The catheter to vein ratio and rates of symptomatic venous thromboembolism in patients with a peripherally inserted central catheter (PICC): a prospective cohort study

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ABSTRACT:

Background: Peripherally inserted central catheters (PICCs) are a common vascular access device used in clinical practice. Their use may be complicated by adverse events such as venous thromboembolism (VTE). The size of the vein used for PICC insertion and thus the catheter to vein ratio is thought to be a controllable factor in the reduction of VTE rates in patients who have a PICC. However, an optimal catheter to vein ratio for PICC insertion has not previously been investigated to inform clinical practice.

Objectives: To determine the effect of the catheter to vein ratio (proportion of the vein measured at the insertion point taken up by the catheter) on rates of symptomatic VTE in patients with a PICC and identify the optimal ratio cut-off point to reduce rates of this adverse event.

Method: Adult patients waiting for PICC insertion at a large metropolitan teaching hospital were recruited between May and December 2013. Vein diameter at the PICC insertion site was measured using ultrasound with in-built callipers. Participants were followed up at eight weeks to determine if they developed symptomatic VTE.

Results: Data were available for 136 patients (50% cancer; 44% infection; 6% other indication for PICC). Mean age was 57 years with 54% males. There were four cases of confirmed symptomatic VTE (two involving the deep veins, one peripheral vein and one pulmonary embolism). Receiver operator characteristic (ROC) analysis determined that a 45% catheter to vein ratio was the ideal cut off point to maximise sensitivity and specificity (AUC 0.761; 95% CI 0.681- 0.830). When a ratio of 46% or above was compared to one that was less than or equal to 45% using a log binomial generalized linear model it was found that participants with a catheter to vein ratio >45% were 13 times more likely to suffer VTE (relative risk 13, p=0.022; CI 1.445-122.788).

Conclusion: It was found that a 45% catheter to vein ratio was the optimal cut off with high sensitivity and specificity to reduce the risk of VTE. However, further research is needed to confirm these results as although adequately powered; the number of cases of VTE was comparatively small, resulting in wide confidence intervals.

Introduction

Peripherally inserted central catheters (PICCs) are used for many patient groups including those requiring chemotherapy agents and antibiotics (Chopra et al., 2012). PICC use has increased worldwide due to cost-effective nurse insertion teams, increased patient satisfaction and to facilitate out of hospital care (Horattas et al., 2001; Sharp et al., 2014). However, the use of these devices has seen a concurrent rise in thrombus rates. Venous thromboembolism (VTE) which incorporates upper extremity thrombosis and pulmonary embolism, causes discomfort, interrupts treatment and may be associated with increased morbidity and mortality (Liem et al., 2012).

Stasis is a key element in the formation of thrombus according to Virchow's triad (Yacopetti, 2008). Blood flow is laminar (with greatest velocity at the centre) and therefore a PICC, which often sits at the centre of the vein, has a sizeable impact on blood flow (Athanasiou & Natoli, 2008). Nifong and McDevitt (2011) used mechanaical models to determine the effect of the catheter to vein ratio on blood flow. Glass cylinders were used to approximate the size of the basilic, brachial and cepahlic veins and stainless steel wires to reflect the diameter of PICCs. They found that flow was dependant on the catheter and cylinder (or vein) size and PICCs commonly used in clinical practice may impede blood flow between 40-80% depending on catheter and vein size (Nifong and McDevitt, 2011). This may explain why larger PICCs are associated with higher rates of symptomatic VTE. Several prospective and retrospective studies set in acute care facilities have determined higher rates of VTE with patients who have a larger diameter PICC (Grove & Pevec, 2000; Chopra et al., 2014).

The diameter of the vein used for PICC insertion and thus the catheter to vein ratio may be a controllable factor in the rate of thrombosis due to the possibility of reducing stasis. However, there are few protocols to guide clinicians regarding safe parameters for catheter to vein ratios to reduce the risk of VTE. Current guidelines suggest that the smallest catheter that meets the treatment needs of the patients be inserted; but it is a clinical reality that larger, multi-lumen PICCs are required for some patient-groups (Infusion Nurses Society, 2011). Typically, French size increases in accordance with the number of lumens, and these are determined by the treatment needs of the patient. For example, for simple antibiotic treatment a single lumen PICC is used, but as treatment becomes complex with incompatible infusions, more lumens are required (Grove & Pevec, 2000).

