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Comparison of Venous Thrombosis Complications in Midlines Versus Peripherally Inserted Central Catheters: Are Midlines the Safer Option?

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Abstract

Catheter-related (CR) thrombosis is a significant complication of midline catheters (MCs) and peripherally inserted central catheters (PICCs). Limited existing data for MCs suggest a favorable complication profile for MCs. To compare incidence of CR thrombosis between MCs and PICCs and to evaluate the impact of quantity of lumens and catheter diameter on CR thrombosis. This was a retrospective comparison spanning 13 months of MCs and PICCs for symptomatic CR thrombosis at an 1100 bed tertiary care academic medical center. Adult patients who had an MC or a PICC placed by the were included. Data were collected using the electronic medical record. Statistical analysis was performed using SAS software. A total of 2577 catheters were included in the analysis with 1094 MCs and 1483 PICCs. One hundred thirty (11.88%) MCs developed CR thrombosis (deep vein thrombosis [DVT] or superficial venous thrombophlebitis [SVT]) as compared to 112 (6.88%) PICCs (odds ratio [OR]: 1.82; $P < .0001$). Midline catheters had a 53% greater odds of developing CR DVT than PICCs (7.04% MCs and 4.72% PICCs; OR: 1.53; $P = .0126$). For CR SVT, MCs have a 2.29-fold greater odds of developing CR SVT than PICCs (4.84% MCs and 2.16% PICCs; OR: 2.29; $P = .0002$). For MCs and PICCs, the incidence of CR thrombosis was 13.50% for double lumen/5F lines and was 6.92% for single lumen/4F lines (OR: 2.10; $P = <.0001$). Symptomatic CR thrombosis is a serious, life-threatening complication that occurs more frequently in MCs compared to PICCs. Inserters should consider placement of single lumen catheters with the smallest diameter to reduce this risk when a midline is used.

Keywords

catheter-related thrombosis, deep venous thrombosis, pulmonary embolism, superficial venous thrombophlebitis, venous thromboembolism

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Introduction

Establishment and maintenance of intravenous access are core processes in providing medical care for hospitalized patients. For patients requiring extended duration of therapy, the point-of-care vascular access team (VAT) is often consulted for patient assessment and vascular access device (VAD) placement at many hospitals. Peripherally inserted central catheters (PICC) are central catheters that are placed via peripheral vein under ultrasound guidance and may be used for patients with difficult venous access for long-term central or peripheral infusion therapies as well as central venous pressure monitoring in a critical care setting.[1,2] Although PICCs provide a great option for some patients, these catheters have known complications including catheter-related (CR) bloodstream infection, CR venous thrombosis, malfunction, and high cost.[3,4] Midline catheters (MCs) represent a potentially attractive alternative to PICCs for peripheral infusions. Midline catheters are inserted into peripheral veins of the upper arm and terminate

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before the distal axillary vein.[5] These catheters have been utilized since the mid-1980s but fell out of favor in the early 1990s due to reports of acute life-threatening hypersensitivity reactions.[6,7] In the past few years, following product modification to lessen adverse events, MCs have made a resurgence in the market and are Food and Drugs Administration cleared for use in patients requiring intermediate- to long-term infusion therapies.[2] As these catheters terminate in a peripheral vein, these VADs do not carry the risk of central line-associated bloodstream infection.

Limited research currently exists regarding the complication profile of MCs with no definitive conclusions. A few small retrospective studies suggest a decrease in life-threatening complications such as infection and thrombosis relative to PICCs. On the other hand, MCs have significantly more minor complications such as pain, occlusion, and edema compared to PICCs.[8-10] Cather-related venous thrombosis is one of the most serious complications of catheter insertion. Catheter-related thrombosis (either superficial venous thrombophlebitis [SVT] or deep vein thrombosis [DVT]) refers to the formation of clots in the vasculature or adhesive wall of the catheter after catheter insertion due to endothelial trauma and inflammation, patient-related factors, or CR factors.[9] Thrombosis interrupts and delays venous therapy, increases cost of care, and often leads to other complications such as pain, bloodstream infections, and pulmonary embolism (PE).[10,11] As currently limited data exist on this important topic, we aim to evaluate the difference in symptomatic CR upper extremity thrombosis between PICCs and MCs.

