Patterns and Predictors of Peripherally Inserted Central Catheter Occlusion: The 3P-O Study

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ABSTRACT

Purpose: To evaluate patterns and predictors of peripherally inserted central catheter (PICC)–related occlusion.

Materials and Methods: Data from a multihospital study were used to examine factors associated with PICC occlusion. Occlusion was defined if documented in the medical record or when tissue plasminogen activator was administered for occlusion-related concerns. Mixed-effects logistic regression was used to predict occlusion, controlling for patient-, provider-, device-, and hospital-level characteristics.

Results: A total of 14,278 PICCs placed in 13,408 patients were included. Of these, occlusion developed in 1,716 PICCs (12%) in 1,684 patients. The most common indications for PICC insertion were intravenous antibiotic therapy (32.7%), difficult intravenous access (21.5%), and central access (13.7%). PICCs placed in the right arm had decreased odds of occlusion compared with those in the left arm (odds ratio [OR] = 0.82; 95% confidence interval [CI] = 0.72–0.94). Verification of catheter tip position following insertion was associated with reduction in occlusion (OR = 0.75; 95% CI = 0.61–0.92). Although normal saline solution or heparin flushes did not reduce occlusion, PICCs flushed with normal saline solution and "locked" with heparin were less likely to become occluded (OR = 0.54; 95% CI = 0.33–0.88). Compared with single-lumen devices, double- and triple-lumen PICCs were associated with greater incidences of occlusion (double, OR = 3.07; 95% CI = 2.56–3.67; triple, OR = 3.72; 95% CI = 2.92–4.74). Catheter tip malposition was also associated with occlusion (OR = 1.46; 95% CI = 1.14–1.87).

Conclusions: Several patient, provider, and device characteristics appear associated with PICC occlusion. Interventions targeting these factors may prove valuable in reducing this complication.

ABBREVIATIONS

CI = confidence interval, ICU = intensive care unit, OR = odds ratio, PICC = peripherally inserted central catheter, SASH = saline, administer medicine, saline, heparin [infusion technique], TPA = tissue plasminogen activator

Increasing use of peripherally inserted central catheters (PICCs) has led to new insights regarding benefits and risks. Compared with central venous catheters (CVCs), PICCs offer several benefits, including lower risk of insertion complications and reliable access for medium- to long-term treatment. Conversely, PICCs are also associated with complications, including infection and venous thrombosis (1–3). Although these adverse events have garnered much interest, minor complications from PICC use such as occlusion have received comparatively less attention.

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This asymmetry is unfortunate, as minor complications are not only more frequent than major complications, but also interrupt treatment and may necessitate device removal (4,5).

One of the most common minor complications associated with PICC use is occlusion, defined as a temporary or permanent inability to aspirate blood or infuse therapeutic agents through a lumen (6). Occlusion of a PICC and damage to its corresponding vein has important sequelae, including potential failure of future arteriovenous grafts or fistulae in patients with chronic kidney disease, ultimately requiring dialysis (7,8). Despite these important aspects, which patient-, provider-, and device-associated factors influence the probability of PICC occlusion remains unknown (9). Given these knowledge gaps, data from a multihospital collaborative quality initiative was used to conduct a retrospective cohort study (the 3P-O study) to understand (*i*) patterns of PICC occlusion and (*ii*) which patient-, provider-, and device-related factors were associated with this event.

MATERIALS AND METHODS

Study Setting and Participants

The present study used data from a collaborative clinical quality initiative supported by Blue Cross Blue Shield and Blue Care Network that is focused on preventing adverse events in hospitalized patients. The design and setting of this consortium have been previously described (10,11). Since December 2013, 51 hospitals have engaged in a prospective cohort study to examine PICC use and outcomes. Adult patients admitted to a general medicine ward or intensive care unit (ICU) who received a PICC for any reason during clinical care were eligible for inclusion. Patients who were (*i*) younger than 18 years of age, (*ii*) pregnant, (*iii*) admitted to a nonmedical service (eg, general surgery), or (*iv*) admitted under observation status were excluded.

At each hospital, dedicated medical record abstractors used a standardized protocol and template to collect data. Patients with PICCs were sampled on a 14-day cycle with the use of a convenience sampling method. Abstractors selected the first eligible PICC inserted each cycle day from 1 to 14, then the second, and so on, for as many as 17 cases. As available, we asked abstractors to select seven PICCs that were inserted in an ICU setting. All patients were followed until death, PICC removal, or 70 days from insertion, whichever occurred first. Follow-up was restricted to the medical record if patients remained hospitalized or underwent PICC removal before hospital discharge; patients discharged with a PICC underwent medical record review and telephone follow-up. Sample size, 14-day sample cycle, and 70-day censoring were all selected to fit abstractor workload and the fact that 90% of PICCs were removed by this time point. Sampling for this project is ongoing. To ensure data accuracy, random audits are performed annually at each site.

