

Peripherally Inserted Central Catheter Thrombosis After Placement via Electrocardiography vs Traditional Methods



Tricia M. Kleidon, MNSci (Nurs. Prac) RNe,^{a,b,c} Jennifer Horowitz, MA,^d Claire M. Rickard, PhD, RN,^{b,c,e}
Amanda J. Ullman, PhD, RN,^{a,b,c,e} Nicole Marsh, PhD, RN,^{b,c,e} Jessica Schults, (PhD), RN,^{a,b,c,e} David Ratz, MPH,^d
Vineet Chopra, MD, MSc^d

^aDepartment of Anesthesia, Queensland Children's Hospital, Brisbane, Australia; ^bAlliance for Vascular Access Teaching and Research, Griffith University, Brisbane, Australia; ^cNursing and Midwifery Research Centre, The Royal Brisbane and Women's Hospital, Brisbane, Australia; ^dPatient Safety Enhancement Program, Division of Hospital Medicine, University of Michigan Health System, Ann Arbor; ^eSchool of Nursing, Griffith University, Brisbane, Australia.

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 with 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 ratio [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; $P = .0098$).

CONCLUSION: The use of electrocardiography 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.

Published by Elsevier Inc. • *The American Journal of Medicine* (2021) 134:e79–e88

KEYWORDS: Catheter, Electrocardiography; Peripherally inserted central catheter; Venous thromboembolism

Funding: See last page of article.

Conflict of Interest: See last page of article.

Authorship: See last page of article.

Requests for reprints should be addressed to Vineet Chopra, MD, MSc, Patient Safety Enhancement Program, Division of Hospital Medicine,

University of Michigan Health System, 2800 Plymouth Road, Building 16
432W, Ann Arbor, MI 48109.

E-mail address: vineetc@med.umich.edu

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 third of the superior vena cava at the cavoatrial junction—a region where blood flow is greatest and risk of thrombosis is lowest.^{3,4} When catheters terminate in more proximal positions—such as mid to upper third 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 postinsertion x-ray imaging confirmed placement using 2-dimensional imaging.^{6,7} However, x-ray studies 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 4–5 cm in a craniocaudal direction).^{8,9} Similarly, while 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 electrocardiogram. 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 electrocardiography 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 with traditional methods.^{11,16}

In comparison with landmark or traditional methods, a theoretical advantage of electrocardiography 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 2 approaches with respect to risk of catheter-associated deep vein thrombosis. To address this gap, we compared peripherally inserted central catheters placed via electrocardiography with nonelectrocardiography (ie, x-ray study) 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 with peripherally inserted central catheters placed 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 about 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: 1) under the age of 18 years; 2) pregnant; 3) admitted to a nonmedical service (eg, general surgery); or 4) admitted under observation status, are excluded. Because 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

CLINICAL SIGNIFICANCE

- Electrocardiographic tip confirmation is a relatively new technique to help guide peripherally inserted central catheter tip positioning at the bedside.
- Real-time electrocardiography-guided placement was associated with a reduced rate of deep vein thrombosis compared with conventional radiographic placement.
- Electrocardiographic placement of peripherally inserted central catheters is convenient, safe, and may prevent thrombosis.

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;^{3,20-22} thus, conventional central venous catheters or catheters placed in lower extremity or chest veins were excluded. Data about peripherally inserted central catheter characteristics (eg, 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 (eg, Sherlock II Tip Location System and Sherlock 3CG [BD-Bard Access Systems, Inc., Salt Lake City, Utah], 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 study 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 (ie, 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 (eg, ultrasound or computed tomography) ipsilateral upper-extremity deep vein thrombosis occurring after peripherally inserted central catheter placement (eg, peripherally inserted central catheter-related deep vein thrombosis). At all sites, testing for deep vein thrombosis occurs only in the presence of clinical symptoms (eg, 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 prior to 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 2 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 2-tailed; $P < .05$ 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 electrocardiography, compared with 21,098 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 nonelectrocardiographic/traditional peripherally inserted central catheter placement, including advanced age (46.8% vs 52.0% ≥ 65 years), 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 with 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 with 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% vs 40.7%; $P < .01$). 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% vs 41.7%; $P < .01$).

