Do antimicrobial and antithrombogenic peripherally inserted central catheter (PICC) materials prevent catheter complications? An analysis of 42,562 hospitalized medical patients

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Peripherally inserted central catheter materials to prevent bloodstream infection, thrombosis and occlusion: an analysis of 42,562 patients

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Abstract

Purpose: To examine the effectiveness of anti-microbial and anti-thrombogenic materials incorporated into peripherally inserted central catheters (PICCs) to prevent bloodstream infection, thrombosis, and catheter occlusion.

Methods: Prospective cohort study involving data from 52 hospitals participating in the Michigan Hospital Medicine Safety Consortium. All adult hospitalised medical patients who received a PICC between January 2013 and October 2019 were included. Coated and impregnated catheters were identified based on name, brand, and device marketing or regulatory materials. Multivariable Cox proportional hazards models with robust sandwich standard error estimates were used to identify factors associated with PICC complications in coated vs. non-coated devices across general care, ICU, and oncology patients. Results were expressed as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs).

Results: Of the 42,562 patients who had PICCs placed, 93.5% (n=39,806) were plain polyurethane, while 5.3% (n=2,263) incorporated anti-microbial materials, and 2.2% (n=921) incorporated anti-thrombogenic materials. Most PICCs were inserted in general ward settings (66.0%; n=28,111), with 28.4% (n=12,078) and 3.3% (n=1,407) placed in in critical care and oncological settings, respectively. Within the entire cohort 1.3% (n=540) developed thrombosis, 1.8% (n=745) developed bloodstream infection, and 9.6% (n=4,090) developed catheter occlusion. Following adjustment for known risk factors, anti-microbial PICCs were not associated with reduction in infections (HR=1.16 [95% CI 0.82-1.64]), and anti-thrombogenic PICCs were not associated with reduction in thrombosis and occlusion (HR=1.15 [95% CI 0.92-1.44]). Results were consistent across all patient populations and care settings.

Conclusions: In this large observational study, anti-microbial and anti-thrombogenic PICCs were not associated with a reduction in major complications.

Keywords

Central venous catheter thrombosis; central venous catheters; deep vein thrombosis; peripheral venous catheterisation; catheter-related infections

INTRODUCTION

Peripherally inserted central catheters (PICCs) are used to deliver medical therapies, ranging between anti-microbials, nutrition, anti-cancer agents, and inotropes. The use of PICCs has grown in recent years, largely due to the ease of insertion compared to traditional central venous catheters (CVCs). However, PICC complications are common with up to 30% of PICCs associated with serious complications and premature failure [1, 2]. These serious, healthcare-associated complications result in treatment delays, high healthcare costs, morbidity, and mortality [3, 4]. Central line -associated bloodstream infection (CLABSI), deep vein thrombosis (DVT), and occlusion are common PICC adverse events and are twice as likely to occur in high-risk patient populations such as those in intensive care units (ICU) or oncology wards [1, 3]. This increased risk is largely due to clinical (e.g., sepsis, neutropenia, coagulopathy), and therapeutic (e.g., infusate viscosity, administration frequency) characteristics.

Anti-microbial and anti-thrombogenic technologies have been incorporated into PICC materials (via coating, impregnation, and integration) as a strategy to prevent specific complications associated with PICC use [5]. These materials are designed to reduce intraluminal bacterial contamination (via anti-microbial exposure, e.g., chlorhexidine), and catheter occlusion or thrombosis (via hydrophobic/philic surfaces) [6]. Innovative PICC materials were developed and introduced following the effectiveness of anti-microbial CVCs to prevent CLABSI in critical care. Previous meta-analysis concluded that catheter impregnation, in comparison to plain polyurethane CVCs, significantly reduced catheter-related BSI (risk ratio [RR] 0.62; 95% confidence interval [CI] 0.52-0.74), with the greatest reduction of catheter-related BSI by minocycline-rifampicin-impregnated CVCs (RR 0.26; 95% CI 0.13- 0.49)[7]. However, many of the trials were manufacturer funded, and all were completed prior to the routine use of modern infection prevention practices, such as alcohol-

containing chlorhexidine gluconate for skin antisepsis. Thus, the incremental effectiveness of coatings to reduce CLABSI in the modern care setting is less clear.

