Peripherally Inserted Central Catheter Thrombosis Following placement via electrocardiography vs. traditional methods: an analysis of 42,687 patients

Tricia M Kleidon ^{a,b,c}, MNSci (Nurs. Prac) RNe

Jennifer Horowitz^d, MA

Claire M Rickard ^{b,c,e} PhD, RN

Amanda J Ullman ^{a,b,c,e} PhD, RN

Nicole Marsh ^{b,c,e} PhD, RN

Jessica Schults ^{a,b,c,e} (PhD), RN

David Ratz^d, MPH

Vineet Chopra^d, MD, MSc

^(a) The Department of Anesthesia, Queensland Children's Hospital, Brisbane, Australia;

^(b) Alliance for Vascular Access Teaching and Research, Griffith University, ^(c) Nursing and Midwifery Research Centre, The Royal Brisbane and Women's Hospital, Brisbane, Australia, ^(d) Patient Safety Enhancement Program, Division of Hospital Medicine, University of Michigan Health System, Ann Arbor, MI 48104, ^(e) School of Nursing, Griffith University, Brisbane, Australia.

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Email addresses:

Tricia.kleidon@health.qld.gov.au

jenhorow@med.umich.edu

C.rickard@griffith.edu.au

a.ullman@griffith.edu.au

Nicole.marsh@health.qld.gov.au

j.schults@griffith.edu.au

ratzd@med.umich.edu

vineetc@med.umich.edu

Address for correspondence:

Vineet Chopra MD, MSc

2800 Plymouth Road, Building 16 432W

Ann Arbor, MI 48109

e-mail – vineetc@med.umich.edu

Conflicts of Interest:

Tricia Kleidon reports investigator-initiated research grants and speaker fees provided to Griffith University from vascular access product manufacturers 3M Medical, Access Scientific, BD-Bard, Baxter; Cardinal Health, unrelated to the current project.

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Running Head:

Peripherally Inserted Central Catheter Thrombosis Following Electrocardiographic Placement

Data Access:

All authors had access to the data and played a role in writing the manuscript.

Highlights

1. Electrocardiographic tip confirmation is a relatively new technique to help guide peripherally inserted central catheter tip positioning at the bedside.

2. Real-time electrocardiographic-guided placement was associated with a reduced rate of deep vein thrombosis compared to conventional placement.
3. Electrocardiographic placement of peripherally inserted central catheter is convenient, safe and may prevent thrombosis.

ABSTRACT

Background: Peripherally inserted central catheter tip placement at the cavoatrial junction is associated with reduced catheter-related deep vein thrombosis .

Electrocardiographic tip confirmation purportedly improves accuracy of tip placement, but whether this approach can reduce deep vein thrombosis is unknown.

Methods: Prospectively collected data from patients that received peripherally inserted central catheters at 52 Michigan hospitals were analyzed. The method used to confirm tip confirmation at insertion and deep vein thrombosis outcomes were extracted from medical records. Multivariate models (accounting for the clustered nature of the data) were fitted to assess the association between peripherally inserted central catheter-related deep vein thrombosis and method of tip confirmation (Electrocardiographic vs. radiographic imaging).

Results: A total of 42,687 peripherally inserted central catheters (21,098 radiology vs. 21,589 Electrocardiographic) were included. Patients receiving Electrocardiographic - confirmed peripherally inserted central catheters had fewer comorbidities compared to those that underwent placement via radiology. Overall, deep vein thrombosis occurred in 594 (1.3%) of all peripherally inserted central catheters. Larger catheter size (odds

radio [OR]=1.32 [95% confidence interval [CI] 0.93–1.90] per unit increase in gauge), history of deep vein thrombosis, and cancer were associated with increased risk of deep vein thrombosis (OR=2.00 [95%CI 1.65-2.43] and OR=1.62 [95%CI 1.16-2.26], respectively) using logistic regression. Following adjustment, electrocardiographic guidance was associated with a significant reduction in peripherally inserted central catheter-related deep vein thrombosis compared with radiographic imaging (OR=0.74, 95% [CI=0.58-0.93, p=0.0098]).

Conclusion: The use of electrocardiographic to confirm peripherally inserted central catheter tip placement at the cavoatrial junction was associated with significantly fewer deep vein thrombosis events than radiographic imaging. Use of this approach for peripherally inserted central catheter insertion may help improve patient safety, particularly in high risk patients.

Key Words: Venous Thromboembolism, PICC, Catheter, EKG

Clinical Significance

1. Electrocardiographic (EKG) tip confirmation is a relatively new technique to help guide PICC tip positioning at the bedside.
2. Real-time EKG-guided placement was associated with a reduced rate of deep vein thrombosis compared to conventional radiographic placement.
3. EKG placement of PICCs is convenient, safe and may prevent thrombosis.

