BMJ Open

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-058866
Article Type:	Original research
Date Submitted by the Author:	01-Nov-2021
Complete List of Authors:	Bayoumi, Mohammad; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), van Rens, Roland; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Shaltout, Deena; Hamad Medical Corporation, Medical Education Department, CHANDRA, PREM; Hamad Medical Corporation, Medical Research Center, Elmalik, Einas; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Hammoudeh, Samer; Hamad Medical Corporation, Medical Research Center (MRC),
Keywords:	NEONATOLOGY, Neonatal intensive & critical care < INTENSIVE & CRITICAL CARE, PERINATOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Mohammad A. A. Bayoumi[1], Matheus van Rens[1], Deena A. D. A. Shaltout[2], Prem Chandra[3], Einas E. Elmalik[1], Samer Hammoudeh[3]

[1] Neonatal Intensive Care Unit, Women's Wellness and Research Center, Hamad Medical Corporation, Doha, Qatar
[2] Department of Medical Education, Hamad Medical Corporation, Doha, Qatar
[3] Medical Research Center, Hamad Medical Corporation, Doha, Qatar

Author's emails:
Mohammad A. A. Bayoumi: moh.abdelwahab@hotmail.com
Matheus van Rens: rolandvanrens@gmail.com
Prem Chandra: pchandra@hamad.qa
Deena A. D. A. Shaltout: dshaltout@hamad.qa
Einas E. Elmalik: einas_e@yahoo.com
Samer Hammoudeh: shammoudeh@hamad.qa

Corresponding Author's Contact Details:
Dr Mohammad A. A. Bayoumi
Neonatal Intensive Care Unit, Women's Wellness and Research Center, Hamad Medical Corporation, P.O. Box: 3050, Doha, Qatar
Fax Number: +97444439571
Mobile Number: +97477671584
Email: moh.abdelwahab@hotmail.com

Abstract:

Background: Central venous access is essential in Neonatal Intensive Care Units (NICUs). We aimed to compare Peripherally Inserted Central Catheters (PICCs) with non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) including femoral, jugular, brachiocephalic and subclavian lines in our NICU.

Methods: A retrospective study (n=1333) was designed to compare between 1264 PICCs and 69 non-tunnelled USG-CVCs from January 2016 to December 2018. A successful catheter insertion means a catheter inserted into a proper central venous position that can be used with its tip located either in the superior or inferior vena cava.

Results: The overall success rate was 88.4% in the USG-CVCs (61/69) compared to 90% in the PICCs (1137/1264) group (P=0.68). However, the first prick success rate was 69.4% in USG-CVCs (43/69) compared to 63.6% in the PICCs (796/1264) group. Leaking and Central Line-Associated Blood Stream Infection (CLABSI) were significantly higher in the USG-CVC group compared to the PICC group (Leaking 16.4% vs. 2.3%, P=0.0001) (CLABSI 8.2% vs. 3.1%, P=0.03). CLABSI rates in the PICC group were 1.75 per 1000 catheter days in 2016 and 3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the USG-CVCs. USG-CVCs had to be removed more often before completion of their intended use due to catheter-related complications (52.5%) compared to PICCs (29.9%), P=0.0001. In 2018, we did not have any non-tunnelled USG-CVCs insertions in our NICU.

Conclusions: The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Keywords:

Neonatal Intensive Care Unit, Neonate, Vascular Access, Peripherally Inserted Central Catheter, Non-Tunneled Ultrasound-Guided Central Venous Catheters.

Strengths and limitations of this study:

- This is an observational study including a large sample of 1333 neonates.
- The study provides information on the insertion success rates and complications of peripherally inserted central catheters and non-tunnelled ultrasound guided central venous catheters in neonates.
- It is based on retrospective analyses of collected data.

What is known about the subject?

- Peripherally Inserted Central Catheters are increasingly used in NICU, especially for extremely premature infants to administer drugs and fluids.
- Non-tunnelled ultrasound-guided Central Venous Catheters including femoral, jugular, brachiocephalic and subclavian lines have limited indications in neonates.

What does this study add?

- Proper central venous device selection and timing, early Peripherally Inserted Central Catheter insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Introduction:

Vascular access is a crucial part of providing care for neonates (1) and is considered the most frequently used invasive procedure (2, 3). It has been reported that up to 33% of neonates admitted to intensive care units require a central venous catheter insertion during their NICU stay (4).

Peripherally Inserted Central Catheters (PICCs) were described for the first time by Shaw in 1973. Since then, they have been used extensively due to their features (5). PICC insertion by direct superficial peripheral vein puncture offers long-term venous access for both term and preterm neonates and is often indicated in NICU for parental nutrition, long-term IV medications, antibiotic therapy, and vesicant drug administration (1, 6).

Non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) are inserted in neonates in special circumstances e.g. central venous pressure monitoring, blood withdrawal, hemodialysis, and for all other infusions and medications when PICC insertion fails (7). They are inserted in the internal jugular, brachiocephalic, subclavian, and femoral veins under ultrasound guidance (5, 8-10).

Both PICCs and non-tunnelled USG-CVCs have risks associated with their usage. Immediate risks include injury to local structures, accidental arterial puncture, phlebitis at the insertion site, air embolism, hematoma, arrhythmia, and catheter damage and malposition. Late complications include infection, occlusion, thrombosis, infiltration, extravasation, and catheter migration (11-

13). Infection, thrombosis, embolization, hydrocephalus, are complications reported in premature babies receiving central venous lines (6).

Umbilical venous catheters are commonly used in neonates. Broviac and Hickman's catheters are vascular access devices that provide central venous access and are rarely used in neonates. These devices are not included in our study.

This study aimed to compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU between 2016 and 2018.

Methods:

This single-centre retrospective study was conducted in the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation (HMC), Doha, Qatar. WWRC is the main specialist hub for women and newborns health services in Qatar with more than 18000 deliveries per year. The NICU in WWRC is a level III mainly medical unit with 112 beds and more than 2000 admissions per year with limited congenital cardiac or surgery cases.

A total of 1333 cases were evaluated in this study. This includes 1264 babies who had PICC insertion and 69 who had non-tunnelled USG-CVC insertion. Related information for all cases between January 2016 and December 2018 was collected from the electronic medical system at the NICU. The study was approved by the Institutional Review Board (IRB) at HMC before the study procedures commenced (MRC-01-18-151).

A fully dedicated PICC insertion team was launched in January 2017. The PICC team has been expanded over time to include 15 neonatologist physicians, one neonatal nurse practitioner as well as 7 NICU Nurses. The team was trained in central line simulation workshops to insert PICC by the catheter-over-needle technique and the modified Seldinger technique (MST) (14, 15). The central line simulation workshop is a full-day workshop that was founded by the neonatal simulation team and is accredited by the Department of Healthcare Professions (DHP) in the Ministry of Public Health (MOPH) with a total of 7 Continuous Professional Development (CPD) hours both category I (1/7) and category III (6/7). The PICC team works in harmony and collaboration with 30 well-trained NICU nurses who are members of the Neonatal Specialized Nursing (NSN) Team. The NSN determines the patient's eligibility, takes care of the central line maintenance using transparent semipermeable dressing, enters the data in the electronic database, and gets the blood samples. There is no difference in the central line type of care, frequency or personnel in all types of catheters. In addition to their role in central line insertion and maintenance, the NSN team attends high-risk deliveries and play a pivotal role in neonatal transportation.

In our NICU, the indications for PICC insertions are the birth weight of < 1500 gm, the requirement of IV fluids for > 5 days, the requirement of IV medications for > 7 days, the requirement of hyperosmolar IV fluid therapy > 700 mosmol/L, and the requirement of > 3 Peripheral Intravenous Catheters (PIVC) insertions in the last 24 hours (16). A successful catheter insertion means a catheter inserted into a proper central venous position that can be used with its tip located either in the superior or inferior vena cava. As per our institutional guideline,

2 pricks are allowed per operator with a maximum of 3 in difficult lines. After 3 unsuccessful pricks, the procedure should be terminated.

Figure 1 shows the 3 types of PICCs available in our NICU; (NutriLine 2 Fr; Vygon), (PremiCath 1 Fr; Vygon), and (PremiStar 1 Fr; Vygon). The most common veins used for PICC insertions are the great saphenous vein, small saphenous vein, posterior tibial vein, antecubital vein, cephalic vein, basilic vein, and ulnar vein. Figure 2 shows the non-tunnelled CVC available in our unit which is (MultiCath 2; 4.5 Fr; Vygon). The most common veins used for USG-CVC insertions are the internal jugular vein, femoral vein, brachiocephalic vein, and subclavian vein.

In our practice, non-tunnelled USG-CVC was used only when PICC insertion has failed by 2-3 operators; 2 pricks for each. USG-CVCs were inserted either by the pediatric surgeon or the pediatric anaesthetist on-call physician under US guidance. Currently, we use the handheld wireless probe-type ultrasound scanner machine to guide the catheter insertion and for the catheter tip location.

We followed the Centers for Disease Control and Prevention (CDC) definition for central line-associated bloodstream infection (CLABSI) and CLABSI rate. CLABSI is defined as a laboratory-confirmed bloodstream infection where an eligible bloodstream infection (BSI) organism is identified, and an eligible central line is present on the laboratory-confirmed bloodstream infection (LCBI) date of the event (DOE) or the day before. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility. CLABSI rate is the total number of CLABSI divided by the total number of device days 1000 (17, 18).

The differential time to positivity (DTP) is defined as a difference in time to positivity of ≥ 2 h between peripheral blood culture and a CVC blood culture (peripheral DTP) or between 2 CVC blood cultures from different lumens of a multi-lumen catheter (CVC DTP) (19). Due to its limitation reported in the literature, our unit does not prefer to use the differential time to positivity (DTP) for the diagnosis of CLABSI (20).
The authors designed an electronic system-based data collection sheet to collect all catheter-related parameters in the 2 groups.

Statistical Analysis:
Descriptive statistics were used to summarize and determine the sample characteristics and distribution of participants' data. The normally distributed data and results were reported with mean and standard deviation (SD); the remaining results were reported with median and inter-quartile range (IQR). Categorical data were summarized using frequencies and proportions. Associations between two or more qualitative data variables were assessed using Chi-square ($\chi 2$) test or Fisher Exact test as appropriate. Quantitative data between the two independent groups (USG-CVC and PICC) were analyzed using unpaired t (for normally distributed data) or Mann Whitney U test (for skewed or non-normally distributed data) as appropriate. Univariate and multivariate logistic regression analysis was applied to determine and assess the potential factors and predictors associated with the catheter insertion success rate adjusted for potential factors and predictors such as catheter types, gestational age, birth weight, the reason for catheter insertion, side of the body, site of insertion and number of pricks. For multivariate logistic

regression models, predictor variables were included considering both statistical and clinical significance. The results of logistic regression analysis were presented as odds ratios (OR) with corresponding 95% confidence intervals (CI). Thereafter, we used the receiver operating characteristic curve (ROC) to evaluate the discriminative ability (predictive accuracy of the developed logistic regression model) of potentially significant variables associated with catheter insertion success rate. Box plots were constructed depicting the distribution of gestational age and birth weight across two catheter types. All P values presented were two-tailed, and P values <0.05 were considered statistically significant. All statistical analyses were performed using statistical packages SPSS version 27.0 (Armonk, NY: IBM Corp) and Epi-info (Centers for Disease Control and Prevention, Atlanta, GA) software.

Results:

Among the three years that this study covered, the usage of USG-CVC has progressively declined to zero in 2018, on which the catheter insertion success rate increased to 97%. Shown in table 1 are the distribution of patients and catheter-related variables associated with the types of catheters. When USG-CVC was compared to PICC about gestational age, the former was significantly higher (33.88±6.34 vs. 29.32±4.03, P=0.0001). Birth weight was also significantly higher among USG-CVC compared to PICC (2161.25±1140.26 vs. 1234.57±624.90, respectively, P=0.0001). Figure 3 shows the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types. The duration of catheter insertion was however not significant (USG-CVC 11.69±9.23, PICC 14.57±12.56, P=0.14). Further comparisons between USG-CVC and PICC on several parameters. PICC had a higher success rate (90% vs. 88.4%), however, the difference did not reach statistical significance.

Table 1: Distribution of patients' profiles and catheter-related parameters and their association with the catheter types

Variables	Total n=1333	USG-CVC 69 (5.2%)	PICC 1264 (94.8%)	P-value
Year				0.001
2016	376 (28.2)	42 (60.9)	334 (26.4)	
2017	507 (38)	27 (39.1)	480 (38)	
2018	450 (33.8)	0 (0)	450 (35.6)	
Side of the body				0.002
Left	498 (41.1)	14 (22.6)	484 (42.1)	
Right	715 (58.9)	48 (77.4)	667 (57.9)	
Site of Insertion				0.001
Upper Extremities	360 (29.5)	37 (53.6)	323 (28)	
Lower Extremities	861 (70.5)	32 (46.4)	829 (72)	
Number of Pricks				0.001
First Prick	839 (63.9)	43 (69.4)	796 (63.6)	
Second Prick	305 (23.2)	8 (12.9)	297 (23.7)	
Third Prick	145 (11)	6 (9.7)	139 (11.1)	
Fourth Prick	22 (1.7)	4 (6.5)	18 (1.4)	
Fifth Prick	1 (0.1)	0 (0)	1 (0.1)	
Sixth Prick	2 (0.2)	1 (1.6)	1 (0.1)	
Reason for Insertion				0.47
Difficult IV Insertion	8 (0.6)	0 (0)	8 (0.6)	

Hypoglycemia	10 (0.8)	0 (0)	10 (0.8)	
Long term IV fluid therapy	1286 (96.6)	68 (100)	1218 (96.4)	
Long term IV medication therapy	27 (2)	0 (0)	27 (2.1)	
Catheter insertion Success Rate				0.68
Successful	1198 (89.9)	61 (88.4)	1137 (90)	
Not Successful	135 (10.1)	8 (11.6)	127 (10)	
Reason for Removal				
CLABSI	40 (3.4)	5 (8.2)	35 (3.1)	0.031
Leaking	36 (3)	10 (16.4)	26 (2.3)	0.001
Accidental Removal	8 (0.7)	1 (1.6)	7 (0.6)	0.40
Broken Catheter	7 (0.6)	0 (0)	7 (0.6)	0.69
Local redness and swelling	104 (8.7)	5 (8.2)	99 (8.8)	0.88
Occlusion	42 (3.5)	0 (0)	42 (3.7)	0.13
Malposition	13 (1.1)	0 (0)	13 (1.1)	0.50
Elective	833 (69.9)	29 (47.5)	804 (71.1)	0.001
Death	39 (3.3)	5 (8.2)	34 (3)	0.03
Phlebitis	70 (5.9)	6 (9.8)	64 (5.7)	0.18
Gestational Age (weeks), Mean ±SD	29.55±4.30	33.88±6.34	29.32±4.03	0.001
Median (IQR)	29 (27, 31)	37 (26, 40)	29 (27, 31)	
Gestational Age				0.001
22 to 28 weeks	602 (45.2)	22 (31.9)	580 (45.9)	
> 28 to 32 weeks	490 (36.8)	4 (5.8)	486 (38.4)	
> 32 to 36 weeks	100 (7.5)	8 (11.6)	92 (7.3)	
> 36 weeks	141 (10.6)	35 (50.7)	106 (8.4)	
Birth Weight (gm), Mean ±SD	1282.6±692.1	2161.4±1140.3	1234.6±624.9	0.001
Median (IQR)	1095 (850, 1400)	2530 (970, 3122)	1080 (840, 1370)	
Birth Weight				0.001
BW <=1 kg	561 (42.1)	21 (30.4)	540 (42.7)	
BW > 1 to 2 kg	618 (46.5)	10 (14.5)	608 (48.1)	
BW > 2 to 3 kg	87 (6.5)	16 (23.2)	71 (5.6)	
BW >3 kg	67 (5)	22 (31.9)	42 (3.6)	

This is a retrospective study design and for some parameters, the data values were incomplete due to the unavailability of the information in the patients' record files. All percentage (%) was computed using non-missing data values. IQR: Inter-Quartile range.

We performed univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with dichotomous outcome variable catheter types (USG-CVC and PICC), it was observed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal (elective vs non-elective), duration of gestation and birth weight were significantly associated with catheter types. The multivariate logistic regression analysis showed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal, and birth weight were remained significantly associated with catheter types adjusting other predictors and factors shown in table 2. The discriminative ability of the significant predictors (observed in multivariate analysis) in predictive catheter types were found to be good with an area under the ROC curve value of 0.927 (95% CI 0.90, 0.96), which indicates that this developed regression model demonstrated an excellent fit, Figure 4.