Observational studies and small randomised controlled trials (RCTs) have highlighted the potential for anti-microbial and anti-thrombogenic coatings and impregnations to prevent PICC-related CLABSI, thrombosis, and occlusion [5, 6, 8]. Whether such coated devices will also bring about clinical effectiveness in general and high-risk populations is unknown. Additionally, each of these new technologies increase healthcare costs, so may be best targeted at populations at high risk of the complications which they are designed to prevent (i.e. anti-microbial for infection prevention; anti-thrombogenic for occlusion and thrombosis prevention).

To guide clinical decision-making, we aimed to compare the performance of PICC coatings to prevent CLABSI, venous thromboembolism (VTE), and occlusion in general and high-risk populations (i.e., ICU, cancer care).

METHODS

Design, participants and setting

A cohort study of prospectively collected data was undertaken, via the Michigan Hospital Medicine Safety (HMS) Consortium in the United States. The design and setting of the HMS Consortium have been previously described. [9-11] HMS hospitals have been prospectively collecting data on PICC use and outcomes since 2013, using a systematic probability sampling strategy, with oversampling of ICU patients, across 52 hospitals in the State of Michigan. Adult medical patients admitted to a general ward or an ICU of a participating hospital for any reason are eligible for inclusion. Patients are excluded if they were (a) ≤18 years old; (b) pregnant; (c) admitted to a non-medical service (e.g., general

surgery); or (d) admitted under observation status. All patients are followed until PICC removal, death, or up to 70 days, whichever occurs first.

Study procedures

Within each hospital, dedicated and trained medical records abstractors use a standardised protocol to collect data directly from medical records of patients that receive PICCs during clinical care. Patients with PICCs 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.

Data regarding PICC characteristics (e.g., gauge, lumens) and indication for PICC placement are obtained directly from insertion notes or the order for PICC placement. Detailed medical history including comorbidities, physical findings, laboratory, and medication data are routinely 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 haematological malignancy, active cancer (defined as receipt of chemotherapy while PICC was in place), and life threatening illness (defined as the patient having a history of serious life-threatening illness that required care in the ICU) are collected. To categorise comorbidity burden, the Charlson comorbidity index score is calculated for each patient. Additionally, treatment characteristics including receipt of haemodialysis, chemotherapy or blood administration during hospitalisation, presence of a CVC when PICC was placed (yes/no), use of VTE 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), use of aspirin, statins, erythropoiesis stimulating agents, and antibiotic therapies are also abstracted directly from medical records. Laboratory values

including white blood cell count, haemoglobin, platelet count, and international normalised ratio at the time of PICC placement are collected from the medical record.

Data collection for the overarching HMS Consortium is ongoing, with complete data from January 2013 and October 2019 included in this analysis.

Definitions and variables

PICCs are defined as vascular access devices inserted in veins of the upper extremity that terminate at the cavo-atrial junction [12-15]. PICC material categorisation (anti-microbial, anti-thrombogenic) were determined based on brand names or device details that indicate: (a) coating or impregnation with an antibiotic agent (e.g. minocycline/rifampicin) or antiseptic agent (e.g., chlorhexidine) [5], (i.e. anti-microbial PICC); (b) engineering with a hydrophilic or hydrophobic surface, or use of a biological or medication agent aimed towards prevention of thrombus adherence / accumulation on the PICC surface [6] (i.e. anti-thrombogenic PICCs).

Catheter outcomes are recorded in accordance with established definitions. CLABSI is defined as meeting the Centers for Disease Control and Prevention's National Healthcare Safety Network definition for BSI, removing the PICC with reason for removal documented as "infection," or documentation of line sepsis or line bacteraemia in the medical record [16, 17]. Catheter-associated VTE is defined as upper extremity DVT or pulmonary embolism, presenting symptomatically, and radiographically confirmed (either by positive ultrasound or computerized tomography scan [CT]) [18]. Catheter occlusion is defined as either: (a) documentation in the medical record by a medical provider; or (b) use of tissue plasminogen activator to treat problems suggestive of occlusion (e.g., poor blood return, sluggish flow)[19].

The study population was *a priori* categorised to subgroups according to altered complication risk, specifically PICCs inserted in ICU, PICCs used in oncology settings, and

non-ICU, non-oncology, general medical hospitalised patients.

Statistical analysis

Analysis was performed using PICCs as the unit of analysis. Missing data were assumed to be missing at random, and missing values were imputed through a 10-fold multiple imputation procedure [20]. Descriptive statistics were first used to summarise characteristics of all, non-coated, anti-microbial, anti-thrombogenic PICCs, then further categorised across predefined populations.