INTRODUCTION

The tip position of central venous catheters and peripherally inserted central catheters is an important predictor of catheter-related thrombosis.^{1, 2} Best practice dictates that central venous catheter and peripherally inserted central catheter tips should be placed in the region of the lower 1/3rd of the superior vena cava at the cavoatrial junction – a

region where blood flow is greatest and risk of thrombosis, lowest.^{3, 4} When catheters terminate in more proximal positions – such as mid to upper 1/3rd of the superior vena cava – patients are known to experience greater rates of catheter-related deep vein thrombosis.^{1, 5}

Traditionally, catheter tip position was confirmed via radiographic imaging of the chest or fluoroscopy following device placement. Anatomical landmarks and anthropometric estimates were used as a guide to determine initial tip placement, and post-insertion X-ray imaging confirmed placement using two-dimensional imaging.^{6, 7} However, X-rays have important limitations, including delays in performance of the test, cost, cumulative radiation exposure, variation in image acquisition and technique, subjective interpretation of tip location, and respiratory movement of the catheter (which may move the tip as much as 4-5cm in cranio-caudal direction).^{8, 9} Similarly, whilst fluoroscopy provides lower radiation exposure, the cost and need for a dedicated imaging suite limits its utility in everyday practice.

The introduction of real-time intracavitary electrocardiography-based peripherally inserted central catheter tip confirmation represents a viable solution to these problems.¹⁰ Electrocardiographic-catheter positioning systems incorporate a guidewire that obtains an internal tracing of the P-wave superimposed on a surface electrocardiographic. The P-wave originates from the sinoatrial node within the cavoatrial junction in a structurally intact heart. Convergence of the internal and externally tracked P-waves (beginning with increasing P-wave amplitude, maximal deflection and an absence of biphasic P [which suggests one has gone too far¹¹]), serves to verify cavoatrial junction placement.¹² Real-time tip location when peripherally

inserted central catheters are placed via electrocardiographic have been shown to result in faster placement and lower cost,¹³ without X-ray exposure across adult and pediatric populations.^{14, 15} In addition, this approach is thought to lead to more accurate tip positioning compared to traditional methods.^{11, 16}

In comparison to landmark or traditional methods, a theoretical advantage of electrocardiographic is that it is more physiologic when it comes to tip location. Therefore, it is plausible that catheters inserted using this approach are not only more accurately positioned, but also less likely to result in thrombotic complications. However, to date, no study has compared the two approaches with respect to risk of catheter associated deep vein thrombosis. To address this gap, we compared peripherally inserted central catheters placed via electrocardiographic to non-electrocardiographic (i.e., X-ray) techniques for deep vein thrombosis outcomes. We hypothesized that electrocardiographic peripherally inserted central catheter placement would be associated with a reduction in deep vein thrombosis complications compared to peripherally inserted central catheters placed and/or confirmed with radiology (X-ray or fluoroscopic techniques).

METHODS

Study Setting and Participants

The study was conducted using data from the Michigan Hospital Medicine Safety (HMS) Consortium; a 52-hospital collaborative quality initiative supported by Blue Cross Blue Shield of Michigan and Blue Care Network. The design and setting of this consortium have been previously described.¹⁷⁻¹⁹ In brief, HMS hospitals have been

prospectively collecting data regarding peripherally inserted central catheter use and outcomes using a purposive sampling strategy at participating hospitals since 2015.¹⁷ Adult medical patients admitted to a general ward or intensive care unit of a participating hospital who received a peripherally inserted central catheter for any reason during clinical care and have peripherally inserted central catheter tip confirmation technique are eligible for inclusion. Patients who are: (a) under the age of 18; (b) pregnant; (c) admitted to a non-medical service (e.g., general surgery); or (d) admitted under observation status, are excluded. Since we were interested in comparing peripherally inserted central catheters placed via electrocardiographic-guidance to those placed using anatomical landmarks and x-ray to confirm tip placement, we also excluded peripherally inserted central catheters placed by fluoroscopic guidance in this analysis.

At each hospital, dedicated, trained medical record abstractors use a standardized protocol to collect clinical data directly from health records of patients. Patients with peripherally inserted central catheters are sampled on a 14-day cycle, and data from the first 17 cases that meet eligibility criteria within each cycle are collected and stored within a patient registry. To ensure adequate representation of critically ill patients, 7 of the 17 cases include peripherally inserted central catheter placement in an intensive care unit-setting. All patients are followed until peripherally inserted central catheter removal, death, or 70 days, whichever occurs first. Data collection for the HMS project is ongoing; for this analysis, complete data from patients enrolled in the study between October 2015 and May 2019 were included.

Definitions and Variables

Peripherally inserted central catheters were defined as vascular access devices inserted in veins of the upper extremity that terminate at the cavoatrial junction^{3, 20, 21, 22}; thus, conventional central venous catheters or catheters placed in lower extremity or chest veins were excluded. Data regarding peripherally inserted central catheter characteristics (e.g., gauge, lumens, tip position verification) and indication for peripherally inserted central catheter placement were obtained directly from vascular nursing or interventional radiology insertion notes or the order for peripherally inserted central catheter placement. Electrocardiographic-guidance to place peripherally inserted central catheter was identified when use of commercially available electrocardiographic-placement technologies (e.g., Sherlock® II Tip Location System [BD-Bard Access Systems, Inc. Salt Lake City, USA], Sherlock 3CG® [BD-Bard Access Systems, Inc. Salt Lake City, USA], The Arrow® VPS G4™ [Teleflex, Morrisville, NC]) and confirmation of the peripherally inserted central catheter tip position via the electrocardiographic route was documented in the medical record. Peripherally inserted central catheters placed at the bedside, and confirmed via X-ray, were considered radiologically confirmed peripherally inserted central catheters.

