

Original Article

Peripherally inserted central venous catheter-associated complications exert negative effects on body weight gain in neonatal intensive care units

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Background and Objectives: The placement of a peripherally inserted central venous catheter (PICC) is an essential procedure in neonatal intensive care units (NICU). The aim of this study was to determine the risk of PICC complications in NICU, and further identify the effects of PICC complications on body weight gain in premature infants. **Methods and Study Design:** A total of 304 premature infants who had a PICC inserted in NICU were enrolled in this study. The weight-for-age z-score (WAZ) at the time of PICC insertion and removal were calculated, and changes of WAZ in different groups were compared using a *t*-test. Risk factors for PICC complications were assessed using the chi-squared test and multiple logistic regression analysis. **Results:** Thirty (9.97%) PICCs were removed due to complications. Of them, 14 PICCs were removed because of non-infectious complications and 16 PICCs were removed for central-line-associated bloodstream infections (CLABSIs). Multiple logistic regression analysis showed that premature infants with birth weight >1,500 g were less likely to have PICC complications than infants with birth weight ≤1,500 g (OR, 0.29; 95% CI: 0.10-0.82; *p*=0.020). In addition, the changes in WAZ between PICC insertion and removal were significantly different in both infectious (-0.144±0.122, *p*<0.005) and non-infectious (-0.65±0.528, *p*<0.001) complications groups, compared with the no complications group (0.291±0.552). **Conclusions:** Findings from this study suggest that birth weight is a risk factor for PICC-associated complications in the NICU, and both infectious and non-infectious PICC complications are associated with poor body weight gain in premature infants.

Key Words: PICC complications, infectious complications, non-infectious complications, body weight, birth weight

INTRODUCTION

Placement of a peripherally inserted central venous catheter (PICC), an essential procedure in neonatal intensive care units (NICUs),¹ is used to provide fluids, medications, and nutritional support to premature infants,² especially low birth-weight neonates.³ Using PICC can decrease the number of painful procedures and needle sticks, without significantly increasing the rate of sepsis.⁴ In addition, PICCs can be placed without general anesthesia and can be left in place for months.⁵ However, infectious and non-infectious complications do occasionally occur,^{6,7} including central line-associated bloodstream infections (CLABSIs),⁸ which are the most common type of infection in NICU.^{9,10} Many studies have suggested that the duration of PICCs use was a risk factor for catheter-related complications, such as CLABSIs. Although the catheter material, the catheter tip position, gestational age and birth weight may affect the risk of complications,¹¹ there is no clear consensus which factor is most important. In this study, the risk of PICC complications,

such as CLABSIs and catheter-related non-infectious complications was investigated in the NICU of Xinhua Hospital in Shanghai. Changes in weight-for-age z-score (WAZ) between the time of PICC insertion and removal were calculated to determine whether PICC-associated complications affect body weight gain among premature infants in the NICU.

METHODS

A total of 304 premature infants who were admitted to

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Xinhua Hospital and had a PICC inserted in NICU between January 2010 and December 2014, were enrolled in the study. For patients with multiple PICC lines, only the first PICC was included in the analysis. Of the 304 patients, 3 were excluded because the PICC lines were removed within 48 h of insertion. Thus, 301 patients were included in the analysis. This study was reviewed and approved by Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine.

The pediatric PICC team placed all PICCs and established a database of patients with PICCs. Data collected included patient characteristics (gestational age, age at insertion, and birth weight) and catheter information (duration and complications). Extremely low-birth weight (ELBW) was defined as birth weight $\leq 1,000$ g and very low-birth weight (VLBW) as $1,000 < \text{birth weight} \leq 1,500$ g. PICC duration was defined as days from PICC insertion to PICC removal. The WAZ at the time of PICC insertion and removal were calculated using the Centers for Disease Control Epi-Info program (Centers for Disease Control, Atlanta, GA, U.S.).