A Cox proportional hazards model with robust sandwich standard error estimates was used to examine the presence of an association between complications (PICC-associated CLABSI; VTE and occlusion [combined]); and PICC coating/impregnation (non-coated, anti-microbial, anti-thrombogenic), due to the risk of complications varying across devices and over time [21, 22]. Characteristics previously published and externally validated to be clinically relevant or predictive of specific PICC complications (PICC-associated CLABSI [17]; VTE and occlusion [19, 23]) were included as additional controls in all Cox models. Results are expressed as hazard ratios (HR) and 95% CI. $P<0.05$ was considered statistically significant. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

Ethical and Regulatory Oversight

The University of Michigan Medical School's Institutional Review Board reviewed this study and assigned it a "Not Regulated" status, HUM00078730.

RESULTS

Patient, device and provider characteristics

Complete data on 42,562 adult patients with PICCs were available and included in the analysis. Within this cohort, 93.5% of PICCs (n=39,806) inserted were uncoated polyurethane devices, 5.3% (n=2,263) were anti-microbial coated and 2.2% (n=921) were anti-thrombogenic coated/impregnated. Most PICCs were inserted during admission to general ward settings (66.0%; n=28,111), with 28.4% (n=12,078) in critical care and 3.3% (n=1,407) in oncological settings. Median patient age was 65 years (interquartile range [IQR] 54 – 76), and 51.1% were male (n=29,323). Intravenous antibiotics were the primary indication for PICC placement (n= 21,079; 50%), followed by difficult access (n= 8,927; 22.4%), medications requiring central access (n= 5,460; 13.7%), and parenteral nutrition (n=2,878; 7.2%). The median PICC gauge was 5Fr (IQR 4-5), but 38.5% were 4Fr and 5.6% were 6Fr.

With respect to coated catheters, fewer anti-microbial PICCs were single lumen (n=770; 34.0%) as compared with other PICC coatings / impregnations (47.1% non-coated; 50.2% anti-thrombogenic PICCs). Anti-thrombogenic PICCs were only inserted by vascular access nurses and interventional radiologists, and they were largely inserted in large, academic hospitals. (Table 1). The indication for a substantial proportion of anti-microbial PICCs was unknown or other (51.7%; n=1,170).

<Insert Table 1>

Association between anti-microbial materials and CLABSI

A total of 745 patients (1.8%) met criteria for CLABSI in the dataset. Of the patients that developed CLABSI, 2.1% received anti-microbial PICCs (n=48), whereas 1.7% received non-antimicrobial PICCs (n=707). Following adjustment for patient-, provider-, and device-characteristics, anti-microbial PICCs (n = 2,263) were not significantly associated with

reduction in risk of CLABSI (HR = 1.16; 95% CI, 0.82 – 1.64, *p* = .40). Findings were similar for PICCs placed in patients that were in the ICU (HR = 1.10; 95% CI, 0.60 - 1.99, *p* = .77) and devices placed in patients with cancer (HR = 2.14; 95% CI, 0.61 – 7.53, *p* = .23) (Table 2).

<Insert Table 2>

Association between anti-thrombogenic materials and VTE and occlusion

A total of 540 patients (1.3%) met criteria for VTE while 4,090 (9.6%) developed catheter occlusion. VTE and occlusion occurred in 13.7% of anti-thrombogenic PICCs (n=127), and 10.8% of non-anti thrombogenic PICCs (n=4,503). After adjustment, patients with anti-thrombogenic PICCs (n=921) did not experience a significantly reduced risk of VTE or occlusion (HR = 1.15, 95% CI, 0.92-1.44, *p* = .21). Similarly, there was no difference in risk of VTE or occlusion between anti-thrombogenic versus non-antithrombogenic PICCs placed in patients in the ICU (HR = 0.86, 95% CI, 0.59-1.26, *p* = .43) or in patients with cancer (HR = 1.37, 95% CI, 0.54-3.47 , *p* = .51). However, anti-thrombogenic PICCs were associated with an increased risk of VTE/occlusion for general hospitalised patients, outside of ICU and oncology (HR=1.39, 95% CI, 1.03, 1.86, *p*= .03). (Table 3).

