology populations, and are unlikely to be related to disease characteristics alone.²⁶ While 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, that may be offset by earlier placement of ports in patients with solid tumors.^{28,29,30,31,32} Understanding drivers of PICC use and 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 was 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 as this was 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, while 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 variation in use and outcomes of PICCs in patients with solid tumors during hospitalization suggest 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. Additionally, frequent use of PICCs in the ICU and placement of PICCs for TPN, especially in patients with metastatic disease, is problematic as 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.³³An 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.

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Table 1. Patient, Device, and Provider Characteristics among hospitalized patients with solid tumors that received PICCs (stratified by metastatic vs. non-metastatic disease)

		Metastatic (n = 1477), n (%)	Non- metastatic (n = 1758), n (%)	P-value	Total (n = 3235), n (%)
Age					
	18-49 y	156 (10.6%)	147 (8.4%)	<.001	303 (9.4%)
	50-69 y	733 (49.6%)	758 (43.1%)		1491 (46.1%)
	≥70 y	541 (36.6%)	801 (45.6%)		1342 (41.5%)
Gender					
	Male	735 (49.8%)	939 (53.4%)	0.04	1674 (51.7%)
	Female	742 (50.2%)	819 (46.6%)		1561 (48.3%)
Race					
	White	1073 (72.6%)	1306 (74.3%)	0.47	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%)	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%)	0.001	1115 (34.5%)
	Blood Transfusion or Blood Products	15 (1.0%)	12 (0.7%)	0.30	27 (0.8%)
	Chemotherapy	307 (20.8%)	202 (11.5%)	<.001	509 (15.7%)
	Chemotherapy Only	226 (73.6%)	166 (82.2%)	0.02	392 (77.0%)
	Chemotherapy and Additional Indication	81 (26.4%)	36 (17.8%)	0.02	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%)	0.37	413 (12.8%)
	Multiple Incompatible Fluids	40 (2.7%)	44 (2.5%)	0.71	84 (2.6%)
	Parenteral Nutrition	300 (20.3%)	278 (15.8%)	0.001	578 (17.9%)

	Medications Requiring Central Access - Per Hospital Policy	2 (0.1%)	3 (0.2%)	0.8	5 (0.2%)
	Unknown	140 (9.5%)	175 (10.0%)	0.65	315 (9.7%)
Attending Physician Specialty					
	Hematologist/Oncologist	188 (12.7%)	180 (10.2%)	<.001	368 (11.4%)
	Non-Hematologist/Oncologist	1289 (87.3%)	1578 (89.8%)		2867 (88.6%)
Insertion attempts					
	1	1284 (86.9%)	1533 (87.2%)	0.66	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%)	0.01	1003 (31.0%)
Hospital Characteristics					
	Metropolitan	1356 (91.8%)	1610 (91.6%)	0.82	2966 (91.7%)
	Nonprofit	1264 (85.6%)	1538 (87.5%)	0.11	2802 (86.6%)
	Teaching	834 (56.5%)	1081 (61.5%)	0.004	1915 (59.2%)
Bed Size					
	1-249 beds	238 (16.1%)	305 (17.3%)	0.42	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					
	2-4.5-French	413 (28.0%)	576 (32.8%)	0.003	989 (30.6%)
	5-7-French	1021 (69.1%)	1126 (64.1%)	0.002	2147 (66.4%)
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%)	0.35	89 (2.8%)
	Line Duration, Median (IQR)	11.0 (5.0-30.0)	14.0 (6.0-30.0)	<.001	13.0 (6.0-30.0)
	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%)
	Peripherally Inserted Central Catheter	25 (7.7%)	20 (8.3%)	0.81	45 (8.0%)
	Central Venous Catheter (Non-Dialysis)	275 (84.9%)	199 (82.2%)	0.4	474 (83.7%)
	Central Venous Catheter for Renal Dialysis	27 (8.3%)	24 (9.9%)	0.51	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%)	0.01	28 (7.6%)
	Irritant/Vesicant	50 (24.5%)	44 (26.6%)	0.14	94 (25.5%)
	Other chemotherapy drug	93 (45.6%)	69 (41.8%)	0.002	162 (43.9%)
Accidental Dislodgement or Removal of PICC		45 (3.1%)	46 (2.6%)	0.461	91 (2.8%)
Catheter Tip Migration		62 (4.2%)	50 (2.8%)	0.036	112 (3.5%)
Labs at time of PICC placement					
	Creatinine (mg/dL), median (IQR)	0.8 (0.6-1.2)	0.9 (0.7-1.3)	0.44	0.9 (0.6-1.2)
	Hemoglobin (g/dL), median (IQR)	9.6 (8.4-11.1)	9.8 (8.6-11.4)	0.73	9.7 (8.5-11.3)
	Platelet Count ($\times 10^9/L$), median (IQR)	229.0 (142.0-329.0)	236.0 (160.0-326.0)	0.52	234.0 (153.0-328.0)
	WBC ($\times 10^9/L$), median (IQR)	9.8 (6.5-14.6)	9.1 (6.3-13.2)	0.32	9.4 (6.3-13.9)
	INR, median (IQR)	1.2 (1.1-1.3)	1.1 (1.0-1.3)	0.98	1.2 (1.1-1.3)
	eGFR (mL/min/m ²), median (IQR)	79.0 (60.0-119.0)	66.0 (51.6-108.0)	0.57	73.0 (55.0-113.0)
Type of cancer					
	Lung non-small 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%)	0.42	346 (10.7%)
	Prostate	143 (9.7%)	169 (9.6%)	0.95	312 (9.6%)
	Lung small cell	127 (8.6%)	88 (5.0%)	<.001	215 (6.6%)
	Bladder	74 (5.0%)	118 (6.7%)	0.04	192 (5.9%)
	Pancreas	109 (7.4%)	70 (4.0%)	<.001	179 (5.5%)
	Stomach	75 (5.1%)	66 (3.8%)	0.07	141 (4.4%)
	Uterine	57 (3.9%)	68 (3.9%)	0.99	125 (3.9%)
	Liver	62 (4.2%)	54 (3.1%)	0.09	116 (3.6%)
	Kidney	60 (4.1%)	39 (2.2%)	0.002	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%)	0.14	80 (2.5%)