Detailed medical history including comorbidities, physical findings, laboratory, and medication data were collected from the medical record at the time of hospital admission. Demographic and diagnostic variables including age, sex, race, body mass index, tobacco use (never, former, current), diagnosis on admission, presence and site of active infection, past or present hematological malignancy and active cancer (defined as receipt of chemotherapy while peripherally inserted central catheter was in place)

were collected. We calculated a Charlson comorbidity score for each patient. Additionally, treatment characteristics including; hemodialysis, chemotherapy or blood administration during hospitalization, existing central venous catheter when peripherally inserted central catheter was placed (yes/no), venous thromboembolism prophylaxis (i.e., receipt of subcutaneous heparin twice or thrice daily regimens or use of enoxaparin at prophylactic doses or treatment dose anticoagulation for any reason), aspirin, statin, erythropoiesis stimulating agents, and antibiotic administration were also abstracted directly from medical records. Laboratory values including white blood cell count, hemoglobin, platelet count, and international normalized ratio at the time of peripherally inserted central catheter placement were also collected from the medical record.

Ascertainment of Outcomes

The primary outcome was radiographically confirmed (e.g., ultrasound or computed tomography) ipsilateral upper-extremity deep vein thrombosis occurring after peripherally inserted central catheter placement (e.g., peripherally inserted central catheter-related deep vein thrombosis). At all sites, testing for deep vein thrombosis occurs only in the presence of clinical symptoms (e.g., arm pain, swelling). To ensure accuracy, patients with suspected deep vein thrombosis without imaging confirmation or patients with pulmonary embolism but absence of a confirmed upper-extremity deep vein thrombosis were excluded. Similarly, patients with deep vein thrombosis documented on the day of peripherally inserted central catheter insertion were also

excluded, as we could not determine whether thrombosis occurred before or after peripherally inserted central catheter placement.

Statistical Analyses

The unit of analysis was the peripherally inserted central catheter. Because our exposure of interest was technique of tip localization, the study population was stratified into those that underwent peripherally inserted central catheter insertion via electrocardiographic vs. those placed using traditional radiographic techniques. Descriptive statistics were first used to summarize differences between these two groups. Bivariate logistic regression was next used to estimate unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between risk factors and deep vein thrombosis in the electrocardiographic-guided and radiologically confirmed cohorts. We used a previously published and externally validated conceptual model of predictors of peripherally inserted central catheter complications to structure our analytical approach and identify putative risk factors.^{4, 23} In brief, this framework was created by systematic synthesis of evidence that identified risk factors associated with deep vein thrombosis in patients that received peripherally inserted central catheters. Thus, adjustment for baseline characteristics and entry of candidate variables into multivariable models was made using clinical and scientific principles, rather than statistical findings. Logistic generalized estimating equation models, accounting for hospital clustering were fit to the outcome of peripherally inserted central catheter-related deep vein thrombosis. Electrocardiographic-guidance was entered as an independent predictive variable in this model along with other candidate variables.

All analyses were performed in SAS, v9.4 (SAS Institute Inc., Cary, NC) and Stata v16 (Stata Corp., College Station, TX). All statistical tests were two-tailed; $P < 0.05$ was considered statistically significant.

Ethical and Regulatory Oversight

The University of Michigan Medical School's Institutional Review Board reviewed this study and assigned it a "Not Regulated" status.

RESULTS

Between October 2015 and May 2019, a total of 42,687 peripherally inserted central catheters placed in 52 HMS hospitals were available and included in this analysis. Of these devices, 21,589 peripherally inserted central catheters were placed using electrocardiographic compared to 21,098 peripherally inserted central catheters placed with radiological confirmation. Table 1 reports participant demographics, half of all patients undergoing peripherally inserted central catheter placement were male, with a mean participant age of 64 years. The median Charlson score of the study population was 3. Most patients were in the hospital for 4 days (median=2 days) prior to receiving a peripherally inserted central catheter. Once inserted, the median duration of peripherally inserted central catheter use was 14 days (range: 1-70 days). The majority of peripherally inserted central catheters (69%) were placed by vascular access nurses on patients in general medical/surgical units (67% of all peripherally inserted central catheters). Approximately one-third of all devices were placed in the intensive care unit (28.3%), with single (45%) and double (44%) lumen devices more commonly inserted.

Patients that received electrocardiographic peripherally inserted central catheters appeared to have fewer comorbidities than those that underwent non-electrocardiographic/traditional peripherally inserted central catheter placement, including advanced age (46.8% vs 52.0% ≥ 65), presence of hypertension (66.5% vs. 69.6%), dementia (7.7% vs. 8.8%), and diabetes - uncomplicated (18.0% vs. 19.5%). With respect to placement characteristics, more electrocardiographic peripherally inserted central catheters were placed in the right arm compared to traditional methods (72.1% vs. 67.4%). The most common indications for groups were intravenous antibiotics (49.9% and 46.9%) difficult intravenous access (25.2% and 19.1%), and central venous access (16.4% and 9.6%). Compared to traditional/radiological placement, electrocardiographic peripherally inserted central catheters were more prevalent in academic settings (71.1% vs. 48.7%) and were more often placed by vascular access nurses (96.1% v 40.7%; $p < 0.01$). Close to half of all peripherally inserted central catheters placed were single lumen devices, but differences in the number of single-lumen devices by electrocardiographic vs. X-ray placement were noted (48.6% v 41.7%; $p < 0.01$).