Some clinicians recommend that no more than 33-50% of the vein be occupied by the catheter but these parameters are arbitrary (Lacy, 2012). Previous research, which has set a minimum vein size for PICC

insertion, has found decreased thrombus rates associated with lower catheter to vein ratios, but the definitive maximum ratio that can be used is not apparent (Meyer, 2011; Itkin et al., 2014). When a minimum 4mm vein size protocol for PICC insertion with a maximum of 50% catheter to vein ratio was introduced at one acute care facility (n= 1300), the thrombus rate halved from 2.9% to 1.4% (Meyer, 2011). But a recent retrospective cohort study set in a Veteran Affairs hospital in the United States with mainly male subjects (n=747) found a higher VTE rate of 3.4% with the same maximum 50% catheter to vein ratio (Chopra et al., 2014). To our knowledge there has not been a prospective study that has examined the association between the catheter to vein ratio and risk of VTE or that has determined a safe maximum ratio to guide clinical practice.

Aims

To determine the effect of the catheter to vein ratio (proportion of the vein measured at the insertion point taken up by the catheter) on rates of symptomatic VTE in patients with a PICC and identify the optimal ratio cut-off point to reduce rates of this adverse event.

Method:

Design

This was a prospective cohort study, set in a large, metropolitan teaching hospital in Adelaide, Australia. This 680 bed tertiary health care service operates a nurse-led PICC service within the Radiology Department. At the hospital where the study was set, PICCs are predominantly inserted to facilitate out of hospital care. Patients may have both PICC insertion and treatment entirely as outpatients (this is common for patients with malignancies who require chemotherapy). An equal number have a PICC inserted so that they are able to be discharged home where they complete treatment (usually intravenous antibiotics). A smaller proportion of patients have a PICC inserted and are hospitalised for their entire treatment.

A Registered Nurse with nearly 10 years experience as a PICC nurse was the sole inserter in the study. Participants were recruited from the waiting area of the Radiology Department between May and December 2013.

Participants

Inclusion criteria

All participants over the age of 18 scheduled to have a PICC inserted in the Radiology Department of the hospital by the PICC nurse as part of their ongoing medical care were invited to take part in the study.

Exclusion criteria

Participants were excluded if they were unable to provide informed consent due to cognitive barriers (diagnosis of dementia; uncontrolled mental illness or deficits) or were unable to read, write or understand English.

Power analysis

A power analysis was conducted using a logistic regression model based on an expected increased odds of VTE (odds ratio 3.00) with patients who had a high catheter to vein ratio compared to a low/ average ratio (1 standard deviation difference). This analysis was calculated using PASS 11 (NCSS, Utah, USA) and determined that to achieve 80% power and 0.05 significance level 136 participants were required. An extra 20% were recruited to allow for loss to follow up.

Primary outcome measure

The primary outcome measure was VTE, which included symptomatic thrombus that occurred in the superficial (SVT) or deep venous system (DVT) or pulmonary embolism (PE) post PICC insertion. SVT was defined as occlusive thrombus in a superficial vein in which the PICC was inserted (basilic or cephalic veins). DVT included occlusive thrombus in the vein the PICC was inserted (if brachial) or if it extended into adjacent deep vasculature (axillary or subclavian veins). All cases were confirmed radiologically after clinical signs and symptoms triggered diagnostic testing.

