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ORIGINAL RESEARCH

Screening for Novel Risk Factors Related to Peripherally Inserted Central Catheter-Associated Complications

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BACKGROUND: Peripherally inserted central catheters (PICCs) are increasingly utilized. Patient and system factors that increase risk of complications should be identified to avoid preventable patient harm.

METHODS: A case control analysis of adult inpatients who underwent PICC placement from January 2009 to January 2010 at Scott & White Memorial Hospital was conducted to determine the incidence and risk factors for complications. One hundred seventy cases of inpatients who experienced PICC-related complications were identified. Age- and gender-matched controls were randomly selected among patients who underwent PICC placement without documented complications during this time.

RESULTS: A total of 1444 PICCs were placed, with a complication rate of 11.77% (95% confidence interval: 10.11%-13.44%). Complications included catheter-associated thrombosis (3%), mechanical complications (4%), catheter-associated bloodstream infections (2%), and cellulitis (1%). In multivariable logistic regression analyses, malnutrition and after-hours placement were significantly associated with increased risk of complications, as was body mass index (BMI) >30 after adjusting for anticoagulation and time of placement. In a secondary multivariable logistic regression analysis, after-hours placement and malnutrition were significantly associated with increased risk of nonmechanical complications. Additionally, in conditional univariate analyses, length of stay, malnutrition, and after-hours placement were associated with increased risk of catheter-associated thrombosis. In our multivariable logistic regression analyses, use of anticoagulation/antiplatelet agents was associated with decreased risk of all-cause complications, nonmechanical complications, and catheter-associated thrombosis.

CONCLUSIONS: Screening of patients undergoing PICC placement with attention to malnutrition, BMI >30, and length of stay may reduce the risk of PICC-associated complications. Use of anticoagulation/antiplatelet agents and avoiding after-hours placement may reduce complications and enhance patient safety. *Journal of Hospital Medicine* 2014;9:481–489. © 2014 Society of Hospital Medicine

Peripherally inserted central venous catheters (PICCs) are used for a variety of indications, including administration of long-term intravenous (IV) antibiotics, home IV medications, chemotherapy, and parenteral nutrition.[1–3] Additionally, PICCs have also been recognized as an alternative to large-bore central venous catheters such as subclavian or internal jugular central venous catheters. PICCs have been associated with fewer bloodstream infections in patients with cancer than tunneled catheters.[4] Compared to central venous catheters, they demonstrate reduced complication rates,[5] decreased cost,[6] and increased safety for longer durations of use.[1–3,7–9]

Despite the numerous benefits of PICCs, Prandoni et al. estimate an all-cause complication rate of 12% to 17% with the use of PICCs.[10] Associated complications include infection,[11] pain, bleeding, and mechanical dysfunction, all of which contribute to patient discomfort and additional healthcare costs.[12] Bloodstream infections, for example, had previously been thought to occur at a substantially lower rate in PICCs than central venous catheters.[13] However, a recent systematic review suggests the rate of PICC-associated bloodstream infections in the inpatient setting is actually comparable to that of central venous catheters.[14] Perhaps the most serious PICC-associated complication is catheter-related venous thrombosis. A recent systematic review and meta-analysis found evidence to suggest the rate of catheter-related venous thrombosis was highest in patients with cancer or critical illness[15]; additionally, rates of thrombosis associated with PICCs were higher than those associated with subclavian or internal jugular central venous catheters.[15,16] Fletcher et al. showed an 8.1% incidence of symptomatic PICC-related upper extremity deep vein thrombosis (DVT) in the neurosurgical intensive care unit, with 15% of patients subsequently developing a pulmonary embolism.[17] A recent prospective, randomized controlled trial by Itkin et al. similarly demonstrated symptomatic DVT rates of

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approximately 4%.[18] However, in this study, when PICCs were routinely screened for thrombosis (with or without associated symptoms), approximately 72% demonstrated thrombosis,[18] suggesting that many PICC-associated thromboses may be clinically undetected. This may have far-reaching clinical significance, as pulmonary embolism complicates upper extremity DVT in 9% of cases and can result in a mortality rate as high as 25%.[10,19]

Some strategies to reduce the rate of catheter-related complications include identification of characteristics that put patients at risk. Many potential risk factors have been investigated, including catheter size,[12,20–24] choice of vein,[24] location of catheter tip,[25] and history of malignancy or prior DVT.[12] However, to date, no definitive consensus has been reached. Special attention has been paid to the investigation of underlying risk factors and treatment for catheter-related DVT, given its significant morbidity and mortality. Results have been equivocal, though, and in some instances, complicated by a diagnosis of underlying malignancy.[26–28]

As PICCs become more widely utilized, assessments of factors that place patients at greater risk of PICC-related complications are needed.[21] The purpose of this study was to establish the incidence of complications associated with PICCs placed in the inpatient setting and examine risk factors predisposing patients to these complications.