Among the 42,687 peripherally inserted central catheters, 594 (1.4%) experienced peripherally inserted central catheter-related deep vein thrombosis. Compared to those that did not experience thrombosis, patients that experienced peripherally inserted central catheter-related deep vein thrombosis had a higher prevalence of cancer (11.8% vs. 7.2%) or history of cancer (29.3% vs. 23.4%). A higher percentage of patients with peripherally inserted central catheter-related deep vein thrombosis had a history of receiving a peripherally inserted central catheter or central

venous catheter within the past six months (27.1% vs. 19.6%). Peripherally inserted central catheter-related deep vein thrombosis was more prevalent among patients whose peripherally inserted central catheters were inserted in an intensive care unit setting (45.5% vs. 28.9%), as well as patients who had a history of prior deep vein thrombosis (16.7% vs. 10.1%). With respect to device characteristics, most peripherally inserted central catheter-related deep vein thromboses occurred in double- and triple lumen catheters (461/594, 77.6% of all events).

In the multivariable logistic regression model (see Table 3), patients with a history of deep vein thrombosis were at greater risk of peripherally inserted central catheter-related deep vein thrombosis than those with no such prior events (OR=2.00, 95%CI 1.65-2.43). Similarly, patients with active cancer were at greater risk of thrombosis (OR=1.62, 95%CI 1.16-2.26). An increase in the number of lumens (catheter size) was associated with an increase in the risk of thrombosis (OR=1.64, 95%CI=1.12-2.40) for triple lumen catheters vs. single lumen devices). For each increase in catheter gauge from 3 Fr. to 6 Fr., the odds of peripherally inserted central catheter-related deep vein thrombosis increased by 1.32 [95%CI 0.93–1.90).

Within the multivariate model, electrocardiographic-guided tip-confirmation was associated with a significant reduction in the odds of peripherally inserted central catheter-related deep vein thrombosis compared to traditional X-ray based methods (OR=0.74, 95% CI=0.58-0.93, $p<0.001$).

DISCUSSION

Deep vein thrombosis is a potentially deleterious complication of peripherally inserted central catheter insertion with lifelong sequelae for patients.²³⁻²⁵ Despite various measures implemented to reduce this risk, including focusing on appropriateness of use,^{4, 23, 26, 27} limiting use of multi-lumen catheters,²⁸⁻³⁰ consideration of catheter-to-vein ratio during insertion,^{26, 31} and ensuring catheter tip placement at cavoatrial junction,^{30, 32} deep vein thrombosis continues to affect 3-15% of all peripherally inserted central catheter recipients.²⁷ In this large secondary data analysis spanning multiple hospitals, we found the use of electrocardiographic to confirm peripherally inserted central catheter tip placement appeared to be protective against deep vein thrombosis. Assuming an average deep vein thrombosis rate of 2%, a total of 192 patients would need to receive an electrocardiographic-guided peripherally inserted central catheter to prevent one catheter-related deep vein thrombosis. Given how often peripherally inserted central catheters are used in clinical care, these findings have important patient safety implications for the thousands of patients that receive these devices across the world.

Preventing hospital-acquired deep vein thrombosis is an important focus of quality improvement initiatives. In particular, catheter-related deep vein thrombosis is frequently asymptomatic², but when diagnosed, has significant clinical impact (disruption and delays to treatment), economic consequences (prolonged hospitalization, need for additional resources) and patient safety implications on future vessel health and preservation. Our study provides further confirmatory data to the growing body of evidence that reports an increased risk of catheter-related deep vein thrombosis in the context of placing peripherally inserted central catheters in the

intensive care unit,²⁴ in patients with history of deep vein thrombosis,^{2, 23, 33} cancer,^{15, 23, 34} and use of multi-lumen catheters.^{27, 29} Multi-lumen catheters are often necessary when caring for critically ill patient; however, device choice is a modifiable risk factor²⁷ and the decision to insert a peripherally inserted central catheter vs. a traditional central device and number of lumens should be a thoughtful decision.²² We also found that insertion of peripherally inserted central catheters by experienced vascular access nurses and use of single lumen catheters were less likely to be associated with deep vein thrombosis. Taken together, these findings are important and extend what is known about peripherally inserted central catheters and thrombosis in hospitalized patients.

