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SYSTEMATIC REVIEW

Influencing factors of neonatal peripherally inserted central venous catheter (PICC)-related phlebitis: a systematic review, meta-analysis and network meta-analysis

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Abstract

A peripherally inserted central venous catheter (PICC) plays an important role in the security of newborns, especially very low birth weight infants and extremely very low birth weight infants. However, PICC-related phlebitis can seriously affect the normal use of catheters and even cause unplanned removals of catheters. In this review, we systematically reviewed and explored the influencing factors of neonatal PICC-related phlebitis. The PubMed, Embase, CENTRAL, CINAHL, CBM, Wanfang and CNKI databases were searched to collect relevant studies on influencing factors of neonatal PICC-related phlebitis. Review Manager software version 5.3 (RevMan; the Cochrane Collaboration 2012, The Nordic Cochrane Center, Copenhagen, Denmark) and GeMTC software version 0.14.3 (Gert van Valkenhoef, Groningen, The Netherlands) were used for the meta-analysis and network meta-analysis. A total of 32 studies were included, including 14 randomized controlled trials (RCTs), 2 case-control studies, and 16 cohort studies, involving a total of 8278 neonates. The meta-analysis results showed that the influencing factors of neonatal PICC-related phlebitis were catheter malposition (OR (Odds Ratio) = 5.53, 95% CI (Confidence Interval) (1.22, 25.15)), catheter occlusion (OR = 7.18, 95% CI (3.54, 14.56)), gestational age (OR = 2.51, 95% CI (1.35, 4.66)), using a dexamethasone solution to infiltrate the catheter (OR = 0.26, 95% CI (0.17, 0.41)), and innovative nursing interventions (OR = 0.17, 95% CI (0.07, 0.42)). The network meta-analysis results showed that, compared with lower limb veins, the use of scalp veins (OR = 3.57, 95% CI (1.39, 10.18)) and upper limb veins (OR = 1.89, 95% CI (1.08, 3.37)) had a statistically significant difference in the incidence of phlebitis, while there was no statistically significant difference in the incidence of phlebitis between scalp veins and upper limb veins (OR = 0.53, 95% CI (0.20, 1.26)). PICC puncture of the lower limb veins was most likely to lead to phlebitis, followed by upper limb vein puncture, followed by scalp vein puncture. Catheter malposition, catheter occlusion and being small for gestational age were risk factors for PICC-related phlebitis, while dexamethasone solution infiltration of catheters and innovative nursing interventions were protective factors. Venipuncture of the lower limbs is the most likely location to cause PICC-related phlebitis.

Keywords

Newborn; Meta-analysis; Influencing factors; PICC

1. Introduction

A peripherally inserted central venous catheter (PICC) is a type of central venous catheter that is inserted through peripheral veins. Neonates' peripheral veins with small vascular lumens are always difficult to puncture. In addition, preterm infants, especially very preterm and extremely preterm infants, require prolonged parenteral nutrition support, which makes their peripheral veins easy to destroy. Thus, a PICC provides important intravenous access to protect neonates' peripheral veins by reducing repeated puncture. The incidence of PICC-related complications in neonates is reported to be 27–47% [1–3], and phlebitis is a relatively high proportion of these complications, which affects the normal use of PICCs. Some cases of severe phlebitis even require catheter removal, resulting in an increased rate of unplanned PICC removals. There are many factors that influence the occurrence of PICC phlebitis in neonates, some of which are objective factors for which it is difficult for us to intervene (gestational age, birth weight, *etc.*), while others are factors for which we can intervene. Although a number of original studies have explored the factors influencing PICC phlebitis in neonates, these studies have presented mixed results. No previous systematic reviews have integrated the evidence related to PICC-related phlebitis in neonates. Thus, we systematically retrieved relevant evidence to determine the factors influencing PICC-related phlebitis in neonates.

2. Materials and Methods

The study was based on the preferred reporting items for systematic reviews and meta-analyses.