	Metastatic with unknown origin	49 (3.3%)	0 (0.0%)	<.001	49 (1.5%)
	Unknown	5 (0.3%)	11 (0.6%)	0.25	16 (0.5%)
	Other	272 (18.4%)	328 (18.7%)	0.86	600 (18.5%)

Abbreviations:

CLABSI, central line-associated bloodstream infection; DVT, deep vein thrombosis; eGFR, estimated glomerular filtration rate; INR, international normalized ration; IQR, interquartile range, LEDVT, lower extremity deep vein thrombosis; PE, pulmonary embolism; PICC, Peripherally Inserted Central Catheter; UEDVT, upper extremity deep vein thrombosis; VTE, venous thromboembolism

Footnotes:

'Other' tumor type includes appendiceal cancer, esophageal cancer, esthesioneuroblastoma, fibrosarcoma, histiocytoma, kaposi sarcoma, malignant pleural effusion without unspecified cancer, squamous cell carcinoma (non-lung derived), testicular cancer, and tonsillar cancer.

Table 2. Device Related Complications

Complications					
	Any major complication	211 (14.3%)	280 (15.9%)	0.19	491 (15.2%)
	CLABSI – confirmed and suspected	33 (2.2%)	49 (2.8%)	0.32	82 (2.5%)
	DVT	59 (4.0%)	57 (3.2%)	0.25	116 (3.6%)
	PE	9 (0.6%)	11 (0.6%)	0.95	20 (0.6%)
	VTE - includes PE, LEDVT and UEDVT	65 (4.4%)	67 (3.8%)	0.40	132 (4.1%)
	Catheter Occlusion	131 (8.9%)	191 (10.9%)	0.06	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%)	0.42	21 (18.1%)
	PE	2 (22.2%)	2 (18.2%)	0.82	4 (20.0%)
	VTE	11 (16.9%)	14 (20.9%)	0.34	25 (18.9%)
VTE prophylaxis before major event (% of patients with positive event)					
	DVT	39 (66.1%)	32 (56.1%)	0.27	71 (61.2%)
	PE	5 (55.6%)	9 (81.8%)	0.56	14 (70.0%)
	VTE	41 (63.1%)	41 (61.2%)	0.82	82 (62.1%)
Any treatment anticoagulant		346 (23.4%)	403 (22.9%)	0.74	749 (23.2%)
Any VTE prophylaxis		907 (61.4%)	1065 (60.6%)	0.63	1972 (61.0%)

Table 3. Peripherally inserted central catheter complications (by tumor type)

	Any major complication, n (%)	CLABSI, n (%)	DVT (UE and LE), n (%)	PE, n (%)	VTE, n (%)	Catheter Occlusion, n (%)	Death, n (%)	Total, n (%)
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 non-small 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; LE, lower extremity; PE, pulmonary embolism; UE, upper extremity; VTE, venous thromboembolism

Footnotes:

^a Due to the data collection process, types of cancer are collected through positive patient histories of cancer. Patients with multiple positive histories of cancer (n = 437) will be counted in each category row.