MATERIALS AND METHODS

Study Design

A case control analysis of adult inpatients who underwent PICC placement between January 2009 and January 2010 was conducted at Scott & White Healthcare (now Baylor Scott & White Healthcare) to determine the incidence and risk factors for PICC-associated complications.

Study Site

The study took place at Scott & White Memorial Hospital in Temple, Texas, a 636-bed multispecialty teaching hospital and level 1 trauma center. It is part of a healthcare system that includes 12 hospitals and more than 60 regional clinics, all of which share an electronic medical record to enable full integration.

Human Subjects Approval

This study received approval from the institutional review board at Scott & White Healthcare.

PICC Placement Technique

Inpatient PICC placement was performed by the PICC consult service. The consult service was comprised of 3 separate provider teams: (1) internal medicine, including select hospitalists and internal medicine residents; (2) radiology, including interventional radiologists and radiology residents; and (3) nursing, including registered nurses with advanced training in PICC placement. Following placement of a consult, the PICC consult service assessed the patient, obtained consent, and subsequently placed the catheter. Members of the PICC consult service followed a system-wide protocol wherein target veins were identified by ultrasound prior to attempting catheter placement, and actual placement of the PICC was ultrasound guided. Images obtained during the procedure were permanently documented in the medical record. At the time of this study, no formal protocol existed wherein target veins were mapped for caliber. Operators relied on their professional judgment to determine if vein caliber appeared sufficient to accommodate catheter placement.

All PICCs were placed using industry standard sterile precautions. A universally accepted modified Seldinger technique was used to obtain venous access.[29] A guidewire was then positioned in the desired vessel to facilitate proper venous placement of the catheter. During the course of the study period, catheters used were either single- (4 Fr) or double lumen (5 Fr).

Catheters were placed at the bedside by hospitalists or registered nurse teams; the location of the catheter tip at the cavoatrial junction was confirmed by chest radiography. Catheter insertions by radiologists were performed in the interventional radiology suite, and confirmation of location of the catheter tip was obtained with fluoroscopy.

PICC Maintenance

Following placement, nurses managed the PICC site according to nursing policy. Per policy, the site was assessed each shift. Documentation of assessment was recorded in nursing notes. Routine dressing changes were performed every 7 days, and as needed, to maintain a sterile site. Date and time of dressing changes were documented in nursing notes and on the PICC dressing. Catheter hubs and injection ports were disinfected with an antiseptic preparation for 15 seconds and allowed to air dry for 30 seconds prior to accessing the catheter. Catheters were flushed with 10 mL of normal saline before and after use. Any abnormality noted during PICC assessment was relayed to the primary provider. If the catheter did not flush readily or demonstrate appropriate blood return, nursing staff obtained an order for alteplase to be administered in an effort to salvage the line. PICCs were discontinued at the discretion of the healthcare provider.

Participants

Records of all patients 18 years of age and older who underwent PICC placement between January 2009 and January 2010 were reviewed (N = 1444) for study inclusion. There were no exclusion criteria.

Data Collection

Patients who experienced complications were identified by electronic medical record review. One-to-one

matching was performed for age and gender-matched controls randomly selected from inpatients who underwent PICC placement during the same time period without complications. A total of 170 cases with PICC-related complications were identified. One hundred seventy exact age- and gender-matched controls, who based upon documentation available in the electronic medical record did not experience complications, were then randomly selected. Prior to data collection, the research team reviewed and discussed the data collection form and agreed upon a standardized protocol for data collection. Data collection was completed by authors J.M. and J.H. on the standardized data collection form. Although a formal analysis of inter-rater agreement was not performed, J.M. and J.H. discussed any items where questions arose and arrived at a consensus decision regarding completion of the data point.

End points of the chart review were completion of medical therapy for which the PICC was indicated (eg, IV antibiotics or total parenteral nutrition [TPN]) or documentation of a complication that led to 1 of the following: discontinuation of the PICC or adjustment of either catheter placement or medical therapy. All complications were identified via International Classification of Diseases, 9th Revision codes and systematic chart review.