Table 2: Logistic regression analysis with potential factors and predictors associated with catheter types USG-CVC and PICC

Variables		Univariate analysis			Multivariate analysis		
	Catheter type- PICC, n (%)	Unadjusted Odds ratio (OR)	95% CI for OR	P-value	Adjusted Odds ratio (OR)	95% CI for OR	P-value
Year							
2016	334 (88.8)	1.0 (reference)			1.0 (reference)		
2017	480 (94.7)	2.24	1.35, 3.70	0.002	3.43	1.79, 6.54	0.001
2018	450 (100)	--	--	--	--	--	--
Side of the body							
Left	484 (97.2)	1.0 (reference)			1.0 (reference)		
Right	667 (93.3)	0.40	0.22, 0.74	0.003	0.34	0.17, 0.70	0.003
Site of Insertion							
Upper Extremities	323 (89.7)	1.0 (reference)			1.0 (reference)		
Lower Extremities	829 (96.3)	2.97	1.82, 4.85	0.001	3.39	1.81, 6.33	0.001
Number of Pricks							
One Prick	796 (94.9)	1.0 (reference)			1.0 (reference)		
Two Prick	297 (97.4)	2.01	0.93, 4.32	0.075	2.58	0.97, 6.86	0.058
≥ 3 Pricks	171 (90.5)	0.51	0.29, 0.91	0.023	0.39	0.16, 0.95	0.037
Reason for catheter insertion							
Long term IV fluid therapy	1218 (94.7)	1.0 (reference)			1.0 (reference)		
Others*	45 (100)	--	--	--	--	--	--
Catheter Insertion Success Rate							
Not Successful	127 (94.1)	1.0 (reference)	0.55, 2.51	0.679	1.0 (reference)	0.59, 2.46	0.569
Successful	1137 (94.9)	1.17			1.14		
Reasons for removal							
Non-Elective	327 (91.1)	1.0 (reference)			1.0 (reference)		
Elective	804 (96.5)	2.71	1.62, 4.56	0.001	2.16	1.16, 4.01	0.015
Gestational age (weeks) PICC vs USG-CVC	29.3 ± 4.1 vs 33.9 ± 6.3	0.82	0.78, 0.86	0.001	1.03	0.90, 1.17	0.715
Birth Weight (gm) PICC vs USG-CVC	1235.6 ± 624.9 vs 2161.4 ± 1140.3	0.98	0.98, 0.99	0.001	0.99	0.98, 0.99	0.001

Catheter types- USG-CVC was considered as the reference group; CI: Confidence interval
**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

CLABSI and Leaking were noted to be significantly higher in the USG-CVC group compared to the PICC group. CLABSI rate is defined as the total number of CLABSI divided by the total number of device days 1000 (17, 18). CLABSI rates in the PICC group were 1.75 in 2016 and

3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the non-tunnelled USG-CVCs. We did not have any USG-CVC inserted in 2018.

In the PICC group, 804 (71.1%) were removed electively after completion of therapy compared to 29 (47.5%) in the USG-CVC group. No significant difference was noted between the 2 groups regarding the other catheter-related complications. No serious or long term complications e.g cardiac arrhythmia, accidental arterial puncture, cardiac tamponade, pericardial or pleural effusion (21), was noted in both groups across the three years.

The results of univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with catheter insertion success rates are presented in Tables 3 and 4. Univariate results indicated that year of catheter insertion, birth weight and the number of pricks had a significant effect on the likelihood of catheter insertion success rates. In patients who had two pricks (unadjusted OR 0.03; 95% CI 0.01, 0.07, P=0.028) and ≥3 pricks (unadjusted OR 0.01; 95% CI 0.01, 0.03, P=0.013) were significantly associated with a decreased likelihood of catheter insertion success rates compared to patients who had one prick. In addition, it was noted that catheter type PICC was associated with a higher rate of catheter insertion success rates, however, this difference was statistically insignificant (P=0.679).

Table 3: Univariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate, n (%)	Unadjusted odds ratio (OR)	95% CI for OR	P-value
Catheter Types				
USG-CVC	61 (88.4)	1.0 (refernce)		
PICC	1137 (90)	1.17	0.55, 2.51	0.679
Year				
2016	309 (81.7)	2.0 (refernce)		
2017	450 (88.6)	1.73	1.18, 2.52	0.004
2018	439 (97.6)	8.91	4.64, 17.12	0.001
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.01	0.96, 1.04	0.954
Birth Weight (g)	1270.1 ± 677.5 vs 1394.2 ± 803.3	0.98	0.98, 0.99	0.045
Reason for catheter insertion				
Long term IV fluid therapy	1156 (89.9)	2.0 (refernce)		
Others*	42 (93.3)	1.57	0.48, 1.51	0.453
Side of the body				
Left	491 (98.6)	2.0 (refernce)		
Right	706 (98.7)	1.12	0.41, 3.03	0.826
Site of Insertion				
Upper Extremities	353 (98.1)	2.0 (refernce)		

Lower Extremities	845 (98.1)	1.05	0.43, 2.57	0.920
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.03	0.01, 0.07	0.028
≥ 3 Pricks	121 (63.7)	0.01	0.01, 0.03	0.013

CI: Confidence interval

**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

The multivariate logistic regression analysis showed that duration of gestation (weeks) and the number of pricks were remained significantly (P<0.05) associated with the catheter insertion success rate after controlling and adjusting potential factors and predictors as shown in Table 4. The higher catheter insertion success rates were associated with increasing gestational age (adjusted OR 1.23; 95% CI 1.03, 1.44, P=0.015). Whereas, in patients who had two pricks (adjusted OR 0.07; 95% CI 0.01, 0.57, P=0.014) and ≥3 pricks (adjusted OR 0.02; 95% CI 0.01, 0.13, P=0.001) were significantly associated with a reduction in the likelihood of catheter insertion success rates when compared to patients who had one prick. Thereafter, we computed a prediction model to evaluate the discriminative ability of potentially significant predictors (observed in the developed multivariate logistic regression model) associated with catheter insertion success rates using ROC curve analysis. The value of area under the curve (AUC) observed was found to be 0.841 (95% CI 0.81, 0.87), which is indicating that this developed regression model demonstrated an excellent fit, Figure 5.

Table 4: Multivariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate N (%)	Adjusted odds ratio (OR)	95% CI for OR	P-value
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.23	1.03, 1.44	0.015
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.07	0.01, 0.57	0.014
≥ 3 Pricks	121 (63.7)	0.02	0.01, 0.13	0.001

CI: Confidence interval

Discussion:

The current study compared PICC to USG-CVC in a sample of cases from Qatar. The results also showed a progressive reduction in the usage of USG-CVC across the 3 years till reached 0% in 2018. This is due to the implementation of a PICC insertion team in early 2017 with a progressive build-up of the team skills (22). Since then, overall success and first prick rates have significantly increased. Reports of an overall success rate of 94% were indicated elsewhere (23). A systematic review highlighted the importance and necessity of a vascular access team in the

NICU, as it reflects positively on the rate of bloodstream infections (24). This was also confirmed in another study where the rate of infections was reduced by 50% after the establishment of a PICC team in the NICU (25).

Only 29 (47.5%) of our USG-CVC were electively removed after completion of therapy while the rest were removed due to death, phlebitis, CLABSI, or other catheter-related complications. In the PICC group, elective removal was noted to be significantly higher 804 (71.1%) than USG-CVC (P= 0.0001). The higher rate of CLABSI in USG-CVCs compared to PICCs is mainly related to the vulnerable insertion sites being close to infection or joint areas (26). Also, the higher rate of catheter leaking in USG-CVCs might be due to occlusions resulting from mechanical or postural factors, catheter malpositioning, or undesirable catheter-tip location. CLABSI and thrombosis might also lead to catheter leaking (27). Approximately one-third of PICCs were associated with complications in another study which is close to our PICC data (28).

Ragavan et al described the advantages of using PICCs inserted in the cubital veins as to have a reduced complication incidence rate, as well as maintenance rates in comparison to USG-CVCs inserted in the internal jugular vein. The authors concluded by recommending the usage of PICCs routinely when dealing with neonatal surgical patients (29). On the other hand, a recent study reported a 100% success rate of 30 preterm babies who underwent an ultrasound-guided brachio-cephalic central venous catheter insertion. No case of accidental arterial or pleural puncture was noted by the researchers (30). In another study involving neonates with femoral central venous catheterization (31), the overall success rate was 100% of neonates (n = 82/82), first attempt 63/74 (85%), second attempt 8/74 (11%), and third attempt 3/74 (4%). In another report, no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (7, 32).

The limitation of this study is being retrospective with potential risks of bias and confounding factors especially when single centre studies. The imbalance in numbers between the two groups suggest that the inferences may not be robust. Another limitation of the study is that the PICC team was properly trained to insert PICCs while the USG-CVC were placed by operators not belonging to the team (surgeons or anaesthetists). Potential bias by indication might be an issue as percutaneous central venous catheters were considered if some attempts for a PICC insertion failed. As reported by other researchers (31), USG-CVCs sometimes needed multiple pricks to get the catheter successfully inserted as reported in our study. This might be related to the level of experience, the number of exposures and lack of training as this task is not the main task daily performed by the operators (surgeons and anaesthetists). Besides, being inserted as rescue mode, not for selected patients is a stressor that might be a factor in increasing the number of pricks.

No USG-CVC was inserted in our unit for the last 2 years, however, it might be needed in the future in certain indications. Randomized controlled trials to study the feasibility of intracavitary ECG in catheter insertion and tip location in neonates are strongly recommended. Also, the use of US guidance during peripheral intravenous catheters insertion and the frequency of its use in tip location monitoring of correctly positioned central lines to confirm the tip positions and diagnose catheter migration are both rich areas for future prospective studies.

Conclusion:

The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Data Availability Statement:

The data that support the findings of this study are available upon reasonable request from the corresponding author. Data requests should be made to Bayoumi M., moh.abdelwahab@hotmail.com

Patient consent for publication:

Not required.

Ethics approval:

This research was approved by the Institutional Review Board (IRB) of the Medical Research Center, Hamad Medical Corporation, Doha, Qatar (MRC-01-18-151). A waiver for the requirement of informed consent from the mothers whose records were analyzed was granted by the Chair of the Medical Research Center on the grounds of being a minimal risk study. All methods were performed following the relevant guidelines and regulations. The author signs for and accepts responsibility for releasing this material on behalf of all co-authors.

Acknowledgement:

This research was funded and supported by the Medical Research Center (MRC), HMC, Doha, Qatar. Special thanks to the entire PICC and NSN teams in WWRC who provide high-quality care to our newborns.

Conflict of Interest:

No competing interests.

Contributors:

MAAB and DADAS conceptualized and designed the study. MVR and MAAB collected, cleaned, and anonymized the data. PC designed and performed the data analysis. MAAB, PC, and SH drafted the initial manuscript. MAAB and PC designed the figures. EEE, MAAB, and PC intellectually revised the manuscript. All authors reviewed and revised the manuscript, and approved the final submitted manuscript.

Funding:

This work was supported by the Medical Research Center (MRC), Hamad Medical Corporation, Doha, Qatar (Protocol number MRC-01-18-151).

Patient and public involvement:

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Provenance and peer review:

Not commissioned; externally peer-reviewed.

References:

1. McCay AS, Elliott EC, Walden M. Videos in clinical medicine. PICC placement in the neonate. N Engl J Med. 2014;370(11):e17.
2. Soong WJ, Jeng MJ, Hwang B. The evaluation of percutaneous central venous catheters--a convenient technique in pediatric patients. Intensive Care Med. 1995;21(9):759-65.
3. van Rens M, Hugill K, Mahmah MA, Bayoumi M, Francia ALV, Garcia KLP, et al. Evaluation of unmodifiable and potentially modifiable factors affecting peripheral intravenous device-related complications in neonates: a retrospective observational study. BMJ Open. 2021;11(9):e047788.
4. Njere I, Islam S, Parish D, Kuna J, Keshtgar AS. Outcome of peripherally inserted central venous catheters in surgical and medical neonates. J Pediatr Surg. 2011;46(5):946-50.
5. Barone G, Pittiruti M. Epicutaneo-caval catheters in neonates: New insights and new suggestions from the recent literature. J Vasc Access. 2020;21(6):805-9.
6. Yu X, Yue S, Wang M, Cao C, Liao Z, Ding Y, et al. Risk Factors Related to Peripherally Inserted Central Venous Catheter Nonselective Removal in Neonates. Biomed Res Int. 2018;2018:3769376.
7. Foo R, Fujii A, Harris JA, LaMorte W, Moulton S. Complications in tunneled CVL versus PICC lines in very low birth weight infants. J Perinatol. 2001;21(8):525-30.
8. Araujo CC, Lima MC, Falbo GH. Percutaneous subclavian central venous catheterization in children and adolescents: success, complications and related factors. J Pediatr (Rio J). 2007;83(1):64-70.
9. Lausten-Thomsen U, Merchaoui Z, Dubois C, Eleni Dit Trolli S, Le Sache N, Mokhtari M, et al. Ultrasound-Guided Subclavian Vein Cannulation in Low Birth Weight Neonates. Pediatr Crit Care Med. 2017;18(2):172-5.
10. Tan Y, Tu Z, Ye P, Xu Y, Ye M, Bai L, et al. Ultrasound guidance for internal jugular vein cannulation in neonates: Modified dynamic needle tip positioning short-axis out-of-plane technique versus long-axis in-plane technique, a randomized controlled trial. J Vasc Access. 2021:11297298211015043.
11. Kornbau C, Lee KC, Hughes GD, Firstenberg MS. Central line complications. Int J Crit Illn Inj Sci. 2015;5(3):170-8.
12. Wrightson DD. Peripherally inserted central catheter complications in neonates with upper versus lower extremity insertion sites. Adv Neonatal Care. 2013;13(3):198-204.
13. Santos FKY, Flumignan RLG, Areias LL, Sarpe AKP, Amaral FCF, Ávila RBd, et al. Peripherally inserted central catheter versus central venous catheter for intravenous access: A protocol for systematic review and meta-analysis. Medicine. 2020;99(30):e20352.

14. Uygun I, Okur MH, Otcu S, Ozturk H. Peripherally inserted central catheters in the neonatal period. Acta Cir Bras. 2011;26(5):404-11.
15. Qin KR, Nataraja RM, Pacilli M. Long peripheral catheters: Is it time to address the confusion? J Vasc Access. 2019;20(5):457-60.
16. Gorski LA, Hadaway L, Hagle ME, Broadhurst D, Clare S, Kleidon T, et al. Infusion Therapy Standards of Practice, 8th Edition. J Infus Nurs. 2021;44(1S Suppl 1):S1-S224.
17. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
18. Hussain ASS, Ali SR, Ariff S, Arbab S, Demas S, Zeb J, et al. A protocol for quality improvement programme to reduce central line-associated bloodstream infections in NICU of low and middle income country. BMJ Paediatr Open. 2017;1(1):e000008.
19. Al-Juaid A, Walkty A, Embil J, Crockett M, Karlowsky J. Differential time to positivity: vascular catheter drawn cultures for the determination of catheter-related bloodstream infection. Scand J Infect Dis. 2012;44(10):721-5.
20. Orihuela-Martin J, Rodriguez-Nunez O, Morata L, Cardozo C, Puerta-Alcalde P, Hernandez-Meneses M, et al. Performance of differential time to positivity as a routine diagnostic test for catheter-related bloodstream infections: a single-centre experience. Clin Microbiol Infect. 2020;26(3):383 e1- e7.
21. Yu X, Wang X, Fan L, Cao N, Yang F, Li J, et al. Iatrogenic Pleural Effusion Due to Extravasation of Parenteral Nutrition via an Epicutaneo Cava Catheter in Neonates: A Prospective Cohort Study. Front Pediatr. 2020;8:570978.
22. Bayoumi MAA, Van Rens MFP, Chandra P, Francia ALV, D'Souza S, George M, et al. Effect of implementing an Epicutaneo-Caval Catheter team in Neonatal Intensive Care Unit. J Vasc Access. 2021;22(2):243-53.
23. Linck DA, Donze A, Hamvas A. Neonatal peripherally inserted central catheter team. Evolution and outcomes of a bedside-nurse-designed program. Adv Neonatal Care. 2007;7(1):22-9.
24. Legemaat MM, Jongerden IP, van Rens RM, Zielman M, van den Hoogen A. Effect of a vascular access team on central line-associated bloodstream infections in infants admitted to a neonatal intensive care unit: a systematic review. Int J Nurs Stud. 2015;52(5):1003-10.
25. Taylor T, Massaro A, Williams L, Doering J, McCarter R, He J, et al. Effect of a dedicated percutaneously inserted central catheter team on neonatal catheter-related bloodstream infection. Adv Neonatal Care. 2011;11(2):122-8.
26. Haddadin Y, Annamaraju P, Regunath H. Central Line Associated Blood Stream Infections. StatPearls. Treasure Island (FL)2021.
27. Bonizzoli M, Batacchi S, Cianchi G, Zagli G, Lapi F, Tucci V, et al. Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. Intensive Care Med. 2011;37(2):284-9.
28. Pet GC, Eickhoff JC, McNevin KE, Do J, McAdams RM. Risk factors for peripherally inserted central catheter complications in neonates. J Perinatol. 2020;40(4):581-8.
29. Ragavan M, Gazula S, Yadav DK, Agarwala S, Srinivas M, Bajpai M, et al. Peripherally inserted central venous lines versus central lines in surgical newborns--a comparison. Indian J Pediatr. 2010;77(2):171-4.
30. Barone G, Pittiruti M, Ancora G, Vento G, Tota F, D'Andrea V. Centrally inserted central catheters in preterm neonates with weight below 1500 g by ultrasound-guided access to the brachio-cephalic vein. J Vasc Access. 2020:1129729820940174.
31. Ostroff M, Zauk A, Chowdhury S, Moureau N, Mobley C. A retrospective analysis of the clinical effectiveness of subcutaneously tunneled femoral vein cannulations at the bedside: A low risk central venous access approach in the neonatal intensive care unit. J Vasc Access. 2020:1129729820969291.

32. Hosseinpour M, Mashadi MR, Behdad S, Azarbad Z. Central venous catheterization in neonates: Comparison of complications with percutaneous and open surgical methods. J Indian Assoc Pediatr Surg. 2011;16(3):99-101.