Descriptive analyses were performed to assess the characteristics of patients and catheters. Median values were reported for range of age, PICC duration, gestational age, and birth weight. Risk factors for complications, CLA-BSIs and non-infectious complications necessitating PICC removal, including birth weight categories, gestational age categories, age categories, and duration categories, were assessed using the chi-squared test and multiple logistic regression analysis. Statistical analysis was performed using Statview5.0-J (SAS, Cary, NC, U.S.). A normal distribution of the data was tested by using the normality test and distribution curve, and the changes of WAZ in different groups were compared by using *t*-test. A 2-tailed *p* value of 0.05 was considered statistically significant.

RESULTS

This study included 301 patients treated from January 1, 2010 to December 31, 2014. The median gestational age was 31 weeks (range, 27-37). The total observation time was 8,223 catheter-days, with a median of 23 catheter-days (range, 3-122) per patient. The median birth weight was 1,400 g (range, 800-3,150), and the median age at the time of PICC insertion was 4 days (interquartile range, 3-7) (Table 1). In this cohort, 57.1% of neonates' gestational age was < 32 weeks, and 67.1% had birth weight $\leq 1,500$ g. Twenty six neonates (8%) were classified as ELBW and 176 (58%) as VLBW. The mean PICC duration was significantly longer in the ELBW and VLBW groups than that in the other two groups (Table 1).

Most PICCs (271, 90%) were removed on completion of the treatment, and 30 (9.97%) PICCs were removed due to a complication during 8,223 catheter days (incidence rate 3.64 per 1,000 catheter days), including 14 PICCs being removed because of non-infectious complications and 16 PICCs being removed for CLABSIs (Table 1). Of the 16 patients with CLA-BSIs, 87.5% had a birth weight of $\leq 1,500$ g, and 68.8% had a gestational age of < 32 weeks, and 62.5% were ≤ 7 days. Among the CLA-BSIs, the most common organism was staphylococcus

epidermidis (50%) (Table 1).

Independent predictors of PICC complications, including birth weight categories, gestational age categories, chronological age categories and duration of PICC, were assessed through univariate analysis and multiple logistic regression analysis. Results showed there to be no significant association between gestational age and chronological age with the risk of PICC complications, while birth weight was an independent contributor to complications (Table 2 and Table 3). After adjusting for other variables including gestational age, age and duration of PICC, premature infants with birth weight $> 1,500$ g were less likely to have PICC complications than infants with birth weight $\leq 1,500$ g (OR, 0.29; 95% CI: 0.10-0.82; $p=0.0201$) in multiple logistic regression analysis. In terms of duration of PICC, PICCs with a dwell time of 20-40 days had a higher incidence of complications (OR: 2.04; 95% CI: 0.92-4.55; $p=0.009$) than PICCs left in place for under 20 days. PICCs left in place for 40-70 after PICC insertion,

Table 1. Characteristics of 301 patients with PICCs

Characteristics	n=301
Age at PICC insertion, median (range), d	4 (1-60)
Birth weight, median (range), g	1,400 (800-3,150)
Gestational age, median (range), w	31 (27-37)
PICC dwell times, n (%)	
<20 d	136 (45.2)
20 d-40 d	107 (35.3)
>40 d	58 (19.3)
Year of study, n (%)	
2010	62 (20.6)
2011	31 (10.3)
2012	60 (19.9)
2013	56 (18.6)
2014	92 (30.6)
PICC duration in different groups, mean (range), d	
ELBW group	32 (6-89)
VLBW group	29 (7-122)
1,500 g-2,000 g group	22 (3-59)
>2,000 g group	14 (6-34)
Catheter disposition, n (%)	
Removed - no longer needed	271 (90.0)
Removed - infectious complications	16 (5.3)
Removed - non infectious complications	14 (4.7)
Local Infiltration	3 (0.99)
Leakage	4 (1.31)
Occlusion	5 (1.6)
Dislodgement	1 (0.3)
Breakage	1 (0.3)
Pathogens that caused CLA-BSIs, n (%)	
Klebsiella pneumoniae	2 (12.5)
Enterococcus faecium	1 (6.25)
Staphylococcus capitis	1 (6.25)
Staphylococcus epidermidis	8 (50.0)
Bacillus subtilis	1 (6.25)
Microbacterium	1 (6.25)
Alcaligenes xylosoxidans	1 (6.25)
Hominis Staphylococcus hyicus	1 (6.25)

ELBW: extremely low-birth weight; VLBW: very low-birth weight.