Our findings are consistent with existing studies. For example, in a randomized controlled trial comparing radiology confirmed peripherally inserted central catheter to electrocardiographic inserted peripherally inserted central catheters in patients with cancer, Li et al. demonstrated superiority of the electrocardiographic group.¹⁵ Electrocardiographic-guided peripherally inserted central catheter placement resulted in significantly greater first-attempt success, 89.2% (95% CI, 86.5% to 91.9%), compared to 77.4% (95% CI, 73.7% to 81.0%) in the anatomical landmark group ($P < 0.0001$), as well as optimal tip placement ($P=0.0016$).¹⁵ Although deep vein thrombosis (1.4%) in our cohort was lower than previously reported,^{27, 35} the safety and efficacy of electrocardiographic-peripherally inserted central catheters guidance coupled with growing use of this technology in practice may explain these findings.^{7, 15, 16}

Our study has limitations including those inherent to the observational design that allow us to determine associations, not causation. Second, deep vein thromboses in this study were identified only when symptoms led to diagnostic testing; thus, we may have

underestimated the true rate of peripherally inserted central catheters-associated deep vein thrombosis and potentially the benefit of electrocardiographic guidance. Third, we did not consider the cost, training and effort required to become proficient with electrocardiographic guidance and instead, focused on patient outcomes. Hospitals seeking to transition to this technology may therefore need to take these initial capital and human aspects into consideration.

Our study also has strengths. First, we included a large sample size and a broad range of patients within a prospective cohort design. These aspects coupled with results that span 52 hospitals lend a high degree of rigor and validity to our findings. Second, the fact that peripherally inserted central catheters placed with electrocardiographic technology were associated with reduced risk of catheter-related deep vein thrombosis is a novel finding that has important safety implications. Given the growth of this technology and myriad other benefits including lack of radiation exposure, greater use of electrocardiographic-guidance is recommended. Third, all thrombotic events in our study were detected based on clinical suspicion and verified by documented imaging findings, a process that is highly consistent with “real world” clinical care.

Our findings have important policy implications and suggest that the current ‘gold standard’ for peripherally inserted central catheters tip verification by post insertion chest X-ray may need to be revisited.^{36 - 38} Anatomical landmarks (e.g. carina) used to determine the location of the cavoatrial junction are not located in the same plane, leading to subjectivity, inter-observer inconsistency and errors in tip position verification.^{37, 38} Furthermore, the immediacy of this technology at the bedside reduces delays to peripherally inserted central catheter tip confirmation, post-procedural catheter

manipulation and time to availability of peripherally inserted central catheter for use.^{10,}

^{14, 15} Coupled with the reduction in deep vein thrombosis observed in our analysis, there is little reason to not move to intra-cavitary electrocardiographic as the standard for insertion of peripherally inserted central catheters.

CONCLUSION

Strategies to help reduce the risk of thrombosis associated with peripherally inserted central catheters are needed for the many patients that receive these devices. The use of electrocardiographic to confirm peripherally inserted central catheter tip placement at cavo-atrial junction appears to be associated with a significant reduction in deep vein thrombosis. Whilst further research is needed to determine causation, adoption of electrocardiographic for peripherally inserted central catheter insertion may ameliorate patient safety, particularly in high risk patients such as those with a history of deep vein thrombosis or cancer diagnosis.

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TABLE 1. STUDY POPULATION (STRATIFIED BY TIP CONFIRMATION TECHNIQUE)

Variable		X-Ray Localization (n=21,098)	EKG-Guidance (n=21,589)	p
Patient Characteristics				
Gender	Male	10619 (50.4%)	11090 (51.4%)	0.03
Race	White	15572 (75.6%)	16015 (76.0%)	0.39
Age	Median (IQR) ¹	65.83 (54.35-76.85)	63.75 (52.79-74.23)	<.01
Charlson Comorbidity Score	Median (IQR) ¹	3.00 (2.00-5.00)	3.00 (2.00-5.00)	<.01
Basal Metabolic Index	Median (IQR) ¹	28.73 (23.92-35.38)	28.73 (24.00-35.15)	0.79
Hyperlipidemia	Yes	22 (0.1%)	35 (0.2%)	0.10
Hypertension	Yes	14676 (69.6%)	14360 (66.5%)	<.01
Myocardial Infarction	Yes	825 (3.9%)	880 (4.1%)	0.38
Congestive Heart Failure	Yes	3083 (14.6%)	2470 (11.4%)	<.01
Peripheral vascular disease	Yes	3546 (16.8%)	3300 (15.3%)	<.01
Cerebrovascular disease	Yes	3390 (16.1%)	3296 (15.3%)	0.02
Dementia	Yes	1854 (8.8%)	1654 (7.7%)	<.01
Chronic Obstructive Pulmonary Disease	Yes	2026 (9.6%)	1968 (9.1%)	0.08
Diabetes-uncomplicated	Yes	4111 (19.5%)	3876 (18.0%)	<.01