Materials and Methods

Study Design and Setting

This was a retrospective chart review of PICC and MC insertions by the point-of-care VAT for 13 months between July 2016 and August 2017, at a single-site, suburban, 1100 bed academic, tertiary care referral center. The study was approved by the institutional review board.

Selection of Participants

Patients eligible for enrollment included adults older than 18 years who had an MC or a PICC placed by the VAT. Pediatric patients and patients who had a line insertion performed by another service such as interventional radiology were excluded from the analysis. Patients were also excluded for lines that were not explicitly documented as single lumen/4F lines or double lumen/5F lines, or if insertion records contained incomplete data. Table 1 demonstrates enrollment scheme.

Nearly 95% of MCs and PICCs placed during the study period were either single lumen/4F or double lumen/5F, so analysis was restricted to these lines. For MCs and PICCs, all single lumen catheters were 4F and all double lumen catheters were 5F.

Table 1. Enrollment Scheme.

	All Lines	MC	PICC
Number of vascular access team MC or PICC placements, July 2016 through August 2017	2890	1139	1751
Exclusion of patients <18 years of age at time of line placement	−74	−5	−69
Exclusion of lines that were not explicitly documented as single lumen 4F lines or double lumen 5F lines	−232	−36	−196
Exclusion of cases with incomplete data necessary to the study	−7	−4	−3
Final sample size	2577	1094	1483

Abbreviations: MC, midline catheter; PICC, peripherally inserted central catheter.

Data Collection

Patient charts were accessed via the electronic medical record, Epic Systems Corporation. The standard process for documenting all MCs and PICCs includes creating an LDA, a format for electronic documentation for all lines, drains, and airways (LDA). The LDA for VADs includes date and time of line placement, type of line, diameter of line, number of line lumens, catheter-to-vein ratio, vein accessed, line laterality, number of attempts, and indication for line. The catheter-to-vein ratio was recently added to the LDA and was not available for the cases included in this study cohort.

Patient charts were further queried for upper extremity venous duplex ultrasonography order and results from the date of line placement plus 30 days. All venous Doppler results were reviewed by the radiologist of record and the VAT medical director, and the presence or absence of SVT or DVT or both were noted. Thrombosis was further lateralized as CR or contralateral. Catheter-related thrombosis was defined as noncompressibility of the vein or adjacent veins in which the catheter was inserted. Isolated CR SVT was defined as an SVT. Isolated CR DVT was defined as a DVT. Combined CR SVT and DVT was defined as a DVT. Contralateral thrombosis followed the same definition scheme except that if the patient had bilateral arm thrombosis, the case was defined only as CR thrombosis. Venous Dopplers were ordered by the primary team for symptoms concerning for thrombosis. The cohort was also queried for computed tomography of the chest and ventilation–perfusion scans for an end point of PE. Data collection also included the presence or absence of patient history of PE and/or DVT prior to line insertion.

VAT Characteristics

The VAT is composed of 15 advanced practice providers who place all bedside MCs and PICCs for the institution. Vascular access device placements are performed daily from 8 AM to 6 PM with annual volume of insertions ranging from 2500 to 3000 placements. The medical director of this group is an emergency medicine physician with advanced fellowship training in

Table 2. Demographic and Catheter Variables, Descriptive Statistics, and Comparisons by Line Type.