Among the 42,687 peripherally inserted central catheters, 594 (1.4%) experienced peripherally inserted central catheter-related deep vein thrombosis. Compared with 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 6 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) (**Table 2**).

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, electrocardiography-guided tip-confirmation was associated with a significant reduction in the odds of peripherally inserted central catheter-related deep vein thrombosis, compared with traditional x-ray-based methods (OR 0.74; 95% CI, 0.58-0.93; $P < .001$).

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 the 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 electrocardiography 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 electrocardiography-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 asymptomatic,² 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

Table 1 Study Population (Stratified by Tip Confirmation Technique)

Variable		X-Ray Localization (n = 21,098)	ECG Guidance (n = 21,589)	P Value
Patient Characteristics				
Sex	Male	10,619 (50.4%)	11,090 (51.4%)	.03
Race	White	15,572 (75.6%)	16,015 (76.0%)	.39
Age	Median (IQR)	65.83 (54.35-76.85)	63.75 (52.79-74.23)	< .01
Charlson Comorbidity Score	Median (IQR)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	< .01
Basal metabolic index	Median (IQR)	28.73 (23.92-35.38)	28.73 (24.00-35.15)	.79
Hyperlipidemia	Yes	22 (0.1%)	35 (0.2%)	.10
Hypertension	Yes	14,676 (69.6%)	14,360 (66.5%)	< .01
Myocardial infarction	Yes	825 (3.9%)	880 (4.1%)	.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%)	.02
Dementia	Yes	1854 (8.8%)	1654 (7.7%)	< .01
Chronic obstructive pulmonary disease	Yes	2026 (9.6%)	1968 (9.1%)	.08
Diabetes - uncomplicated	Yes	4111 (19.5%)	3876 (18.0%)	< .01
Diabetes-complicated	Yes	4595 (21.8%)	4727 (21.9%)	.77
Renal Failure	Yes	7826 (37.1%)	8056 (37.3%)	.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%)	.03
Cancer history	Yes	4992 (23.7%)	5013 (23.2%)	.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 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*	Yes	4283 (20.3%)	4130 (19.1%)	< .01
Presence of another central venous catheter†	Yes	3019 (14.3%)	2573 (11.9%)	< .01
Placement attempts	>1	2013 (10.0%)	2552 (11.9%)	< .01
Device characteristics				
Insertion arm	Right arm	14,207 (67.4%)	15,550 (72.1%)	< .01
Insertion vein	Basilic	12,183 (57.7%)	13,470 (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%)	20,740 (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%)	10,477 (48.6%)	< .01
	Double	10,096 (48.0%)	8567 (39.7%)	
	Triple	2178 (10.3%)	2523 (11.7%)	
Power peripherally inserted central catheter	Yes	18,298 (86.7%)	20,521 (95.1%)	< .01

Table 1 (Continued)

Variable		X-Ray Localization (n = 21,098)	ECG Guidance (n = 21,589)	P Value
Antimicrobial coated	Yes	1820 (8.6%)	580 (2.7%)	< .01
Antithrombotic coated	Yes	374 (1.8%)	536 (2.5%)	< .01
Peripherally inserted central catheter length	Median (IQR)	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%)	10,765 (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	10,274 (48.7%)	15,358 (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)*	372.00 (250.00-632.00)	372.00 (291.00-573.00)	< .01
Annual discharges	Median	18,439.00 (11,072.00-31,081.00)	19,097.00 (12,453.00-30,375)	< .01

ECG = electrocardiographic; IQR = interquartile range.

*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?

†Does the patient have an existing indwelling central venous catheter at the time the peripherally inserted central catheter was placed?

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 patients; 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 catheters to electrocardiography peripherally inserted central catheters in patients with cancer, Yuan et al¹⁵ demonstrated superiority of the electrocardiography group. Electrocardiography-guided peripherally inserted central catheter placement resulted in significantly greater first-attempt success, 89.2% (95% CI, 86.5%–91.9%), compared with 77.4% (95% CI, 73.7%–81.0%) in the anatomical landmark group ($P < .0001$), as well as optimal tip placement ($P = .0016$).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 catheter-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