Procedure

The PICC inserter used ultrasound to measure the anteroposterior diameter of the relevant vein (basilic, brachial or cephalic) at the insertion point. No tourniquet was used during the measurement process to reflect the natural vein diameter. The measurement was conducted using inbuilt callipers in a SonoSite™ S-Series ultrasound (SonoSite, Bothell, WA). The reliability of the PICC inserter for vein measurement had been established previously (Sharp et al., 2013). The largest vein was chosen for PICC insertion unless contraindicated (presence of an automated external defibrillator, previous upper extremity DVT, poor skin integrity or lymph clearance on the same side). Whilst the PICC used in the study had the capability for reverse taper, this feature was not used in the study. An allowance was made when the trim length was calculated to ensure that the reverse taper part of the catheter lay outside of the vein. The catheter was

trimmed using a scalpel. All PICCs were inserted using the modified Seldinger technique (MST). The tip was verified at the superior vena cava/ right atrium junction using fluoroscopy. An AngioDynamics proximal valve power-injectable PICC was used in the study (Xcela). This PICC does not have an anti-thrombotic coating. All PICCs were flushed using normal saline 0.9%. The size of the PICC inserted (4, 5 or 6 French) was determined by the medical/infusion needs of the patient in consultation with their treating physician. PICC diameter was obtained from manufacturer information (outer diameter).

Participants were included only once in the study and followed up at eight weeks post insertion. This follow-up period is based on research that determined most adverse events associated with a PICC occurred within eight weeks (Jennings et al., 2011, Sperry et al., 2012). Participant unit record numbers were used to access hospital information systems for Doppler ultrasound reports performed on the same upper extremity as where the PICC was inserted. These were performed by Sonographers and triggered by symptoms of thrombus (oedema, pain or clinical suspicion). Cases of PE were included when symptomatic and verified using spiral computed tomography (CT) angiography scan post PICC insertion.

Medical records were hand searched to obtain participant co-morbidities, clinical treatment and PICC removal dates. The hospital where the study was set services a wide geographical area including rural and remote areas and as such some participants were discharged to other health care services. If the participant was discharged with the PICC and not managed by a medical unit within the hospital, participants were interviewed via telephone to determine adverse events, medications infused and the PICC removal date. When the PICC required exchange due to malposition, occlusion or need for increased lumens due to change in medical treatment; the exchange date was coded as the removal date.

Ethics

The Human Research Ethics Committees of the university and the hospital where the study was conducted provided approval prior to the study's commencement (Protocol no. 31301 and 130217 respectively). Potential participants were given an information sheet by the researcher, allowed time to read it and were encouraged to ask questions. After this, participants were invited to take part and written consent was obtained.

Analysis

Descriptive statistics were used to present information about the study population in the form of simple percentages. Catheter to vein ratios was determined by dividing PICC diameter by vein diameter and multiplying by 100 to generate a percentage. The association between the catheter to vein ratio as well as

the influence of comorbidities and medication on the risk of VTE were analysed using a log binomial generalized linear model. When this would not converge, robust Poisson regression or exact logistic regression models were used (Stata 11 statistical package, Stata Corp., College Station, Texas, USA).

Receiver operator characteristic (ROC) analysis was used to plot the sensitivity and specificity of each ratio measurement using MedCalc for Windows, version 12.5 (MedCalc Software, Ostend, Belgium). The area under the curve (AUC) and Youden's index (sensitivity + specificity -1) were determined to identify the ideal catheter to vein ratio cut off point with the aim to maximize sensitivity and specificity. All results with $p<0.05$ were considered statistically significant. A VTE rate per 1000 PICC days was generated by dividing the VTE rate by the number of days the PICC was inserted which was then multiplied by 1000.

Results

Study population

Of those assessed for eligibility, 59 declined to take part and 47 were unable to consent (confusion, low Glasgow Coma Scale score or inability to read, write or understand English). Of the participants recruited, 27 were lost to follow up at eight weeks (13 died – which was not PICC related and 14 were transferred to another facility and were unable to be contacted via telephone). The study population retained for analysis was 136 participants (figure 1).