	All Lines, n = 2577	MC, n = 1094	PICC, n = 1483	*P* Value[a]
Age of patient (n = 2577)				
Mean (standard deviation)	63.70 (17.28)	63.71 (17.84)	63.69 (16.87)	.9755
Median (interquartile range)	65 (54, 76)	65 (52, 77)	66 (55, 76)	
Minimum value, maximum value	18, 105	18, 105	18, 101	
Biological sex of patient (n = 2577)				
Female	1400 (54.33%)	695 (65.53%)	705 (47.54%)	<.0001
Male	1177 (45.67%)	399 (36.47%)	778 (52.46%)	
Lumen/line size (n = 2577)				
Single/4F	1762 (68.37%)	840 (76.78%)	922 (62.17%)	<.0001
Double/5F	815 (31.63%)	254 (23.22%)	561 (37.83%)	
Location of line placement (n = 2577)				
Basilic	1689 (65.54%)	654 (59.78%)	1035 (69.79%)	<.0001
Brachial	752 (29.18%)	357 (32.63%)	395 (26.64%)	
Cephalic	109 (4.23%)	71 (6.49%)	38 (2.56%)	
Other/unknown	27 (1.05%)	12 (1.10%)	15 (1.01%)	
History of DVT or PE (n = 2577)				
Yes	452 (17.54%)	225 (20.57%)	227 (15.31%)	.0005
No	2125 (82.46%)	869 (79.43%)	1256 (84.69%)	
Number of attempts (n = 2577)				
1	2315 (91.03%)	977 (89.31%)	1338 (90.22%)	.6217
2	177 (6.96%)	83 (7.59%)	94 (6.34%)	
3+	51 (2.00%)	21 (1.92%)	30 (2.02%)	
Unknown	34 (0.91%)	13 (1.19%)	21 (1.42%)	
Line side (n = 2577)				
Left	758 (29.41%)	339 (30.99%)	419 (28.25%)	.1322
Right	1819 (70.59%)	755 (69.01%)	1064 (71.75%)	
Indication for line (n = 2577)				
Antibiotics	1322 (51.30%)	396 (36.20%)	926 (62.44%)	<.0001
Chemotherapy	60 (2.33%)	3 (0.27%)	57 (3.84%)	
Difficult access/blood draws	669 (25.96%)	572 (52.29%)	97 (6.54%)	
Medications requiring central access	44 (1.71%)	0 (0.00%)	44 (2.97%)	
Multiple incompatible IV fluids	83 (3.22%)	20 (1.83%)	63 (4.25%)	
TPN	190 (7.37%)	0 (0.00%)	190 (12.81%)	
Other/unknown	209 (8.11%)	103 (9.41%)	106 (7.15%)	

Abbreviation: DVT, deep vein thrombosis; IV, intravenous; MC, midline catheter; PE, pulmonary embolism; PICC, peripherally inserted central catheter; TPN, total parenteral nutrition.

[a]*P* Value is generated by the use of 2 samples independent *t* tests for continuously measured variables and χ^2 tests for categorical variables.

emergency ultrasound and 15 years of experience with ultrasound-guided vascular access procedures. During the study period, no new inserters were added to the group. Further, all inserters had at least 2 years of experience on the team prior to the study period.

Outcomes

The goal of this study was to compare incidence of CR thrombosis between MCs and PICCs. Specifically, the focus of the investigation was to evaluate the impact of quantity of lumens and catheter diameter on the primary outcome.

Statistical Analysis

Descriptive statistics were reported for all variables and comparisons were made for demographics and catheter variables between MC and PICC using independent samples *t* tests and χ^2 tests. Univariate/unadjusted analysis uses univariate logistic regressions to present the results in terms of odds ratios (OR), with corresponding 95% confidence intervals (95% CI) and *P* values. Multivariate/adjusted logistic regression models display adjusted odds ratios (AOR). Firth penalized likelihood was used reduce potential bias because thrombotic outcomes were rare in this cohort (<10% of all line insertions) and there were some highly predictive risk factors for thrombotic outcomes. Models adjusted for age, sex, lumen and size, location of line, history or DVT or PE, number of attempts, and indication. All analysis was performed in SAS 9.4 (SAS Institute Inc, Cary, North Carolina). Any *P* value <.05 indicates statistical significance.

Results

The final data set includes 2577 MC or PICC line insertions in adult patients, which was comprised of 1094 MCs and 1483 PICCs that were inserted between July 2016 and August 2017.

Table 3. Univariate/Unadjusted Analysis for Effect of Line Type on Thrombosis Events.