<Insert Table 3>

Variation in CLABSI, VTE, and Occlusion between patient-, provider-, and device-characteristics

Across the cohort, CLABSI risk was increased with double (HR=2.52, 95% CI 1.88-3.38, *p* <.001) and triple/quadruple lumen PICCs (HR=3.28, 95% CI 2.09- 5.13, *p* <.001) (in

comparison to single lumen). Similarly, risk of CLABSI was greater among patients with active cancer (HR= 1.78, 95% CI 1.38- 2.29, p <.0001) and those with an existing CVC at the time of PICC insertion (HR= 2.22, 95% CI 1.80 - 2.74, p <.0001). Within the ICU, a life-threatening illness such as sepsis was also associated with increased risk of CLABSI (HR =1.83, 1.26 - 2.65, p = .001).

Comparatively, risk of VTE/occlusion was greater with double (HR=5.49, 95% CI 4.85 -6.23, p <.0001) and triple/quadruple lumen PICCs (HR=7.10, 95% CI 5.92 -8.51, p <.0001) in comparison to single lumen devices. Patients with a history of DVT (HR= 1.19, 95% CI 1.07- 1.51, p= .0015), presence of an existing CVC at the time of PICC insertion (HR= 1.10, 95% CI 1.01 – 1.20, p= .0289), and life- threatening illness (HR = 1.91, 95% CI, 1.68-2.17, p < .001) were also associated with a higher risk of VTE/occlusion. Although larger PICC gauge was not associated with risk of VTE in the ICU population (HR = 1.38, 95% CI, 0.93-2.03, p =0.107), among patients with cancer, PICC gauge was associated with a significantly increased risk of VTE and occlusion (HR = 1.73, 95% CI, 1.03-2.91, p < .038).

DISCUSSION

CLABSI, VTE, and catheter occlusion can cause catastrophic harm to our most vulnerable populations [24-27]. Inventive and concerned clinicians are motivated to identify and implement promising technologies to prevent this harm. However, within our large, observational dataset, we have found the use of novel PICC coatings, materials, and impregnation technology were not associated with reductions in these major complications. While the theoretical value of these innovations is promising[5, 6, 8], further research, (preferably via RCTs), needs to be undertaken to establish clinical and economic effectiveness when it comes to PICCs.

These results were echoed in the clinical subgroups, with no reduction in CLABSI or VTE/occlusion evident for patients in intensive care or oncological settings. Comparatively, anti-thrombogenic PICCs were associated with increased risk of VTE and occlusion for general medical, non-ICU, non-oncological settings (HR 1.39; 95% CI 103-1.86; $p = 0.0289$). This finding, while non-intuitive, could be related to difficulty with the insertion procedure associated with these 'newer' technologies that often change the physical characteristics and handling of the device. A recent pilot RCT evaluated the effectiveness of a hydrophobic PICC, in comparison to plain polyurethane PICCs, reported reduced PICC inserter satisfaction (median: 7/10 [IQR 5-9] anti-thrombogenic vs 10/10 [IQR 7-10] uncoated polyurethane), and more 'difficult' insertions (36% [20/56] anti-thrombogenic vs 24% [13/55] uncoated polyurethane)[28]. Difficulty and trauma during the PICC insertion procedure has been proposed as an important risk factor for increased VTE [21, 29, 30].

Our results differ significantly from a systematic review and meta-analysis evaluating the effectiveness of coated CVCs[7]. This may be due to the care settings for these non-tunnelled CVCs which are inserted and managed in operating theatres and ICU settings, for consistent indications and a short dwell (indicated up to 14 days therapy)[31]. Comparatively, aside from inherent differences in device characteristics, PICCs are inserted and managed across diverse settings (including at home), with varied indications and longer dwell times (no maximum therapy duration)[31]. These patient, provider, and device differences influence the risk of infective and thrombotic complications. However, these differences also dilute the impact of a single technology to result in significant, clinical effectiveness to prevent multi-layered complications.

Our findings suggest that catheter material technologies may be reaching a plateau of maturation[32]. Early research in critical care highlighted the potential of catheter materials to dramatically change clinical outcomes, inflating broad expectations. The sustainability and

impact of these innovations outside of specific patient groups and clinical environments are potentially now in question. Moving forward we need to appropriately target these innovations, via high quality, interventional research.