Covariates and Outcomes of Interest

Catheter occlusion was identified when either of the following two criteria were met: (*i*) catheter occlusion was documented in the medical record by a medical provider or (*ii*) tissue plasminogen activator (TPA) was administered to treat problems suggestive of occlusion (eg, poor blood return, sluggish flow). Occlusion was further categorized as irreversible (defined as catheter removal or exchange within 24 h of occlusion with documentation that the reason for removal was occlusion) or transient (ie, catheter remained in place and no device exchange occurred).

Patient-, provider-, and device-related predictors of catheter occlusion were selected a priori based on a conceptual model of PICC complications (12). Patient factors including age, sex, tobacco use (current, former, never), body mass index, uncomplicated or complicated diabetes, severe liver disease, renal failure, coagulopathy, hyperlipidemia, hypertension, and indication for PICC use were included. Because statins, aspirin, and antiplatelet agents are associated with thrombosis (13), these were included if administered while the PICC was in situ. Baseline values for creatinine, hemoglobin, and white blood cell count at the time of PICC insertion were also included. Because the risk of PICC complications is greater in critically ill patients, ICU status was included as an indicator variable if (*i*) the patient underwent PICC placement in an ICU or (*ii*) received care in an ICU setting before device occlusion. Although PICC dwell time was included, data were censored at 70 days due to follow-up terminating at this time.

Provider factors including vein selected for insertion (basilic, brachial, cephalic, other), arm of insertion, and type of operator inserting the PICC (vascular access nurse vs. other) were recorded. Additionally, ascertainment of appropriate PICC tip position (by radiography or electrocardiography) and occurrence of catheter malposition (defined as radiographic evidence of PICC tip localization at any site other than the cavoatrial junction) before PICC occlusion were recorded. As some infusates are associated with increased incidence of occlusion, delivery of chemotherapeutic agents and specific antibiotic agents (vancomycin, cefepime, or piperacillin/tazobactam) through the PICC was also examined.

Device-related factors included total PICC length, number of lumens, and type of PICC (power-injectable vs not). Additionally, the effect of catheter coating or impregnation (antimicrobial, antithrombotic, or both) and valve presence were evaluated as risk factors for occlusion. To understand the effect of flushing and catheter care, protocols for PICC flushing from each hospital were incorporated. Flushing frequency was coded as daily, twice daily, or three times daily. Flush type was coded as normal saline solution, heparin, or normal saline solution followed by drug administration, 10 mL normal saline solution flush, and 3-mL heparin "lock" (known as the SASH technique). The 2016 Infusion Nursing Standards (14) provide more details regarding this technique.

Costs associated with TPA administration at all follow-up intervals (maximum of five doses per catheter) were evaluated to quantify economic consequences associated with PICC occlusion. In accordance with previous economic evaluations (15,16) and the average wholesale price of 2 mg Cathflo Activase (Genentech, South San Francisco, California) (17), a conservative estimate of $100 per TPA dose or treatment was used. Costs associated with declotting via TPA were therefore estimated by the number of TPA doses administered multiplied by $100 per treatment.

Statistical Analysis

Mixed-effects binary logistic regression was used to predict any occlusion, controlling for patient-, provider-, device-, and hospital-level characteristics. Bivariate tests of association were examined first, followed by the full multivariable model. For all analyses, the PICC was the level of analysis, with patient- and hospital-level random effects included to account for patients who received multiple PICCs and clustering of patients within hospitals. Results were expressed as odds ratios (OR) with corresponding 95% confidence intervals (CIs).

To further distinguish among predictors of different types of occlusion (none, transient, irreversible), a two-level multinomial regression model was estimated, again adjusting for patient-, device-, provider-, and facility-level variables. Patient- and hospital-level random effects, constrained to be equal across types of occlusion, were included to account for unobserved variation at the patient and hospital levels. Stata MP/SE software (version 14.1, StataCorp, College Station, Texas) was used for all analyses. Two-tailed significance testing was used throughout; $P < .05$ was considered statistically significant. This study received a "not regulated" status by our institutional review board.

RESULTS

A total of 14,278 PICCs placed in 13,408 patients spanning 307,320 catheter-days were available for analysis. With respect to PICC characteristics (**Table 1**), 7,222 PICCs (50.6%) were double-lumen catheters, 4,965 (34.8%) were single-lumen catheters, and 2,091 (14.6%) were triple-lumen (or greater) catheters. The majority of PICCs (n = 13,000; 91.1%) were capable of power injection. Vascular-access nurses inserted the majority of devices (n = 10,525; 73.7%), followed by interventional radiologists (n = 2,356; 16.5%). All PICCs were inserted under ultrasound or fluoroscopy guidance. Most PICCs were placed in the right upper extremity (n = 9,864; 69.1%) and basilic vein (n = 8,671; 60.7%). The most common indications for PICC insertion were intravenous antibiotic therapy (4,666; 32.7%), difficult intravenous access (3,072; 21.5%), and central venous access for medication delivery or hemodynamic monitoring (1,955, 13.7%). The mean dwell time for PICCs was 21.5 days (median, 12 d; interquartile range, 6–30 d).