	All Lines, n = 2577	MC, n = 1094	PICC, n = 1483	OR (95% CI)[a]	*P* Value
Catheter-related events					
Thrombosis (DVT or SVT)	232 (9.00%)	130 (11.88%)	102 (6.88%)	1.82 (1.39-2.39)	<.0001
DVT	147 (5.70%)	77 (7.04%)	70 (4.72%)	1.53 (1.10-2.13)	.0126
SVT	85 (3.30%)	53 (4.84%)	32 (2.16%)	2.29 (1.47-3.57)	.0002
Contralateral events					
Thrombosis (DVT or SVT)	62 (2.41%)	29 (2.65%)	33 (2.23%)	1.20 (0.73-1.98)	.4784
DVT	28 (1.09%)	13 (1.19%)	15 (1.01%)	1.18 (0.57-2.46)	.6543
SVT	34 (1.32%)	16 (1.46%)	18 (1.21%)	1.21 (0.62-2.37)	.5731
Contralateral and/or bilateral events					
Thrombosis (DVT or SVT)	122 (4.73%)	60 (5.48%)	62 (4.18%)	1.33 (0.93-1.91)	0.1230
DVT	50 (1.94%)	25 (2.29%)	25 (1.69%)	1.36 (0.78-2.38)	0.2730
SVT	86 (3.34%)	44 (4.02%)	42 (2.83%)	1.44 (0.94-2.20)	0.0969
PE events					
PE	42 (1.63%)	18 (1.65%)	24 (1.62%)	1.02 (0.56-1.88)	.9396

Abbreviation: CI, confidence interval; DVT, deep vein thrombosis; MC, midline catheter; OR, odds ratio; PE, pulmonary embolism; PICC, peripherally inserted central catheter; SVT, superficial venous thrombophlebitis.
[a]The odds ratio compares the odds of developing a thrombolytic event in MCs relative to the odds of developing a thrombolytic event in PICCs.

Table 4. Multivariate/Adjusted Analysis for Effect of Line Type on Thrombosis Events.

	MC Adjusted[a]	PICC Adjusted[a]	AOR (95% CI)[b]	*P* Value
Catheter-related events				
Thrombosis (DVT or SVT)	22.30%	12.34%	2.04 (1.46-2.86)	<.0001
DVT	12.53%	6.85%	1.95 (1.28-2.97)	.0019
SVT	5.56%	2.91%	1.96 (1.18-3.25)	.0090
Contralateral events				
Thrombosis (DVT or SVT)	4.04%	4.40%	0.91 (0.50-1.66)	.7706
DVT	1.46%	1.59%	0.91 (0.39-2.13)	.8360
SVT	3.66%	4.05%	0.90 (0.43-1.90)	.7814
PE events				
PE	7.19%	4.88%	1.51 (0.74-3.09)	.2606

Abbreviation: AOR, adjusted odds ratio; CI, confidence interval; DVT, deep vein thrombosis; MC, midline catheter; PE, pulmonary embolism; PICC, peripherally inserted central catheter; SVT, superficial venous thrombophlebitis.
[a]The percentages refer to the model-adjusted predicted probabilities of developing a thrombosis event.
[b]AOR refers to the model-adjusted odds of developing a thrombolytic event in MCs relative to the odds of developing a thrombosis event in PICCs. The model is adjusted for the effect of age, sex, lumen/size, location, DVT/PE history, number of attempts, line side, and indication.

A total of 82.46% of patients had no prior documented history of DVT or PE. More than two-thirds of lines (68.37%) were single lumen/4F lines. More than 90% of insertions (91.03%) were successful on the first attempt. The most common indication for line placement was antibiotics (51.30%), followed by difficult access/blood draws (25.96%). See Table 2 for complete descriptive statistics.

In all, 130 (11.88%) MCs developed symptomatic CR thrombosis (DVT or SVT) as compared to 112 (6.88%) PICCs (OR: 1.82; $P < .0001$; Table 3). Midline catheters had a 53% greater odds of developing CR DVT than PICCs (7.04% MCs and 4.72% PICCs; OR: 1.53; $P = .0126$; Table 3). When evaluating CR SVT, MCs have a 2.29-fold greater odds of developing CR SVT than PICCs (4.84% MCs and 2.16% PICCs; OR: 2.29; $P = .0002$; Table 3). Multivariate analysis confirmed that MC is an independent predictor of increased odds for development of CR thrombosis (AOR: 2.04; $P = <0.0001$; Table 4), CR DVT (AOR: 1.95; $P = .0019$; Table 4), and CR SVT (AOR: 1.96; $P = .0090$; Table 4). The average time from catheter insertion to diagnosis of CR thrombosis in PICCs was a median of 8.1 days for DVT and 7.84 days for SVT. Similarly, the average time from catheter insertion to diagnosis of CR thrombosis in MCs was a median of 8.3 days for DVT and 8.02 days for SVT.