Complications resulting in discontinuation of the PICC, adjustment of catheter placement, or change in medical therapy were identified by review of nursing or physician documentation, and were categorized as follows: mechanical complications (defined as loss of the ability of the catheter to flush or draw properly, inadvertent catheter dislodgement, or retained portion of the catheter following catheter removal), catheter-associated bloodstream infection (development of a positive blood culture attributable to the central catheter with no other clearly identifiable source of bacteremia present), cellulitis (defined as cellulitis in the extremity where the catheter was placed), bleeding from the site of catheter, fever (for which no other cause could be identified), and catheter-associated thrombosis (identified by Doppler ultrasonography in patients exhibiting symptoms such as pain, swelling, redness, or warmth in the extremity in which the PICC was placed).[30]

Demographic data were collected, including insurance status, age, ethnicity, and gender. Clinical data included body mass index (BMI), presence of malnutrition (defined by a serum albumin of less than 3 g/dL),[31] previous or active cancer, previous DVT, use of anticoagulants (eg, warfarin, heparin, or low-molecular-weight heparin) or antiplatelet agent (eg, aspirin or clopidogrel) at the time of placement, and indication for PICC placement. A patient's history of previous or active cancer and previous DVT were identified by clinical documentation. Indications for PICC placement included: treating infectious processes (ie, infusion of antimicrobials), providing TPN, chemotherapy administration, and IV access. Catheter-specific data were also collected and included venous access obtained (cephalic, basilic, brachial), catheter size (single lumen [4 Fr] or double lumen [5 Fr]), type of complication, and time to complication. The procedure note accompanying PICC placement was reviewed for data regarding time of day inserted (with after hours defined as documentation of placement occurring after 5 PM), and procedure operator to identify type of team (internal medicine, radiology, nursing) responsible for placement.

Data Analysis

Demographic characteristics and potential risk factors for patients in both the case and control groups of the study were summarized using descriptive statistics: mean (± standard deviation [SD]) for continuous variables and frequency (percent) for categorical variables. Univariate and multivariable conditional logistic regression analyses of variables that were potential risk factors of PICC-related complications were utilized. A stepwise selection method was used for multivariable conditional logistic regression models. Alpha = 0.2 was used for the significance to enter the model, and $\alpha = 0.05$ was used for significance level to remain in the model. Attribution of PICC-related complications was evaluated in terms of odds ratios (OR) and 95% confidence interval (CI). A P value of <0.05 indicated statistical significance. No prospective power analysis was performed. However, for a retrospective power analysis for 1:1 matching with 170 cases and 170 matched controls, assuming 20% of controls were affected and an α of 0.05, one would achieve 80% power to detect an odds ratio of 2. SAS 9.2 (SAS Institute Inc., Cary, NC) was used for data analysis.

RESULTS

In 2009, 1444 PICCs were placed, and 170 cases in which patients experienced complications associated with PICC placement were identified, resulting in a complication rate of 11.77% (95% CI: 10.11%-13.44%). The most common complications experienced by our patient population included catheter-associated thrombosis (3%, n = 46), mechanical complications (4%, n = 67), inadvertent catheter dislodgement (2%, n = 36), mechanical dysfunction (2%, n = 30), retained portion of the catheter following catheter removal (<1%, n = 1), catheter-associated bloodstream infections (2%, n = 24), and cellulitis at the catheter insertion site (1%, n = 15). Other documented complications included unexplained fever and bleeding (Table 1).

The mean age of the total cohort (N = 340), comprised of case (N = 170) and control (N = 170) groups, was 58 years (SD 17), and 55% (n = 94) were females. There were no significant differences in complications between groups based on ethnicity

TABLE 1. Type of Complication

Complication	N (%)
Thrombosis	46 (3)
Infection	24 (2)
Cellulitis	15 (1)
Mechanical complications*	67 (4)
Unexplained fever	15 (1)
Bleeding	3 (0)
No complication	1,274 (88)

NOTE: N = 1,444. Mechanical dysfunction (N = 30), retained portion of the catheter (N = 1 [0%]). Sum of the % in the columns were not exactly 100% for some cases due to rounding. *Inadvertent catheter dislodgement (N = 36).

($P = 0.66$). In the case group, 46% (n = 78) of PICCs were placed by the radiology team, 41% (n = 69) were placed by the internal medicine team, and 14% (n = 23) were placed by nursing. In the control group, 44% (n = 74) of PICCs were placed by radiology, 36% (n = 62) by internal medicine, and 20% (n = 34) by nursing. Based on univariate conditional analysis, provider team was not significantly associated with complications ($P = 0.29$).