Diabetes-complicated	Yes	4595 (21.8%)	4727 (21.9%)	0.77
Renal Failure	Yes	7826 (37.1%)	8056 (37.3%)	0.64
Hemodialysis	Yes	828 (3.9%)	490 (2.3%)	<.01
Mild liver disease	Yes	1245 (5.9%)	1553 (7.2%)	<.01
Moderate/severe liver disease	Yes	743 (3.5%)	847 (3.9%)	0.03
Cancer history	Yes	4992 (23.7%)	5013 (23.2%)	0.28
Active cancer	Yes	1446 (6.9%)	1661 (7.7%)	<.01
Hematological cancer	Yes	619 (2.9%)	835 (3.9%)	<.01
Cerebrovascular Accident/ Transient Ischemic Attack	Yes	3615 (17.1%)	3387 (15.7%)	<.01
Deep vein thrombosis ¹ history	No	18254 (86.5%)	18945 (87.8%)	<.01
	Positive history	2239 (10.6%)	2115 (9.8%)	
Prior Central Venous Catheter/Peripherally Inserted Central Catheter ²	Yes	4283 (20.3%)	4130 (19.1%)	<.01
Presence of another Central Venous Catheter ³	Ye	3019 (14.3%)	2573 (11.9%)	<.01
Placement attempts	>1	2013 (10.0%)	2552 (11.9%)	<.01
Device Characteristics				
Insertion arm	Right Arm	14207 (67.4%)	15550 (72.1%)	<.01
Insertion vein	Basilic	12183 (57.7%)	13470 (62.4%)	<.01
	Brachial	6832 (32.4%)	6723 (31.1%)	
	Cephalic	948 (4.5%)	1208 (5.6%)	
	Other	1135 (5.4%)	188 (0.9%)	
Operator	Vascular Access Nurse	8596 (40.7%)	20740 (96.1%)	<.01
	Interventional Radiologist	7422 (35.2%)	475 (2.2%)	
	Physician	231 (1.1%)	40 (0.2%)	
	Advanced Practice Professional	4476 (21.2%)	316 (1.5%)	
	Other	373 (1.8%)	18 (0.1%)	
Number of Peripherally Inserted Central Catheter lumens	Single	8778 (41.7%)	10477 (48.6%)	<.01
	Double	10096 (48.0%)	8567 (39.7%)	
	Triple	2178 (10.3%)	2523 (11.7%)	

Power Peripherally Inserted Central Catheter	Yes	18298 (86.7%)	20521 (95.1%)	<.01
Anti-microbial coated	Yes	1820 (8.6%)	580 (2.7%)	<.01
Anti-thrombotic coated	Yes	374 (1.8%)	536 (2.5%)	<.01
Peripherally Inserted Central Catheter Length	Median (IQR) ¹	42.00 (38.00-45.00)	43.00 (39.00-46.00)	<.01
Location of Insertion	Intensive Care Unit	5729 (28.3%)	6348 (29.8%)	<.01
Indication: Antibiotics	Yes	9897 (46.9%)	10765 (49.9%)	<.01
Indication: Chemotherapy	Yes	605 (2.9%)	821 (3.8%)	<.01
Indication: Difficult access	Yes	4030 (19.1%)	5433 (25.2%)	<.01
Indication: Central infusates	Yes	2027 (9.6%)	3542 (16.4%)	<.01
Indication: Parenteral Nutrition	Yes	1572 (7.5%)	1438 (6.7%)	<.01
Indication: Other/unknown	Yes	4848 (23.0%)	3531 (16.4%)	<.01
Catheter Size (French)	>5 French	1590 (7.9%)	1156 (5.4%)	<.01
Hospital Characteristics				
Academic	Yes	10274 (48.7%)	15358 (71.1%)	<.01
Area	Rural	378 (1.8%)	680 (3.1%)	<.01
Profit Status	For Profit	926 (4.4%)	1995 (9.2%)	<.01
Bed size	Median (IQR) ¹	372.00 (250.00-632.00)	372.00 (291.00-573.00)	<.01
Annual Discharges	Median	18439.00 (11072.00-31081.00)	19097.00 (12453.00-30375)	<.01

¹ IQR = interquartile range;

² Prior to Peripherally Inserted Central Catheter insertion, did the patient have a Peripherally Inserted Central Catheter or Central Venous Catheter placed in the past 6 months?

³ Does the patient have an existing indwelling Central Venous Catheter at the time the Peripherally Inserted Central Catheter was placed?

TABLE 2. UNIVARIATE ASSOCIATIONS OF VARIABLES WITH DEEP VEIN THROMBOSIS

Variable		OR (95% CI)	P-value
Gender	Male vs. Female	1.06 (0.85, 1.32)	0.61
Race	White vs. Non-White	0.84 (0.64, 1.11)	0.22
Age group	>=65 vs. <65	1.11 (0.97, 1.27)	0.14
Hyperlipidemia	Yes vs. No	1.32 (0.24, 7.26)	0.75
Hypertension	Yes vs. No	0.96 (0.80, 1.15)	0.66
Myocardial Infarction	Yes vs. No	1.24 (0.85, 1.81)	0.27
Congestive Heart Failure	Yes vs. No	0.70 (0.51, 0.95)	0.02