^b 'Other' tumor type includes appendiceal cancer, esophageal cancer, esthesioneuroblastoma, fibrosarcoma, histiocytoma, kaposi sarcoma, malignant pleural effusion without unspecified cancer, squamous cell carcinoma (non-lung derived), testicular cancer, and tonsillar cancer.

Table 4. Hospital Variation in PICC characteristics and complications

		Range across hospitals							
		Min	10th Pctl	25th Pctl	Med.	75th Pctl	90th Pctl	Max	p*
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%	0.002
	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
Number of lumens									
	Single lumen	10.2%	16.7%	27.7%	33.5%	43.0%	48.6%	73.2%	<.001
	Double lumen	24.4%	41.7%	48.6%	54.4%	66.9%	76.0%	85.4%	<.001
	Triple lumen	0.0%	0.0%	0.0%	5.7%	13.8%	21.3%	36.7%	<.001
Line duration		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%	0.34
	DVT - UEDVT and LEDVT	0.0%	0.0%	1.7%	3.1%	4.2%	7.1%	10.6%	0.01
	PE	0.0%	0.0%	0.0%	0.0%	1.3%	2.1%	2.9%	0.34
	VTE	0.0%	0.0%	2.0%	3.8%	5.2%	7.9%	10.6%	0.01
	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%	0.01
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; LE, lower extremity; PE, pulmonary embolism; UE, upper extremity; VTE, venous thromboembolism

Disclosure Purpose: CNCR-22-0198.R2

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9. **Are there other financial or non-financial interests that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work not disclosed above.**

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10. **Was any of the work in this manuscript funded directly or indirectly from tobacco companies or their subsidiaries? (Please note that this does not include work from organizations that sponsor research from funds won by U.S. states and federal governments as part of tobacco settlements that are intended to promote research and care toward alleviating the suffering of individuals affected by tobacco products.)**

No

Certification

I certify that I have answered every question and the information provided in this disclosure is complete and accurate.

Author Manuscript

Disclosure Purpose: CNCR-22-0198.R2

Employment Information: Currently Employed

Disclosure Information:

1. **Are you the corresponding author?**

No

2. **What is the manuscript title?**

Patterns of Use and Outcomes of Peripherally Inserted Central Catheters in Hospitalized Patients with Solid Tumors: A Multi-Center Study

3. **Please select which of the following apply to each relationship or activity:**

- a. **Employment** Comprehensive Cancer Center, University of Michigan

The relationship is in direct support of the work reported in the manuscript anytime from when the work was conceived

4. **I confirm I have disclosed all direct support for the present manuscript (e.g. funding, provision of study materials, medical writing, article processing charges, etc.) There is no time limit for this item.**

Yes

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No, I have no relevant interests of this type

- b. **Grants or contracts for research (If you need to add an interest, please scroll to the top of the page, click "add interest" and select "Grant/Contract")**

No, I have no relevant interests of this type

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No, I have no relevant interests of this type

- e. **Payment for service on an advisory board (If you need to add an interest, please scroll to the top of the page, click "add interest" and select "Independent Contractor," and choose "Other")**

No, I have no relevant interests of this type

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- g. **Expert witness testimony (If you need to add an interest, please scroll to the top of the page, click "add interest" and select "Independent Contractor")**

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- l. **Support for attending meetings or other travel (If you need to add an interest, please scroll to the top of the page, click "add interest" and select "Travel")**

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6. **Was any individual paid to provide professional writing assistance with this manuscript?**

No.

7. **Have you or your institution received equipment, materials, drugs, or services in direct support of the work in the manuscript (without time limit) not disclosed above?**

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3. Please select which of the following apply to each relationship or activity:

a. **Employment** Department of Hematology and Oncology, University of Pittsburgh Medical Center

The relationship is outside the work reported in the manuscript but topically related and within the past 36 months

b. **Employment** Department of Internal Medicine, University of Michigan

The relationship is in direct support of the work reported in the manuscript anytime from when the work was conceived

c. **Travel** Department of Internal Medicine, University of Michigan

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Patterns of Use and Outcomes of Peripherally Inserted Central Catheters in Hospitalized Patients with Solid Tumors: A Multi-Center Study.

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Neither

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Neither

b. Independent Contractor - Consultant World Health Organization

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c. Employment Linköpings Universitet

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i. Patents planned, issued, or pending, whether or not you receive royalties (If you need to add an interest, please scroll to the top of the page, click "add interest" and select "Patents")

No, I have no relevant interests of this type

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