Predictors of All-Cause Complications

Based upon univariate conditional logistic regression analyses of complications related to PICC placement (N = 340), the following variables demonstrated a statistically significant increased risk for complications: malnutrition (OR: 1.88 [95% CI: 1.02–3.44], $P = 0.04$) and after-hours placement (OR: 8.67 [95% CI: 2.62-28.63], $P = 0.0004$) (Table 2). Anticoagulation was associated with a decreased risk of complications (OR: 0.27 [95% CI: 0.16-0.45], $P = 0.04$). Based upon multivariable logistic regression analysis, after-hours placement (OR: 9.52 [95% CI: 2.68-33.78], $P = 0.0005$) and BMI >30 (OR: 1.98 [95% CI: 1.09-3.61], $P = 0.02$) were significantly associated with an increased risk of PICC-associated complications. Conversely, anticoagulation/antiplatelet use was associated with a decreased risk of complications (OR: 0.24 [95% CI: 0.14-0.43], $P < 0.0001$).

Predictors of Nonmechanical Complications

To study risk factors related to nonmechanical complications, a secondary analysis (N = 206) was performed in which all patients who experienced mechanical complications (N = 67) and matched controls (N = 67) were excluded. Based upon multivariable logistic regression analysis, after-hours placement (OR: 6.93 [95% CI: 1.35-35.56], $P = 0.02$) and malnutrition (OR: 2.83 [95% CI: 1.03–7.81], $P = 0.04$) were significantly associated with increased risk of nonmechanical complications. The use of anticoagulation/antiplatelet agents was associated with decreased risk of nonmechanical complications (OR: 0.17 [95% CI: 0.07-0.40], $P < 0.0001$). Variables not significantly associated with nonmechanical complications included BMI>30, previous history of DVT, history of cancer, catheter size, and venous access choice (Table 3).

Predictors of Thrombotic Complications

Of 1444 patients who underwent PICC placement, 3% (n = 46) were subsequently diagnosed with a catheter-associated thrombosis, representing 27% of all observed complications. In an attempt to better identify factors predisposing patients to thrombotic complications, an additional subgroup analysis (N = 92) was performed on those patients who experienced catheter-associated thrombosis (N = 46) and matched controls (N = 46). Variables examined in the analysis included BMI, length of stay (LOS), history of DVT, history of cancer, utilization of anticoagulation/antiplatelet agents, malnutrition, and catheter size.

Based on conditional univariate analyses, the following variables were significantly associated with increased risk of catheter-associated thrombosis: LOS (as a continuous variable) (OR: 1.04 [95% CI: 1.00–1.09], $P = 0.05$), malnutrition (OR: 4 [95% CI: 1.13–14.18], $P = 0.03$), and after-hours placement (OR: 8.00 [95% CI: 1.00–63.96], $P = 0.05$) (Table 4). Use of anticoagulation/antiplatelet agents (OR: 0.29 [95% CI: 0.11-0.80], $P = 0.02$) was associated with decreased risk of thrombosis. History of previous DVT and history of cancer were nonsignificant. In the multivariable logistic regression model, malnutrition (OR: 10.16 [95% CI: 1.76-58.71], $P = 0.01$) remained associated with increased risk of catheter-associated thrombosis, whereas use of anticoagulation/antiplatelet agents (OR: 0.11 [95% CI: 0.02-0.51], $P = 0.005$) was associated with decreased risk of catheter-associated thrombosis (Table 4).

DISCUSSION

The goal of this study was to identify factors related to PICC placement that place the general population of patients at risk. The type and rate of complications associated with PICCs in this study were similar to those previously reported in the literature including catheter-related infection and thrombosis.[10,32] Two unique risk factors, not well recognized previously,[10,27,28,33] were observed in this study: malnutrition and after-hours placement. Malnutrition, defined as serum albumin <3 g/dL was associated with an increase in PICC-related complications (such as catheter-associated bloodstream infections and cellulitis) and catheter-related thrombosis. Malnutrition itself has long been associated with a decreased resistance to infection[34]; in addition, low serum albumin may also be a marker of the presence of other severe comorbidities, which may contribute to increased risk of thrombosis. It has been noted in previous studies that critical illness increases risk of thrombosis.[15] Despite an exhaustive search of the literature, we have been unable to find additional studies examining the extent to which malnutrition may impact PICC-associated complications.