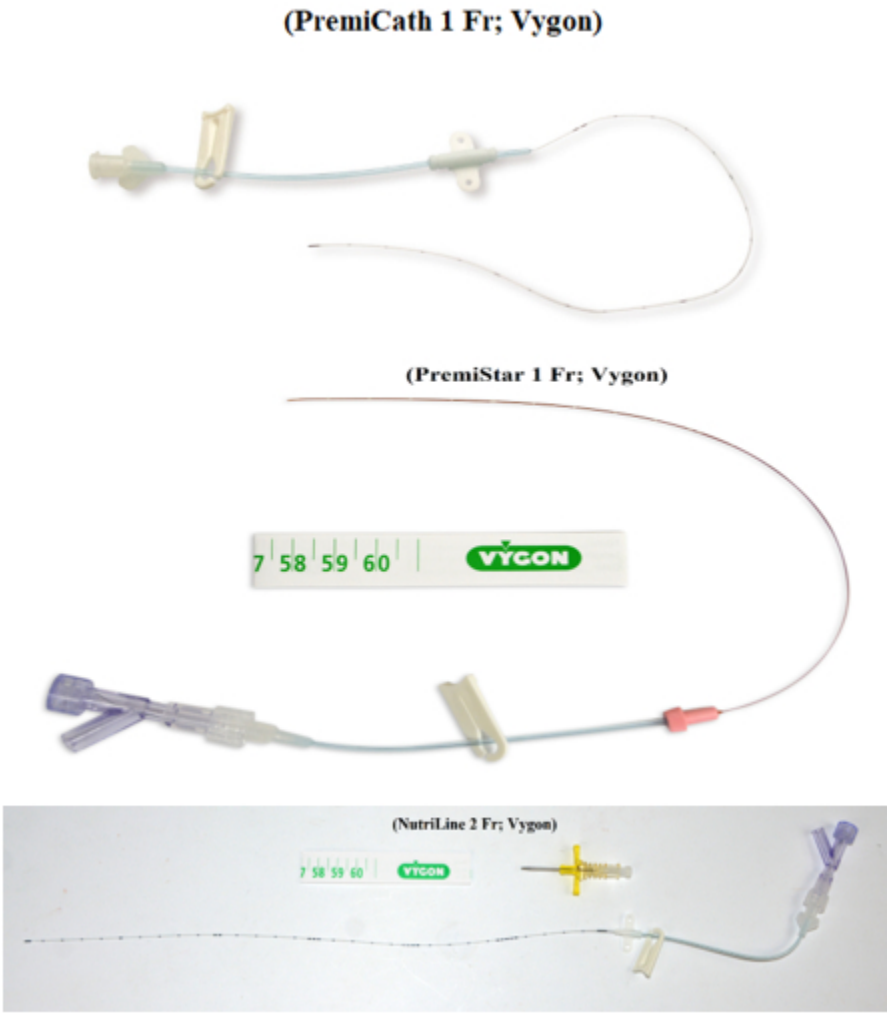


Figure 1: Three types of Peripherally Inserted Central Catheters (PICCs).

296x342mm (38 x 38 DPI)

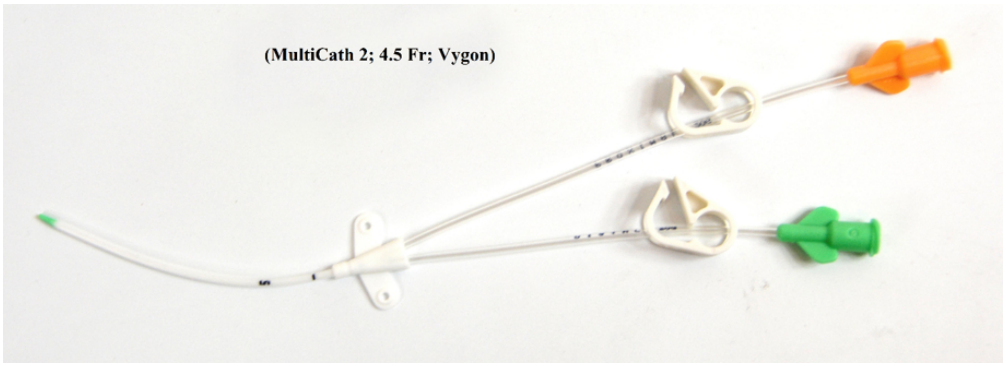


Figure 2. Non-tunnelled Ultrasound-Guided Central Venous Catheter (USG-CVC).

611x219mm (38 x 38 DPI)

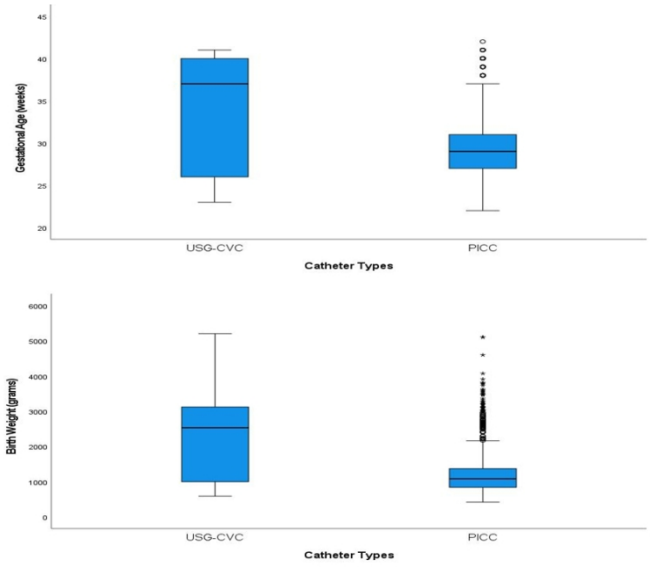
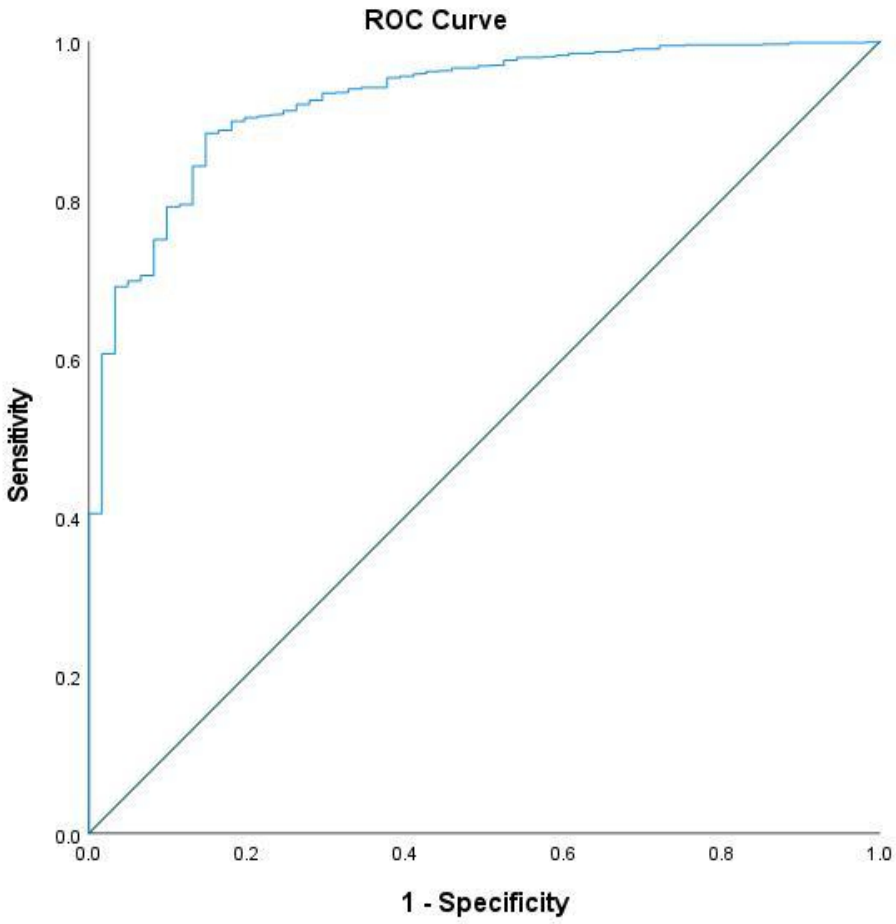


Figure 3. Box plot depicting the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types

855x481mm (38 x 38 DPI)



[Area under the curve (AUC) value was 0.927 (95% CI 0.90, 0.96), P=0.001]

Figure 4. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter types (USG-CVC and PICC)

211x211mm (72 x 72 DPI)

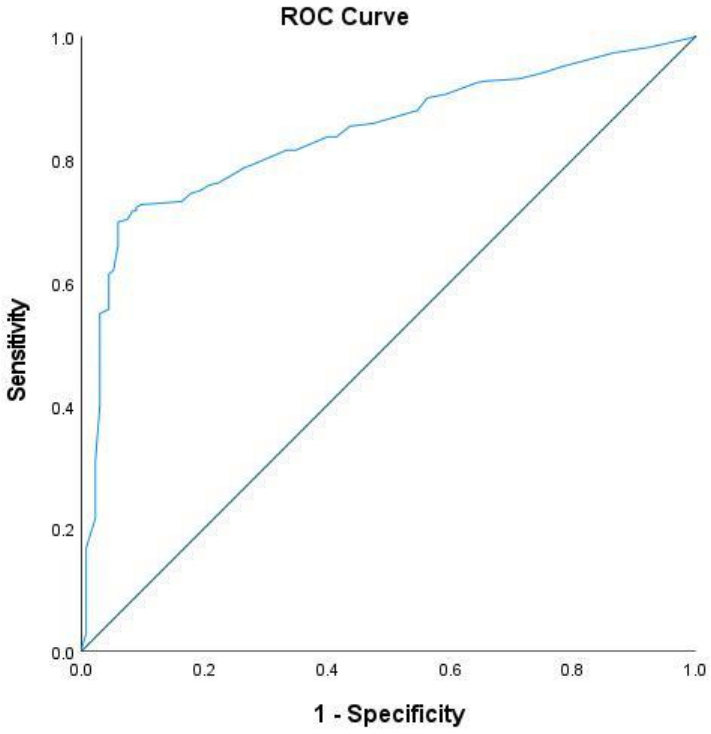


Figure 5. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter insertion success rate (successful/not successful)

234x188mm (72 x 72 DPI)

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	In the abstract. In the abstract. Not applicable.
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported		PICCs and non-tunnelled USG-CVCs have risks associated with their usage.	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses		To compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU	Aims and objectives
Methods					
Study Design	4	Present key elements of study design early in the paper		Data are collected retrospectively	Title
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		A total of 1333 cases were evaluated who had PICC insertion and non-tunneled USG-CVC insertion. Related information for all cases between	Methods

				January 2016 and December 2018 was collected from the electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar.	
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	In the methods. Babies who had PICC insertion and non-tunneled USG-CVC insertion at NICU were enrolled.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details			Data were collected from the

		of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar.
Bias	9	Describe any efforts to address potential sources of bias		Being restrospective research design, appropriate comparable groups, physicians experience, and missing obervations on important condounders can not be ruled out.	Limitation of the study
Study size	10	Explain how the study size was arrived at		1264 babies who had PICC insertion and non-tunneled USG-CVC insertion between January 2016 and December 2018 were included in the research	Methods
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how			Yes, described in the methods under statistical analysis

		matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Described in methods
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	CERNER
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic,			Descrbed in table 1 and 2

		clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Given in table 2,3, and 4
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			N/A
Discussion					

Key results	18	Summarise key results with reference to study objectives			The success rate is higher when using PICC. It also has less incidence of complications when compared to the non-tunnelled USG-CVCs.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Limitation of the study
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.	Conclusion
Generalisability	21	Discuss the generalisability (external validity) of the study results			The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled

					USG-CVCs. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			N/A
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Corresponding author is responsible for it

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

*Checklist is protected under Creative Commons Attribution (CC BY) license.

BMJ Open

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-058866.R1
Article Type:	Original research
Date Submitted by the Author:	13-Jan-2022
Complete List of Authors:	Bayoumi, Mohammad; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), van Rens, Roland; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Shaltout, Deena; Hamad Medical Corporation, Medical Education Department, CHANDRA, PREM; Hamad Medical Corporation, Medical Research Center, Elmalik, Einas; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Hammoudeh, Samer; Hamad Medical Corporation, Medical Research Center (MRC),
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Qualitative research
Keywords:	NEONATOLOGY, Neonatal intensive & critical care < INTENSIVE & CRITICAL CARE, PERINATOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Mohammad A. A. Bayoumi[1], Matheus van Rens[1], Deena A. D. A. Shaltout[2], Prem Chandra[3], Einas E. Elmalik[1], Samer Hammoudeh[3]

[1] Neonatal Intensive Care Unit, Women's Wellness and Research Center, Hamad Medical Corporation, Doha, Qatar
[2] Department of Medical Education, Hamad Medical Corporation, Doha, Qatar
[3] Medical Research Center, Hamad Medical Corporation, Doha, Qatar

Author's emails:
Mohammad A. A. Bayoumi: moh.abdelwahab@hotmail.com
Matheus van Rens: rolandvanrens@gmail.com
Prem Chandra: pchandra@hamad.qa
Deena A. D. A. Shaltout: dshaltout@hamad.qa
Einas E. Elmalik: einas_e@yahoo.com
Samer Hammoudeh: shammoudeh@hamad.qa

Corresponding Author's Contact Details:
Dr Mohammad A. A. Bayoumi
Neonatal Intensive Care Unit, Women's Wellness and Research Center, Hamad Medical Corporation, P.O. Box: 3050, Doha, Qatar
Fax Number: +97444439571
Mobile Number: +97477671584
Email: moh.abdelwahab@hotmail.com

Manuscript Checklist

Abstract:

Objectives: We aimed to compare the success rates and other catheter-related parameters between Peripherally Inserted Central Catheters (PICCs) and non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) including femoral, jugular, brachiocephalic and subclavian lines.

Design: This was a retrospective observational study.

Setting: The study was performed in a Level III neonatal intensive care unit in Qatar, as a single-site study.

Participants: This study included 1333 neonates who required central venous catheter insertion in the NICU from January 2016 to December 2018. Of those, we had 1264 PICCs and 69 non-tunnelled USG-CVCs.

Outcome measures: The main outcome was the success rate and other catheter-related complications leading to unplanned removal of the catheter before completion of the planned therapy in the 2 groups.

Results: The overall success rate was 88.4% in the USG-CVCs (61/69) compared to 90% in the PICCs (1137/1264) group (P=0.68). However, the first prick success rate was 69.4% in USG-CVCs (43/69) compared to 63.6% in the PICCs (796/1264) group. Leaking and Central Line-Associated Blood Stream Infection (CLABSI) were significantly higher in the USG-CVC group compared to the PICC group (Leaking 16.4% vs. 2.3%, P=0.0001) (CLABSI 8.2% vs. 3.1%, P=0.03). CLABSI rates in the PICC group were 1.75 per 1000 catheter days in 2016 and 3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the USG-CVCs. USG-CVCs had to be removed more often before completion of their intended use due to catheter-related complications (52.5%) compared to PICCs (29.9%), P=0.0001. In 2018, we did not have any non-tunnelled USG-CVCs insertions in our NICU.

Conclusions: The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Keywords:

Neonatal Intensive Care Unit, Neonate, Vascular Access, Peripherally Inserted Central Catheter, Non-Tunneled Ultrasound-Guided Central Venous Catheters.

Strengths and limitations of this study:

- This is an observational study including a large sample of 1333 neonates.
- The study provides information on the insertion success rates and complications of peripherally inserted central catheters and non-tunnelled ultrasound-guided central venous catheters in neonates.
- It is based on retrospective analyses of collected data.

What is known about the subject?

- Peripherally Inserted Central Catheters are increasingly used in NICU, especially for extremely premature infants to administer drugs and fluids.
- Non-tunnelled ultrasound-guided Central Venous Catheters including femoral, jugular, brachiocephalic and subclavian lines have limited indications in neonates.

What does this study add?

- Proper central venous device selection and timing, early Peripherally Inserted Central Catheter insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Introduction:

Peripherally Inserted Central Catheters (PICCs) were described for the first time by Shaw in 1973. Since then, they have been used extensively due to their features (1). PICC insertion by direct superficial peripheral vein puncture offers long-term venous access for both term and preterm neonates and is often indicated in NICU for parental nutrition, long-term IV medications, antibiotic therapy, and vesicant drug administration (2, 3).

Non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) are inserted in neonates in special circumstances e.g. central venous pressure monitoring, blood withdrawal, hemodialysis, and for all other infusions and medications when PICC insertion fails (4). They are inserted in the internal jugular, brachiocephalic, subclavian, and femoral veins under ultrasound guidance (1, 5-7).

There is a limited number of studies comparing PICCs with USG-CVCs in neonates that necessitated further research and comparative analysis. This study aimed to compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU between 2016 and 2018.

Methods:

This single-centre retrospective study was conducted in the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation (HMC), Doha, Qatar. WWRC is the main specialist hub for women and newborns health services in Qatar with more than 18000 deliveries per year. The NICU in WWRC is a level III mainly medical unit with 112 beds and more than 2000 admissions per year with limited congenital cardiac or surgery cases.

Patient and Public Involvement:
Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Participants:
A total of 1333 cases were evaluated in this study. This includes 1264 babies who had PICC insertion and 69 who had non-tunnelled USG-CVC insertion. Related information for all cases between January 2016 and December 2018 was collected from the electronic medical system at the NICU. The study was approved by the Institutional Review Board (IRB) at HMC before the study procedures commenced (MRC-01-18-151).

A fully dedicated PICC insertion team was launched in January 2017. The PICC team has been expanded over time to include 15 neonatologist physicians, one neonatal nurse practitioner as well as 7 NICU Nurses. The team was trained in central line simulation workshops to insert PICC by the catheter-over-needle technique and the modified Seldinger technique (MST) (8, 9). The central line simulation workshop is a full-day workshop that was founded by the neonatal simulation team and is accredited by the Department of Healthcare Professions (DHP) in the Ministry of Public Health (MOPH) with a total of 7 Continuous Professional Development (CPD) hours both category I (1/7) and category III (6/7). The PICC team works in harmony and collaboration with 30 well-trained NICU nurses who are members of the Neonatal Specialized Nursing (NSN) Team. The NSN determines the patient's eligibility, takes care of the central line maintenance using transparent semipermeable dressing, enters the data in the electronic database, and gets the blood samples. There is no difference in the central line type of care, frequency or personnel in all types of catheters. In addition to their role in central line insertion and maintenance, the NSN team attends high-risk deliveries and play a pivotal role in neonatal transportation.