Catheter-related thrombosis was higher in double lumen/5F lines as compared to single lumen/4F lines, as shown in Table 5. For MCs and PICCs, the incidence of CR thrombosis was 13.50% for double lumen/5F lines and was 6.92% for single lumen/4F lines (OR: 2.10; $P \leq .0001$; Table 5). Catheter-related DVT in double lumen/5F MC lines was 13.38% as compared to 5.12% of single lumen/4F MC lines (OR: 2.87; $P \leq .0001$; Table 5). Similarly, in MCs, CR SVT was 7.09% in double lumen/5F lines as compared to 4.17% for single lumen/4F lines; however, there was no significant difference (OR: 1.78; $P = .0530$; Table 5). Catheter-related DVT in double lumen/5F PICC lines was 8.20% as compared to 2.60% of

Table 5. Effect of Lumen/Size on Thrombosis Events, Overall, and Stratified by Line Type.

	MC and PICC					
	Double/5F, n = 815	Single/4F, n = 1762	OR (95% CI)[a]	*P* Value	AOR (95% CI)[b]	*P* Value
Catheter-related events						
Thrombosis (DVT or SVT)	110 (13.50%)	122 (6.92%)	2.10 (1.60-2.75)	<.0001	2.48 (1.80-3.42)	<.0001
DVT	80 (9.82%)	67 (3.80%)	2.75 (1.97-3.84)	<.0001	2.82 (1.91-4.18)	<.0001
SVT	30 (3.68%)	55 (3.12%)	1.20 (0.76-1.87)	.4386	1.83 (1.11-3.02)	.0187
Contralateral events						
Thrombosis (DVT or SVT)	23 (2.82%)	39 (2.21%)	1.29 (0.77-2.17)	.3293	0.91 (0.50-1.67)	.7717
DVT	11 (1.35%)	17 (0.96%)	1.43 (0.67-3.02)	.3528	1.23 (0.55-7.75)	.6160
SVT	12 (1.47%)	22 (1.25%)	1.20 (0.60-2.42)	0.6024	0.72 (0.33-1.59)	.4164
PE events						
PE	26 (3.19%)	16 (0.91%)	3.55 (1.91-6.61)	<.0001	3.22 (1.59-6.52)	.0012
	MC					
	Double/5Fr, n = 254	Single/4Fr, n = 840	OR (95% CI)[a]	*P* Value	AOR (95% CI)[b]	*P* Value
Catheter-related events						
Thrombosis (DVT or SVT)	52 (20.47%)	78 (9.29%)	2.52 (1.72-3.69)	<.0001	2.74 (1.83-4.10)	<.0001
DVT	34 (13.38%)	43 (5.12%)	2.87 (1.79-4.60)	<.0001	3.06 (3.04-3.09)	<.0001
SVT	18 (7.09%)	35 (4.17%)	1.78 (0.99-3.17)	.0530	2.02 (1.10-3.70)	.0232
Contralateral events						
Thrombosis (DVT or SVT)	8 (3.15%)	21 (2.50%)	1.32 (0.59-2.95)	.5071	0.92 (0.41-2.08)	.8473
DVT	5 (1.97%)	8 (0.95%)	2.16 (0.73-6.38)	.1638	1.64 (0.62-4.39)	.3210
SVT	3 (1.18%)	13 (1.55%)	0.85 (0.26-2.79)	.7928	0.51 (0.17-1.59)	.2462
PE events						
PE	7 (2.76%)	11 (1.31%)	2.19 (0.86-5.55)	.1001	1.71 (0.70-4.19)	.2431
	PICC					
	Double/5Fr, n = 561	Single/4Fr, n = 922	OR (95% CI)[a]	*P* Value	AOR (95% CI)[b]	*P* Value
Catheter-related events						
Thrombosis (DVT or SVT)	58 (10.34%)	44 (4.77%)	2.29 (1.53-3.44)	<.0001	2.64 (1.50-4.64)	.0007
DVT	46 (8.20%)	24 (2.60%)	3.31 (2.00-5.46)	<.0001	2.86 (1.46-5.62)	.0023
SVT	12 (2.14%)	20 (2.17%)	1.00 (0.49-2.04)	.9968	2.24 (0.93-5.44)	.0735
Contralateral events						
Thrombosis (DVT or SVT)	15 (2.67%)	18 (1.95%)	1.39 (0.70-2.75)	.3485	0.94 (0.38-2.34)	.8973
DVT	6 (1.07%)	9 (0.98%)	1.13 (0.41-3.07)	.8179	0.94 (0.28-3.10)	.9127
SVT	9 (1.60%)	9 (0.98%)	1.65 (0.67-4.09)	.2768	0.94 (0.30-2.92)	.9137
PE events						
PE	19 (3.39%)	6 (0.65%)	6.00 (2.31-15.5)	.0002	7.34 (2.47-21.8)	.0003