Table 2 Univariate Associations of Variables with Deep Vein Thrombosis

Variable		OR (95% CI)	P Value
Sex	Male vs female	1.06 (0.85-1.32)	.61
Race	White vs non-white	0.84 (0.64-1.11)	.22
Age group, years	≥65 vs <65	1.11 (0.97-1.27)	.14
Hyperlipidemia	Yes vs no	1.32 (0.24-7.26)	.75
Hypertension	Yes vs no	0.96 (0.80-1.15)	.66
Myocardial infarction	Yes vs no	1.24 (0.85-1.81)	.27
Congestive heart failure	Yes vs no	0.70 (0.51-0.95)	.02
Peripheral vascular disorders	Yes vs no	0.75 (0.58-0.98)	.03
Cerebrovascular disease	Yes vs no	1.18 (0.98-1.41)	.08
Dementia	Yes vs no	1.20 (0.89-1.62)	.24
Chronic obstructive pulmonary disease	Yes vs no	0.94 (0.63-1.40)	.75
Rheumatoid arthritis	Yes vs no	0.63 (0.08-4.79)	.66
Peptic ulcer disease	Yes vs no	1.74 (1.31-2.31)	.0001
Diabetes-uncomplicated	Yes vs no	0.95 (0.77-1.17)	.63
Diabetes-complicated	Yes vs no	0.91 (0.75-1.10)	.31
Renal failure	Yes vs no	0.89 (0.74-1.07)	.22
Kidney transplant	Yes vs no	1.22 (0.44-3.41)	.70
Hemodialysis	Yes vs no	1.42 (0.89-2.28)	.14
Peritoneal dialysis	Yes vs no	1.63 (0.26-10.00)	.60
Hemi-/paraplegia	Yes vs no	1.04 (0.68-1.61)	.85
Mild liver disease	Yes vs no	0.82 (0.57-1.18)	.28
Moderate/severe liver disease	Yes vs no	0.59 (0.35-1.00)	.05
Acquired immune deficiency syndrome	Yes vs no	0.21 (0.02-1.95)	.17
Cancer history	Yes vs no	1.36 (1.13-1.64)	.001
Active cancer	Yes vs no	1.74 (1.28-2.37)	.0005
Coagulopathy	Yes vs no	1.52 (1.03-2.22)	.03
Central line-associated bloodstream infection history	Yes vs no	1.01 (0.43-2.36)	.99
Inflammatory bowel disease	Yes vs no	1.78 (0.84-3.78)	.013
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)	.01
Sepsis	Yes vs no	1.18 (1.01-1.39)	.04
Cerebrovascular accident/transient ischemic attack	Yes vs no	1.09 (0.88-1.34)	.43
Venous stasis	Yes vs no	0.67 (0.45-1.00)	.05
Statin	Yes vs no	1.56 (1.26-1.94)	< .0001
Aspirin	Yes vs no	1.25 (1.04-1.51)	.02
Aspirin or statin	Yes vs no	1.50 (1.22-1.85)	.0002
Other antiplatelet therapy	Yes vs no	1.14 (0.85-1.53)	.39
Prior central venous catheter/peripherally inserted central catheter	Yes vs no	1.44 (1.17-1.78)	.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)	.96
Insertion arm	Right arm vs left arm	0.86 (0.73-1.02)	.09
Power peripherally inserted central catheter	Yes vs no	0.70 (0.51-0.96)	.03
Antimicrobial coated	Yes vs no	1.42 (0.81-2.47)	.22
Antithrombotic coated	Yes vs no	0.47 (0.08-2.85)	.41
Valved	Yes vs no	0.69 (0.49-0.97)	.03
Lymphoma	Yes vs no	1.10 (0.69-1.76)	.68
Hematological cancer	Yes vs no	1.44 (1.02-2.03)	.04
Metastatic cancer	Yes vs no	0.99 (0.62-1.57)	.95
Nonmetastatic cancer	Yes vs no	1.30 (1.05-1.61)	.01
Endocarditis	Yes vs no	1.19 (0.46-3.09)	.72
Osteomyelitis	Yes vs no	0.62 (0.47-0.82)	.0006
Pancreatitis	Yes vs no	1.62 (0.83-3.18)	.16
Short gut syndrome	Yes vs no	1.54 (0.14-16.91)	.72
Cellulitis	Yes vs no	0.56 (0.43-0.73)	< .0001