In our NICU, the indications for PICC insertions are the birth weight of < 1500 gm, the requirement of IV fluids for > 5 days, the requirement of IV medications for > 7 days, the requirement of hyperosmolar IV fluid therapy > 700 mosmol/L, and the requirement of > 3 Peripheral Intravenous Catheters (PIVC) insertions in the last 24 hours (10). A successful catheter insertion means a catheter inserted into a proper central venous position that can be used with its tip located either in the superior or inferior vena cava. As per our institutional guideline, 2 pricks are allowed per operator with a maximum of 3 in difficult lines. After 3 unsuccessful pricks, the procedure should be terminated.

Figure 1 shows the 3 types of PICCs available in our NICU; (NutriLine 2 Fr; Vygon), (PremiCath 1 Fr; Vygon), and (PremiStar 1 Fr; Vygon). PremiStar 1 Fr; Vygon is an

antimicrobial impregnated catheter that is used in our unit for babies born less than 28 weeks gestation or when sepsis is suspected. We use NutriLine 2 Fr; Vygon, when a double lumen PICC or a long line is needed in big babies as its length is 30 cm. PremiCath 1 Fr; Vygon is used for the rest of our NICU babies who need PICC insertion. The most common veins used for PICC insertions are the great saphenous vein, small saphenous vein, posterior tibial vein, antecubital vein, cephalic vein, basilic vein, and ulnar vein. Figure 2 shows the non-tunnelled CVC available in our unit which is (MultiCath 2; 4.5 Fr; Vygon). The most common veins used for USG-CVC insertions are the internal jugular vein, femoral vein, brachiocephalic vein, and subclavian vein.

In our practice, non-tunnelled USG-CVC was used only when PICC insertion has failed by 2-3 operators; 2 pricks for each. USG-CVCs were inserted either by the pediatric surgeon or the pediatric anaesthetist on-call physician under US guidance. Currently, we use the handheld wireless probe-type ultrasound scanner machine to guide the catheter insertion and for the catheter tip location.

We followed the Centers for Disease Control and Prevention (CDC) definition for central line-associated bloodstream infection (CLABSI) and CLABSI rate. CLABSI is defined as a laboratory-confirmed bloodstream infection where an eligible bloodstream infection (BSI) organism is identified, and an eligible central line is present on the laboratory-confirmed bloodstream infection (LCBI) date of the event (DOE) or the day before. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility. CLABSI rate is the total number of CLABSI divided by the total number of device days 1000 (11, 12).

The differential time to positivity (DTP) is defined as a difference in time to positivity of ≥ 2 h between peripheral blood culture and a CVC blood culture (peripheral DTP) or between 2 CVC blood cultures from different lumens of a multi-lumen catheter (CVC DTP) (13). Due to its limitation reported in the literature, our unit does not prefer to use the differential time to positivity (DTP) for the diagnosis of CLABSI (14).
The authors designed an electronic system-based data collection sheet to collect all catheter-related parameters in the 2 groups.

Statistical Analysis:
Descriptive statistics were used to summarize and determine the sample characteristics and distribution of participants' data. The normally distributed data and results were reported with mean and standard deviation (SD); the remaining results were reported with median and inter-quartile range (IQR). Categorical data were summarized using frequencies and proportions. Associations between two or more qualitative data variables were assessed using Chi-square ($\chi 2$) test or Fisher Exact test as appropriate. Quantitative data between the two independent groups (USG-CVC and PICC) were analyzed using unpaired t (for normally distributed data) or Mann Whitney U test (for skewed or non-normally distributed data) as appropriate. Univariate and multivariate logistic regression analysis was applied to determine and assess the potential factors and predictors associated with the catheter insertion success rate adjusted for potential factors and predictors such as catheter types, gestational age, birth weight, the reason for catheter insertion, side of the body, site of insertion and number of pricks. For multivariate logistic

regression models, predictor variables were included considering both statistical and clinical significance. The results of logistic regression analysis were presented as odds ratios (OR) with corresponding 95% confidence intervals (CI). Thereafter, we used the receiver operating characteristic curve (ROC) to evaluate the discriminative ability (predictive accuracy of the developed logistic regression model) of potentially significant variables associated with catheter insertion success rate. Box plots were constructed depicting the distribution of gestational age and birth weight across two catheter types. All P values presented were two-tailed, and P values <0.05 were considered statistically significant. All statistical analyses were performed using statistical packages SPSS version 27.0 (Armonk, NY: IBM Corp) and Epi-info (Centers for Disease Control and Prevention, Atlanta, GA) software.

Results:

Among the three years that this study covered, the usage of USG-CVC has progressively declined to zero in 2018, on which the catheter insertion success rate increased to 97%. Shown in table 1 are the distribution of patients and catheter-related variables associated with the types of catheters. When USG-CVC was compared to PICC about gestational age, the former was significantly higher (33.88±6.34 vs. 29.32±4.03, P=0.0001). Birth weight was also significantly higher among USG-CVC compared to PICC (2161.25±1140.26 vs. 1234.57±624.90, respectively, P=0.0001). Figure 3 shows the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types. The duration of catheter insertion was however not significant (USG-CVC 11.69±9.23, PICC 14.57±12.56, P=0.14). Further comparisons between USG-CVC and PICC on several parameters. PICC had a higher success rate (90% vs. 88.4%), however, the difference did not reach statistical significance.

Table 1: Distribution of patients' profiles and catheter-related parameters and their association with the catheter types

Variables	Total n=1333	USG-CVC 69 (5.2%)	PICC 1264 (94.8%)	P-value
Year				0.001
2016	376 (28.2)	42 (60.9)	334 (26.4)	
2017	507 (38)	27 (39.1)	480 (38)	
2018	450 (33.8)	0 (0)	450 (35.6)	
Side of the body				0.002
Left	498 (41.1)	14 (22.6)	484 (42.1)	
Right	715 (58.9)	48 (77.4)	667 (57.9)	
Site of Insertion				0.001
Upper Extremities	360 (29.5)	37 (53.6)	323 (28)	
Lower Extremities	861 (70.5)	32 (46.4)	829 (72)	
Number of Pricks				0.001
First Prick	839 (63.9)	43 (69.4)	796 (63.6)	
Second Prick	305 (23.2)	8 (12.9)	297 (23.7)	
Third Prick	145 (11)	6 (9.7)	139 (11.1)	
Fourth Prick	22 (1.7)	4 (6.5)	18 (1.4)	
Fifth Prick	1 (0.1)	0 (0)	1 (0.1)	
Sixth Prick	2 (0.2)	1 (1.6)	1 (0.1)	
Reason for Insertion				0.47
Difficult IV Insertion	8 (0.6)	0 (0)	8 (0.6)	

Hypoglycemia	10 (0.8)	0 (0)	10 (0.8)	
Long term IV fluid therapy	1286 (96.6)	68 (100)	1218 (96.4)	
Long term IV medication therapy	27 (2)	0 (0)	27 (2.1)	
Catheter insertion Success Rate				0.68
Successful	1198 (89.9)	61 (88.4)	1137 (90)	
Not Successful	135 (10.1)	8 (11.6)	127 (10)	
Reason for Removal				
CLABSI	40 (3.4)	5 (8.2)	35 (3.1)	0.031
Leaking	36 (3)	10 (16.4)	26 (2.3)	0.001
Accidental Removal	8 (0.7)	1 (1.6)	7 (0.6)	0.40
Broken Catheter	7 (0.6)	0 (0)	7 (0.6)	0.69
Local redness and swelling	104 (8.7)	5 (8.2)	99 (8.8)	0.88
Occlusion	42 (3.5)	0 (0)	42 (3.7)	0.13
Malposition	13 (1.1)	0 (0)	13 (1.1)	0.50
Elective	833 (69.9)	29 (47.5)	804 (71.1)	0.001
Death	39 (3.3)	5 (8.2)	34 (3)	0.03
Phlebitis	70 (5.9)	6 (9.8)	64 (5.7)	0.18
Gestational Age (weeks), Mean ±SD	29.55±4.30	33.88±6.34	29.32±4.03	0.001
Median (IQR)	29 (27, 31)	37 (26, 40)	29 (27, 31)	
Gestational Age				0.001
22 to 28 weeks	602 (45.2)	22 (31.9)	580 (45.9)	
> 28 to 32 weeks	490 (36.8)	4 (5.8)	486 (38.4)	
> 32 to 36 weeks	100 (7.5)	8 (11.6)	92 (7.3)	
> 36 weeks	141 (10.6)	35 (50.7)	106 (8.4)	
Birth Weight (gm), Mean ±SD	1282.6±692.1	2161.4±1140.3	1234.6±624.9	0.001
Median (IQR)	1095 (850, 1400)	2530 (970, 3122)	1080 (840, 1370)	
Birth Weight				0.001
BW <=1 kg	561 (42.1)	21 (30.4)	540 (42.7)	
BW > 1 to 2 kg	618 (46.5)	10 (14.5)	608 (48.1)	
BW > 2 to 3 kg	87 (6.5)	16 (23.2)	71 (5.6)	
BW >3 kg	67 (5)	22 (31.9)	42 (3.6)	

This is a retrospective study design and for some parameters, the data values were incomplete due to the unavailability of the information in the patients' record files. All percentage (%) was computed using non-missing data values. IQR: Inter-Quartile range.

We performed univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with dichotomous outcome variable catheter types (USG-CVC and PICC), it was observed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal (elective vs non-elective), duration of gestation and birth weight were significantly associated with catheter types. The multivariate logistic regression analysis showed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal, and birth weight were remained significantly associated with catheter types adjusting other predictors and factors shown in table 2. The discriminative ability of the significant predictors (observed in multivariate analysis) in predictive catheter types were found to be good with an area under the ROC curve value of 0.927 (95% CI 0.90, 0.96), which indicates that this developed regression model demonstrated an excellent fit, Figure 4.

Table 2: Logistic regression analysis with potential factors and predictors associated with catheter types USG-CVC and PICC

Variables		Univariate analysis			Multivariate analysis		
	Catheter type- PICC, n (%)	Unadjusted Odds ratio (OR)	95% CI for OR	P-value	Adjusted Odds ratio (OR)	95% CI for OR	P-value
Year							
2016	334 (88.8)	1.0 (reference)			1.0 (reference)		
2017	480 (94.7)	2.24	1.35, 3.70	0.002	3.43	1.79, 6.54	0.001
2018	450 (100)	--	--	--	--	--	--
Side of the body							
Left	484 (97.2)	1.0 (reference)			1.0 (reference)		
Right	667 (93.3)	0.40	0.22, 0.74	0.003	0.34	0.17, 0.70	0.003
Site of Insertion							
Upper Extremities	323 (89.7)	1.0 (reference)			1.0 (reference)		
Lower Extremities	829 (96.3)	2.97	1.82, 4.85	0.001	3.39	1.81, 6.33	0.001
Number of Pricks							
One Prick	796 (94.9)	1.0 (reference)			1.0 (reference)		
Two Prick	297 (97.4)	2.01	0.93, 4.32	0.075	2.58	0.97, 6.86	0.058
≥ 3 Pricks	171 (90.5)	0.51	0.29, 0.91	0.023	0.39	0.16, 0.95	0.037
Reason for catheter insertion							
Long term IV fluid therapy	1218 (94.7)	1.0 (reference)			1.0 (reference)		
Others*	45 (100)	--	--	--	--	--	--
Catheter Insertion Success Rate							
Not Successful	127 (94.1)	1.0 (reference)	0.55, 2.51	0.679	1.0 (reference)	0.59, 2.46	0.569
Successful	1137 (94.9)	1.17			1.14		
Reasons for removal							
Non-Elective	327 (91.1)	1.0 (reference)			1.0 (reference)		
Elective	804 (96.5)	2.71	1.62, 4.56	0.001	2.16	1.16, 4.01	0.015
Gestational age (weeks) PICC vs USG-CVC	29.3 ± 4.1 vs 33.9 ± 6.3	0.82	0.78, 0.86	0.001	1.03	0.90, 1.17	0.715
Birth Weight (gm) PICC vs USG-CVC	1235.6 ± 624.9 vs 2161.4 ± 1140.3	0.98	0.98, 0.99	0.001	0.99	0.98, 0.99	0.001

Catheter types- USG-CVC was considered as the reference group; CI: Confidence interval
**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

CLABSI and Leaking were noted to be significantly higher in the USG-CVC group compared to the PICC group. CLABSI rate is defined as the total number of CLABSI divided by the total number of device days 1000 (11, 12). CLABSI rates in the PICC group were 1.75 in 2016 and

3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the non-tunnelled USG-CVCs. We did not have any USG-CVC inserted in 2018.

In the PICC group, 804 (71.1%) were removed electively after completion of therapy compared to 29 (47.5%) in the USG-CVC group. No significant difference was noted between the 2 groups regarding the other catheter-related complications. No serious or long term complications e.g cardiac arrhythmia, accidental arterial puncture, cardiac tamponade, pericardial or pleural effusion (15), was noted in both groups across the three years.

The results of univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with catheter insertion success rates are presented in Tables 3 and 4. Univariate results indicated that year of catheter insertion, birth weight and the number of pricks had a significant effect on the likelihood of catheter insertion success rates. In patients who had two pricks (unadjusted OR 0.03; 95% CI 0.01, 0.07, P=0.028) and ≥3 pricks (unadjusted OR 0.01; 95% CI 0.01, 0.03, P=0.013) were significantly associated with a decreased likelihood of catheter insertion success rates compared to patients who had one prick. In addition, it was noted that catheter type PICC was associated with a higher rate of catheter insertion success rates, however, this difference was statistically insignificant (P=0.679).

Table 3: Univariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate, n (%)	Unadjusted odds ratio (OR)	95% CI for OR	P-value
Catheter Types				
USG-CVC	61 (88.4)	1.0 (refernce)		
PICC	1137 (90)	1.17	0.55, 2.51	0.679
Year				
2016	309 (81.7)	2.0 (refernce)		
2017	450 (88.6)	1.73	1.18, 2.52	0.004
2018	439 (97.6)	8.91	4.64, 17.12	0.001
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.01	0.96, 1.04	0.954
Birth Weight (g)	1270.1 ± 677.5 vs 1394.2 ± 803.3	0.98	0.98, 0.99	0.045
Reason for catheter insertion				
Long term IV fluid therapy	1156 (89.9)	2.0 (refernce)		
Others*	42 (93.3)	1.57	0.48, 1.51	0.453
Side of the body				
Left	491 (98.6)	2.0 (refernce)		
Right	706 (98.7)	1.12	0.41, 3.03	0.826
Site of Insertion				
Upper Extremities	353 (98.1)	2.0 (refernce)		

Lower Extremities	845 (98.1)	1.05	0.43, 2.57	0.920
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.03	0.01, 0.07	0.028
≥ 3 Pricks	121 (63.7)	0.01	0.01, 0.03	0.013

CI: Confidence interval

**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

The multivariate logistic regression analysis showed that duration of gestation (weeks) and the number of pricks were remained significantly (P<0.05) associated with the catheter insertion success rate after controlling and adjusting potential factors and predictors as shown in Table 4. The higher catheter insertion success rates were associated with increasing gestational age (adjusted OR 1.23; 95% CI 1.03, 1.44, P=0.015). Whereas, in patients who had two pricks (adjusted OR 0.07; 95% CI 0.01, 0.57, P=0.014) and ≥3 pricks (adjusted OR 0.02; 95% CI 0.01, 0.13, P=0.001) were significantly associated with a reduction in the likelihood of catheter insertion success rates when compared to patients who had one prick. Thereafter, we computed a prediction model to evaluate the discriminative ability of potentially significant predictors (observed in the developed multivariate logistic regression model) associated with catheter insertion success rates using ROC curve analysis. The value of area under the curve (AUC) observed was found to be 0.841 (95% CI 0.81, 0.87), which is indicating that this developed regression model demonstrated an excellent fit, Figure 5.

Table 4: Multivariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate N (%)	Adjusted odds ratio (OR)	95% CI for OR	P-value
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.23	1.03, 1.44	0.015
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.07	0.01, 0.57	0.014
≥ 3 Pricks	121 (63.7)	0.02	0.01, 0.13	0.001

CI: Confidence interval

Discussion:

Both PICCs and non-tunnelled USG-CVCs have risks associated with their usage. Immediate risks include injury to local structures, accidental arterial puncture, phlebitis at the insertion site, air embolism, hematoma, arrhythmia, and catheter damage and malposition. Late complications include infection, occlusion, thrombosis, infiltration, extravasation, and catheter migration (16-18). Infection, thrombosis, embolization, hydrocephalus, are complications reported in premature babies receiving central venous lines (3).

The current study compared PICC to USG-CVC in a sample of cases from Qatar. The results also showed a progressive reduction in the usage of USG-CVC across the 3 years till reached 0% in 2018. This is due to the implementation of a PICC insertion team in early 2017 with a progressive build-up of the team skills (19). Since then, overall success and first prick rates have significantly increased. Reports of an overall success rate of 94% were indicated elsewhere (20). A systematic review highlighted the importance and necessity of a vascular access team in the NICU, as it reflects positively on the rate of bloodstream infections (21). This was also confirmed in another study where the rate of infections was reduced by 50% after the establishment of a PICC team in the NICU (22).