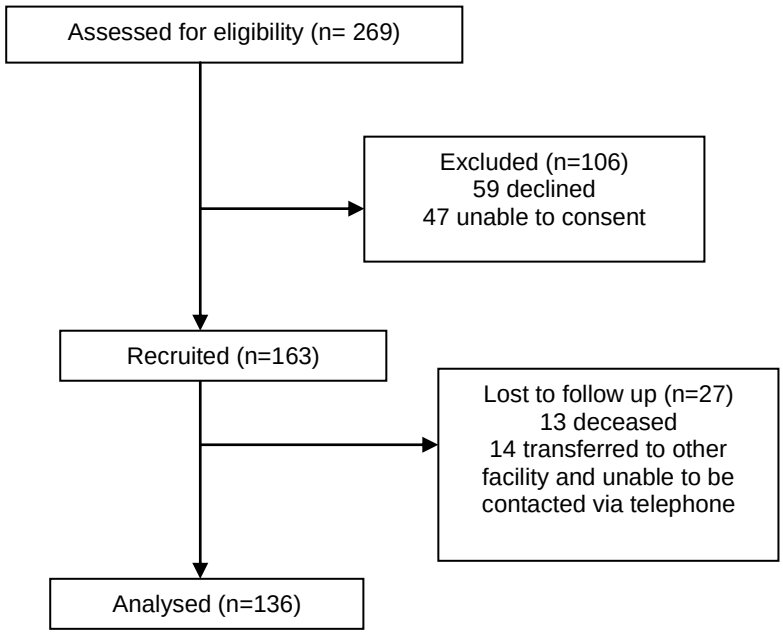

Figure 1: Study flow diagram

Most participants were managed by a hospital based treatment unit, 16 participants were discharged with a PICC and managed by other health care organisations. These participants were interviewed via telephone

to determine adverse events, medications infused and the PICC removal date. None of the participants followed up by telephone described symptoms that could indicate a VTE (upper arm pain, oedema or shortness of breath) or further investigations that could imply a clinical suspicion of this adverse event. At PICC insertion a third of participants were outpatients, of these most were receiving treatment for a malignancy (69% a solid tumour and 27% a haematological condition). Of the participants who were in-patients when they received a PICC, 63% were discharged after insertion to finish treatment at home (44% of the total sample). Only a quarter (n=34) of participants had a PICC inserted and completed their treatment in an acute care facility.

Clinical characteristics of the participants are displayed in Table 1. There were similar numbers of men and women included in the sample. Most participants had a malignancy or infection primary diagnosis (50% and 44% respectively) and were independent in mobility (68%). Many participants did not receive prophylactic subcutaneous unfractioned or low-molecular-weight heparin (62%). Prophylactic subcutaneous anticoagulants are not usually prescribed for patients receiving outpatient therapy at the hospital where the study was set, and most participants received a PICC as an outpatient or were discharged after PICC insertion. None of the patient factors analysed were associated with increased risk of VTE (table 1). Only one participant who developed a VTE had a previous history of a thrombotic event which was a DVT in a lower extremity.