A total of 1,716 PICCs (12.0%) placed in 1,684 patients developed occlusion at some point during their dwell time: 1,532 (10.7%) showed one occlusion event, 171 (1.2%) showed two events, and 13 (0.1%) showed three events during follow-up. Time to occlusion varied from 0 to 70 days (median, 7 d; interquartile range, 4–14 d; **Fig**). With respect to type of occlusion, 1,363 PICCs (9.6% overall or 79% of all occlusions) developed transient occlusion whereas 353 PICCs (2.5% overall or 21% of occluded PICCs) were removed as a result of irreversible occlusion. Most PICCs with transient occlusion (n = 1,242; 91.1%) were treated with TPA.

Predictors of PICC Occlusion

In multivariable modeling, several patient-, provider-, and device-related factors were associated with occlusion (**Table 2**). Compared with non–critically ill patients, PICC use in the ICU was associated with greater odds of occlusion (OR = 1.32; 95% CI = 1.14–1.52). Aspirin, statins, or antiplatelet agent (clopidogrel, aspirin, and ticagrelor) therapy did not affect catheter occlusion rates. White blood cell count and creatinine level at the time of PICC placement were not associated with catheter occlusion; however, hemoglobin level < 10 g/dL was associated with greater odds of occlusion (OR = 1.17; 95% CI = 1.04–1.32).

Several provider-related factors were associated with occlusion. PICCs placed in the right arm were associated with decreased odds of occlusion compared with those placed in the left arm (OR = 0.82, 95% CI = 0.72–0.94). Compared with catheters whose tip position was not documented/confirmed or was inappropriate, verification of appropriate catheter tip position following insertion was associated with reduction in subsequent occlusion (OR = 0.74; 95% CI = 0.60–0.91). Infusion of cefepime (OR = 1.45; 95% CI = 1.23–1.70), piperacillin/tazobactam (OR = 1.21; 95% CI = 1.02–1.44), and vancomycin (OR = 1.81; 95% CI = 1.57–2.07) through the PICC was associated with greater odds of occlusion. Transfusion of packed red blood cells through the PICC was also associated with greater odds of occlusion (OR = 1.35; 95% CI = 1.12–1.63). More frequent flushing of the PICC (twice or three times vs once daily) did not reduce occlusion. Although flushing the catheter with 0.9% normal saline solution or heparin was not associated with occlusion, PICCs flushed with 0.9% normal saline solution and locked with heparin (ie, SASH method) had significantly lower rates of occlusion than saline alone (OR = 0.53; 95% CI = 0.32–0.88).

Device-related factors were among the strongest predictors of catheter occlusion. Gauge and lumen number were significant predictors in bivariate models of occlusion; however, as a result of high collinearity, only lumens were included in the multivariable model. Compared with single-lumen devices, double- and triple-lumen PICCs were

Table 1. Descriptive Statistics for Patient, Device, Provider, and Facility Predictors of Occlusion by PICC Occlusion Status