Variable		OR (95% CI)	P-value
Peripheral vascular disorders	Yes vs. No	0.75 (0.58, 0.98)	0.03
Cerebrovascular disease	Yes vs. No	1.18 (0.98, 1.41)	0.08
Dementia	Yes vs. No	1.20 (0.89, 1.62)	0.24
Chronic Obstructive Pulmonary Disease	Yes vs. No	0.94 (0.63, 1.40)	0.75
Rheumatoid arthritis	Yes vs. No	0.63 (0.08, 4.79)	0.66
Peptic Ulcer Disease	Yes vs. No	1.74 (1.31, 2.31)	0.0001
Diabetes-uncomplicated	Yes vs. No	0.95 (0.77, 1.17)	0.63
Diabetes-complicated	Yes vs. No	0.91 (0.75, 1.10)	0.31
Renal Failure	Yes vs. No	0.89 (0.74, 1.07)	0.22
Kidney transplant	Yes vs. No	1.22 (0.44, 3.41)	0.70
Hemodialysis	Yes vs. No	1.42 (0.89, 2.28)	0.14
Peritoneal Dialysis	Yes vs. No	1.63 (0.26, 10.00)	0.60
Hemi/paraplegia	Yes vs. No	1.04 (0.68, 1.61)	0.85
Mild liver disease	Yes vs. No	0.82 (0.57, 1.18)	0.28
Moderate/severe liver disease	Yes vs. No	0.59 (0.35, 1.00)	0.05
Acquired immune deficiency syndrome	Yes vs. No	0.21 (0.02, 1.95)	0.17
Cancer history	Yes vs. No	1.36 (1.13, 1.64)	0.001
Active cancer	Yes vs. No	1.74 (1.28, 2.37)	0.0005
Coagulopathy	Yes vs. No	1.52 (1.03, 2.22)	0.03
Central Line-Associated Bloodstream Infection history	Yes vs. No	1.01 (0.43, 2.36)	0.99
Inflammatory bowel disease	Yes vs. No	1.78 (0.84, 3.78)	0.13
Lung disease	Yes vs. No	1.61 (1.30, 1.99)	<.0001
Life-threatening illness	Yes vs. No	2.13 (1.72, 2.65)	<.0001
Pneumonia	Yes vs. No	1.35 (1.08, 1.70)	0.01
Sepsis	Yes vs. No	1.18 (1.01, 1.39)	0.04
Cerebrovascular Accident/ Transient Ischemic Attack	Yes vs. No	1.09 (0.88, 1.34)	0.43
Venous stasis	Yes vs. No	0.67 (0.45, 1.00)	0.05
Statin	Yes vs. No	1.56 (1.26, 1.94)	<.0001
Aspirin	Yes vs. No	1.25 (1.04, 1.51)	0.02
Aspirin or statin	Yes vs. No	1.50 (1.22, 1.85)	0.0002
Other antiplatelet therapy	Yes vs. No	1.14 (0.85, 1.53)	0.39

Variable		OR (95% CI)	P-value
Prior Central Venous Catheter/Peripherally Inserted Central Catheter	Yes vs. No	1.44 (1.17, 1.78)	0.0007
Presence of another Central Venous Catheter	Yes vs. No	1.87 (1.52, 2.30)	<.0001
Placement attempts	>1 vs. 1	1.01 (0.75, 1.35)	0.96
Insertion arm	Right Arm vs. Left Arm	0.86 (0.73, 1.02)	0.09
Power Peripherally Inserted Central Catheter	Yes vs. No	0.70 (0.51, 0.96)	0.03
Antimicrobial coated	Yes vs. No	1.42 (0.81, 2.47)	0.22
Anti-thrombotic coated	Yes vs. No	0.47 (0.08, 2.85)	0.41
Valved	Yes vs. No	0.69 (0.49, 0.97)	0.03
Lymphoma	Yes vs. No	1.10 (0.69, 1.76)	0.68
Hematological cancer	Yes vs. No	1.44 (1.02, 2.03)	0.04
Metastatic cancer	Yes vs. No	0.99 (0.62, 1.57)	0.95
Non-metastatic cancer	Yes vs. No	1.30 (1.05, 1.61)	0.01
Endocarditis	Yes vs. No	1.19 (0.46, 3.09)	0.72
Osteomyelitis	Yes vs. No	0.62 (0.47, 0.82)	0.0006
Pancreatitis	Yes vs. No	1.62 (0.83, 3.18)	0.16
Short gut syndrome	Yes vs. No	1.54 (0.14, 16.91)	0.72
Cellulitis	Yes vs. No	0.56 (0.43, 0.73)	<.0001
Swollen legs	Yes vs. No	1.15 (0.93, 1.41)	0.19
Smoking status	Former/Current vs. Never	0.97 (0.80, 1.17)	0.74
Level of care, binary	Emergency Room/Intensive Care Unit vs. Inpatient Med Floor/Outpatient	1.98 (1.63, 2.40)	<.0001
Inserted Intensive Care Unit	Intensive Care Unit vs. non-Intensive Care Unit	2.01 (1.66, 2.44)	<.0001
Indication antibiotics	Yes vs. No	0.53 (0.43, 0.65)	<.0001
Indication chemotherapy	Yes vs. No	1.71 (1.25, 2.34)	0.0008
Indication difficult access	Yes vs. No	1.46 (1.11, 1.93)	0.01
Indication central access	Yes vs. No	1.15 (0.85, 1.55)	0.37
Indication multiple fluids	Yes vs. No	0.96 (0.46, 2.00)	0.92
Indication Total Parenteral Nutrition	Yes vs. No	1.45 (1.13, 1.86)	0.0038
Indication other/unknown	Yes vs. No	1.42 (1.01, 1.98)	0.04
5 French	>5 vs. ≤5	2.14 (1.69, 2.70)	<.0001