Our study has limitations, primarily those inherent to the observational design that allow us to explore associations, not causation. Second, the interventions under examination are new so they are not as represented in the dataset, especially outside of academic centres, impacting statistical power and generalisability. Yet, our study also has significant strengths, including the large sample size, broad range of patients, and rigorous outcome assessment. To our knowledge, this remains the largest study on this topic conducted to date. Overall, we highlight an area of clinical practice being changed without sufficient evidence, but with increases in costs.

Our findings have important policy and clinical implications. Most international clinical practice guidelines have reserved the implementation of the impregnated CVCs after ensuring high quality baseline practices (e.g., education, maximal sterile barrier precautions, chlorhexidine-based skin decontamination).[33, 34] Our results support these recommendations being extended to impregnated PICCs. These more expensive and unproven technologies should remain in reserve unless all other practices are optimised, and further research is available to establish their effectiveness.

CONCLUSION

Infections and thrombosis associated with PICCs are unlikely to be 'fixed' by a single practice or technology, such as implementing new PICC coatings and impregnations. These are complex problems, requiring multi-faceted approaches. However, these new technologies may still be a piece of the CLABSI, VTE, and occlusion prevention puzzle. Further

interventional research is required to evaluate their clinical and economic effectiveness. Until then, impregnated and coated PICCs should not be implemented as routine practice to prevent significant complications.

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Table 1. Patient, device and provider characteristics for non-coated, anti-microbial, anti-thrombogenic and all PICCs (*N*=42,562)

Category/Variable, *n* (%)	Non-coated (*n* = 39,806)	Anti-microbial (*n* = 2,263)	Anti-thrombogenic (*n* = 921)	All (*n* =42,562)
Patient characteristics				
Gender (male)	20323 (51.1%)	1161 (51.3%)	509 (55.3%)	21729 (51.1%)
Age, median years (IQR)	65.1 (54.1-75.8)	62.4 (50.9-73.2)	65.0 (53.1-75.8)	65.0 (53.8-75.7)
Charlson-Deyo, median (IQR)	3.00 (2.00-5.00)	3.00 (1.00-5.00)	4.00 (2.00-6.00)	3.00 (2.00-5.00)
Hospital stay prior to PICC, median days (IQR)	4.00 (2.00-7.00)	5.00 (2.00-8.00)	5.00 (3.00-8.00)	4.00 (2.00-7.00)
Diagnoses				
Pneumonia	8041 (20.2%)	438 (19.4%)	186 (20.2%)	8586 (20.2%)
Lung Disease	12069 (30.3%)	598 (26.4%)	443 (48.1%)	12905 (30.3%)
Hypertension	27031 (67.9%)	1427 (63.1%)	652 (70.8%)	28810 (67.7%)
Renal failure	14652 (36.8%)	707 (31.2%)	380 (41.3%)	15560 (36.6%)
Congestive heart failure	4917 (12.4%)	413 (18.3%)	172 (18.7%)	5417 (12.7%)
Endocarditis	363 (0.9%)	37 (1.6%)	14 (1.5%)	409 (1%)
Osteomyelitis	5085 (12.8%)	240 (10.6%)	170 (18.5%)	5395 (12.7%)
Pancreatitis	512 (1.3%)	32 (1.4%)	16 (1.7%)	557 (1.3%)
Short gut syndrome	34 (0.1%)	6 (0.3%)	5 (0.5%)	41 (0.1%)
Cellulitis	7004 (17.6%)	259 (11.4%)	193 (21.0%)	7350 (17.3%)
Cerebrovascular disease	6273 (15.8%)	324 (14.3%)	207 (22.5%)	6682 (15.7%)
Indications for PICC				
Antibiotics	20195 (50.7%)	609 (26.9%)	533 (57.9%)	21079 (49.5%)
Difficult access	8927 (22.4%)	295 (13.0%)	126 (13.7%)	9284 (21.8%)
Medications requiring central access	5460 (13.7%)	100 (4.4%)	54 (5.9%)	5594 (13.1%)
Parenteral nutrition	2878 (7.2%)	98 (4.3%)	125 (13.6%)	3046 (7.2%)
Multiple incompatible	979 (2.5%)	11 (0.5%)	21 (2.3%)	1006 (2.4%)
Chemotherapy	1349 (3.4%)	43 (1.9%)	30 (3.3%)	1407 (3.3%)
Other/Unknown	6737 (16.9%)	1170 (51.7%)	96 (10.4%)	7981 (18.8%)
Cancer				
Active cancer	2907 (7.3%)	124 (5.5%)	83 (9.0%)	3068 (7.2%)
Cancer history	9310 (23.4%)	520 (23.0%)	237 (25.7%)	9953 (23.4%)
Hematological cancer	1299 (3.3%)	59 (2.6%)	30 (3.3%)	1373 (3.2%)
Metastatic cancer	1549 (3.9%)	51 (2.3%)	54 (5.9%)	1634 (3.8%)
Non-metastatic cancer	5454 (13.7%)	245 (10.8%)	149 (16.2%)	5773 (13.6%)
Coagulopathy	1328 (3.3%)	92 (4.1%)	49 (5.3%)	1441 (3.4%)
Critical illness				
Life threatening illness	8879 (22.3%)	581 (25.7%)	198 (21.5%)	9561 (22.5%)
Sepsis	13496 (33.9%)	605 (26.7%)	310 (33.7%)	14265 (33.5%)
CVA/TIA	6534 (16.4%)	304 (13.4%)	151 (16.4%)	6933 (16.3%)
Myocardial Infarction	1613 (4.1%)	94 (4.2%)	60 (6.5%)	1730 (4.1%)
Hemodialysis	1114 (2.8%)	127 (5.6%)	22 (2.4%)	1256 (3%)
CLABSI history	493 (1.2%)	26 (1.1%)	20 (2.2%)	527 (1.2%)
VTE history				
No	33790 (84.9%)	1922 (84.9%)	786 (85.3%)	36120 (84.9%)
Positive history	4686 (11.8%)	235 (10.4%)	110 (11.9%)	4988 (11.7%)
Within previous 30 days	1330 (3.3%)	106 (4.7%)	25 (2.7%)	1454 (3.4%
Presence of another CVC	5027 (12.6%)	411 (18.2%)	105 (11.4%)	5494 (12.9%)
Prior CVC/PICC	6828 (17.2%)	431 (19.0%)	209 (22.7%)	7377 (17.3%)
Device characteristics				
Gauge (Fr), median (IQR)	5 (4.0-5.0)	5 (5.0-5.0)	5 (4.5-5.0)	5 (4.0-5.0)
Lumen number				
Single	18719 (47.1%)	770 (34.0%)	462 (50.2%)	19708 (46.3%)
Double	16728 (42.1%)	1179 (52.1%)	399 (43.4%)	18164 (42.7%)
Triple/Quad	4295 (10.8%)	313 (13.8%)	59 (6.4%)	4624 (10.9%)
Provider characteristics				