Predictors	Total (N = 14,278)	Occlusion (n = 1,716)	No Occlusion (n = 12,562)	*P* Value*
Patient-Related				
Age (y)	63.90 ± 16.3	62.35 ± 15.9	64.11 ± 16.4	< .001
Sex				
Female	7,321 (51.3)	904 (52.7)	6,417 (51.1)	Reference
Male	6,957 (48.7)	812 (47.3)	6,145 (48.9)	.74
Tobacco use				
Never	5,910 (41.4)	717 (41.8)	5,193 (41.3)	Reference
Former	5,200 (36.4)	597 (34.8)	4,603 (36.6)	.15
Current	3,168 (22.2)	402 (23.4)	2,766 (22.0)	.70
Comorbidities				
Uncomplicated diabetes	2,979 (20.9)	422 (24.6)	2,557 (20.4)	.001
Complicated diabetes	2,731 (19.3)	360 (21.0)	2,371 (18.9)	.001
Severe liver disease	579 (4.1)	48 (2.8)	531 (4.2)	.002
Renal failure	4,746 (33.2)	580 (33.8)	4,166 (33.2)	.10
Hyperlipidemia	5,103 (35.7)	583 (34.0)	4,520 (36.0)	.46
Hypertension	9,723 (68.1)	1,194 (69.6)	8,529 (67.9)	.08
Coagulopathy	475 (3.3)	47 (2.7)	428 (3.4)	.43
Body mass index (kg/m^2)	30.49 ± 8.9	31.93 ± 9.1	30.29 ± 8.86	< .001
Creatinine level				
Low/normal (≤ 1.5 mg/dL)	11,323 (79.3)	1,360 (79.3)	9,963 (79.3)	Reference
Elevated (> 1.5 mg/dL)	2,955 (20.7)	356 (20.7)	2,599 (20.7)	.41
Hemoglobin level				
Low (< 11 g/dl)	6,768 (47.4)	922 (53.7)	5,846 (46.5)	Reference
Normal (11–18 g/dL)	7,491 (52.5)	792 (46.2)	6,699 (53.3)	< .001
High (> 18 g/dL)	19 (0.1)	2 (0.1)	17 (0.1)	.98
White blood cells				
Low (< 4 × 10^9/L)	788 (5.5)	89 (5.2)	699 (5.6)	.54
Normal (4–12 × 10^9/L)	9,213 (64.5)	1,001 (58.3)	8,212 (65.4)	Reference
High (> 12 × 10^9/L)	4,277 (30.0)	626 (36.5)	3,651 (29.1)	< .001
In intensive care unit	5,592 (39.2)	932 (54.3)	4,660 (37.1)	< .001
Indication				
At-home antibiotics	4,666 (32.7)	426 (24.8)	4,240 (33.8)	Reference
Chemotherapy	434 (3.0)	80 (4.7)	354 (2.8)	< .001
Difficult access	3,072 (21.5)	426 (24.8)	2,646 (21.1)	< .001
Meds requiring central access	1,955 (13.7)	224 (13.1)	1,731 (13.9)	< .001
Total parenteral nutrition	789 (5.5)	111 (6.5)	678 (5.4)	.001
Other/unknown	3,362 (23.5)	449 (26.2)	2,913 (23.2)	< .001
Dwell time (d)	21.52 ± 21.5	27.88 ± 21.9	20.66 ± 21.3	< .001
Device-Related				
Lumens				
Single	4,965 (34.8)	265 (15.4)	4,700 (37.4)	Reference
Double	7,222 (50.6)	1,059 (61.7)	6,163 (49.1)	< .001
Triple/quadruple	2,091 (14.6)	392 (22.8)	1,699 (13.5)	< .001
Gauge				
≤ 4	4,357 (30.5)	261 (15.2)	4,096 (32.6)	Reference
4.5 or 5	8,528 (59.7)	1,251 (72.9)	7,277 (57.9)	< .001
> 5	1,393 (9.8)	204 (11.9)	1,189 (9.5)	< .001
Coated				
None	13,119 (91.9)	1,536 (89.5)	11,583 (92.2)	Reference
Antimicrobial	816 (5.7)	149 (8.7)	667 (5.3)	.006
Antithrombotic	261 (1.8)	16 (0.9)	245 (1.9)	.96
Both	82 (0.6)	15 (0.9)	67 (0.5)	.53

continued

Table 1. Descriptive Statistics for Patient, Device, Provider, and Facility Predictors of Occlusion by PICC Occlusion Status *(continued)*

Predictors	Total (N = 14,278)	Occlusion (n = 1,716)	No Occlusion (n = 12,562)	*P* Value*
Power-injectable PICC	13,000 (91.0)	1,549 (90.3)	11,451 (91.2)	.91
Valved	3,689 (25.8)	376 (21.9)	3,313 (26.4)	.12
Length (cm)	42.09 ± 5.0	42.09 ± 5.0	42.09 ± 5.0	< .001
Provider-Related				
Vein				
Basilic	8,671 (60.7)	1,068 (62.2)	7,603 (60.5)	Reference
Brachial	4,498 (31.5)	490 (28.5)	4,008 (31.9)	.85
Cephalic	760 (5.3)	110 (6.4)	650 (5.2)	.004
Other	349 (2.4)	48 (2.8)	301 (2.4)	.03
Arm				
Left	4,414 (30.9)	566 (33.0)	3,848 (30.6)	Reference
Right	9,864 (69.1)	1,150 (67.0)	8,714 (69.4)	< .001
Vascular access nurse insertion†	10,525 (73.7)	1,295 (73.5)	9,230 (75.5)	.15
Malposition or migration	711 (5.0)	103 (6.0)	608 (4.8)	< .001
Tip position				
PICC confirmation system	5,432 (38.0)	613 (35.7)	4,819 (38.4)	< .001
Other system (x-ray, fluoroscopy)	5,189 (36.3)	563 (32.8)	4,626 (36.8)	.06
Both	1,423 (10.0)	198 (11.5)	1,225 (9.8)	.35
No confirmation	2,234 (15.7)	342 (19.9)	1,892 (15.1)	Reference
Infusates				
Chemotherapy	423 (3.0)	87 (5.1)	336 (2.7)	< .001
Cefepime	1,860 (13.0)	398 (23.2)	1,462 (11.6)	< .001
Piperacillin/tazobactam	1,486 (10.4)	273 (15.9)	1,213 (9.7)	< .001
Vancomycin	3,880 (27.2)	737 (42.9)	3,143 (25.0)	< .001
Medications provided				
Statins	5,044 (35.3)	635 (37.0)	4,409 (35.1)	.04
Aspirin	4,325 (30.3)	504 (29.4)	3,821 (30.4)	.05
Antiplatelet agents	2,191 (15.4)	300 (17.5)	1,891 (15.1)	.22
Blood transfusion through PICC	1,117 (7.8)	230 (13.4)	887 (7.1)	< .001
Hospital-Related				
Flush frequency				
Daily or less than daily	4,308 (30.2)	320 (18.7)	3,988 (31.7)	Reference
Twice daily	5,307 (37.2)	851 (49.6)	4,456 (35.5)	.20
Three times daily	4,663 (32.7)	545 (31.8)	4,118 (32.8)	.17
Flush with				
Saline solution	8,628 (60.4)	1,329 (77.5)	7,299 (58.1)	Reference
Heparin	705 (4.9)	54 (3.1)	651 (5.2)	.67
Heparin and saline solution (SASH)	4,945 (34.6)	333 (19.4)	4,612 (36.7)	.03