Characteristic		Venous thromboembolism					
		Yes (n=4)	No (n=132)	Total (n=136)	Univariate analysis		
		n (%)	n (%)	n (%)	RR/OR	95% CI	Sig[a]
Gender	Male	2 (50)	72 (55)	74 (54)	0.838	0.122-5.776	0.857
	Female	2 (50)	60 (45)	62 (46)			
Age (years)					0.998 [b]	0.936-1.064	0.949
	19-45	1 (25)	27 (20)	28 (20)			
	46-65	1 (25)	66 (50)	67 (49)			
	66-79	2 (50)	30 (23)	32 (24)			
	80+	0 (0)	9 (7)	9 (7)			
Treatment organisation [c]							
	OPD	2 (50)	40 (30)	42 (31)	1.000		
	Discharged with PICC	1 (25)	59 (45)	60 (44)	1.619	0.153-17.104	0.689
	Inpatient	1 (25)	33 (25)	34 (25)	0.567	0.037- 8.773	0.684
BMI [d]					0.910 [b]	0.890-1.120	0.980
	<18	1 (25)	8 (6)	9 (7)			
	19-24	1 (25)	50 (38)	51 (38)			
	25-30	0 (0)	36 (27)	36 (27)			
	>31	2 (50)	38 (29)	40 (30)			
Diagnosis[e]	Solid tumour	0 (0)	35 (27)	35 (26)	5.490	0.672-∞	0.120
	Haematological cancer	4 (100)	29 (22)	33 (24)			
	Infection	0 (0)	60 (45)	60 (44)			
	Other	0 (0)	8 (6)	8 (6)			
Mobility					0.697 [f]	0.075-6.511	0.752
	Independent	3 (75)	89 (67)	92 (68)			
	Used assistive device	1 (25)	32 (24)	33 (24)			
	Chair bound	0 (0)	5 (4)	5 (4)			
	Bed bound	0 (0)	6 (5)	6 (4)			
CVA	Y	1 (25)	1 (1)	2 (2)	37.961 [g]	0.418-3448.298	0.116
	N	3 (75)	131 (99)	134 (98)			
PMX-VTE (PE+DVT)	Y	1 (25)	21 (16)	22 (16)	1.727	0.188- 15.851	0.629
	N	3 (75)	111 (84)	114 (84)			
PMX-PE	Y	0 (0)	13 (10)	13 (10)	1.783 [g]	0-15.153	1.000
	N	4 (100)	119 (90)	123 (90)			
PMX-DVT	Y	1 (25)	11 (8)	12 (9)	3.444	0.388-30.600	0.267
	N	3 (75)	121 (92)	124 (91)			
DM	Y	0 (0)	31 (23)	31 (23)	0.629 [g]	0-5.179	0.701
	N	4 (100)	101 (77)	105 (77)			
Recent Surgery	Y	1 (25)	51 (39)	52 (38)	0.538	0.058-5.041	0.587
	N	3 (75)	81 (61)	84 (62)			
Anti-coagulant							
oral	Y	0 (0)	12 (9)	12 (9)	1.950 [g]	0-16.658	1.000
	N	4 (100)	120 (91)	124 (91)			
Subcutaneous (prophylactic)	Y	0 (0)	52 (39)	52 (38)	0.297 [g]	0-2.438	0.283
	N	4 (100)	80 (61)	84 (62)			
APA	Y	0 (0)	18 (14)	18 (13)	1.227 [g]	0-10.272	1.000
	N	4 (100)	114 (86)	118 (87)			
Tobacco[h]	Y	0 (0)	38 (29)	38 (28)	0.477 [g]	0-3.916	0.530
	N	4 (100)	94 (71)	98 (72)			

[a] Based on log binomial generalized linear model unless otherwise stated; CI=confidence interval; RR=relative risk; OR=odds ratio

[b] Analysed as a continuous variable

[c] Participants discharged home with a PICC to complete treatment and those who completed treatment in an acute care facility compared to those who solely received outpatient treatment; OPD=outpatient department treatment

[d] BMI= body mass index (there was one missing value)

[e] analysed as malignancy (solid tumour and haematological malignancy) versus none; ∞ = infinity

[f] Analysed as independent vs. assisted, chair or bedfast; CVA=cerebral vascular accident; PMX-DVT =Previous history of deep vein thrombosis (upper or lower extremity); PMX-PE= Previous history pulmonary embolism; DM= Diabetes Mellitus; Recent surgery = within 8 weeks of PICC insertion

[g] Odds ratio - based on exact logistic regression; Surgery= >1 hour, within 8 weeks of insertion; APA= antiplatelet agents

[h] current or previous smoker

PICC insertion factors

The basilic vein on the right side was most often punctured for PICC insertion (Table 2). Few participants needed more than one attempt (8%) and the majority of participants had a single lumen PICC inserted (74%). The most common indication for PICC insertion was intravenous antibiotics (62%). Most participants had the PICC for up to 6 weeks (82%). At the 8-week follow up time 18% of participants still had the PICC in situ. The vein and arm used for PICC insertion, number of attempts or duration of time that the participants had the PICC were not associated with increased risk of VTE. Catheter size did have a large influence on risk - for each increase in French size there was 9 times increased risk of VTE.