Category/Variable, *n* (%)	**Non-coated (*n* = 39,806)**	**Anti-microbial (*n* = 2,263)**	**Anti-thrombogenic (*n* = 921)**	**All (*n* =42,562)**
Professional inserting PICC				
Vascular Access Nurse	28353 (79.7%)	1022 (51.5%)	627 (87.3%)	29589 (69.5%)
Interventional Radiologist	6649 (18.7%)	942 (47.5%)	91 (12.7%)	7662 (18%)
Physician	251 (0.7%)	6 (0.3%)	-	257 (0.6%)
Advance Practice Professional	10 (0.0%)	1 (0.1%)	-	11 (0%)
Other	330 (0.9%)	14 (0.7%)	-	344 (0.8%)
Insertion vein				
Basilic	24065 (60.5%)	1429 (63.1%)	664 (72.1%)	25824 (60.7%)
Brachial	12495 (31.4%)	693 (30.6%)	224 (24.3%)	13328 (31.3%)
Cephalic	2049 (5.1%)	67 (3.0%)	31 (3.4%)	2137 (5%)
Other	1197 (3.0%)	74 (3.3%)	2 (0.2%)	1273 (3%)
>1 insertion attempts	4307 (11.2%)	69 (3.1%)	88 (10.1%)	4440 (10.4%)
Hospital characteristics				
Rural	999 (2.5%)	2 (0.1%)	1 (0.1%)	1002 (2.4%)
Profit	2706 (6.8%)	5 (0.2%)	200 (21.7%)	2910 (6.8%)
Academic	24076 (60.5%)	1452 (64.2%)	27 (2.9%)	25542 (60%)
Hospital size (number of beds), median (IQR)	356 (255-573)	852 (383-852)	377 (377-632)	372 (255-584)
Annual hospital discharges, median (IQR)	18439 (11241-30375)	31081 (18810-58627)	18810 (18810-30611)	18810 (12209-30611)