Abbreviation: AOR, adjusted odds ratio; CI, confidence interval; DVT, deep vein thrombosis; MC, midline catheter; OR, odds ratio; PE, pulmonary embolism; PICC, peripherally inserted central catheter; SVT, superficial venous thrombophlebitis.

[a]The odds ratio compares the odds of developing a thrombolytic event in double lumen/5F lines relative to the odds of developing a thrombosis event in single lumen/4F lines.

[b]AOR refers to the model-adjusted odds of developing a thrombosis event in double lumen/5F lines relative to the odds of developing a thrombosis event in single lumen/4Fr lines. The model is adjusted for the effect of age, sex, location, DVT/PE history, number of attempts, line side, and indication.

single lumen/4F PICC lines (OR: 3.31; $P \leq .0001$; Table 5). Similarly, in PICCs, CR SVT was 2.14% in double lumen/5F lines as compared to 2.17% for single lumen/4F lines; however, there was again no significant difference (OR: 1.00; $P = .9968$; Table 5). Higher incidence of CR thrombosis and CR DVT in both MC and PICC double lumen/5F lines was confirmed in multivariate analysis.

Eighteen (1.65%) MCs developed a PE as compared to 24 PICCs (1.62%; OR: 1.02; $P = .9396$; Table 3). The PE rate increased to 3.11% and 3.09% for MCs and PICCs, respectively, when only double lumen lines are considered. The rate of PE was 2.76% MCs and 3.39% PICCs in double lumen/5F catheters, while the rate of PE was 1.31% of MCs and 0.65% of PICCs in single lumen/4F catheters. Multivariate analysis showed that there was not enough evidence to conclude a significant interaction in the rate of PE between single lumen/4F catheters and double lumen/5F catheters (interaction $P = .1137$).

Isolated contralateral thrombosis occurred in 2.41% of lines. Contralateral DVT occurred in 13 MCs (1.19%) as compared

15 (1.01%) PICCs (OR: 1.18; $P = .6543$; Table 3). Similarly, contralateral SVT occurred in 16 (1.46%) MCs as compared to 18 (1.21%) PICCs (OR: 1.21; $P = .7531$; Table 3). Table 3 summarizes isolated contralateral and concurrent CR thrombosis results.

In all, 452 patients had a history of DVT or PE while 2125 did not. A total of 12.39% of patients with a history of DVT or PE developed CR thrombosis while 8.28% of patients with no history of DVT or PE developed CR thrombosis (OR: 1.57; $P = .0111$). A total of 15.56% of MCs with a history of DVT or PE developed CR thrombosis while 10.93% of MCs with no history of DVT or PE developed CR thrombosis (OR: .99; $P = .0543$). A total of 9.25% of PICCs with a history of DVT or PE developed CR thrombosis while 6.45% of PICCs with no history of DVT or PE developed CR thrombosis (OR: 0.91; $P = .0896$).

Discussion

The limited published data on MC outcomes have been either inconclusive or suggest that MCs are safer with a decreased complication profile compared to PICCs.[8,12-14] In recent years, many hospitals, including our institution, have migrated to the use of MCs based on published guidelines recommending their use for intermediate duration of therapy and to reduce central line–associated bacterial infection occurrences.[2] Midline catheters are touted as versatile lines with a low complication rate, long dwell time, and a high rate of first-attempt placement.[15] Some research suggests significant cost-saving benefits for hospital systems with the use of MCs.[16]