TABLE 2. Any Complication: Descriptive Statistics and Conditional Logistic Regression Analysis

			Univariate		Multivariable	
Variable	Case, N (%)	Control, N (%)	OR (95% CI)	*P* Value	AOR (95% CI)	*P* Value
Age, y, mean ± SD	58 ± 17	58 ± 17	—	—		
BMI, mean ± SD	29.2 ± 9.5	27.9 ± 7.9	1.02 (0.99–1.05)	0.12		
≤30	108 (64)	116 (68%)	1.00		1.00	
>30	62 (36)	54 (32%)	1.29 (0.79–2.11)	0.32	1.98 (1.09–3.61)	0.02
Length of stay, d, mean ± SD	18 ± 22	14 ± 16	1.01 (1.00–1.03)	0.06		
Length of stay group, d				0.11*		
<7	41 (24)	52 (31)	1.00			
7–29	101 (59)	103 (61)	1.19 (0.72–1.98)	0.49		
≥30	28 (16)	15 (9)	2.21 (1.07–4.58)	0.03		
Gender						
Female	94 (55)	94 (55)	—	—		
Male	76 (45)	76 (45)				
Ethnicity				0.66*		
Caucasian	131 (77)	125 (74)	1.00			
African American	26 (15)	28 (16)	0.88 (0.48–1.60)	0.67		
Hispanic/Asian	13 (8)	17 (10)	0.70 (0.31–1.58)	0.38		
Provider team				0.29*		
Radiology	78 (46)	74 (44)	1.00			
Internal medicine	69 (41)	62 (36)	1.05 (0.68–1.64)	0.82		
Nursing	23 (14)	34 (20)	0.65 (0.35–1.19)	0.16		
Insurance†				0.22*		
Private insurance	46 (27)	42 (25)	1.00			
Uninsured	17 (10)	24 (14)	0.73 (0.35–1.55)	0.41		
Medicare	57 (34)	62 (37)	0.73 (0.38–1.40)	0.34		
Medicaid	39 (23)	25 (15)	1.51 (0.74–3.06)	0.26		
Tricare/Veterans Administration	11 (6)	16 (9)	0.59 (0.24–1.45)	0.25		
History of DVT	27 (16)	26 (15)	1.05 (0.58–1.91)	0.88		
Malnutrition†	149 (88)	134 (79)	1.88 (1.02–3.44)	0.04		
Cancer	25 (15)	36 (21)	0.58 (0.31–1.09)	0.09		
Fluoroscopy	129 (76)	139 (82)	0.71 (0.42–1.19)	0.19		
Anticoagulation use	50 (29)	100 (59)	0.27 (0.16–0.45)	<0.0001	0.24 (0.14–0.43)	<0.0001
Multilumen‡	99 (58)	111 (66)	0.70 (0.44–1.11)	0.13		
Vein†				0.39*		
Basilic	98 (58)	86 (51)	1.00			
Cephalic	11 (6)	8 (5)	1.37 (0.48–3.89)	0.55		
Brachial	61 (36)	74 (44)	0.70 (0.45–1.09)	0.12		
Internal mammary	0 (0)	1 (1)	<0.001 (<0.001–>999)	0.99		
Time of day†						
Morning/afternoon	144 (85)	166 (98)	1.00		1.00	
After hours	26 (15)	3 (2)	8.67 (2.62–28.63)	0.0004	9.52 (2.68–33.78)	0.0005
Indication for PICC				0.02*		
Infection§	88 (52)	71 (42)	1.00			
Pneumonia	21 (12)	14 (8)	1.07 (0.50–2.29)	0.87		
Chemotherapy	5 (3)	2 (1)	1.84 (0.34–9.93)	0.48		
IV access	36 (21)	66 (39)	0.44 (0.25–0.75)	0.003		
Total parenteral nutrition	20 (12)	17 (10)	0.96 (0.44–2.14)	0.93		

NOTE: N = 170 in each group. Sum of the % in the columns was not exactly 100% for some cases due to rounding. **Abbreviations:** AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; DVT, deep vein thrombosis; IV, intravenous; OR, odds ratio; PICC, peripherally inserted central venous catheter; SD, standard deviation.

*Overall significance of the factor.

†Frequency missing = 1.

‡Frequency missing = 2.

§Osteomyelitis, abscess, cellulitis, pyelonephritis, meningitis.

After-hours placement was also associated with increased nonmechanical complications, as well as catheter-related thrombosis. In an effort to improve both patient and consulting provider satisfaction and provide more expedient service, PICCs were often placed after hours (between 5 PM and 8 AM) by both interventional radiology (n = 14) and internal medicine (n = 15) teams.