Only 29 (47.5%) of our USG-CVC were electively removed after completion of therapy while the rest were removed due to death, phlebitis, CLABSI, or other catheter-related complications. In the PICC group, elective removal was noted to be significantly higher 804 (71.1%) than USG-CVC (P= 0.0001). The higher rate of CLABSI in USG-CVCs compared to PICCs is mainly related to the vulnerable insertion sites being close to infection or joint areas (23). Also, the higher rate of catheter leaking in USG-CVCs might be due to occlusions resulting from mechanical or postural factors, catheter malpositioning, or undesirable catheter-tip location. CLABSI and thrombosis might also lead to catheter leaking (24). Approximately one-third of PICCs were associated with complications in another study which is close to our PICC data (25).

Ragavan et al described the advantages of using PICCs inserted in the cubital veins as to have a reduced complication incidence rate, as well as maintenance rates in comparison to USG-CVCs inserted in the internal jugular vein. The authors concluded by recommending the usage of PICCs routinely when dealing with neonatal surgical patients (26). On the other hand, a recent study reported a 100% success rate of 30 preterm babies who underwent an ultrasound-guided brachio-cephalic central venous catheter insertion. No case of accidental arterial or pleural puncture was noted by the researchers (27). In another study involving neonates with femoral central venous catheterization (28), the overall success rate was 100% of neonates (n = 82/82), first attempt 63/74 (85%), second attempt 8/74 (11%), and third attempt 3/74 (4%). Another 2 studies reported no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (4, 29).

The limitation of this study is being retrospective with potential risks of bias and confounding factors especially when single centre studies. The imbalance in numbers between the two groups suggest that the inferences may not be robust. Another limitation of the study is that the PICC team was properly trained to insert PICCs while the USG-CVC were placed by operators not belonging to the team (surgeons or anaesthetists). Potential bias by indication might be an issue as percutaneous central venous catheters were considered if some attempts for a PICC insertion failed. As reported by other researchers (28), USG-CVCs sometimes needed multiple pricks to get the catheter successfully inserted as reported in our study. This might be related to the level of experience, the number of exposures and lack of training as this task is not the main task daily performed by the operators (surgeons and anaesthetists). Besides, being inserted as rescue mode, not for selected patients is a stressor that might be a factor in increasing the number of pricks.

No USG-CVC was inserted in our unit for the last 2 years, however, it might be needed in the future in certain indications. Randomized controlled trials to study the feasibility of intracavitary ECG in catheter insertion and tip location in neonates are strongly recommended. Also, the use of US guidance during peripheral intravenous catheters insertion and the frequency of its use in tip location monitoring of correctly positioned central lines to confirm the tip positions and diagnose catheter migration are both rich areas for future prospective studies.

Conclusion:

The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Data Availability Statement:

The data that support the findings of this study are available upon reasonable request from the corresponding author. Data requests should be made to Bayoumi M., moh.abdelwahab@hotmail.com

Patient consent for publication:

Not required.

Ethics approval:

This research was approved by the Institutional Review Board (IRB) of the Medical Research Center, Hamad Medical Corporation, Doha, Qatar (MRC-01-18-151). A waiver for the requirement of informed consent from the mothers whose records were analyzed was granted by the Chair of the Medical Research Center on the grounds of being a minimal risk study. All methods were performed following the relevant guidelines and regulations. The author signs for and accepts responsibility for releasing this material on behalf of all co-authors.

Acknowledgement:

This research was funded and supported by the Medical Research Center (MRC), HMC, Doha, Qatar. Special thanks to the entire PICC and NSN teams in WWRC who provide high-quality care to our newborns.

Conflict of Interest:

No competing interests.

Contributors:

MAAB and DADAS conceptualized and designed the study. MVR and MAAB collected, cleaned, and anonymized the data. PC designed and performed the data analysis. MAAB, PC, and SH drafted the initial manuscript. MAAB and PC designed the figures. EEE, MAAB, and PC intellectually revised the manuscript. All authors reviewed and revised the manuscript, and approved the final submitted manuscript.

Funding:

This work was supported by the Medical Research Center (MRC), Hamad Medical Corporation, Doha, Qatar (Protocol number MRC-01-18-151).

Provenance and peer review:

Not commissioned; externally peer-reviewed.

References:

1. Barone G, Pittiruti M. Epicutaneo-caval catheters in neonates: New insights and new suggestions from the recent literature. J Vasc Access. 2020;21(6):805-9.
2. McCay AS, Elliott EC, Walden M. Videos in clinical medicine. PICC placement in the neonate. N Engl J Med. 2014;370(11):e17.
3. Yu X, Yue S, Wang M, Cao C, Liao Z, Ding Y, et al. Risk Factors Related to Peripherally Inserted Central Venous Catheter Nonselective Removal in Neonates. Biomed Res Int. 2018;2018:3769376.
4. Foo R, Fujii A, Harris JA, LaMorte W, Moulton S. Complications in tunneled CVL versus PICC lines in very low birth weight infants. J Perinatol. 2001;21(8):525-30.
5. Araujo CC, Lima MC, Falbo GH. Percutaneous subclavian central venous catheterization in children and adolescents: success, complications and related factors. J Pediatr (Rio J). 2007;83(1):64-70.
6. Lausten-Thomsen U, Merchaoui Z, Dubois C, Eleni Dit Trolli S, Le Sache N, Mokhtari M, et al. Ultrasound-Guided Subclavian Vein Cannulation in Low Birth Weight Neonates. Pediatr Crit Care Med. 2017;18(2):172-5.
7. Tan Y, Tu Z, Ye P, Xu Y, Ye M, Bai L, et al. Ultrasound guidance for internal jugular vein cannulation in neonates: Modified dynamic needle tip positioning short-axis out-of-plane technique versus long-axis in-plane technique, a randomized controlled trial. J Vasc Access. 2021:11297298211015043.
8. Uygun I, Okur MH, Otcu S, Ozturk H. Peripherally inserted central catheters in the neonatal period. Acta Cir Bras. 2011;26(5):404-11.
9. Qin KR, Nataraja RM, Pacilli M. Long peripheral catheters: Is it time to address the confusion? J Vasc Access. 2019;20(5):457-60.
10. Gorski LA, Hadaway L, Hagle ME, Broadhurst D, Clare S, Kleidon T, et al. Infusion Therapy Standards of Practice, 8th Edition. J Infus Nurs. 2021;44(1S Suppl 1):S1-S224.
11. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
12. Hussain ASS, Ali SR, Ariff S, Arbab S, Demas S, Zeb J, et al. A protocol for quality improvement programme to reduce central line-associated bloodstream infections in NICU of low and middle income country. BMJ Paediatr Open. 2017;1(1):e000008.

13. Al-Juaid A, Walkty A, Embil J, Crockett M, Karlowsky J. Differential time to positivity: vascular catheter drawn cultures for the determination of catheter-related bloodstream infection. Scand J Infect Dis. 2012;44(10):721-5.
14. Orihuela-Martin J, Rodriguez-Nunez O, Morata L, Cardozo C, Puerta-Alcalde P, Hernandez-Meneses M, et al. Performance of differential time to positivity as a routine diagnostic test for catheter-related bloodstream infections: a single-centre experience. Clin Microbiol Infect. 2020;26(3):383 e1- e7.
15. Yu X, Wang X, Fan L, Cao N, Yang F, Li J, et al. Iatrogenic Pleural Effusion Due to Extravasation of Parenteral Nutrition via an Epicutaneo Cava Catheter in Neonates: A Prospective Cohort Study. Front Pediatr. 2020;8:570978.
16. Kornbau C, Lee KC, Hughes GD, Firstenberg MS. Central line complications. Int J Crit Illn Inj Sci. 2015;5(3):170-8.
17. Wrightson DD. Peripherally inserted central catheter complications in neonates with upper versus lower extremity insertion sites. Adv Neonatal Care. 2013;13(3):198-204.
18. Santos FKY, Flumignan RLG, Areias LL, Sarpe AKP, Amaral FCF, Ávila RBd, et al. Peripherally inserted central catheter versus central venous catheter for intravenous access: A protocol for systematic review and meta-analysis. Medicine. 2020;99(30):e20352.
19. Bayoumi MAA, Van Rens MFP, Chandra P, Francia ALV, D'Souza S, George M, et al. Effect of implementing an Epicutaneo-Caval Catheter team in Neonatal Intensive Care Unit. J Vasc Access. 2021;22(2):243-53.
20. Linck DA, Donze A, Hamvas A. Neonatal peripherally inserted central catheter team. Evolution and outcomes of a bedside-nurse-designed program. Adv Neonatal Care. 2007;7(1):22-9.
21. Legemaat MM, Jongerden IP, van Rens RM, Zielman M, van den Hoogen A. Effect of a vascular access team on central line-associated bloodstream infections in infants admitted to a neonatal intensive care unit: a systematic review. Int J Nurs Stud. 2015;52(5):1003-10.
22. Taylor T, Massaro A, Williams L, Doering J, McCarter R, He J, et al. Effect of a dedicated percutaneously inserted central catheter team on neonatal catheter-related bloodstream infection. Adv Neonatal Care. 2011;11(2):122-8.
23. Haddadin Y, Annamaraju P, Regunath H. Central Line Associated Blood Stream Infections. StatPearls. Treasure Island (FL)2021.
24. Bonizzoli M, Batacchi S, Cianchi G, Zagli G, Lapi F, Tucci V, et al. Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. Intensive Care Med. 2011;37(2):284-9.
25. Pet GC, Eickhoff JC, McNevin KE, Do J, McAdams RM. Risk factors for peripherally inserted central catheter complications in neonates. J Perinatol. 2020;40(4):581-8.
26. Ragavan M, Gazula S, Yadav DK, Agarwala S, Srinivas M, Bajpai M, et al. Peripherally inserted central venous lines versus central lines in surgical newborns--a comparison. Indian J Pediatr. 2010;77(2):171-4.
27. Barone G, Pittiruti M, Ancora G, Vento G, Tota F, D'Andrea V. Centrally inserted central catheters in preterm neonates with weight below 1500 g by ultrasound-guided access to the brachio-cephalic vein. J Vasc Access. 2020:1129729820940174.
28. Ostroff M, Zauk A, Chowdhury S, Moureau N, Mobley C. A retrospective analysis of the clinical effectiveness of subcutaneously tunneled femoral vein cannulations at the bedside: A low risk central venous access approach in the neonatal intensive care unit. J Vasc Access. 2020:1129729820969291.
29. Hosseinpour M, Mashadi MR, Behdad S, Azarbad Z. Central venous catheterization in neonates: Comparison of complications with percutaneous and open surgical methods. J Indian Assoc Pediatr Surg. 2011;16(3):99-101.

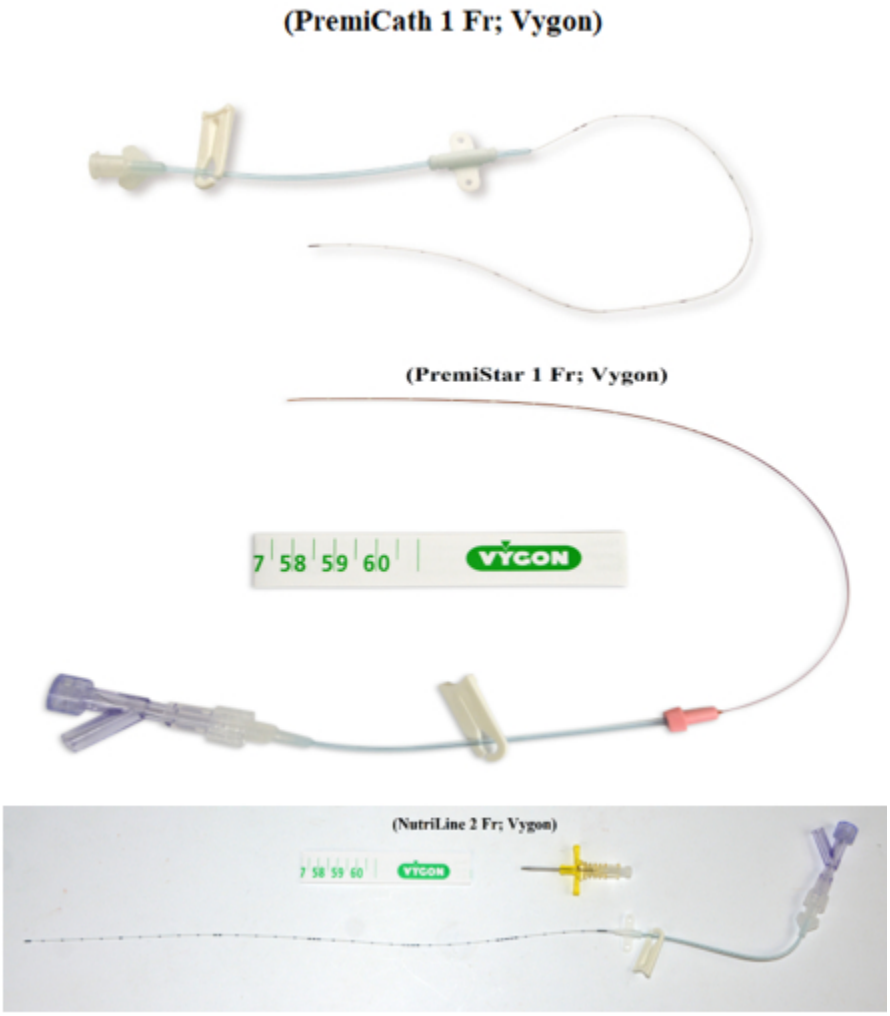


Figure 1: Three types of Peripherally Inserted Central Catheters (PICCs).

296x342mm (38 x 38 DPI)

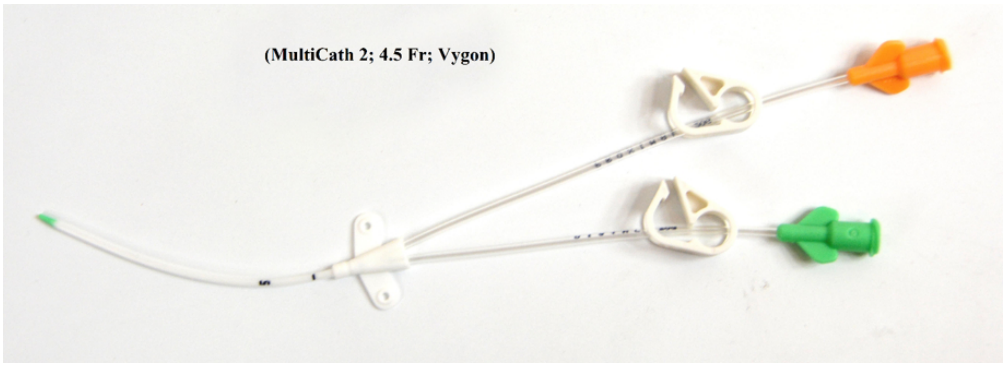


Figure 2. Non-tunnelled Ultrasound-Guided Central Venous Catheter (USG-CVC).

611x219mm (38 x 38 DPI)

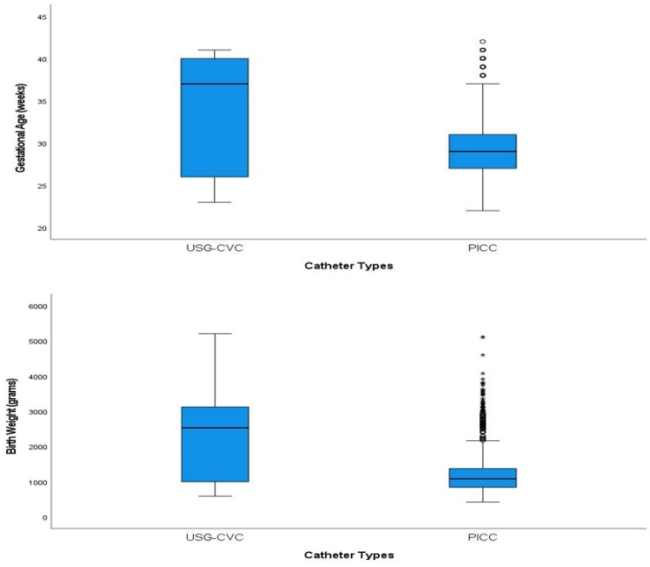
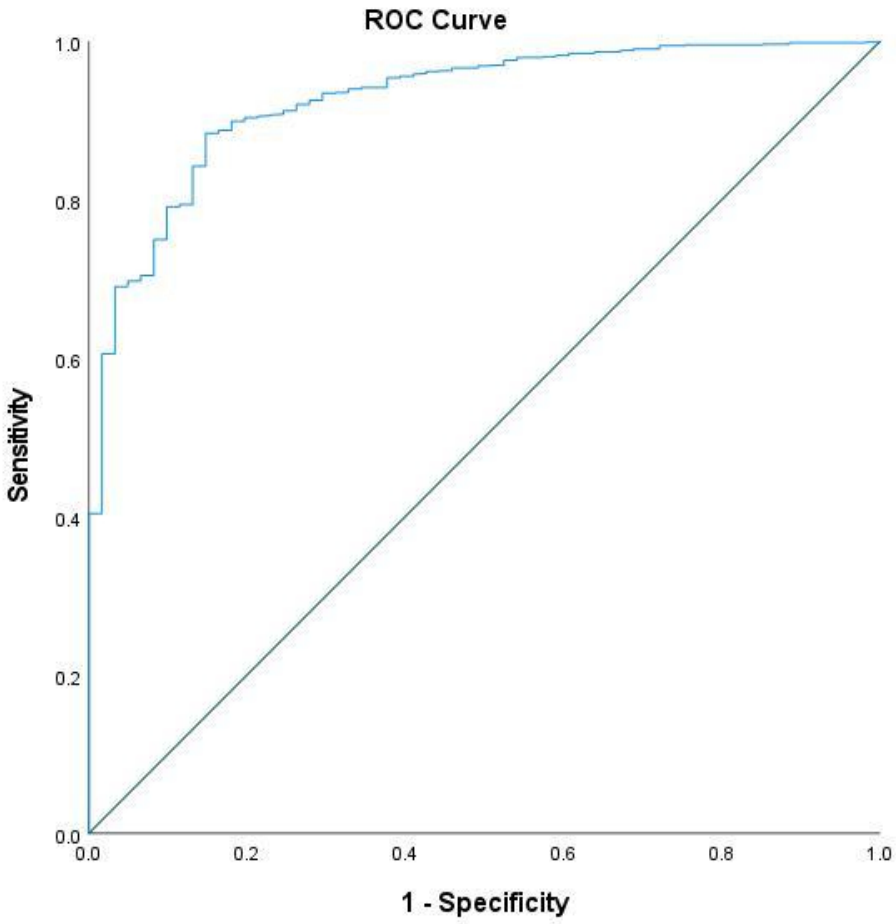