Table 2. Univariate analysis for risk factors of PICC complications

Variable	Complication number (%)	No complication number (%)	OR (95% CI)	<i>p</i> value
Age, d				
≤7	20 (57.1)	123 (46.2)	1.47 (0.79-2.77)	0.225
>7	15 (42.9)	143 (53.8)	0.95 (0.87-1.03)	
Gestational age, m				
<32	21 (60.0)	151 (56.8)	1.13 (0.60-2.13)	0.716
≥32	14 (40.0)	115 (43.2)	0.98 (0.91-1.07)	
Birth weight, g				
≤1,500	30 (85.7)	172 (64.7)	2.94 (1.18-7.35)	0.013
>1,500	5 (14.3)	94 (35.3)	0.90 (0.83-0.97)	
Duration of PICC, d				
<20	11 (31.4)	117 (44.0)	1	0.004
20-40	21 (60.0)	91 (34.2)	2.46 (1.13-5.35)	
>40	3 (8.57)	58 (21.8)	0.55 (0.15-2.05)	

Table 3. Multiple logistic regression analysis for complications, infectious and non-infectious complications

Variable	Complications		Infectious complications		Non-infectious complications	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Age, d						
≤7	1		1		1	
>7	0.67 (0.32-1.40)	0.284	0.49 (0.17-1.44)	0.194	0.91 (0.35-2.34)	0.836
Gestational age, m						
<32	1		1		1	
≥32	1.12 (0.51-2.49)	0.775	2.02 (0.67-6.09)	0.213	0.66 (0.22-1.92)	0.443
Birth weight, g						
≤1,500	1		1		1	
>1,500	0.29 (0.10-0.82)	0.020	0.24 (0.05-1.19)	0.080	0.39 (0.10-1.50)	0.169
Duration of PICC, d						
<20	1		1		1	
20-40	2.04 (0.92-4.55)	0.009	3.78 (1.00-14.3)	0.050	1.24 (0.46-3.34)	0.091
>40	0.46 (0.18-1.76)	0.075	1.49 (0.23-9.83)	0.748	0.18 (0.02-1.50)	0.081

had a lower rates of complications (OR: 0.46; 95% CI: 0.17-1.76; $p=0.075$) (Table 3). Because there may have been different risk factors for CLA-BSIs and non-infectious complications, a sub-analysis was performed to assess risk factors associated with each outcome. Multiple logistic regression analysis showed that the rate of CLA-BSIs tended to decrease as birth weight increased (OR, 0.24; 95% CI: 0.05-1.19, $p=0.080$), and the duration between 20-40 days had a tendency to be related to CLA-BSIs development (OR, 3.78; 95% CI: 1.00-14.3, $p=0.050$), while these trends were not statistically significant (Table 3).

At the time of PICC insertion and removal, the median WAZ was -5.04 (-3.67 to -7.02) and -4.87 (-3.3 to -6.47) in the no complication group, -5.08 (-3.81 to -7.81) and -5.28 (-4.18 to -7.43) in the infectious complication group, and -5.15 (-4.33 to -6.66) and -6.27 (-4.33 to -6.57) in the non-infectious complication group. The results showed that after PICC insertion, the median WAZ was higher in the no complication group, but it was lower in both complication groups. Then, changes in WAZ between PICC insertion and removal were calculated, and the results showed that changes in WAZ between PICC insertion and removal were significantly different between the infectious (-0.144 ± 0.122 , $p<0.005$) and non-infectious (-0.650 ± 0.528 , $p<0.001$) complications groups,

and the no complications group (0.291 ± 0.552) (Figure 1).