LOS has been associated with PICC placement complications in other studies.[12] In both primary and secondary analyses, hospital stays >30 days were associated with a higher risk of complications than

TABLE 3. Complications Other Than Mechanical: Descriptive Statistics and Conditional Logistic Regression Analysis

			Univariate		Multivariable	
Variable	Case, N (%)	Control, N (%)	OR (95% CI)	*P* Value	AOR (95% CI)	*P* Value
Age, y, mean ± SD	58 ± 16	58±16	—	—		
BMI, mean ± SD	29.7 ± 9.8	28.5±7.9	1.03 (0.99–1.07)	0.22		
≤30	64 (62)	68 (66)	1.00			
>30	39 (38)	35 (34)	1.27 (0.64–2.49)	0.49		
Length of stay, d, mean ± SD	20 ± 26	14 ± 18	1.02 (1.00–1.03)	0.08		
Length of stay group, d				0.03*		
<7	22 (21)	28 (27)	1.00			
7–29	60 (58)	68 (66)	0.95 (0.49–1.82)	0.87		
≥30	21 (20)	7 (7)	3.24 (1.23–8.54)	0.02		
Gender						
Female	63 (61)	63 (61)	—	—		
Male	40 (39)	40 (39)				
Ethnicity				0.95*		
Caucasian	75 (73)	75 (73)	1.00			
African American	19 (18)	18 (17)	1.06 (0.51–2.21)	0.87		
Hispanic/Asian	9 (9)	10 (10)	0.88 (0.32–2.44)	0.81		
Provider team				0.81*		
Radiology	43 (42)	44 (43)	1.00			
Internal medicine	45 (44)	41 (40)	1.11 (0.62–1.96)	0.73		
Nursing	15 (15)	18 (17)	0.86 (0.39–1.90)	0.71		
Insurance†				0.22*		
Private insurance	29 (28)	27 (26)	1.00			
Uninsured	13 (13)	12 (12)	1.18 (0.43–3.26)	0.74		
Medicare	32 (31)	40 (39)	0.52 (0.21–1.29)	0.16		
Medicaid	21 (20)	12 (12)	1.81 (0.69–4.74)	0.23		
Tricare/Veterans Administration	8 (8)	11 (11)	0.58 (0.19–1.79)	0.34		
History of DVT	15 (15)	15 (15)	1.00 (0.46–2.16)	1.00		
Malnutrition†	93 (90)	79 (77)	2.86 (1.21–6.76)	0.02	2.83 (1.03–7.81)	0.04
Cancer	17 (17)	22 (21)	0.67 (0.30–1.48)	0.32		
Fluoroscopy	78 (76)	85 (83)	0.65 (0.32–1.31)	0.23		
Anticoagulation use	29 (28)	60 (58)	0.21 (0.10–0.44)	<0.0001	0.17 (0.07–0.40)	<0.0001
Multilumen‡	64 (62)	67 (66)	0.83 (0.46–1.51)	0.55		
Vein†				0.32*		
Basilic	54 (52)	49 (48)	1.00			
Cephalic	8 (8)	3 (3)	2.45 (0.64–9.32)	0.19		
Brachial	41 (40)	49 (48)	0.72 (0.42–1.24)	0.24		
Internal mammary	0 (0)	1 (1)	<0.001 (<0.001–>999)	0.99		
Time of day†						
Morning/afternoon	87 (84)	100 (98)	1.00		1.00	
After hours	16 (16)	2 (2)	8.00 (1.84–34.79)	0.006	6.93 (1.35–35.56)	0.02
Indication for PICC				0.13		
Infection§	52 (50)	45 (44)	1.00			
Pneumonia	14 (14)	7 (7)	1.46 (0.51–4.18)	0.48		
Chemotherapy	5 (5)	0 (0)	>999 (<0.001–>999)	0.99		
IV access	22 (21)	43 (42)	0.48 (0.24–0.96)	0.04		
Total parenteral nutrition	10 (10)	8 (8)	1.08 (0.32–3.62)	0.90		

NOTE: N = 103 in each group. Sum of the % in the columns were not exactly 100% for some cases due to rounding. **Abbreviations:** AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; DVT, deep vein thrombosis; IV, intravenous; OR, odds ratio; PICC, peripherally inserted central venous catheter; SD, standard deviation.

*Overall significance of the factor.

†Frequency missing = 1.

‡Frequency missing = 2.