Figure 3. Box plot depicting the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types

855x481mm (38 x 38 DPI)



[Area under the curve (AUC) value was 0.927 (95% CI 0.90, 0.96), P=0.001]

Figure 4. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter types (USG-CVC and PICC)

211x211mm (72 x 72 DPI)

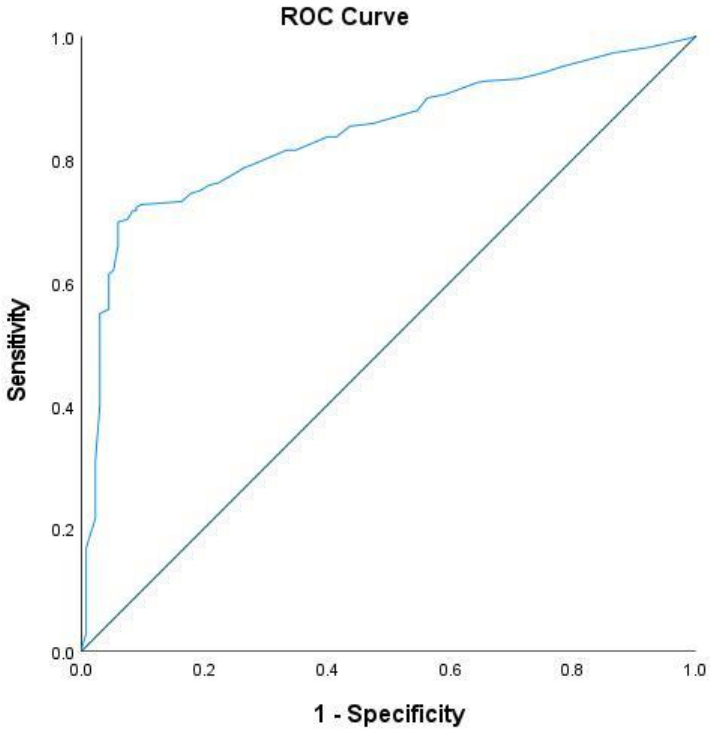


Figure 5. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter insertion success rate (successful/not successful)

234x188mm (72 x 72 DPI)

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	In the abstract. In the abstract. Not applicable.
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported		PICCs and non-tunnelled USG-CVCs have risks associated with their usage.	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses		To compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU	Aims and objectives
Methods					
Study Design	4	Present key elements of study design early in the paper		Data are collected retrospectively	Title
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		A total of 1333 cases were evaluated who had PICC insertion and non-tunneled USG-CVC insertion. Related information for all cases between	Methods

				January 2016 and December 2018 was collected from the electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar.	
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	In the methods. Babies who had PICC insertion and non-tunneled USG-CVC insertion at NICU were enrolled.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details			Data were collected from the

		of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar.
Bias	9	Describe any efforts to address potential sources of bias		Being restrospective research design, appropriate comparable groups, physicians experience, and missing obervations on important condounders can not be ruled out.	Limitation of the study
Study size	10	Explain how the study size was arrived at		1264 babies who had PICC insertion and non-tunneled USG-CVC insertion between January 2016 and December 2018 were included in the research	Methods
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how			Yes, described in the methods under statistical analysis

		matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Described in methods
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	CERNER
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic,			Descrbed in table 1 and 2

		clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Given in table 2,3, and 4
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			N/A
Discussion					

Key results	18	Summarise key results with reference to study objectives			The success rate is higher when using PICC. It also has less incidence of complications when compared to the non-tunnelled USG-CVCs.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Limitation of the study
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled USG-CVCs. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.	Conclusion
Generalisability	21	Discuss the generalisability (external validity) of the study results			The overall success rate is higher in PICCs with less incidence of complications compared to the non-tunnelled

					USG-CVCs. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			N/A
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Corresponding author is responsible for it

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

*Checklist is protected under Creative Commons Attribution (CC BY) license.

BMJ Open

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-058866.R2
Article Type:	Original research
Date Submitted by the Author:	14-Mar-2022
Complete List of Authors:	Bayoumi, Mohammad; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), van Rens, Roland; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), CHANDRA, PREM; Hamad Medical Corporation, Medical Research Center, Shaltout, Deena; Hamad Medical Corporation, Medical Education Department, Gad, Ashraf; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Elmalik, Einas; Hamad Medical Corporation, Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Hammoudeh, Samer; Hamad Medical Corporation, Medical Research Center (MRC),
Primary Subject Heading:	Paediatrics
Secondary Subject Heading:	Qualitative research
Keywords:	NEONATOLOGY, Neonatal intensive & critical care < INTENSIVE & CRITICAL CARE, PERINATOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY

Mohammad A. A. Bayoumi[1], Matheus van Rens[1], Prem Chandra[3], Deena A. D. A. Shaltout[2], Ashraf I. Gad[1], Einas E. Elmalik[1], Samer Hammoudeh[3]

[1] Neonatal Intensive Care Unit (NICU), Women's Wellness and Research Center (WWRC), Hamad Medical Corporation (HMC), Doha, Qatar
[2] Department of Medical Education, Hamad Medical Corporation (HMC), Doha, Qatar
[3] Medical Research Center (MRC), Hamad Medical Corporation (HMC), Doha, Qatar

Author's emails:
Mohammad A. A. Bayoumi: moh.abdelwahab@hotmail.com
Matheus van Rens: rolandvanrens@gmail.com
Prem Chandra: pchandra@hamad.qa
Deena A. D. A. Shaltout: dshaltout@hamad.qa
Ashraf I. Gad: agad2@hamad.qa
Einas E. Elmalik: einas_e@yahoo.com
Samer Hammoudeh: shammoudeh@hamad.qa

Corresponding Author's Contact Details:
Dr Mohammad A. A. Bayoumi
Neonatal Intensive Care Unit, Women's Wellness and Research Center, Hamad Medical Corporation, P.O. Box: 3050, Doha, Qatar
Fax Number: +97444439571
Mobile Number: +97477671584
Email: moh.abdelwahab@hotmail.com

Abstract:

Objectives: We aimed to compare the success rates and other catheter-related parameters between Peripherally Inserted Central Catheters (PICCs) and non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) including femoral, jugular, brachiocephalic and subclavian lines.

Design: This was a retrospective observational study.

Setting: The study was performed in a level III NICU in Qatar, as a single-site study.

Participants: This study included 1333 neonates who required central venous catheter insertion in the NICU from January 2016 to December 2018. Of those, we had 1264 PICCs and 69 non-tunnelled USG-CVCs.

Outcome measures: The success rate and other catheter-related complications in the 2 groups.

Results: The overall success rate was 88.4% in the USG-CVCs (61/69) compared to 90% in the PICCs (1137/1264) group (P=0.68). However, the first prick success rate was 69.4% in USG-CVCs (43/69) compared to 63.6% in the PICCs (796/1264) group. Leaking and Central Line-Associated Blood Stream Infection (CLABSI) were significantly higher in the USG-CVC group compared to the PICC group (Leaking 16.4% vs. 2.3%, P=0.0001) (CLABSI 8.2% vs. 3.1%, P=0.03). CLABSI rates in the PICC group were 1.75 per 1000 catheter days in 2016 and 3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the USG-CVCs. USG-CVCs had to be removed due to catheter-related complications in 52.5% of the cases compared to 29.9% in PICCs, P=0.001. In 2018, we did not have any non-tunnelled USG-CVCs insertions in our NICU.

Conclusions: The overall complication rate, CLABSI and Leaking are significantly higher in non-tunnelled USG-CVCs compared to the PICCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Keywords:

Neonatal Intensive Care Unit, Neonate, Vascular Access, Peripherally Inserted Central Catheter, Non-Tunneled Ultrasound-Guided Central Venous Catheters.

Strengths and limitations of this study:

- This is an observational study including a large sample of 1333 neonates.
- The study provides information on the insertion success rates and complications of peripherally inserted central catheters and non-tunnelled ultrasound-guided central venous catheters in neonates.
- It is based on retrospective analyses of collected data.

Introduction:

Peripherally Inserted Central Catheters (PICCs) were described for the first time by Shaw in 1973. Since then, they have been used extensively due to their features (1). PICC insertion by direct superficial peripheral vein puncture offers long-term venous access for both term and preterm neonates and is often indicated in NICU for parental nutrition, long-term IV medications, antibiotic therapy, and vesicant drug administration (2, 3).

Non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) are inserted in neonates in special circumstances e.g. central venous pressure monitoring, blood withdrawal, hemodialysis, and for all other infusions and medications when PICC insertion fails (4). They are inserted in the internal jugular, brachiocephalic, subclavian, and femoral veins under ultrasound guidance (1, 5-7).

There is a limited number of studies comparing PICCs with USG-CVCs in neonates that necessitated further research and comparative analysis. This study aimed to compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU between 2016 and 2018.

Methods:

This single-centre retrospective study was conducted in the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation (HMC), Doha, Qatar. WWRC is the main specialist hub for women and newborns health services in Qatar with more than 18000 deliveries per year. The NICU in WWRC is a level III mainly medical unit with 112 beds and more than 2000 admissions per year with limited congenital cardiac or surgery cases.

Patient and Public Involvement:

Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Participants:

A total of 1333 cases were evaluated in this study. This includes 1264 babies who had PICC insertion and 69 who had non-tunnelled USG-CVC insertion. Related information for all cases between January 2016 and December 2018 was collected from the electronic medical system at the NICU. The study was approved by the Institutional Review Board (IRB) at HMC before the study procedures commenced (MRC-01-18-151).

A fully dedicated PICC insertion team was launched in January 2017. The PICC team has been expanded over time to include 15 neonatologist physicians, one neonatal nurse practitioner as well as 7 NICU Nurses. The team was trained in central line simulation workshops to insert PICC by the catheter-over-needle technique and the modified Seldinger technique (MST) (8, 9). The central line simulation workshop is a full-day workshop that was founded by the neonatal simulation team and is accredited by the Department of Healthcare Professions (DHP) in the Ministry of Public Health (MOPH) with a total of 7 Continuous Professional Development (CPD) hours both category I (1/7) and category III (6/7). The PICC team works in harmony and collaboration with 30 well-trained NICU nurses who are members of the Neonatal Specialized Nursing (NSN) Team. The NSN determines the patient's eligibility, takes care of the central line maintenance using transparent semipermeable dressing, enters the data in the electronic database, and gets the blood samples. There is no difference in the central line type of care, frequency or personnel in all types of catheters. In addition to their role in central line insertion and maintenance, the NSN team attends high-risk deliveries and play a pivotal role in neonatal transportation.

In our NICU, the indications for PICC insertions are the birth weight of < 1500 gm, the requirement of IV fluids for > 5 days, the requirement of IV medications for > 7 days, the requirement of hyperosmolar IV fluid therapy > 700 mosmol/L, and the requirement of > 3 Peripheral Intravenous Catheters (PIVC) insertions in the last 24 hours (10). A successful catheter insertion means a catheter inserted into a proper central venous position that can be used with its tip located either in the superior or inferior vena cava. As per our institutional guideline, 2 pricks are allowed per operator with a maximum of 3 in difficult lines. After 3 unsuccessful pricks, the procedure should be terminated.

Figure 1 shows the 3 types of PICCs available in our NICU; (NutriLine 2 Fr; Vygon), (PremiCath 1 Fr; Vygon), and (PremiStar 1 Fr; Vygon). PremiStar 1 Fr; Vygon is an antimicrobial impregnated catheter that is used in our unit for babies born less than 28 weeks gestation or when sepsis is suspected. We use NutriLine 2 Fr; Vygon, when a double lumen PICC or a long line is needed in big babies as its length is 30 cm. PremiCath 1 Fr; Vygon is used for the rest of our NICU babies who need PICC insertion. The most common veins used for PICC insertions are the great saphenous vein, small saphenous vein, posterior tibial vein, antecubital vein, cephalic vein, basilic vein, and ulnar vein. Figure 2 shows the non-tunnelled CVC available in our unit which is (MultiCath 2; 4.5 Fr; Vygon). The most common veins used for USG-CVC insertions are the internal jugular vein, femoral vein, brachiocephalic vein, and subclavian vein.

In our practice, non-tunnelled USG-CVC was used only when PICC insertion has failed by 2-3 operators; 2 pricks for each. USG-CVCs were inserted either by the pediatric surgeon or the pediatric anaesthetist on-call physician under US guidance. Currently, we use the handheld wireless probe-type ultrasound scanner machine to guide the catheter insertion and for the catheter tip location.

We followed the Centers for Disease Control and Prevention (CDC) definition for central line-associated bloodstream infection (CLABSI) and CLABSI rate. CLABSI is defined as a laboratory-confirmed bloodstream infection where an eligible bloodstream infection (BSI)

organism is identified, and an eligible central line is present on the laboratory-confirmed bloodstream infection (LCBI) date of the event (DOE) or the day before. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility. CLABSI rate is the total number of CLABSI divided by the total number of device days 1000 (11, 12).

The differential time to positivity (DTP) is defined as a difference in time to positivity of ≥ 2 h between peripheral blood culture and a CVC blood culture (peripheral DTP) or between 2 CVC blood cultures from different lumens of a multi-lumen catheter (CVC DTP) (13). Due to its limitation reported in the literature, our unit does not prefer to use the differential time to positivity (DTP) for the diagnosis of CLABSI (14).
The authors designed an electronic system-based data collection sheet to collect all catheter-related parameters in the 2 groups.

Statistical Analysis:
Descriptive statistics were used to summarize and determine the sample characteristics and distribution of participants' data. The normally distributed data and results were reported with mean and standard deviation (SD); the remaining results were reported with median and inter-quartile range (IQR). Categorical data were summarized using frequencies and proportions. Associations between two or more qualitative data variables were assessed using Chi-square ($\chi 2$) test or Fisher Exact test as appropriate. Quantitative data between the two independent groups (USG-CVC and PICC) were analyzed using unpaired t (for normally distributed data) or Mann Whitney U test (for skewed or non-normally distributed data) as appropriate. Univariate and multivariate logistic regression analysis was applied to determine and assess the potential factors and predictors associated with the catheter insertion success rate adjusted for potential factors and predictors such as catheter types, gestational age, birth weight, the reason for catheter insertion, side of the body, site of insertion and number of pricks. For multivariate logistic regression models, predictor variables were included considering both statistical and clinical significance. The results of logistic regression analysis were presented as odds ratios (OR) with corresponding 95% confidence intervals (CI). Thereafter, we used the receiver operating characteristic curve (ROC) to evaluate the discriminative ability (predictive accuracy of the developed logistic regression model) of potentially significant variables associated with catheter insertion success rate. Box plots were constructed depicting the distribution of gestational age and birth weight across two catheter types. All P values presented were two-tailed, and P values <0.05 were considered statistically significant. All statistical analyses were performed using statistical packages SPSS version 27.0 (Armonk, NY: IBM Corp) and Epi-info (Centers for Disease Control and Prevention, Atlanta, GA) software.

Results:

Among the three years that this study covered, the usage of USG-CVC has progressively declined to zero in 2018, on which the catheter insertion success rate increased to 97%. Shown in table 1 are the distribution of patients and catheter-related variables associated with the types of catheters. When USG-CVC was compared to PICC about gestational age, the former was significantly higher (33.88±6.34 vs. 29.32±4.03, P=0.0001). Birth weight was also significantly higher among USG-CVC compared to PICC (2161.25±1140.26 vs. 1234.57±624.90,

respectively, P=0.0001). Figure 3 shows the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types. The duration of catheter insertion was however not significant (USG-CVC 11.69±9.23, PICC 14.57±12.56, P=0.14). Further comparisons between USG-CVC and PICC on several parameters. PICC had a higher success rate (90% vs. 88.4%), however, the difference did not reach statistical significance.