DISCUSSION

Previous studies have suggested that the risk factors or PICC complications include prematurity or severity of infant condition, PICC duration, tip location, and size of the NICU.^{5,6,11} Here, results showed that patients whose birth weights were $\leq 1,500$ g were at increased risk of complications, while those whose birth weights were

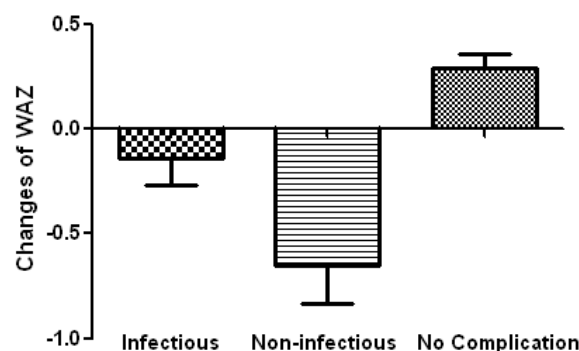


Figure 1. The changes of WAZ between PICC insertion and removal in infectious group, non-infectious group and no complication group. Values are expressed as mean \pm SD with $p<0.001$ (compared with no complication group).

>1,500 g were at lower risk, consistent with previous findings that high birth weight may protect against PICC-associated complications. Among the complications, CLA-BSIs are common cause of morbidity and mortality in premature infants, and the reported prevalence of CR-BSI varies from 0.7% to 4.1%. Risk factors such as age, immaturity and duration of PICC placement have been reported to contribute to the pathogenesis of CLA-BSIs.^{12,13} However, in this study, these factors did not show significant effects on CLA-BSIs, and only low birth weight was found to be related to the incidence of CLA-BSIs. Most CLA-BSIs are caused by commensal skin flora, such as coagulase-positive staphylococcus epidermidis.

Catheter dwell time has been indicated as a risk factor for PICC complications in several studies,¹² some of which showed that placement time to be associated with complications.^{14,15} However, there is no evidence that PICC complications can be prevented through routine replacement of catheters. In this study, the complex interactions between catheter placement time and risk of PICC complications, and infectious and non-infectious complications were illustrated. Time was treated as a continuous variable to track the incidence of PICC complications over time and determine the continuous hazard of developing a PICC complication. PICCs with a dwell time of 20-40 days had a higher rate of complications than PICCs left in place for less than 20 days, while those left in place for 40-70 days had a lower non-significant rate of complications. Furthermore, a sub-analysis showed that the incidence of CLA-BSIs and non-infectious complications tended to increase between 20 and 40 days. In this way, the data assessed in this study did not support the hypothesis that prolonged catheter placement time was associated with increased PICC complications, but additional studies are needed to identify a threshold for catheter replacement.

To further determine the effects of PICC complications on body weight gain, the changes in WAZ between PICC insertion and removal were calculated, and the results showed that WAZ increased over time in the no complications group, but decreased over time in both complications groups. The differences in WAZ between the no complications group and complications groups were statistically significant. As mentioned above, low birth weight is a risk factor for all PICC complications, and PICC-associated complications exerted negative effects on patients' body weight gain, suggesting that clinicians should be more cautious in maintaining a PICC in low birth weight neonates. Finally, several limitations should be considered when interpreting the findings presented here. First, although the study was conducted over a 5-year period, the incidence of CLA-BSIs was low, and only 16 events were recorded. In addition, because PICC-associated complications were investigated at only one institution, a multi-centre cohort study is needed.

Findings from this study suggest that birth weight is a risk factor of PICC-associated complications in NICU, and both infectious and non-infectious PICC complications are associated with poor body weight gain in premature infants. Although efforts have been made to reduce the risk of CLA-BSIs and although the frequency

of individual complications is rare, it is here suggested that clinicians should be more cautious in maintaining a PICC in low-birth-weight infants.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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