Note–Values presented as mean ± standard deviation where applicable. Values in parentheses are percentages.
PICC = peripherally inserted central catheter; SASH = saline, administer medicine, saline, heparin.
*Bivariate association assessed via mixed-effects model including patient- and hospital-level random effects to account for patients who received multiple PICCs and clustering of patients within hospitals.
†Compared with reference of interventional radiologist insertion.

associated with significantly greater odds of occlusion (double, OR = 3.12; 95% CI = 2.56–3.79; triple, OR = 3.81; 95% CI = 2.94–4.94). The association between each additional lumen and occlusion was nonmonotonic, ie, the risk of occlusion with double-lumen catheters was greater than twice that with single-lumen devices ($\chi^2[1] = 21.32$; $P < .001$). Malposition of the catheter tip at any point during the catheter dwell time was also associated with greater subsequent risk of occlusion (OR = 1.47; 95% CI = 1.14–1.89). Antimicrobial- or antithrombotic-coated PICCs did not have lower rates of occlusion compared with other PICCs, nor did valved versus nonvalved PICCs.

Although the prevalence of transient occlusion was far greater than that of irreversible occlusion, multinomial models incorporating identical patient-, provider-, and device-specific risk factors showed no differences in predictors between these two events (**Table E1** [available online at *www.jvir.org*]).

Estimated Costs Associated with PICC Occlusion

A total of 1,499 of 1,716 PICCs (87.3%) were used to administer at least one dose of TPA for treatment of occlusion. In total, 2,495 doses of TPA were administered for declotting purposes during all follow-up intervals. Approximate costs related to administration of this therapy alone are therefore estimated at $249,500. Although the mean doses of TPA provided per catheter occlusion event was 1.45 (median, 1), some PICCs received as many as nine doses of TPA during follow-up. Therefore (assuming an average facility cost of $100), the cost per

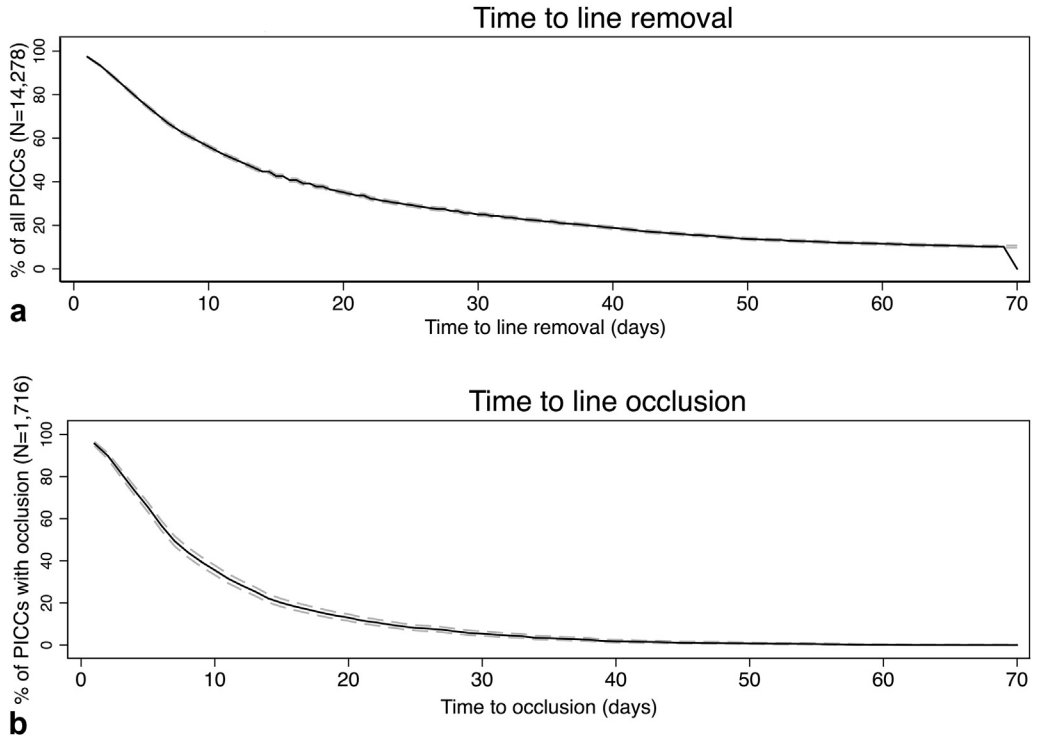

Figure. Times to PICC removal **(a)** or PICC occlusion **(b)**. Dashed lines indicate 95% CIs.

occluded PICC for TPA use averaged $145 but varied from $100 to $900.