Table 1: Distribution of patients' profiles and catheter-related parameters and their association with the catheter types

Variables	Total n=1333	USG-CVC 69 (5.2%)	PICC 1264 (94.8%)	P-value
Year				0.001
2016	376 (28.2)	42 (60.9)	334 (26.4)	
2017	507 (38)	27 (39.1)	480 (38)	
2018	450 (33.8)	0 (0)	450 (35.6)	
Side of the body				0.002
Left	498 (41.1)	14 (22.6)	484 (42.1)	
Right	715 (58.9)	48 (77.4)	667 (57.9)	
Site of Insertion				0.001
Upper Extremities	360 (29.5)	37 (53.6)	323 (28)	
Lower Extremities	861 (70.5)	32 (46.4)	829 (72)	
Number of Pricks				0.001
First Prick	839 (63.9)	43 (69.4)	796 (63.6)	
Second Prick	305 (23.2)	8 (12.9)	297 (23.7)	
Third Prick	145 (11)	6 (9.7)	139 (11.1)	
Fourth Prick	22 (1.7)	4 (6.5)	18 (1.4)	
Fifth Prick	1 (0.1)	0 (0)	1 (0.1)	
Sixth Prick	2 (0.2)	1 (1.6)	1 (0.1)	
Reason for Insertion				0.47
Difficult IV Insertion	8 (0.6)	0 (0)	8 (0.6)	
Hypoglycemia	10 (0.8)	0 (0)	10 (0.8)	
Long term IV fluid therapy	1286 (96.6)	68 (100)	1218 (96.4)	
Long term IV medication therapy	27 (2)	0 (0)	27 (2.1)	
Catheter insertion Success Rate				0.68
Successful	1198 (89.9)	61 (88.4)	1137 (90)	
Not Successful	135 (10.1)	8 (11.6)	127 (10)	
Reason for Removal				
CLABSI	40 (3.4)	5 (8.2)	35 (3.1)	0.031
Leaking	36 (3)	10 (16.4)	26 (2.3)	0.001
Accidental Removal	8 (0.7)	1 (1.6)	7 (0.6)	0.40
Broken Catheter	7 (0.6)	0 (0)	7 (0.6)	0.69
Local redness and swelling	104 (8.7)	5 (8.2)	99 (8.8)	0.88
Occlusion	42 (3.5)	0 (0)	42 (3.7)	0.13
Malposition	13 (1.1)	0 (0)	13 (1.1)	0.50
Elective	833 (69.9)	29 (47.5)	804 (71.1)	0.001
Death	39 (3.3)	5 (8.2)	34 (3)	0.03
Phlebitis	70 (5.9)	6 (9.8)	64 (5.7)	0.18
Gestational Age (weeks), Mean ±SD	29.55±4.30	33.88±6.34	29.32±4.03	0.001
Median (IQR)	29 (27, 31)	37 (26, 40)	29 (27, 31)	
Gestational Age				0.001
22 to 28 weeks	602 (45.2)	22 (31.9)	580 (45.9)	

> 28 to 32 weeks	490 (36.8)	4 (5.8)	486 (38.4)	
> 32 to 36 weeks	100 (7.5)	8 (11.6)	92 (7.3)	
> 36 weeks	141 (10.6)	35 (50.7)	106 (8.4)	
Birth Weight (gm), Mean ±SD	1282.6±692.1	2161.4±1140.3	1234.6±624.9	0.001
Median (IQR)	1095 (850, 1400)	2530 (970, 3122)	1080 (840, 1370)	
Birth Weight				0.001
BW <=1 kg	561 (42.1)	21 (30.4)	540 (42.7)	
BW > 1 to 2 kg	618 (46.5)	10 (14.5)	608 (48.1)	
BW > 2 to 3 kg	87 (6.5)	16 (23.2)	71 (5.6)	
BW >3 kg	67 (5)	22 (31.9)	42 (3.6)	

This is a retrospective study design and for some parameters, the data values were incomplete due to the unavailability of the information in the patients' record files. All percentage (%) was computed using non-missing data values. IQR: Inter-Quartile range.

We performed univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with dichotomous outcome variable catheter types (USG-CVC and PICC), it was observed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal (elective vs non-elective), duration of gestation and birth weight were significantly associated with catheter types. The multivariate logistic regression analysis showed that year of catheter insertion, side of the body, site of insertion, number of pricks ≥3 pricks, reasons for removal, and birth weight were remained significantly associated with catheter types adjusting other predictors and factors shown in table 2. The discriminative ability of the significant predictors (observed in multivariate analysis) in predictive catheter types were found to be good with an area under the ROC curve value of 0.927 (95% CI 0.90, 0.96), which indicates that this developed regression model demonstrated an excellent fit, Figure 4.

Table 2: Logistic regression analysis with potential factors and predictors associated with catheter types USG-CVC and PICC

Variables		Univariate analysis			Multivariate analysis		
	Catheter type- PICC, n (%)	Unadjusted Odds ratio (OR)	95% CI for OR	P-value	Adjusted Odds ratio (OR)	95% CI for OR	P-value
Year							
2016	334 (88.8)	1.0 (reference)			1.0 (reference)		
2017	480 (94.7)	2.24	1.35, 3.70	0.002	3.43	1.79, 6.54	0.001
2018	450 (100)	--	--	--	--	--	--
Side of the body							
Left	484 (97.2)	1.0 (reference)			1.0 (reference)		
Right	667 (93.3)	0.40	0.22, 0.74	0.003	0.34	0.17, 0.70	0.003
Site of Insertion							
Upper Extremities	323 (89.7)	1.0 (reference)			1.0 (reference)		
Lower Extremities	829 (96.3)	2.97	1.82, 4.85	0.001	3.39	1.81, 6.33	0.001
Number of Pricks							
One Prick	796 (94.9)	1.0 (reference)			1.0 (reference)		
	297 (97.4)						

Two Prick	171 (90.5)	2.01	0.93, 4.32	0.075	2.58	0.97, 6.86	0.058
≥ 3 Pricks		0.51	0.29, 0.91	0.023	0.39	0.16, 0.95	0.037
Reason for catheter insertion							
Long term IV fluid therapy	1218 (94.7)	1.0 (reference)			1.0 (reference)		
Others*	45 (100)	--	--	--	--	--	--
Catheter Insertion Success Rate							
Not Successful	127 (94.1)	1.0 (reference)	0.55, 2.51	0.679	1.0 (reference)	0.59, 2.46	0.569
Successful	1137 (94.9)	1.17			1.14		
Reasons for removal							
Non-Elective	327 (91.1)	1.0 (reference)			1.0 (reference)		
Elective	804 (96.5)	2.71	1.62, 4.56	0.001	2.16	1.16, 4.01	0.015
Gestational age (weeks) PICC vs USG-CVC	29.3 ± 4.1 vs 33.9 ± 6.3	0.82	0.78, 0.86	0.001	1.03	0.90, 1.17	0.715
Birth Weight (gm) PICC vs USG-CVC	1235.6 ± 624.9 vs 2161.4 ± 1140.3	0.98	0.98, 0.99	0.001	0.99	0.98, 0.99	0.001

Catheter types- USG-CVC was considered as the reference group; CI: Confidence interval
**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

CLABSI and Leaking were noted to be significantly higher in the USG-CVC group compared to the PICC group. CLABSI rate is defined as the total number of CLABSI divided by the total number of device days 1000 (11, 12). CLABSI rates in the PICC group were 1.75 in 2016 and 3.3 in 2017 compared to 6.91 in 2016 (P=0.0001) and 14.32 in 2017 (P=0.0001) for the non-tunnelled USG-CVCs. We did not have any USG-CVC inserted in 2018.

In the PICC group, 804 (71.1%) were removed electively after completion of therapy compared to 29 (47.5%) in the USG-CVC group. No significant difference was noted between the 2 groups regarding the other catheter-related complications. No serious or long term complications e.g cardiac arrhythmia, accidental arterial puncture, cardiac tamponade, pericardial or pleural effusion (15), was noted in both groups across the three years.

The results of univariate and multivariate logistic regression analysis testing for potential factors and predictors and their possible association with catheter insertion success rates are presented in Tables 3 and 4. Univariate results indicated that year of catheter insertion, birth weight and the number of pricks had a significant effect on the likelihood of catheter insertion success rates. In patients who had two pricks (unadjusted OR 0.03; 95% CI 0.01, 0.07, P=0.028) and ≥3 pricks (unadjusted OR 0.01; 95% CI 0.01, 0.03, P=0.013) were significantly associated with a decreased likelihood of catheter insertion success rates compared to patients who had one prick. In addition, it was noted that catheter type PICC was associated with a higher rate of catheter insertion success rates, however, this difference was statistically insignificant (P=0.679).

Table 3: Univariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate, n (%)	Unadjusted odds ratio (OR)	95% CI for OR	P-value
Catheter Types				
USG-CVC	61 (88.4)	1.0 (refernce)		
PICC	1137 (90)	1.17	0.55, 2.51	0.679
Year				
2016	309 (81.7)	2.0 (refernce)		
2017	450 (88.6)	1.73	1.18, 2.52	0.004
2018	439 (97.6)	8.91	4.64, 17.12	0.001
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.01	0.96, 1.04	0.954
Birth Weight (g)	1270.1 ± 677.5 vs 1394.2 ± 803.3	0.98	0.98, 0.99	0.045
Reason for catheter insertion				
Long term IV fluid therapy	1156 (89.9)	2.0 (refernce)		
Others*	42 (93.3)	1.57	0.48, 1.51	0.453
Side of the body				
Left	491 (98.6)	2.0 (refernce)		
Right	706 (98.7)	1.12	0.41, 3.03	0.826
Site of Insertion				
Upper Extremities	353 (98.1)	2.0 (refernce)		
Lower Extremities	845 (98.1)	1.05	0.43, 2.57	0.920
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.03	0.01, 0.07	0.028
≥ 3 Pricks	121 (63.7)	0.01	0.01, 0.03	0.013

CI: Confidence interval

**Others includes: Difficult IV insertion, hypoglycemia and long term IV medication therapy*

The multivariate logistic regression analysis showed that duration of gestation (weeks) and the number of pricks were remained significantly (P<0.05) associated with the catheter insertion success rate after controlling and adjusting potential factors and predictors as shown in Table 4. The higher catheter insertion success rates were associated with increasing gestational age (adjusted OR 1.23; 95% CI 1.03, 1.44, P=0.015). Whereas, in patients who had two pricks (adjusted OR 0.07; 95% CI 0.01, 0.57, P=0.014) and ≥3 pricks (adjusted OR 0.02; 95% CI 0.01, 0.13, P=0.001) were significantly associated with a reduction in the likelihood of catheter insertion success rates when compared to patients who had one prick. Thereafter, we computed a prediction model to evaluate the discriminative ability of potentially significant predictors (observed in the developed multivariate logistic regression model) associated with catheter insertion success rates using ROC curve analysis. The value of area under the curve (AUC) observed was found to be

0.841 (95% CI 0.81, 0.87), which is indicating that this developed regression model demonstrated an excellent fit, Figure 5.

Table 4: Multivariate logistic regression analyses with potential significant factors and predictors associated with catheter insertion success rates

Variables	Catheter insertion success rate N (%)	Adjusted odds ratio (OR)	95% CI for OR	P-value
Gestational Age (week)	29.56 ± 4.20 vs 29.53 ± 5.12	1.23	1.03, 1.44	0.015
Number of Pricks				
One Prick	833 (99.3)	1.0 (refernce)		
Two Prick	244 (79.5)	0.07	0.01, 0.57	0.014
≥ 3 Pricks	121 (63.7)	0.02	0.01, 0.13	0.001

CI: Confidence interval

Discussion:

Both PICCs and non-tunnelled USG-CVCs have risks associated with their usage. Immediate risks include injury to local structures, accidental arterial puncture, phlebitis at the insertion site, air embolism, hematoma, arrhythmia, and catheter damage and malposition. Late complications include infection, occlusion, thrombosis, infiltration, extravasation, and catheter migration (16-18). Infection, thrombosis, embolization, hydrocephalus, are complications reported in premature babies receiving central venous lines (3).

The current study compared PICC to USG-CVC in a sample of cases from Qatar. The results also showed a progressive reduction in the usage of USG-CVC across the 3 years till reached 0% in 2018. This is due to the implementation of a PICC insertion team in early 2017 with a progressive build-up of the team skills (19). Since then, overall success and first prick rates have significantly increased. Reports of an overall success rate of 94% were indicated elsewhere (20). A systematic review highlighted the importance and necessity of a vascular access team in the NICU, as it reflects positively on the rate of bloodstream infections (21). This was also confirmed in another study where the rate of infections was reduced by 50% after the establishment of a PICC team in the NICU (22).

Only 29 (47.5%) of our USG-CVC were electively removed after completion of therapy while the rest were removed due to death, phlebitis, CLABSI, or other catheter-related complications. In the PICC group, elective removal was noted to be significantly higher 804 (71.1%) than USG-CVC (P= 0.0001). The higher rate of CLABSI in USG-CVCs compared to PICCs is mainly related to the vulnerable insertion sites being close to infection or joint areas (23). Also, the higher rate of catheter leaking in USG-CVCs might be due to occlusions resulting from mechanical or postural factors, catheter malpositioning, or undesirable catheter-tip location.

CLABSI and thrombosis might also lead to catheter leaking (24). Approximately one-third of PICCs were associated with complications in another study which is close to our PICC data (25).

Ragavan et al described the advantages of using PICCs inserted in the cubital veins as to have a reduced complication incidence rate, as well as maintenance rates in comparison to USG-CVCs inserted in the internal jugular vein. The authors concluded by recommending the usage of PICCs routinely when dealing with neonatal surgical patients (26). On the other hand, a recent study reported a 100% success rate of 30 preterm babies who underwent an ultrasound-guided brachio-cephalic central venous catheter insertion. No case of accidental arterial or pleural puncture was noted by the researchers (27). In another study involving neonates with femoral central venous catheterization (28), the overall success rate was 100% of neonates (n = 82/82), first attempt 63/74 (85%), second attempt 8/74 (11%), and third attempt 3/74 (4%). Another 2 studies reported no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (4, 29).

The limitation of this study is being retrospective with potential risks of bias and confounding factors especially when single centre studies. The imbalance in numbers between the two groups suggest that the inferences may not be robust. Another limitation of the study is that the PICC team was properly trained to insert PICCs while the USG-CVC were placed by operators not belonging to the team (surgeons or anaesthetists). Potential bias by indication might be an issue as percutaneous central venous catheters were considered if some attempts for a PICC insertion failed. As reported by other researchers (28), USG-CVCs sometimes needed multiple pricks to get the catheter successfully inserted as reported in our study. This might be related to the level of experience, the number of exposures and lack of training as this task is not the main task daily performed by the operators (surgeons and anaesthetists). Besides, being inserted as rescue mode, not for selected patients is a stressor that might be a factor in increasing the number of pricks.

No USG-CVC was inserted in our unit for the last 2 years, however, it might be needed in the future in certain indications. Randomized controlled trials to study the feasibility of intracavitary ECG in catheter insertion and tip location in neonates are strongly recommended. Also, the use of US guidance during peripheral intravenous catheters insertion and the frequency of its use in tip location monitoring of correctly positioned central lines to confirm the tip positions and diagnose catheter migration are both rich areas for future prospective studies.

Conclusion:

The overall complication rate, CLABSI and Leaking are significantly higher in non-tunnelled USG-CVCs compared to the PICCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.

Data Availability Statement:

The data that support the findings of this study are available upon reasonable request from the corresponding author. Data requests should be made to Bayoumi M., moh.abdelwahab@hotmail.com

Patient consent for publication:

Not required.

Ethics approval:

This research was approved by the Institutional Review Board (IRB) of the Medical Research Center, Hamad Medical Corporation, Doha, Qatar (MRC-01-18-151). A waiver for the requirement of informed consent from the mothers whose records were analyzed was granted by the Chair of the Medical Research Center on the grounds of being a minimal risk study. All methods were performed following the relevant guidelines and regulations. The author signs for and accepts responsibility for releasing this material on behalf of all co-authors.

Acknowledgement:

This research was funded and supported by the Medical Research Center (MRC), HMC, Doha, Qatar. Special thanks to the entire PICC and NSN teams in WWRC who provide high-quality care to our newborns.

Conflict of Interest:

No competing interests.

Contributors:

MAAB and DADAS conceptualized and designed the study. MVR and MAAB collected, cleaned, and anonymized the data. PC designed and performed the data analysis. MAAB, PC, and SH drafted the initial manuscript. MAAB and PC designed the figures. EEE, MAAB, AIG and PC intellectually revised the manuscript. All authors reviewed and revised the manuscript, and approved the final submitted manuscript.

Funding:

This work was supported by the Medical Research Center (MRC), Hamad Medical Corporation, Doha, Qatar (Protocol number MRC-01-18-151).

Provenance and peer review:

Not commissioned; externally peer-reviewed.

References:

1. Barone G, Pittiruti M. Epicutaneo-caval catheters in neonates: New insights and new suggestions from the recent literature. J Vasc Access. 2020;21(6):805-9.
2. McCay AS, Elliott EC, Walden M. Videos in clinical medicine. PICC placement in the neonate. N Engl J Med. 2014;370(11):e17.
3. Yu X, Yue S, Wang M, Cao C, Liao Z, Ding Y, et al. Risk Factors Related to Peripherally Inserted Central Venous Catheter Nonselective Removal in Neonates. Biomed Res Int. 2018;2018:3769376.
4. Foo R, Fujii A, Harris JA, LaMorte W, Moulton S. Complications in tunneled CVL versus PICC lines in very low birth weight infants. J Perinatol. 2001;21(8):525-30.
5. Araujo CC, Lima MC, Falbo GH. Percutaneous subclavian central venous catheterization in children and adolescents: success, complications and related factors. J Pediatr (Rio J). 2007;83(1):64-70.
6. Lausten-Thomsen U, Merchaoui Z, Dubois C, Eleni Dit Trolli S, Le Sache N, Mokhtari M, et al. Ultrasound-Guided Subclavian Vein Cannulation in Low Birth Weight Neonates. Pediatr Crit Care Med. 2017;18(2):172-5.
7. Tan Y, Tu Z, Ye P, Xu Y, Ye M, Bai L, et al. Ultrasound guidance for internal jugular vein cannulation in neonates: Modified dynamic needle tip positioning short-axis out-of-plane technique versus long-axis in-plane technique, a randomized controlled trial. J Vasc Access. 2021:11297298211015043.
8. Uygun I, Okur MH, Otcu S, Ozturk H. Peripherally inserted central catheters in the neonatal period. Acta Cir Bras. 2011;26(5):404-11.
9. Qin KR, Nataraja RM, Pacilli M. Long peripheral catheters: Is it time to address the confusion? J Vasc Access. 2019;20(5):457-60.
10. Gorski LA, Hadaway L, Hagle ME, Broadhurst D, Clare S, Kleidon T, et al. Infusion Therapy Standards of Practice, 8th Edition. J Infus Nurs. 2021;44(1S Suppl 1):S1-S224.
11. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
12. Hussain ASS, Ali SR, Ariff S, Arbab S, Demas S, Zeb J, et al. A protocol for quality improvement programme to reduce central line-associated bloodstream infections in NICU of low and middle income country. BMJ Paediatr Open. 2017;1(1):e000008.
13. Al-Juaid A, Walkty A, Embil J, Crockett M, Karlowsky J. Differential time to positivity: vascular catheter drawn cultures for the determination of catheter-related bloodstream infection. Scand J Infect Dis. 2012;44(10):721-5.
14. Orihuela-Martin J, Rodriguez-Nunez O, Morata L, Cardozo C, Puerta-Alcalde P, Hernandez-Meneses M, et al. Performance of differential time to positivity as a routine diagnostic test for catheter-related bloodstream infections: a single-centre experience. Clin Microbiol Infect. 2020;26(3):383 e1- e7.
15. Yu X, Wang X, Fan L, Cao N, Yang F, Li J, et al. Iatrogenic Pleural Effusion Due to Extravasation of Parenteral Nutrition via an Epicutaneo Cava Catheter in Neonates: A Prospective Cohort Study. Front Pediatr. 2020;8:570978.
16. Kornbau C, Lee KC, Hughes GD, Firstenberg MS. Central line complications. Int J Crit Illn Inj Sci. 2015;5(3):170-8.
17. Wrightson DD. Peripherally inserted central catheter complications in neonates with upper versus lower extremity insertion sites. Adv Neonatal Care. 2013;13(3):198-204.
18. Santos FKY, Flumignan RLG, Areias LL, Sarpe AKP, Amaral FCF, Ávila RBd, et al. Peripherally inserted central catheter versus central venous catheter for intravenous access: A protocol for systematic review and meta-analysis. Medicine. 2020;99(30):e20352.