Variable		OR (95% CI)	P-value
Area	Rural vs. Metropolitan/Micropolitan	0.85 (0.52, 1.38)	0.51
Academic	Yes vs. No	0.67 (0.45, 0.99)	0.05
Deep Vein Thrombosis history	Positive history vs. No	1.89 (1.56, 2.28)	
	Within previous 30 days vs. No	2.88 (1.84, 4.50)	<.0001
Pulmonary Embolism history	Positive history vs. No	1.69 (1.28, 2.23)	
	Within previous 30 days vs. No	0.72 (0.32, 1.62)	0.0001
Venous Thromboembolism history	Positive history vs. No	1.76 (1.45, 2.14)	
	Within previous 30 days vs. No	2.37 (1.59, 3.52)	<.0001
Estimated Glomerular Filtration category ¹	15-29 vs. <15	0.67 (0.37, 1.22)	
	30-44 vs. <15	0.64 (0.40, 1.00)	
	45-59 vs. <15	0.68 (0.40, 1.14)	
	>=60 vs. <15	0.66 (0.41, 1.05)	0.38
Origin of admission	Another hospital vs. Acute rehab	0.61 (0.31, 1.21)	
	Assisted living vs. Acute rehab	0.53 (0.12, 2.37)	
	Skilled nursing home vs. Acute rehab	0.41 (0.23, 0.72)	
	Home vs. Acute rehab	0.56 (0.35, 0.89)	0.02
Insertion vein	Brachial vs. Basilic	1.24 (1.02, 1.50)	
	Cephalic vs. Basilic	0.69 (0.47, 1.03)	
	Other vs. Basilic	1.26 (0.82, 1.95)	0.01
Inserted by	Interventional Radiologist vs. Vascular Access Nurse	1.45 (0.95, 2.20)	
	Physician vs. Vascular Access Nurse	1.30 (0.63, 2.68)	
	Advance Practice Professional vs. Vascular Access Nurse	1.39 (0.86, 2.25)	
	Other vs. Vascular Access Nurse	1.01 (0.56, 1.81)	0.55
Number of Peripherally Inserted Central Catheter lumens ¹	Double vs. Single	2.59 (2.12, 3.16)	
	Triple/Quad vs. Single	3.49 (2.75, 4.42)	<.0001
Age	Per unit increase	1.00 (1.00, 1.01)	0.39
Charlson	Per unit increase	0.98 (0.95, 1.01)	0.22
Basal Metabolic Index	Per unit increase	0.99 (0.98, 1.00)	0.01
Estimated Glomerular Filtration	Per unit increase	1.00 (1.00, 1.00)	0.22

Variable		OR (95% CI)	P-value
White Blood Count	Per unit increase	1.00 (1.00, 1.00)	0.74
Hemoglobin	Per unit increase	0.96 (0.92, 1.00)	0.04
Platelets	Per unit increase	1.00 (1.00, 1.00)	0.06
International Normalized Ratio ¹	Per unit increase	1.03 (0.99, 1.07)	0.12
Gauge	Per unit increase	2.12 (1.87, 2.40)	<.0001
PICC length	Per unit increase	1.00 (0.98, 1.01)	0.78
Hospital Length of Stay prior to Central Venous Catheter	Per unit increase	1.01 (1.00, 1.03)	0.06
Lumens	Per unit increase	1.89 (1.71, 2.09)	<.0001
Bed Size	Per unit increase	1.00 (1.00, 1.00)	0.0012
Discharges	Per unit increase	1.00 (1.00, 1.00)	<.0001

TABLE 3. LOGISTIC GEE MODELS FOR PREDICTORS OF PERIPHERALLY INSERTED CENTRAL CATHETER-RELATED DEEP VEIN THROMBOSIS

Variable		Odds Ratio (95% Confidence Interval)	P
Use of Electrocardiogram - Guidance	Yes vs. No	0.74 (0.58, 0.93)	0.01
History of Deep Vein Thrombosis	Yes vs. No	2.00 (1.65, 2.43)	<.0001
History of Deep Vein Thrombosis within 30 Days	Yes vs. No	2.43 (1.55, 3.81)	0.0001
Active cancer	Yes vs. No	1.62 (1.16, 2.26)	0.01
Catheter Gauge	Per unit increase	1.32 (0.93, 1.90)	0.12
Number of Lumens	Double vs. Single	1.61 (0.82, 3.18)	0.17
	Triple vs. Single	1.64 (1.12, 2.40)	0.01
Power Peripherally Inserted Central Catheter	Yes vs. No	0.79 (0.57, 1.09)	0.15
Existing Central Venous Catheter ¹	Yes vs. No	1.30 (1.05, 1.62)	0.02
Insertion vein	Cephalic vs. Basilic	0.67 (0.45, 1.00)	0.05
	Other vs. Basilic	1.07 (0.73, 1.55)	0.74
	Brachial vs. Basilic	1.15 (0.97, 1.37)	0.11
Insertion in Intensive Care Unit	Yes vs. No	0.96 (0.63, 1.47)	0.85