As limited data exist for MC complications, the main focus of this study was 2-fold: (1) identify incidence of CR thrombosis for MCs and (2) provide a comparison to PICCs for CR thrombosis. A small retrospective study involving 206 PICCs and 200 MCs showed that MCs were associated with more minor complications compared to PICCs, with inconclusive data regarding thrombosis.[8] Another study comparing PICCs to MCs in a cystic fibrosis population with 231 MCs and 97 PICCs found no significant difference between catheters for significant and minor complications.[17] A recent prospective study involving 439 MCs inserted in 430 patients showed symptomatic CR venous thrombosis (combined SVT and DVT) diagnosed in 4.5% of patients with MCs.[18] A meta-analysis of 11 studies showed that PICCs were associated with an increased risk of DVT compared to other CVCs but did not analyze MC-related DVT incidence directly.[1]

To our knowledge, this is the largest comparative evaluation of MCs and PICCs. Our findings detect a significantly higher thrombosis risk of MCs compared to previous evaluations. The symptomatic CR thrombosis rate was 11.88%. Further, unlike other conclusions in the literature, the thrombosis rate of MCs was significantly higher than PICCs. Our finding of CR thrombosis rate of 6.88% for PICCs is consistent with the range published in the literature.[1] Our study also explored the impact of insertion and CR variables on thrombosis. Specifically, quantity of lumens and catheter diameter were related to higher thrombosis rates in both MCs and PICCs. Moving from a single to double lumen and from 4F to 5F increased the odds of thrombosis by 2.10. Although this study is the first evaluation of these characteristics in MCs, the literature for PICCs supports the use of smaller diameter catheters as larger diameter catheters are associated with higher rates of CR thrombosis.[19-21] The relationship between the number of lumens and thrombosis is less conclusive.[22-24]

Increase in contralateral arm thrombosis was an interesting finding of this study. The rates were significantly higher than the incidence of the upper extremity thrombosis in the general population.[25] Although most of the focus of investigations has been on CR thrombosis, there appears to be a significant risk of symptomatic contralateral thrombosis related to line placement. There were also multiple cases in which there was a coexisting CR thrombosis making the true thrombosis rate even higher. There does not appear to be any other study specifically evaluating the risk on contralateral thrombosis in patients with catheters, although one study found that insertion of an upper extremity PICC was an independent risk factor for the development of the lower extremity thrombosis.[26]

Limitations

The retrospective nature of the evaluation is a limitation. There are many factors that may impact thrombosis; it is difficult to account for all confounding variables with this study design. Illness severity, medical history, all indications for line placement, and medication history among other variables may influence the development of symptomatic thrombosis. We also unsuccessfully attempted to account for the impact of caustic medications or fluid therapies on thrombosis. While the medication administration record can be queried retrospectively, we found the data to be incomplete and unreliable for the purposes of this evaluation.

Another limitation of our study was a lack of data on catheter-to-vein ratio. A study of PICCs reported a reduction of CR DVT rates from 2.9% to 1.4% when the vessel diameter was at least twice the outer diameter of the catheter.[27] There are no specific data on catheter-to-vein ratio for MCs. The impact of the intrinsic catheter properties on thrombosis is also unknown and not specifically assessed. The increased thrombosis rate in MCs may be partly due to the intrinsic properties of the catheter or the catheter material itself. Midline catheter devices had traditionally been made from rigid materials that can be irritating to veins; softer materials have been associated with hypersensitivity reactions, thrombosis, or thrombophlebitis.[6,7]

Conclusions

Symptomatic CR thrombosis is a serious, life-threatening complication that occurs more frequently in MCs compared to PICCs. As this complication increases with the larger diameter and dual-lumen catheters, inserters should consider placement of single-lumen catheters with the smallest diameter to reduce

this risk when a midline is used. Inserters should also consider using other VADs beyond midlines for intermediate duration of therapy. Larger prospective trials are needed to evaluate the safety profile of MCs and determine best insertion practices and catheter characteristics needed to reduce complications.

Authors' Note

A. Bahl designed the study, supervised the conduct of the study and data, managed the data, including quality control, provided statistical advice on study design and analyzed the data with assistance from the Research Institute, drafted the manuscript, and takes responsibility for the paper as a whole. P. Karabon designed the study, managed data, provided statistical analysis, and drafted the manuscript. D. Chu collected data, managed data, analyzed the data with assistance from the Research Institute, and drafted the manuscript.

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Declaration of Conflicting Interests

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