§Osteomyelitis, abscess, cellulitis, pyelonephritis, meningitis.

hospitalizations <7 days. In light of the clinical significance of catheter-related thrombosis, a subgroup analysis of patients with an LOS >30 days was conducted. The conditional univariate regression analysis showed an increased risk with greater LOS, malnutrition, and after-hours placement. Use of anticoagulant or antiplatelet agents were associated with decreased risk of thrombosis (Table 4). The association between LOS and PICC-related thrombosis is consistent with findings from Evans et al. involving 1728 patients in a similar center.[12] In these circumstances, increased LOS may be a surrogate marker for increased severity of illness, in that those

TABLE 4. Cathether-Associated Thrombosis: Descriptive Statistics and Conditional Logistic Regression Analysis

			Univariate		Multivariable	
Variable	Case, N (%)	Control, N (%)	OR (95% CI)	*P* Value	AOR (95% CI)	*P* Value
Age, y, mean ± SD	58 ± 18	58 ± 18	—	—		
BMI, mean ± SD	27.7 ± 7.1	27.7 ± 7.8	1.00 (0.93–1.08)	0.98		
≤30	34 (74)	33 (72)				
>30	12 (26)	13 (28)	0.83 (0.25–2.73)	0.76		
Length of stay, d, mean ± SD	17 ± 12	11 ± 9	1.04 (1.00–1.09)	0.05		
Length of stay group, d				0.15		
<7	8 (17)	14 (30)	1.00			
7–29	29 (63)	30 (65)	1.13 (0.41–3.07)	0.82		
≥30	9 (20)	2 (4)	4.65 (0.98–22.13)	0.05		
Gender						
Female	26 (57)	26 (57)	—	—		
Male	20 (43)	20 (43)				
Ethnicity				0.44*		
Caucasian	31 (67)	36 (78)	1.00			
African American	11 (24)	6 (13)	2.02 (0.69–5.93)	0.20		
Hispanic/Asian	4 (9)	4 (9)	1.12 (0.22–5.68)	0.89		
Provider team				0.26*		
Radiology	23 (50)	19 (41)	1.00			
Internal medicine	20 (43)	18 (39)	1.00 (0.43–2.31)	1.00		
Nursing	3(7)	9 (20)	0.33 (0.09–1.27)	0.11		
Insurance†				0.38*		
Private insurance	13 (28)	11 (24)	1.00			
Uninsured	8 (17)	4 (9)	2.01 (0.38–10.58)	0.41		
Medicare	14 (30)	21 (47)	0.39 (0.10–1.47)	0.16		
Medicaid	8 (17)	7 (16)	1.23 (0.28–5.36)	0.78		
Tricare/Veterans Administration	3 (7)	2 (4)	1.01 (0.12–8.27)	1.00		
History of DVT	7 (15)	8 (17)	0.88 (0.32–2.41)	0.80		
Malnutrition†	43 (93)	33 (73)	4.00 (1.13–14.18)	0.03	10.16 (1.76–58.71)	0.01
Cancer	10 (22)	13 (28)	0.67 (0.24–1.87)	0.44		
Fluoroscopy	33 (72)	39 (85)	0.46 (0.16–1.31)	0.14		
Anticoagulation use	16 (35)	28 (61)	0.29 (0.11–0.80)	0.02	0.11 (0.02–0.51)	0.005
Multilumen‡	22 (48)	28 (62)	0.53 (0.23–1.26)	0.15		
Vein†				0.93*		
Basilic	24 (52)	21 (47)	1.00			
Cephalic	1 (2)	1 (2)	0.86 (0.05–14.39)	0.92		
Brachial	21 (46)	22 (49)	0.75 (0.31–1.79)	0.51		
Internal mammary	0 (0)	1 (2)	<0.001 (<0.001–>999)	0.99		
Time of day†						
Morning/afternoon	38 (83)	44 (98)	1.00			
After hours	8 (17)	1 (2)	8.00 (1.00–63.96)	0.05		
Indication for PICC				0.80*		
Infection§	20 (43)	17 (37)	1.00			
Pneumonia	5 (11)	6 (13)	0.60 (0.14–2.56)	0.49		
Chemotherapy	3 (7)	0 (0)	>999 (<0.001–>999)	0.99		
IV access	14 (30)	20 (43)	0.58 (0.23–1.44)	0.24		
Total parenteral nutrition	4 (9)	3 (7)	1.22 (0.19–7.70)	0.83		

NOTE: N = 46 in each group. Sum of the % in the columns were not exactly 100% for some cases due to rounding. **Abbreviations:** AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; DVT, deep vein thrombosis; IV, intravenous; OR, odds ratio; PICC, peripherally inserted central venous catheter; SD, standard deviation.

*Overall significance of the factor.

†Frequency missing = 1.

‡Frequency missing = 2.