CLABSI: Central line associated bloodstream infection; CVA/TIA: Cerebrovascular accident/Transient ischaemic attack; CVC: Central venous catheter; Fr: French; IQR: Interquartile range; PICC: Peripherally inserted central catheter

Table 2. Multivariate Cox Model for CLABSI

Variable	All PICCs *n* = 42,562 HR (95% CI)	*p*	Non-ICU/Non-Oncology *n* = 28,111 HR (95% CI)	*p*	ICU *n* = 12,078 HR (95% CI)	*p*	Oncology *n* = 1,407 HR (95% CI)	*p*
Anti-microbial coating[1]	1.16 (0.82, 1.64)	0.3997	1.22 (0.75, 1.98)	0.4254	1.10 (0.60, 1.99)	0.7655	2.14 (0.61, 7.53)	0.234
Lumens								
Double vs. Single	2.52 (1.88, 3.38)	<.0001	1.58 (1.11, 2.25)	0.0108	19.42 (2.62, 144.07)	0.0037	3.32 (0.84, 13.10)	0.0869
Triple/Quad vs. Single	3.28 (2.09, 5.13)	<.0001	3.34 (1.74, 6.40)	0.0003	21.61 (2.76, 169.31)	0.0034	5.77 (1.15, 28.89)	0.0328
Active cancer[1]	1.78 (1.38, 2.29)	<.0001	1.38 (0.88, 2.15)	0.1566	1.36 (0.77, 2.40)	0.2911	--	--
Existing CVC[1]	2.22 (1.80, 2.74)	<.0001	2.63 (1.92, 3.62)	<.0001	2.17 (1.61, 2.92)	<.0001	2.20 (0.99, 4.89)	0.0532
CHF[1]	1.20 (0.93, 1.55)	0.15	1.21 (0.81, 1.79)	0.3494	1.26 (0.89, 1.78)	0.1917	0.82 (0.11, 6.18)	0.8476
Peripheral vascular disorders[1]	0.67 (0.50, 0.89)	0.0052	0.68 (0.48, 0.97)	0.0312	0.69 (0.41, 1.16)	0.1633	0.77 (0.18, 3.31)	0.7222
Pneumonia[1]	1.23 (0.99, 1.52)	0.057	1.19 (0.85, 1.65)	0.316	1.30 (0.97, 1.74)	0.0815	1.10 (0.32, 3.77)	0.874
Aspirin or statin[1]	1.02 (0.79, 1.31)	0.8808	1.41 (1.02, 1.95)	0.0401	0.74 (0.48, 1.14)	0.1759	0.71 (0.30, 1.69)	0.4451
Gauge (Per unit increase)	1.00 (0.83, 1.21)	0.975	1.16 (0.90, 1.50)	0.2373	0.84 (0.61, 1.17)	0.311	0.85 (0.41, 1.74)	0.6516
Insertion vein								
Cephalic vs. Basilic	0.74 (0.46, 1.17)	0.2004	0.83 (0.44, 1.57)	0.5607	0.78 (0.40, 1.55)	0.4794	0.00 (0.00,)	0.9871
Other vs. Basilic	1.25 (0.81, 1.93)	0.3133	1.00 (0.52, 1.90)	0.998	1.74 (0.85, 3.57)	0.1323	2.19 (0.64, 7.46)	0.21
Brachial vs. Basilic	2.52 (1.88, 3.38)	<.0001	1.58 (1.11, 2.25)	0.0108	19.42 (2.62, 144.07)	0.0037	3.32 (0.84, 13.10)	0.0869
Life-threatening Illness[1]	1.47 (1.08, 2.01)	0.0145	0.86 (0.37, 1.98)	0.7213	1.83 (1.26, 2.65)	0.0014	2.42 (0.28, 20.72)	0.4189
Insertion in ICU[1]	0.66 (0.48, 0.91)	0.0102	--	--	--	--	0.27 (0.03, 2.38)	0.2377

[1]Yes vs. no

CLABSI: Central line associated bloodstream infection; CHF: Congestive heart failure; CI: Confidence interval; CVC: Central venous catheter; HR: Hazard ratio; ICU: Intensive care unit; PICC: Peripherally inserted central catheter