Table 2 (Continued)

Variable		OR (95% CI)	P Value
Swollen legs	Yes vs no	1.15 (0.93-1.41)	.19
Smoking status	Former/current vs never	0.97 (0.80-1.17)	.74
Level of care-binary	Emergency department/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)	.0008
Indication difficult access	Yes vs no	1.46 (1.11-1.93)	.01
Indication central access	Yes vs no	1.15 (0.85-1.55)	.37
Indication multiple fluids	Yes vs no	0.96 (0.46-2.00)	.92
Indication total parenteral nutrition	Yes vs no	1.45 (1.13-1.86)	.0038
Indication other/unknown	Yes vs no	1.42 (1.01-1.98)	.04
5 French	>5 vs ≤5	2.14 (1.69-2.70)	< .0001
Area	Rural vs metropolitan/micropolitan	0.85 (0.52-1.38)	.51
Academic	Yes vs no	0.67 (0.45-0.99)	.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)	.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	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)	.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)	.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)	.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)	.55
Number of peripherally inserted central catheter lumens	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)	.39
Charlson	Per unit increase	0.98 (0.95-1.01)	.22
Basal metabolic index	Per unit increase	0.99 (0.98-1.00)	.01
Estimated glomerular filtration	Per unit increase	1.00 (1.00-1.00)	.22
White blood count	Per unit increase	1.00 (1.00-1.00)	.74
Hemoglobin	Per unit increase	0.96 (0.92-1.00)	.04
Platelets	Per unit increase	1.00 (1.00-1.00)	.06
International normalized ratio	Per unit increase	1.03 (0.99-1.07)	.12
Gauge	Per unit increase	2.12 (1.87-2.40)	< .0001
PICC length	Per unit increase	1.00 (0.98-1.01)	.78
Hospital length of stay prior to central venous catheter	Per unit increase	1.01 (1.00-1.03)	.06
Lumens	Per unit increase	1.89 (1.71-2.09)	< .0001
Bed size	Per unit increase	1.00 (1.00-1.00)	.0012
Discharges	Per unit increase	1.00 (1.00-1.00)	< .0001

CI = confidence interval; OR = odds ratio; PICC = peripherally inserted central catheter.

Table 3 Logistic GEE Models for Predictors of Peripherally Inserted Central Catheter-Related Deep Vein Thrombosis

Variable		Odds Ratio (95% Confidence Interval)	P Value
Use of electrocardiogram guidance	Yes vs no	0.74 (0.58-0.93)	.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)	.0001
Active cancer	Yes vs no	1.62 (1.16-2.26)	.01
Catheter gauge	Per unit increase	1.32 (0.93-1.90)	.12
Number of lumens	Double vs single	1.61 (0.82-3.18)	.17
	Triple vs single	1.64 (1.12-2.40)	.01
Power peripherally inserted central catheter	Yes vs no	0.79 (0.57-1.09)	.15
Existing central venous catheter	Yes vs no	1.30 (1.05-1.62)	.02
Insertion vein	Cephalic vs basilic	0.67 (0.45-1.00)	.05
	Other vs basilic	1.07 (0.73-1.55)	.74
	Brachial vs basilic	1.15 (0.97-1.37)	.11
Insertion in Intensive Care Unit	Yes vs no	0.96 (0.63-1.47)	.85

GEE = generalized estimating equation.

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 postinsertion chest x-ray study may need to be revisited.³⁶⁻³⁸ Anatomical landmarks (eg, carina) used to determine the location of the cavoatrial junction are not located in the same plane, leading to subjectivity, interobserver 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, postprocedural 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 intracavitary electrocardiography 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 electrocardiography to confirm peripherally inserted central catheter tip placement at the cavoatrial junction appears to be associated with a significant reduction in deep vein thrombosis. While further research is needed to determine causation, adoption of electrocardiography 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.