§Osteomyelitis, abscess, cellulitis, pyelonephritis, meningitis.

patients who are more ill require lengthier hospitalizations. In a systematic review and meta-analysis, Chopra et al. observed that increased severity of illness correlated with higher rates of catheter-associated thrombosis, which is supportive of these findings.[15]

In the multivariate logistic regression analysis, BMI >30 was associated with a statistically significant increased risk for PICC-associated complications after adjusting for anticoagulation and time of placement (Table 2). In the secondary analysis, where patients with mechanical complications were removed, BMI >30 was no longer associated with an increased risk for PICC-associated complications (Table 3). This suggests that patients with a BMI >30 had an increased

risk of mechanical complications, but were not necessarily at increased risk of developing other complications, such as catheter-related thrombosis, infection, or bleeding. This finding is congruent with studies by Evans et al.,[12] who found no association between BMI and catheter-associated thrombosis. Our association between BMI and complications is unique; to date, there are few additional studies that examine the extent to which BMI impacts the rate and type of complications associated with PICCs. At this time, the mechanism of the association between mechanical complications (such as inadvertent catheter removal or mechanical malfunction) and BMI is uncertain and warrants further investigation.

Use of Anticoagulant Agents

Anticoagulant (ie, any agent used for DVT prophylaxis or therapeutic anticoagulation) or antiplatelet agent use at the time of PICC placement and during the patient's hospitalization was associated with a decreased risk of thrombosis in our analysis. However, it should be noted that no specific anticoagulant agent was studied, and that antiplatelet agents were included in this analysis, unlike that of Evans et al.[12] Although current literature in oncologic populations, as well as the evidence-based clinical practice guidelines, recommend against routine use of venous thromboprophylaxis in patients with central venous catheters,[33,35–37] we believe this deserves further study, particularly in light of conflicting data in this area.[38,39] Evans et al.[12] noted that although use of anticoagulants initially appeared to be associated with greater incidence of upper extremity venous thrombosis, when previous diagnosis of DVT was removed from the analysis the association was no longer significant.

In our analyses, no associations between catheter size, choice of venous access, history of previous deep venous thrombosis, or history of malignancy and risk for complications were found. Our findings differed from previous studies, where a relationship between increasing catheter bore size and site of access have been associated with increased PICC-related thrombosis or other complications.[12,20,40,41] There were also no significant differences in risk for complications between provider teams (eg, internal medicine, radiology, nursing) for PICCs placed during the morning or afternoon, which is consistent with findings by Funk et al.[1] Yet, after-hours placement of PICCs was associated with greater complications than daytime placement. Although the exploration of factors associated with after-hours placement was beyond the scope of this study, the findings from this study caused the authors, primarily comprised of members of the internal medicine inpatient medicine division, to reexamine the division's protocol on PICC placement. A consensus decision was made to discontinue after-hours placement of PICCs by internal medicine teams in an effort to promote patient safety until further data could be collected. As a result, internal medicine teams no longer place PICCs after regular working hours at our institution.

Limitations

Limitations include the categorization of antiplatelet and anticoagulant agents together. We did not distinguish between high- and low-dose aspirin, nor did we distinguish between therapeutic dosing of heparin and low-molecular-weight heparin versus DVT prophylaxis dosing. Additionally, for patients who were on warfarin or heparin drip, we did not evaluate for therapeutic range of international normalized ratio or partial thromboplastin time, as this was beyond the present scope of this study. In addition, malnutrition defined by albumin alone may have been somewhat narrow, as conditions aside from malnutrition can impact albumin levels. In future evaluations, this relationship may be clarified by including other determinants of clinical malnutrition including BMI <18 or the measurement of prealbumin. For determination of after-hours placement of PICCs, we relied upon time of procedure dictation, assuming that all dictations immediately followed catheter placement. If there was a lapse in time between catheter placement and dictation, the category may have been recorded in error. Another limitation of after-hours categorization was that we were unable to determine whether the PICC was placed on a weekend or holiday.

CONCLUSIONS AND FUTURE DIRECTIONS

Our results suggest that more stringent screening of patients undergoing PICC placement may reduce the risk of complications, with special attention to characteristics such as BMI >30, increased LOS, and protein-calorie malnutrition (albumin <3). Furthermore, placement of PICC lines in emergent or after-hours settings should be carefully considered and weighed against relative risks of central venous catheter placement. Further examination of the role anticoagulant and antiplatelet agents may have in the prevention of catheter-related thrombosis should be undertaken. We hope that the identification of these risk factors will decrease the rate of complications and ultimately enhance patient safety and satisfaction.

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