Table 3. Multivariate Cox Model for VTE and/or Occlusion

Variable	All PICCs *n* = 42,562 HR (95% CI)	*p*	Non-ICU/Non-Oncology *n* = 28,111 HR (95% CI)	*p*	ICU *n* = 12,078 HR (95% CI)	*p*	Oncology *n* = 1,407 HR (95% CI)	*p*
Antithrombotic coating[1]	1.15 (0.92, 1.44)	0.2148	1.39 (1.03, 1.86)	0.0289	0.86 (0.59, 1.26)	0.433	1.37 (0.54, 3.47)	0.5092
DVT History								
Positive History vs. No History	1.19 (1.07, 1.32)	0.0015	1.36 (1.18, 1.58)	<.0001	1.05 (0.88, 1.24)	0.5927	0.56 (0.25, 1.28)	0.1717
Within Previous 3- days vs. No History	1.27 (1.07, 1.51)	0.0066	1.34 (1.02, 1.77)	0.0372	1.22 (0.96, 1.54)	0.1065	1.01 (0.41, 2.53)	0.9767
Lumens								
Double vs. Single	5.49 (4.85, 6.23)	<.0001	4.44 (3.79, 5.19)	<.0001	4.36 (3.03, 6.28)	<.0001	1.89 (0.90, 3.95)	0.0916
Triple/Quad vs. Single	7.10 (5.92, 8.51)	<.0001	6.92 (5.21, 9.20)	<.0001	5.92 (3.98, 8.80)	<.0001	3.53 (1.47, 8.46)	0.0047
Active cancer	1.08 (0.96, 1.22)	0.2109	1.00 (0.81, 1.23)	0.9978	0.93 (0.72, 1.19)	0.5468	--	--
Existing CVC	1.10 (1.01, 1.20)	0.0289	1.14 (0.97, 1.34)	0.1223	1.09 (0.98, 1.21)	0.1123	0.88 (0.52, 1.49)	0.6304
CHF[1]	0.93 (0.85, 1.03)	0.1575	1.02 (0.88, 1.19)	0.7535	0.91 (0.80, 1.03)	0.1409	0.54 (0.22, 1.36)	0.1945
Peripheral vascular disorders[1]	0.95 (0.86, 1.04)	0.2881	0.94 (0.83, 1.07)	0.3427	0.98 (0.84, 1.14)	0.7893	1.00 (0.55, 1.81)	0.9983
Pneumonia[1]	1.06 (0.98, 1.15)	0.1654	1.22 (1.07, 1.39)	0.0025	0.98 (0.88, 1.09)	0.6993	0.98 (0.54, 1.78)	0.9534
Aspirin or statin[1]	1.93 (1.80, 2.07)	<.0001	2.39 (2.17, 2.64)	<.0001	1.48 (1.33, 1.64)	<.0001	2.41 (1.74, 3.33)	<.0001
Gauge (Per unit increase)	0.95 (0.86, 1.05)	0.3538	1.17 (1.01, 1.35)	0.0379	0.76 (0.66, 0.87)	0.0001	1.73 (1.03, 2.91)	0.0378
Insertion vein								
Cephalic vs. Basilic	0.87 (0.81, 0.94)	0.0003	0.92 (0.83, 1.02)	0.1195	0.84 (0.75, 0.94)	0.0024	0.59 (0.40, 0.87)	0.0082
Other vs. Basilic	1.01 (0.87, 1.17)	0.9069	1.02 (0.81, 1.29)	0.8385	1.04 (0.85, 1.27)	0.7122	0.66 (0.29, 1.52)	0.3294
Brachial vs. Basilic	0.86 (0.70, 1.04)	0.1167	0.70 (0.52, 0.95)	0.0197	0.72 (0.50, 1.05)	0.0843	1.29 (0.68, 2.45)	0.4323
Life-threatening Illness[1]	1.91 (1.68, 2.17)	<.0001	0.97 (0.72, 1.31)	0.8342	3.06 (2.57, 3.64)	<.0001	4.86 (1.65, 14.35)	0.0042
Insertion in ICU[1]	0.69 (0.61, 0.79)	<.0001	--	--	--	--	0.30 (0.10, 0.94)	0.0396

[1]Yes vs. no; CHF: Congestive heart failure; CI: Confidence interval; CVC: Central venous catheter; DVT: Deep vein thrombosis; HR: Hazard ratio; ICU: Intensive care unit; PICC: Peripherally inserted central catheter