19. Bayoumi MAA, Van Rens MFP, Chandra P, Francia ALV, D'Souza S, George M, et al. Effect of implementing an Epicutaneo-Caval Catheter team in Neonatal Intensive Care Unit. J Vasc Access. 2021;22(2):243-53.
20. Linck DA, Donze A, Hamvas A. Neonatal peripherally inserted central catheter team. Evolution and outcomes of a bedside-nurse-designed program. Adv Neonatal Care. 2007;7(1):22-9.
21. Legemaat MM, Jongerden IP, van Rens RM, Zielman M, van den Hoogen A. Effect of a vascular access team on central line-associated bloodstream infections in infants admitted to a neonatal intensive care unit: a systematic review. Int J Nurs Stud. 2015;52(5):1003-10.
22. Taylor T, Massaro A, Williams L, Doering J, McCarter R, He J, et al. Effect of a dedicated percutaneously inserted central catheter team on neonatal catheter-related bloodstream infection. Adv Neonatal Care. 2011;11(2):122-8.
23. Haddadin Y, Annamaraju P, Regunath H. Central Line Associated Blood Stream Infections. StatPearls. Treasure Island (FL)2021.
24. Bonizzoli M, Batacchi S, Cianchi G, Zagli G, Lapi F, Tucci V, et al. Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. Intensive Care Med. 2011;37(2):284-9.
25. Pet GC, Eickhoff JC, McNevin KE, Do J, McAdams RM. Risk factors for peripherally inserted central catheter complications in neonates. J Perinatol. 2020;40(4):581-8.
26. Ragavan M, Gazula S, Yadav DK, Agarwala S, Srinivas M, Bajpai M, et al. Peripherally inserted central venous lines versus central lines in surgical newborns--a comparison. Indian J Pediatr. 2010;77(2):171-4.
27. Barone G, Pittiruti M, Ancora G, Vento G, Tota F, D'Andrea V. Centrally inserted central catheters in preterm neonates with weight below 1500 g by ultrasound-guided access to the brachio-cephalic vein. J Vasc Access. 2020:1129729820940174.
28. Ostroff M, Zauk A, Chowdhury S, Moureau N, Mobley C. A retrospective analysis of the clinical effectiveness of subcutaneously tunneled femoral vein cannulations at the bedside: A low risk central venous access approach in the neonatal intensive care unit. J Vasc Access. 2020:1129729820969291.
29. Hosseinpour M, Mashadi MR, Behdad S, Azarbad Z. Central venous catheterization in neonates: Comparison of complications with percutaneous and open surgical methods. J Indian Assoc Pediatr Surg. 2011;16(3):99-101.

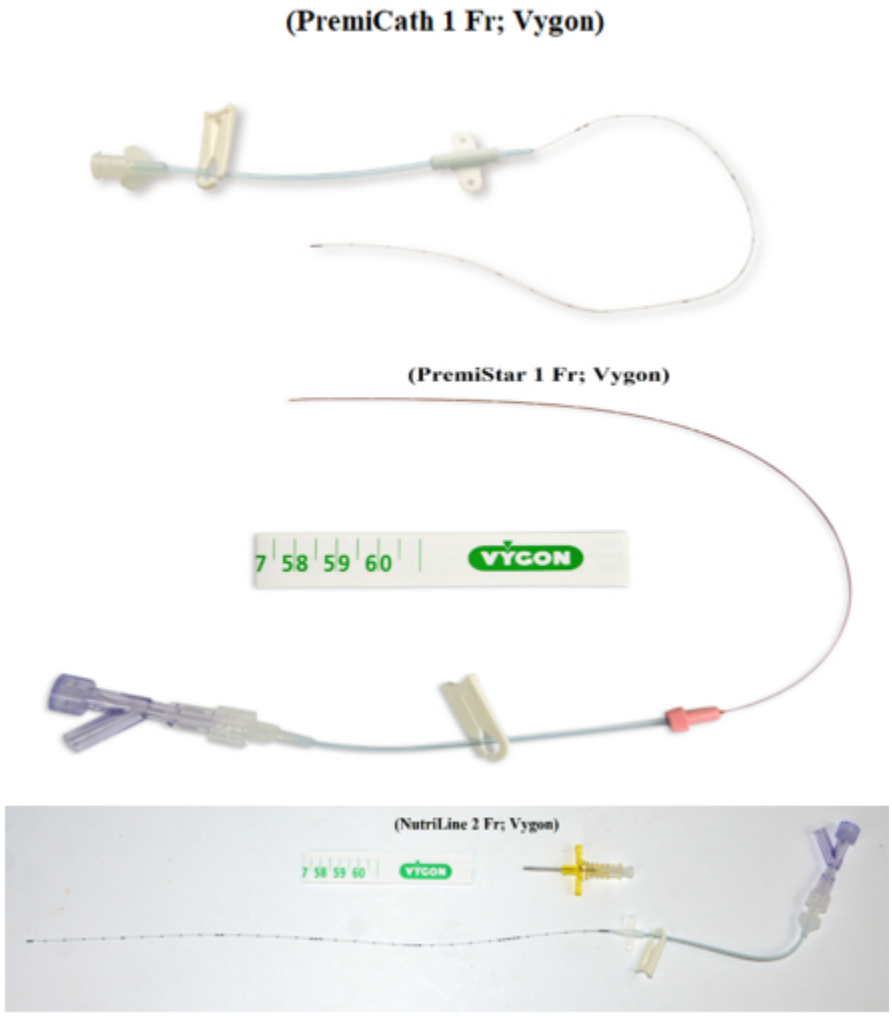


Figure 1: Three types of Peripherally Inserted Central Catheters (PICCs).

296x342mm (38 x 38 DPI)

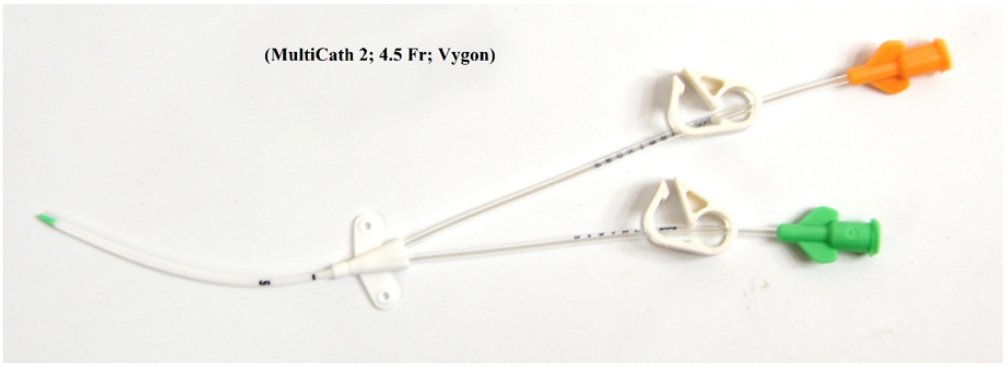


Figure 2. Non-tunnelled Ultrasound-Guided Central Venous Catheter (USG-CVC).

611x219mm (38 x 38 DPI)

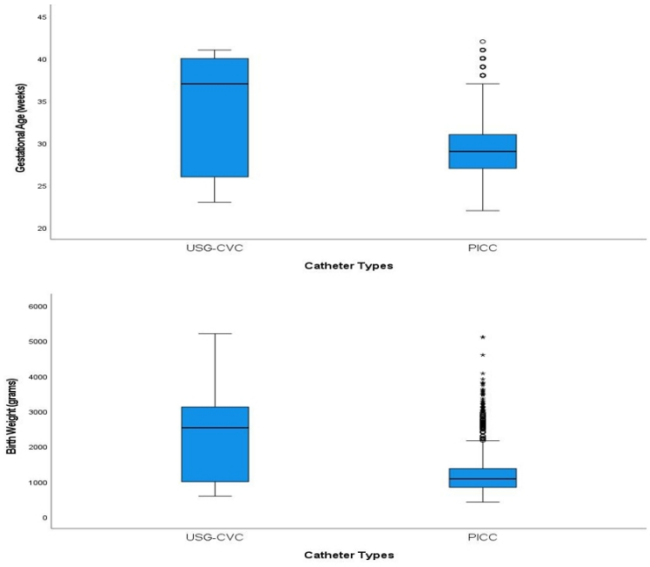
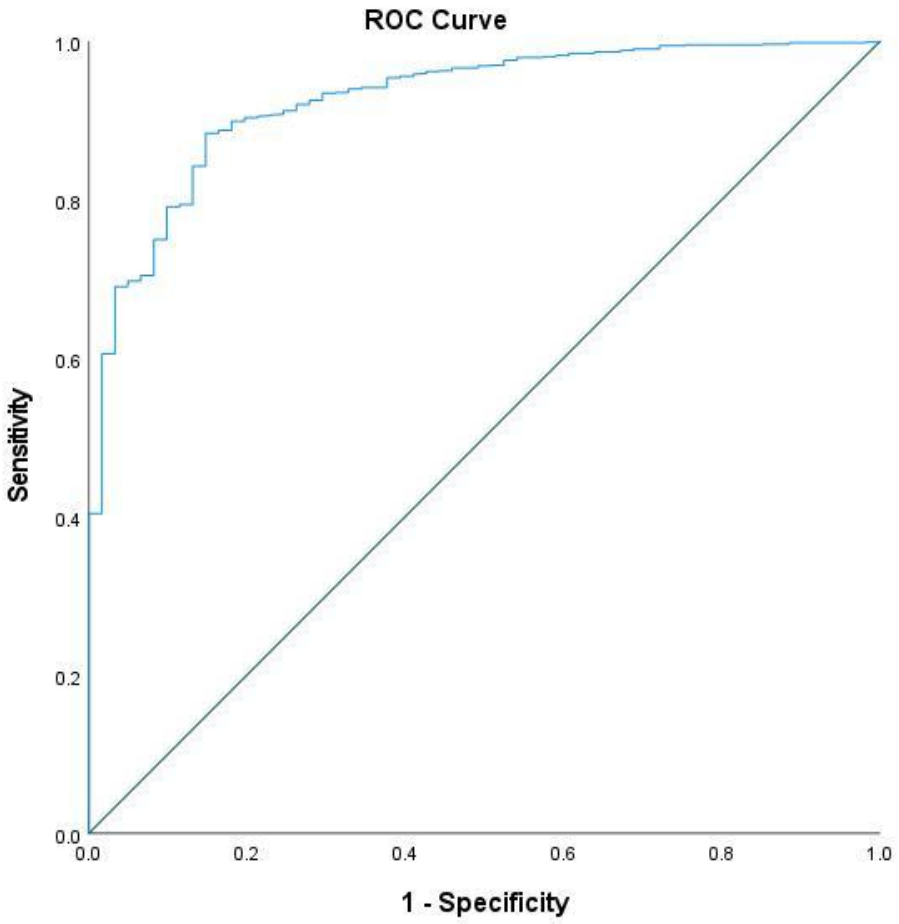


Figure 3. Box plot depicting the distribution of Gestational age (weeks) and Birth weight (gm) across two catheter types

855x481mm (38 x 38 DPI)



[Area under the curve (AUC) value was 0.927 (95% CI 0.90, 0.96), P=0.001]

Figure 4. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter types (USG-CVC and PICC)

211x211mm (72 x 72 DPI)

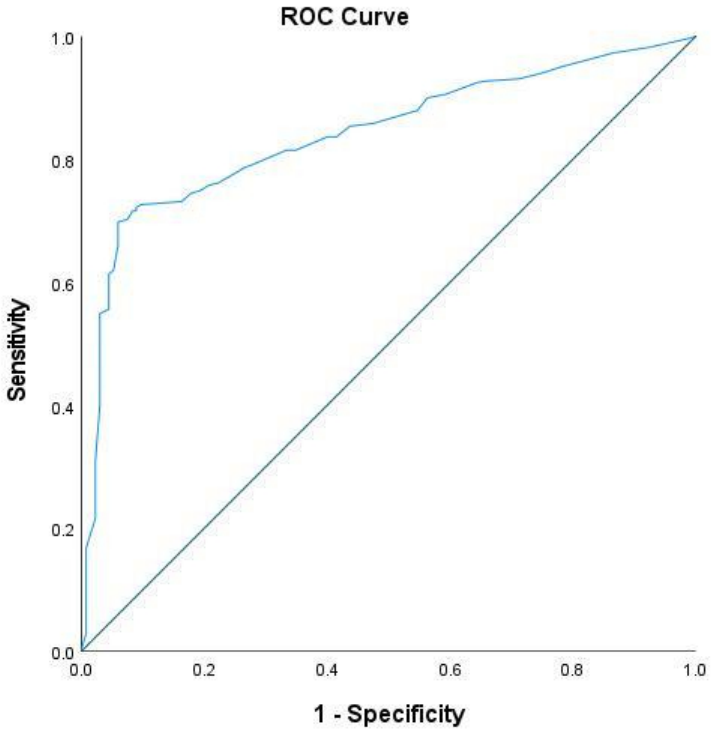


Figure 5. Receiver operating characteristic curve (ROC) to evaluate and assess the predictive accuracy of the developed logistic regression model (using the predicted probabilities) with dichotomous outcome variable catheter insertion success rate (successful/not successful)

234x188mm (72 x 72 DPI)

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	In the abstract (Page 2). In the abstract (Page 2). Not applicable.
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported		PICCs and non-tunnelled USG-CVCs have risks associated with their usage.	Introduction (Page 3)
Objectives	3	State specific objectives, including any prespecified hypotheses		To compare the success rates and other catheter-related parameters in PICCs and the non-tunnelled USG-CVCs in NICU	Aims and objectives (Page 2)
Methods					
Study Design	4	Present key elements of study design early in the paper		Data are collected retrospectively	Title (Page 1)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		A total of 1333 cases were evaluated who had PICC insertion and non-tunneled USG-CVC insertion. Related information for all cases between	Methods (Page 3)

				January 2016 and December 2018 was collected from the electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar.	
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	In the methods (Page 3). Babies who had PICC insertion and non-tunnelled USG-CVC insertion at NICU were enrolled (Page 3).
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods (Page 3)
Data sources/ measurement	8	For each variable of interest, give sources of data and details			Data were collected from the

		of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			electronic medical system at the NICU at the Women's Wellness and Research Centre (WWRC), Hamad Medical Corporation, Doha, Qatar (Page 3).
Bias	9	Describe any efforts to address potential sources of bias		Being restrospective research design, appropriate comparable groups, physicians experience, and missing obervations on important condounders can not be ruled out.	Limitation of the study (Page 3).
Study size	10	Explain how the study size was arrived at		1264 babies who had PICC insertion and non-tunneled USG-CVC insertion between January 2016 and December 2018 were included in the research	Methods (Page 3).
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed			Yes, described in the methods under statistical analysis (Page 5).

		Case-control study - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	Described in methods (Page 3).
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	CERNER (Page 3)
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods (Page 3).

Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			Described in Tables 1 and 2 (Page 6 and 7 of the results section).
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			Given in Tables 2,3, and 4 (Page 7, 9, and 10 of the results section).
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and			N/A

		interactions, and sensitivity analyses			
Discussion					
Key results	18	Summarise key results with reference to study objectives			PICCs have less incidence of complications when compared to the non-tunnelled USG-CVCs (Page 11 in conclusion).
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Limitation of the study (Page 3).
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		The overall complication rate, CLABSI and Leaking are significantly higher in non-tunnelled USG-CVCs compared to the PICCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU.	The overall complication rate, CLABSI and Leaking are significantly higher in non-tunnelled USG-CVCs compared to the PICCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach,

					dedicated vascular access team development, proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU (Page 11 in conclusion).
Generalisability	21	Discuss the generalisability (external validity) of the study results			The overall complication rate, CLABSI and Leaking are significantly higher in non-tunnelled USG-CVCs compared to the PICCs. However, RCTs with larger sample sizes are desired. Proper central venous device selection and timing, early PICC insertion and early removal approach, dedicated vascular access team development,

					proper central venous line maintenance, central line simulation workshops, and US-guided insertions are crucial elements for patient safety in NICU (Page 11 in conclusion).
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			N/A
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	The corresponding author is responsible for it

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.