Table 2: Insertion factors and risk of venous thromboembolism

Characteristic		Venous thromboembolism					
		Yes (n=4)	No (n=132)	Total (n=136)	Univariate analysis		
		n (%)	n (%)	n (%)	RR/OR	95% CI	Sig[a]
Arm	Left	1 (25)	50 (38)	51 (37)	0.556	0.059-5.200	0.606
	Right	3 (75)	82 (62)	85 (63)			
Vein	Basilic	2 (50)	83 (63)	85 (63)	1.00		
	Brachial	1(25)	32 (13)	33 (24)	2.36	0.226-24.680	0.473
	Cephalic	1(25)	17 (24)	18 (13)	1.29	0.120-13.731	0.834
Insertion attempts	1	3 (75)	122 (92)	125 (92)	3.78[b]	0.429-33.429	0.231
	2	1 (25)	9 (7)	10 (7)			
	3 +	0 (0)	1 (1)	1 (1)			
Catheter size (Fr) [c]	4	0 (0)	100 (76)	100 (74)	9.487	2.479-36.303	0.001
	5	2 (50)	28 (21)	30 (22)			
	6	2 (50)	4 (3)	6 (4)			
Days PICC in					0.995	0.980-1.011	0.554[d]
	≤7	1 (25)	33 (25)	34 (25)			
	8-21	3 (75)	27 (21)	30 (22)			
	22-42	0 (0)	48 (36)	48 (35)			
	43+	0 (0)	24 (18)	24 (18)			
Infusion [e]							
Bone marrow transplant		0 (0)	9 (7)	9 (7)	2.683[f]	0-23.416	1.000
Chemotherapy		4 (100)	59 (45)	63 (46)	6.384[f]	0.782-∞	0.087
Blood products		0 (0)	19 (14)	19 (14)	1.151[f]	0-9.620	1.000
Antibiotics		0 (0)	82 (62)	82 (62)	0.119[f]	0-0.969	0.046
TPN		0 (0)	4 (3)	4 (3)	6.501[f]	0-64.485	1.000

[a] Based on log binomial generalized linear model unless otherwise stated; CI=confidence interval; RR=relative risk; OR=odds ratio

[b] 1 attempt vs 2 or more

[c] Fr=French unit, Fr size corresponds to lumen number, 4Fr=1 lumen, 5Fr= 2 lumens, 6Fr=3 lumens

[d] Analysed as a continuous variable

[e] Participants often had more than one infusion type, analysed as yes versus no for that infusion type using exact logistic regression

[f] Odds ratio - based on exact logistic regression ; ∞ = infinity.

Cases of VTE

There were four cases of symptomatic VTE (2.9%). This equated to 0.83 VTE per 1000 PICC days. These comprised two DVTs, one SVT and one PE. One participant with a PE was also symptomatic of DVT (pain and swelling) in the arm in which the PICC was placed, but the veins of the upper arm were not assessed by a Sonographer to confirm diagnosis. This was due to the presence of a thick dressing covering that area (because of a skin reaction) which was not removed by the Sonographer. This was counted as a case of PE

only. The median time from PICC insertion to VTE diagnosis was 17 days (range 10-22 days). Equal numbers of males and females developed a VTE; half were obese and most were independent in mobility (Table 1). All participants who developed a VTE had a haematological cancer diagnosis, a PICC with two or more lumens and received chemotherapy.

Catheter to vein ratio and risk of VTE

Most participant or insertion variables were not associated with VTE hence they were not adjusted for in the main model that analysed for risk of VTE associated with the catheter to vein ratio (table 1 and 2). Although the use of intravenous antibiotics was associated with reduced risk of VTE it was not adjusted for in the main model to avoid over-fitting. Further, adjustment was not made for catheter size as it was already part of the ratio.

Nearly half of the sample had a catheter to vein ratio of less than one third (table 3). There was little difference in risk when comparing the lowest ratio category (18-33%) to the midrange category (34-50%). This was a relative risk (RR) of 1.264 (95% CI 0.809-19.741, p=0.867). There was nearly eight times increased risk of VTE for those with a ratio of more than 50% compared to those with less than 50% (RR=7.5, 95% CI 1.13-49.62, p=0.037).