References

- Fallouh N, McGuirk HM, Flanders SA, Chopra V. Peripherally inserted central catheter-associated deep vein thrombosis: a narrative review. *Am J Med* 2015;128(7):722–38.
- Menendez JJ, Verdu C, Calderon B, et al. Incidence and risk factors of superficial and deep vein thrombosis associated with peripherally inserted central catheters in children. *J Thromb Haemost* 2016;14(11):2158–68.
- Vesely TM. Central venous catheter tip position: a continuing controversy. *J Vasc Interv Radiol* 2003;14(5):527–34.
- Chopra V, Ratz D, Kuhn L, Lopus T, Lee A, Krein S. Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. *J Thromb Haemost*. 2014;12(6):847–54.
- Saber W, Moua T, Williams EC, et al. Risk factors for catheter-related thrombosis (CRT) in cancer patients: a patient-level data (IPD) meta-analysis of clinical trials and prospective studies. *J Thromb Haemost* 2011;9(2):312–9.
- Schuster M, Nave H, Piepenbrock S, Pabst R, Panning B. The carina as a landmark in central venous catheter placement. *Br J Anaesth* 2000;85(2):192–4.
- Cales YK, Rheingans J, Steves J, Moretti M. Electrocardiogram-guided peripherally inserted central catheter tip confirmation using a standard electrocardiogram machine and a wide-mouth electrocardiogram clip compared with traditional chest radiograph. *J Vasc Access* 2016;21(1):44–54.
- Connolly B, Amaral J, Walsh S, Temple M, Chait P, Stephens D. Influence of arm movement on central tip location of peripherally inserted central catheters (PICCs). *Pediatr Radiol* 2006;36(8):845–50.
- Gnannt R, Connolly BL, Parra DA, Amaral J, Moineddin R, Thakor AS. Variables decreasing tip movement of peripherally inserted central catheters in pediatric patients. *Pediatr Radiol* 2016;46(11):1532–8.
- Pittiruti M, La Greca A, Scoppettuolo G. The electrocardiographic method for positioning the tip of central venous catheters. *J Vasc Access* 2011;12(4):280–91.
- Chu KS, Hsu JH, Wang SS, et al. Accurate central venous port-A catheter placement: intravenous electrocardiography and surface landmark techniques compared by using transesophageal echocardiography. *Anesth Analg* 2004;98(4):910–4.
- Smith B, Neuharth RM, Hendrix MA, McDonnell D, Michaels AD. Intravenous electrocardiographic guidance for placement of peripherally inserted central catheters. *J Electrocardiol* 2010;43(3):274–8.
- Dale M, Higgins A, Carolan-Rees G. Sherlock 3CG[®] Tip Confirmation System for Placement of Peripherally Inserted Central Catheters: a NICE Medical Technology Guidance. *Appl Health Econ Health Policy* 2016;14(1):41–9.
- Rossetti F, Pittiruti M, Lamperti M, Graziano U, Celentano D, Capozzoli G. The intracavitary ECG method for positioning the tip of central venous access devices in pediatric patients: results of an Italian multi-center study. *J Vasc Access* 2015;16(2):137–43.
- Yuan L, Li R, Meng A, et al. Superior success rate of intracavitary electrocardiogram guidance for peripherally inserted central catheter