DISCUSSION

Data from the present study of 14,278 PICCs suggest that occlusion affects as many as 12% of PICCs and is associated with significant cost. Selection of putative risk factors finds that obese, diabetic, and critically ill patients experienced greater odds of occlusion than others. Conversely, PICC placement in the right arm was associated with lower rates of occlusion than placement in the left arm, possibly because of shorter catheter length when placed in this limb. The occurrence of catheter malpositioning, infusion of specific antibiotic agents and blood, and number of PICC lumens were among the strongest predictors of catheter occlusion. These findings are important because they highlight specific factors that can be targeted to prevent occlusion.

No differences in odds of occlusion based on frequency of catheter flushing were found. This suggests that the absolute frequency of flushing may not be important; rather, attention to flushing the catheter before and after each use may be more relevant in preventing occlusions. In accordance with a Cochrane review (18), occlusion did not vary between PICCs that were flushed with normal saline solution versus heparin. However, PICCs managed by using the SASH technique, which includes a heparin lock following use, showed a significant reduction in odds of occlusion. Finally, coated or impregnated PICCs did not exhibit lower rates of occlusion than noncoated devices. These findings echo those of a recent study (19), and suggest that continued innovation in device coatings aimed at preventing occlusion is necessary.

In contrast to CVCs that are inserted in the neck or chest, PICCs are inserted in the arm, making them convenient for use. However, because PICCs are placed in veins of smaller caliber than those of the neck or chest, they have smaller cross-sectional diameters than CVCs. In addition, PICCs are longer than CVCs, with greater surface area. Consequently, it is plausible that the length and narrowness of PICCs predisposes them to occlusion. Available data are supportive of this assertion. In a systematic review and meta-analysis (9), catheter dysfunction (often caused by occlusion) was five times more common in patients with PICCs compared with CVCs. In a more recent study of residents at a skilled nursing facility (20), PICC occlusion was the most common complication and often delayed treatment. In a prospective French study (21), PICC occlusion was not only the most common complication, but also the most common reason for premature catheter removal. Collectively, these data highlight the importance and relevance of this event for clinicians who use PICCs for a range of indications.

How may occlusion be prevented? The data suggest some strategies. First, appropriate catheter tip positioning at the cavoatrial junction and prompt recognition of catheter malposition are important. These two factors share in common blood flow, which is greatest at the cavoatrial junction and lesser at other positions, which potentially helps explain why occlusion might be influenced by these variables (22). Second, use of PICCs with the least number of lumens is critical for the prevention of occlusion. As

Table 2. Mixed-Effects Multivariable Binary Logistic Regression of Predictors of Occlusion (N = 14,278)

Predictor	OR (95% CI)
Patient-Related	
Age in decades	0.928* (0.891–0.968)
Male sex	0.994 (0.877–1.126)
Tobacco use (reference: never)	
Former	0.920 (0.807–1.050)
Current	1.076 (0.924–1.252)
Comorbidities (reference: none)	
Uncomplicated diabetes	1.289* (1.113–1.493)
Complicated diabetes	1.309* (1.116–1.534)
Severe liver disease	0.616† (0.443–0.856)
Renal failure	1.068 (0.927–1.231)
Hyperlipidemia	0.895 (0.780–1.027)
Hypertension	1.125 (0.981–1.289)
Coagulopathy	0.745 (0.525–1.056)
Body mass index	1.018* (1.010–1.026)
Elevated creatinine (reference: normal)	0.874 (0.745–1.024)
Hemoglobin (reference: normal)	
Low	1.170‡ (1.038–1.319)
High	0.909 (0.195–4.245)
White blood cells (reference: normal)	
Low	0.892 (0.685–1.162)
High	1.070 (0.946–1.211)
In intensive care unit	1.315* (1.140–1.518)
Indication (reference: home antibiotics)	
Chemotherapy	1.218 (0.772–1.922)
Difficult access	0.987 (0.821–1.186)
Medications requiring central access	0.936 (0.746–1.173)
Total parenteral nutrition	1.252 (0.957–1.638)
Other/unknown	0.970 (0.806–1.168)
Dwell time in days	1.020* (1.017–1.023)
Device-Related	
Lumens (reference: single)	
Double	3.118* (2.564–3.792)
Triple/quadruple	3.807* (2.936–4.936)
Coated (reference: none)	
Antimicrobial	1.065 (0.772–1.470)
Antithrombotic	1.156 (0.612–2.181)
Both	0.711 (0.358–1.414)
Power-injectable PICC	1.028 (0.736–1.436)
Valved	1.009 (0.815–1.250)
PICC length	1.000 (0.985–1.016)
Provider-Related	
Vein (reference: basilic)	
Brachial	1.067 (0.935–1.219)
Cephalic	1.050 (0.819–1.346)
Other	1.241 (0.855–1.800)
Arm (reference: left)	
Right	0.823† (0.720–0.941)
Vascular access nurse insertion	0.831 (0.673–1.026)
Malposition or migration	1.468† (1.139–1.893)
Tip position confirmation (reference: none)	
PICC tip detector system	0.739† (0.597–0.914)
Other system (x-ray, fluoroscopy)	0.834 (0.695–1.001)
Both	0.971 (0.743–1.269)
Infusates (reference: none)	
Cefepime	1.446* (1.228–1.702)
Chemotherapy	1.365 (0.889–2.097)
Piperacillin-tazobactam	1.211‡ (1.022–1.436)
Vancomycin	1.805* (1.571–2.073)
Medications (reference: none)	
Statins	1.055 (0.921–1.210)
Aspirin	1.111 (0.968–1.275)
Antiplatelet agents	1.037 (0.881–1.221)
Blood transfusion through PICC	1.352† (1.118–1.634)
Flush frequency (reference: daily or less)	
Twice daily	1.435 (0.816–2.524)
Three times daily	1.272 (0.664–2.438)
Flush with (reference: saline solution)	
Heparin	0.735 (0.259–2.086)
Heparin and saline solution (SASH)	0.533‡ (0.324–0.879)