Table 3: Catheter to vein ratio and cases of venous thromboembolism

Characteristic		Venous thromboembolism					
		Yes (n=4)	No (n=132)	Total (n=136)	RR	95% CI	Sig.*
		n (%)	n (%)	n (%)			
Catheter to vein ratio	18-33%	1 (25)	66 (50)	67 (49)	1.04	0.99-1.09	0.097
	34-45%	0 (0)	44 (33)	44 (33)			
	46-70%	3 (75)	18 (14)	21 (15)			
	>71%	0 (0)	4 (3)	4 (3)			

*Based on log binomial generalized linear model (analysed as a continuous variable); CI=confidence interval; RR=relative risk

Catheter to vein ratio ROC analysis

ROC analysis was undertaken comparing 100-specificity to sensitivity (figure 2). It was determined that a 45% catheter to vein ratio was the ideal cut off point to maximise sensitivity and specificity (AUC 0.761; 95% CI 0.681- 0.830; sensitivity 75 and specificity 83). Further, at a 45% ratio the Youden's index was 0.58, either side of this cut-off, the index fell sharply (>30% = 0.11; >46% = 0.34).

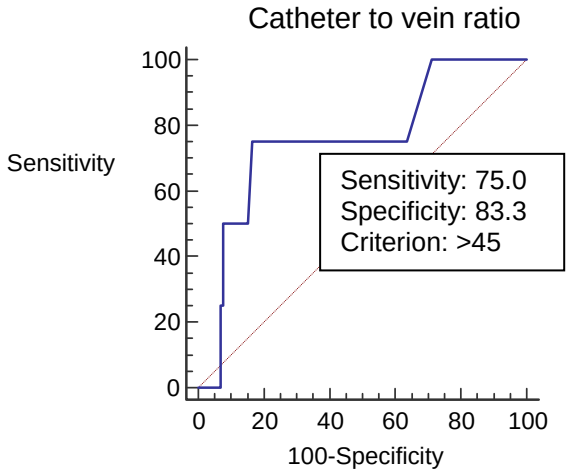

Figure 2: receiver operator characteristic analysis identifying the optimal catheter to vein ratio to reduce the risk of venous thromboembolism

Once the optimal cut off point was determined, the catheter to vein ratio was dichotomised at this point and the log binomial regression model re-run. It was found that participants with a ratio >45% were 13 times more likely to suffer VTE than those with a ratio lower than this (RR 13, p=0.022; CI 1.445-122.788).

Discussion

Catheter to vein ratio

To our knowledge this is the first study to analyse the relationship between the catheter to vein ratio and VTE as well as set out to determine parameters to guide clinical practice. Previous research has set minimum vein sizes for PICC insertion which equate to a 50% catheter to vein ratio (Meyer, 2011; Chopra et al., 2014). The present study did find an eight fold increased risk of VTE when a catheter to vein ratio of more than 50% was compared to one less than this measurement, which supports previous research. However, the risk was higher when analysis was performed using a 45% cut-off point. The present study suggests that the catheter to vein ratio should be less than or equal to 45% for PICC insertion, a ratio greater than this increased the risk of VTE by a factor of 13. Further, the 45% ratio cut off point demonstrated high sensitivity and specificity. There was no difference in risk when lower ratios were included in analysis, indicating that the use of less than 33% catheter to vein ratio may not be necessary. The suggested minimum vein sizes required to achieve a ratio less than or equal to 45% for commonly used PICC sizes used in adult populations are shown in table 4. Anecdotally, it appears many clinicians follow a maximum 50% catheter to vein ratio for PICC insertion in clinical practice. In reality the difference in risk between using a <45% versus <50% ratio is probably marginal, and would need to be confirmed with a larger study.

Table 4: Recommended minimum vein diameter for PICC insertion

French size	PICC outer diameter (mm)	Minimum vein diameter (mm)
4	1.332	3
5	1.665	3.75
6	1.998	4.5

The present study found just four cases of symptomatic VTE in the sample of 136 patients undergoing PICC insertion. This was an overall symptomatic VTE rate of 2.9% (0.83 VTE per 1000 PICC days), which is similar to previous research in comparable populations (Liem et al., 2012; Leroyer et al., 2013; Chopra et al., 2014). The low number of events means that these results should be viewed with caution. Nonetheless, a strong association between the catheter to vein ratio and rates of VTE was found which is unlikely due to chance.