- placement in patients with cancer: a randomized open-label controlled multicenter study. *PLoS One* 2017;12(3):e0171630.
16. Liu G, Hou W, Zhou C, et al. Meta-analysis of intracavitary electrocardiogram guidance for peripherally inserted central catheter placement. *J Vasc Access* 2019;20(6):577–82.
 17. Greene MT, Spyropoulos AC, Chopra V, et al. Validation of risk assessment models of venous thromboembolism in hospitalized medical patients. *Am J Med* 2016;129(9):1001.e1009–.
 18. 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.
 19. Grant PJ, Greene MT, Chopra V, Bernstein SJ, Hofer TP, Flanders SA. Assessing the Caprini score for risk assessment of venous thromboembolism in hospitalized medical patients. *Am J Med* 2016;129(5):528–35.
 20. Scott WL. Central venous catheters. An overview of Food and Drug Administration activities. *Surg Oncol Clin N Am* 1995;4(3):377–93.
 21. Infusion Nurses Society. Infusion therapy: standards of practice. *J Infus Nurs* 2016;39(1 suppl):S1–S156.
 22. 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 suppl):S1–40.
 23. 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):1951–62.
 24. Govindan S, Snyder A, Flanders SA, Chopra V. Peripherally inserted central catheters in the ICU: a retrospective study of adult medical patients in 52 hospitals. *Crit Care Med* 2018;46(12):e1136–44.
 25. Ullman AJ, Marsh N, Mihala G, Cooke M, Rickard CM. Complications of central venous access devices: a systematic review. *Pediatrics* 2015;136(5):e1331–44.
 26. Sharp R, Cummings M, Fielder A, Mikocka-Walus A, Grech C, Esterman A. The catheter to vein ratio and rates of symptomatic venous thromboembolism in patients with a peripherally inserted central catheter (PICC): a prospective cohort study. *Int J Nurs Stud* 2015;52(3):677–85.
 27. Chopra V, Anand S, Hickner A, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. *Lancet* 2013;382(9889):311–25.
 28. Ratz D, Hofer T, Flanders SA, Saint S, Chopra V. Limiting the number of lumens in peripherally inserted central catheters to improve outcomes and reduce cost: a simulation study. *Infect Control Hosp Epidemiol* 2016;37(7):811–7.
 29. Bozaan D, Skicki D, Brancaccio A, et al. Less lumens-less risk: a pilot intervention to increase the use of single-lumen peripherally inserted central catheters. *J Hosp Med* 2019;14(1):42–6.
 30. Kleidon TM, Rickard CM, Schultz JA, et al. Development of a paediatric central venous access device database: A retrospective cohort study of practice evolution and risk factors for device failure. *J Paediatr Child Health* 2020;56(2):289–97.
 31. Sharp R, Grech C, Fielder A, Mikocka-Walus A, Esterman A. Vein diameter for peripherally inserted catheter insertion: a scoping review. *J Vasc Access* 2016;21(3):166–75.
 32. Chopra V, Anand S, Krein SL, Chenoweth C, Saint S. Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: reappraising the evidence. *Am J Med* 2012;125(8):733–41.
 33. Chopra V, Fallouh N, McGuirk H, et al. Patterns, risk factors and treatment associated with PICC-DVT in hospitalized adults: a nested case-control study. *Thromb. Res.* 2015;135(5):829–34.
 34. Rickard CM, Marsh NM, Webster J, et al. Peripherally Inserted Central catheter dressing and securement in patients with cancer: the PISCES trial. Protocol for a 2x2 factorial, superiority randomised controlled trial. *BMJ Open* 2017;7(6):e015291.
 35. Yamashita Y, Morimoto T, Amano H, et al. Deep vein thrombosis in upper extremities: clinical characteristics, management strategies and long-term outcomes from the COMMAND VTE Registry. *Thromb Res* 2019;177:1–9.
 36. Wise M, Richardson D, Lum P. Catheter tip position: a sign of things to come. *J Vasc Access Devices* 2001;6(2):18–27.
 37. Aslamy Z, Dewald CL, Heffner JE. MRI of central venous anatomy: implications for central venous catheter insertion. *Chest* 1998;114(3):820–6.
 38. Chan TY, England A, Meredith SM, McWilliams RG. Radiologist variability in assessing the position of the cavoatrial junction on chest radiographs. *Br J Radiol* 2016;89(1065):20150965.

Funding: This project was supported by funding from Blue Cross/Blue Shield of Michigan / Blue Care Network for the Hospital Medicine Safety Collaborative.

Conflict of Interest: TK 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. CMR reports that Griffith University has received unrestricted investigator-initiated research or educational grants on her behalf from product manufacturers (BD-Bard; Cardinal Health), and Griffith University has received consultancy payments on her behalf from manufacturers (3M, B Braun, BD-Bard); AJU reports investigator-initiated research grants and speaker fees provided to Griffith University from vascular access product manufacturers (3M Medical, Becton Dickinson, Cardinal Health), unrelated to the current project; NM's former employer (Griffith University) has received, on her behalf, from manufacturers of vascular access device products: investigator-initiated research grants and unrestricted educational grants from Becton Dickinson and Cardinal Health, and a consultancy payment from Becton Dickinson; JS reports that Griffith University has received unrestricted investigator-initiated research or educational grants on her behalf from product manufacturers BD-Bard; VC has received grant support from the Agency for Healthcare Research and Quality and the American Hospital Association. He has also received royalties from Wolters Kluwer Health and Oxford University Press related to books he has authored. The other authors have indicated they have no financial relationships relevant to this article to disclose.

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