Note–Model unit of analysis was PICC; models include patient- and hospital-level random effects to account for patients who received multiple PICCs and clustering of patients within hospitals.
CI = confidence interval; OR = odds ratio; PICC = peripherally inserted central catheter; SASH = saline, administer medicine, saline, heparin.
*$P < .001$.
†$P < .01$.
‡$P < .05$.

many providers are unaware of the incremental risk of multilumen devices and often prefer the use of these catheters (23), educational strategies such as the use of mobile applications (24), as well as interventions that limit use of multilumen PICCs, are needed (17,25). Third, use of the SASH technique with a heparin lock following PICC use appears to be protective against occlusion. These results appear novel and are consistent with data that suggest a role for heparin in patency of various vascular devices (26,27).

The present study has limitations. First, this is a retrospective and observational study; therefore, unmeasured confounding may affect study conclusions. Although the variables selected for modeling were based on plausible pathways, it is not possible to establish causal linkages to occlusion. Second, data regarding flushing (eg, frequency and type of flush) were derived from hospital policies. Whether such policies were stringently adhered to and reflective of actual practice is not known. Additionally, details regarding flushing practice (eg, pulsatile push-pause) were not available and may influence findings (28). Third, although certain antibiotic agents and transfusion of blood were found to be associated with occlusion, mechanisms

underpinning these associations are not known. Finally, the assessment of costs associated with occlusion is limited to drug costs and omits costs associated with PICC replacement or additional specialist time for care and management, which are unknown.

Despite these limitations, the present study has important strengths. To our knowledge, this study is the first and largest to examine rates and predictors of PICC occlusion. As it includes medical patients receiving care in multiple hospitals, its findings are likely to be generalizable, externally valid, and applicable to other centers. Second, this study uses robust statistical techniques, including a conceptual model to guide selection of variables and random effects for unmeasured hospital practices and patient variation. Third, by establishing a number of factors associated with occlusion, this study helps inform clinical practice in important ways and advances the research agenda for safety related to PICCs.

In conclusion, PICC occlusion is a prevalent and costly complication that is associated with patient-related factors (eg, obesity, diabetes, and critical illness), as well as catheter malpositioning, infusion of antibiotic agents and blood, and number of PICC lumens. Future studies including data from the present study that focus on the prevention of occlusion appear necessary.

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Table E1. Mixed-Effects Multivariable Multinomial Logistic Regression ORs and 95% CI for Patient, Device, Provider, and Hospital Predictors of Occlusion Type (Reference: No Occlusion; N = 14,278)