The low number of VTE cases may be due to the catheter to vein ratios of participants in the study; most did not have a ratio above 45% (82% had less than or equal to 45%). This is due to the clinical practice of the PICC nursing team, who strive to use the smallest catheter that meets the treatment needs of the patient. Single lumen 4 French PICCs are the default size unless a larger multi-lumen PICC is clinically indicated. Once the PICC request is received, the PICC nurse discusses the risks/benefits of the requested catheter size with the medical team when it does not appear to be clinically justified. This demonstrates the importance of including PICC inserters in clinical decision-making about appropriate device selection. A multi-disciplinary approach is needed which includes the specialist knowledge of PICC nurses as Medical Officers may not always incorporate risks associated with larger catheter size in clinical decision making (Chopra et al., 2013).

Cancer

The use of a maximum catheter to vein ratio appeared to reduce, but not completely remove, the risk of VTE for some participants in the present study. Although malignancy was not associated with increased risk of VTE in our study, larger PICCs were (which are primarily inserted for patients with malignancy at the hospital where the study is set). All of the participants who developed a VTE in our study had a haematological malignancy, either a 5 or 6 French PICC and were receiving chemotherapy. One participant who developed a VTE had a 30% catheter to vein ratio, indicating that some cancer patients may be at risk despite the use of a catheter to vein ratio protocol. Malignancy does increase the risk of VTE, regardless of the presence of a PICC (Chin et al., 2005; Chopra et al., 2014). One study in the Netherlands found nearly an eight-fold increase in risk of upper arm thrombosis for cancer patients without a central venous access device in place (Blom et al., 2005). Previous research which used maximum ratios between 40-50% for

patients requiring 6 French PICCs still found higher risk of VTE in patients with these PICCs compared to smaller catheters (Chopra et al., 2014). Since these larger catheters are often used in patients with malignancies this suggests that the use of a maximum catheter to vein ratio protocol may not be protective for some patients receiving cancer treatment.

DVT and SVT

This study included both superficial and deep vein thrombosis in the outcome measure. There is a paucity of studies analysing PICC associated SVT, but increasingly researchers are including this complication in VTE outcome measures (Periard et al., 2008; Itkin et al., 2014). SVT is uncomfortable for the patient, may result in removal of the device and can extend into deeper vasculature with resulting thromboembolic complications (Decousus et al., 2010; Kitchens, 2011). In the lower extremities, there is increasing evidence that rather than a benign issue, symptomatic SVT is closely associated with VTE and may be a marker of risk (Decousus et al., 2010; Roach et al., 2013). Further research is needed to determine whether treatment should be initiated for patients with a PICC who develop symptomatic SVT.

Limitations

Although adequately powered to detect an association between the catheter to vein ratio and the likelihood of a VTE, our study found only four cases of VTE, resulting in wide confidence intervals around the relative risk. Another important limitation is that all patients who developed a VTE in this study had a malignancy diagnosis requiring chemotherapy which may increase risk independently of the cancer diagnosis. Thus, the infusate itself could be a confounding variable; however, it is difficult to ascertain whether the chemotherapy agent could be an independent risk factor for VTE as the two variables are conflated.

Also, our method did not assess stenosis proximal to the insertion point and venous diameter was only measured once (as veins are dynamic structures diameter may change over time). Some may disagree with the inclusion of thrombus in the superficial venous system in the outcome measure as the clinical significance of this adverse event is still unknown. Further, this study included only symptomatic thrombus in the outcome measure; post-insertional screening was not conducted on all participants post PICC insertion to capture asymptomatic thrombus. Thus, cases of asymptomatic thrombus which is reported to be higher than symptomatic were not recorded. Lastly, staging of patients with a malignancy was not recorded and hence risk associated with varied cancer staging (including presence of metastases) was not performed.

Conclusion

PICCs are an integral part of modern healthcare due to low insertion costs and the facilitation of out of hospital care. However, these devices are associated with adverse events including VTE. It was found that a 45% catheter to vein ratio was the optimal cut off with high sensitivity and specificity to reduce the risk of VTE, although further research is needed to confirm these results. It appears that the use of less than a 45% catheter to vein ratio may reduce the burden of this adverse event for patients who require a PICC. This study reiterates the importance of a complete vasculature assessment using ultrasound to identify an appropriately sized vein to reduce the risk of VTE.

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