Predictor	OR (95% CI)	
	Transient Occlusion	Irreversible Occlusion
Patient-Related		
Age in decades	0.941* (0.900–0.984)	0.887† (0.820–0.960)
Male sex	0.984 (0.861–1.126)	1.028 (0.808–1.307)
Tobacco use (reference: never)		
Former	0.944 (0.819–1.088)	0.862 (0.668–1.110)
Current	1.116 (0.947–1.315)	0.945 (0.706–1.266)
Comorbidities (reference: none)		
Uncomplicated diabetes	1.305† (1.115–1.527)	1.221 (0.919–1.622)
Complicated diabetes	1.346‡ (1.135–1.597)	1.202 (0.884–1.634)
Severe liver disease	0.519‡ (0.355–0.758)	1.048 (0.607–1.810)
Renal failure	1.064 (0.913–1.239)	1.093 (0.836–1.429)
Hyperlipidemia	0.881 (0.760–1.022)	0.958 (0.737–1.246)
Hypertension	1.108 (0.956–1.284)	1.177 (0.905–1.530)
Coagulopathy	0.885 (0.619–1.267)	0.291* (0.106–0.797)
Body mass index	1.015‡ (1.007–1.023)	1.026‡ (1.012–1.041)
Elevated creatinine (reference: normal)	0.891 (0.751–1.056)	0.817 (0.600–1.114)
Hemoglobin (reference: normal)		
Low	1.183† (1.041–1.346)	1.109 (0.879–1.396)
High	0.609 (0.078–4.758)	1.783 (0.224–14.200)
White blood cells (reference: normal)		
Low	1.001 (0.757–1.324)	0.586 (0.329–1.045)
High	1.109 (0.972–1.266)	0.925 (0.729–1.173)
In intensive care unit	1.297‡ (1.113–1.511)	1.358* (1.037–1.777)
Indication (reference: home antibiotics)		
Chemotherapy	1.093 (0.670–1.784)	1.663 (0.703–3.934)
Difficult access	0.985 (0.808–1.200)	0.955 (0.666–1.370)
Medications requiring central access	0.902 (0.708–1.150)	1.048 (0.685–1.604)
Total parenteral nutrition	1.035 (0.769–1.394)	2.200‡ (1.376–3.517)
Other/unknown	0.959 (0.786–1.170)	0.992 (0.693–1.418)
Dwell time	1.024‡ (1.021–1.026)	0.997 (0.991–1.003)
Device-Related		
Lumens (reference: single)		
Double	3.338‡ (2.734–4.076)	2.167‡ (1.524–3.080)
Triple/quadruple	4.114‡ (3.156–5.364)	2.522‡ (1.608–3.955)
Coated (reference: none)		
Antimicrobial	0.978 (0.697–1.371)	1.507 (0.879–2.581)
Antithrombotic	1.465 (0.757–2.837)	0.424 (0.097–1.850)
Both	0.707 (0.341–1.464)	0.744 (0.212–2.608)
Power-injectable PICC	1.004 (0.712–1.414)	1.117 (0.663–1.883)
Valved	0.921 (0.736–1.153)	1.396* (1.007–1.937)
PICC length	0.998 (0.981–1.014)	1.012 (0.984–1.040)
Provider-Related		
Vein (reference: basilic)		
Brachial	1.026 (0.889–1.185)	1.213 (0.945–1.557)
Cephalic	1.104 (0.848–1.438)	0.879 (0.544–1.422)
Other	1.256 (0.843–1.873)	1.184 (0.598–2.343)
Arm (reference: left)		
Right	0.825† (0.714–0.952)	0.808 (0.629–1.037)
Vascular access nurse insertion	0.882 (0.709–1.097)	0.667* (0.479–0.929)
Malposition or migration	1.323* (1.002–1.747)	1.983† (1.291–3.045)

continued

Table E1. Mixed-Effects Multivariable Multinomial Logistic Regression ORs and 95% CI for Patient, Device, Provider, and Hospital Predictors of Occlusion Type (Reference: No Occlusion; N = 14,278) *(continued)*

Predictor	OR (95% CI)	
	Transient Occlusion	**Irreversible Occlusion**
Tip position confirmation (reference: none)		
PICC tip detector system	0.728† (0.584–0.907)	0.832 (0.563–1.231)
Other system (x-ray, fluoroscopy)	0.781* (0.643–0.949)	1.073 (0.756–1.523)
Both	0.905 (0.683–1.200)	1.306 (0.814–2.095)
Infusates (reference: none)		
Cefepime	1.437‡ (1.210–1.706)	1.457† (1.083–1.961)
Chemotherapy	1.317 (0.833–2.083)	1.531 (0.670–3.498)
Piperacillin-tazobactam	1.187 (0.990–1.422)	1.305 (0.949–1.794)
Vancomycin	1.751‡ (1.519–2.018)	1.895‡ (1.470–2.443)
Medications (reference: none)		
Statins	1.118 (0.966–1.294)	0.837 (0.638–1.099)
Aspirin	1.133 (0.977–1.314)	1.044 (0.798–1.366)
Antiplatelet agents	0.991 (0.832–1.180)	1.227 (0.891–1.688)
Blood transfusion through PICC	1.329† (1.087–1.625)	1.440* (1.006–2.063)
Flush frequency (reference: daily or less)		
Twice daily	1.260 (0.715–2.221)	2.087* (1.094–3.980)
Three times daily	1.167 (0.609–2.237)	1.709 (0.815–3.580)
Flush with (reference: saline solution)		
Heparin	0.776 (0.275–2.189)	0.534 (0.145–1.967)
Heparin and saline solution (SASH)	0.468† (0.284–0.775)	0.874 (0.491–1.553)

Note–Model unit of analysis was PICC; models include patient and hospital-level random effects to account for patients who received multiple PICCs and clustering of patients within hospitals.
PICC = peripherally inserted central catheter; SASH = saline, administer medicine, saline, heparin.
* $P < .05$.
† $P < .01$.
‡ $P < .001$.