2.1 Search strategy

We searched for studies in the Public Medicine (PubMed), Excerpta Medica Database (EMbase), the Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index of Nursing & Allied Health Literature (CINAHL), China Biology Medicine (CBM), Wanfang, and China National Knowledge Infrastructure (CNKI) databases using the terms "peripherally inserted central catheter", "PICC", "central catheter", "phlebitis", "phlebophlogosis", "infant, newborn", "neonate", "low birth weight", "LBW", and "VLBW" from the conception of the database to November 2019. The search strategies are listed in **Supplementary material**. The reference lists of the relevant studies were also scrutinized to identify potentially relevant studies.

2.2 Eligibility Criteria

Studies were selected based on the following inclusion criteria: (a) the participants were neonates with a PICC placed; (b) the research topic was the influencing factors of neonatal PICC-related phlebitis; and (c) the study was a randomized controlled trial, a case-control study or a cohort study. The exclusion criteria were as follows: (a) studies that focused on the influencing factors for PICC-related complications rather than phlebitis; (b) the study was a review, an experimental study, or a case report; and (c) complete data were not available.

2.3 Data extraction

Two researchers independently screened the literature, extracted information and cross-checked the studies. Disagreements were resolved by discussion with a third person until a consensus was reached. The following data were extracted: (a) general information of the included studies, such as the title, author, and publication time; (b) type of study design; (c) demographic characteristics of the enrolled patients; and (d) factors related to PICC-related phlebitis in neonates.

2.4 Risk of bias assessment

For RCTs, the risk of bias was assessed by the recommended Cochrane Handbook for Systematic Reviews of Interventions Version 5.2.0 randomized controlled trial quality evaluation standards, which include criteria concerning random sequence generation, allocation concealment, the blinding of participants and personnel, the blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other potential threats to validity. For case-control and cohort studies, the risk of bias was assessed by the Newcastle-Ottawa Quality Assessment (NOS) scale, which consists of 8 items with a total possible score of 9, including 3 domains: selection, comparability, and exposure (for case-control study) outcome (for cohort study). All risk of bias was independently assessed by 2 trained researchers. Disagreements were resolved by discussion with a third person until a consensus was reached.

2.5 Data synthesis and analysis

For the meta-analysis, RevMan 5.3 was used for data analysis. The heterogeneity of the included studies was determined by I^2. A fixed-effects model was used when apparent heterogeneity was detected (I^2 <50%, $p \geq$ 0.05). Otherwise, a random-effects model was used ($I^2 \geq 50\%, p < 0.05$). For the network meta-analysis, stata 14.0 (StataCorp, College Station, TX, USA) was used for network plotting, and GeMTC 0.14.3 was used for data analysis. GeMTC is a nonprogramming software based on Bayesian theory, which makes the computing process of WinBUGS transparent and only requires the operator to enter relevant data to complete the network meta-analysis [4, 5]. GeMTC uses Markov chain Monte Carlo (MCMC) for Bayesian network meta-analysis. In this analysis, 4 Markov chains with 100,000 iterations were used. The first 50,000 were used for annealing to remove the effect of initial values. The potential scale reduction factor (PSRF) was used to detect the degree of model convergence. PSRF values tend to 1, suggesting satisfactory model convergence [6]. The step size was set to 10. A p value $<$ 0.05 was regarded as statistically significant.

3. Results

3.1 Characteristics of the included studies

After searching the databases, 732 potentially eligible studies were identified, of which 522 remained after the removal of duplicates (Fig. 1). After screening the titles and abstracts, 92 studies were obtained. After reading the full texts of these records, 32 studies qualified for inclusion in this review, of which 14 were randomized controlled trials, 2 were case-control studies, and 16 were cohort studies, enrolling a total of 8278 neonates. Eight of the included studies were in English, while 24 were in Chinese. Nineteen studies [7–25] examined the association between PICC puncture sites and PICC-related phlebitis. Thirteen studies [26–38] examined the association between PICC-related phlebitis and factors such as birth weight, catheter malposition, innovative nursing interventions, catheter occlusion, gestational age, sex, asphyxia, and using a dexamethasone solution to infiltrate catheters. The detailed study characteristics of the included studies are reported in Table 1 (Ref. [7–38]).

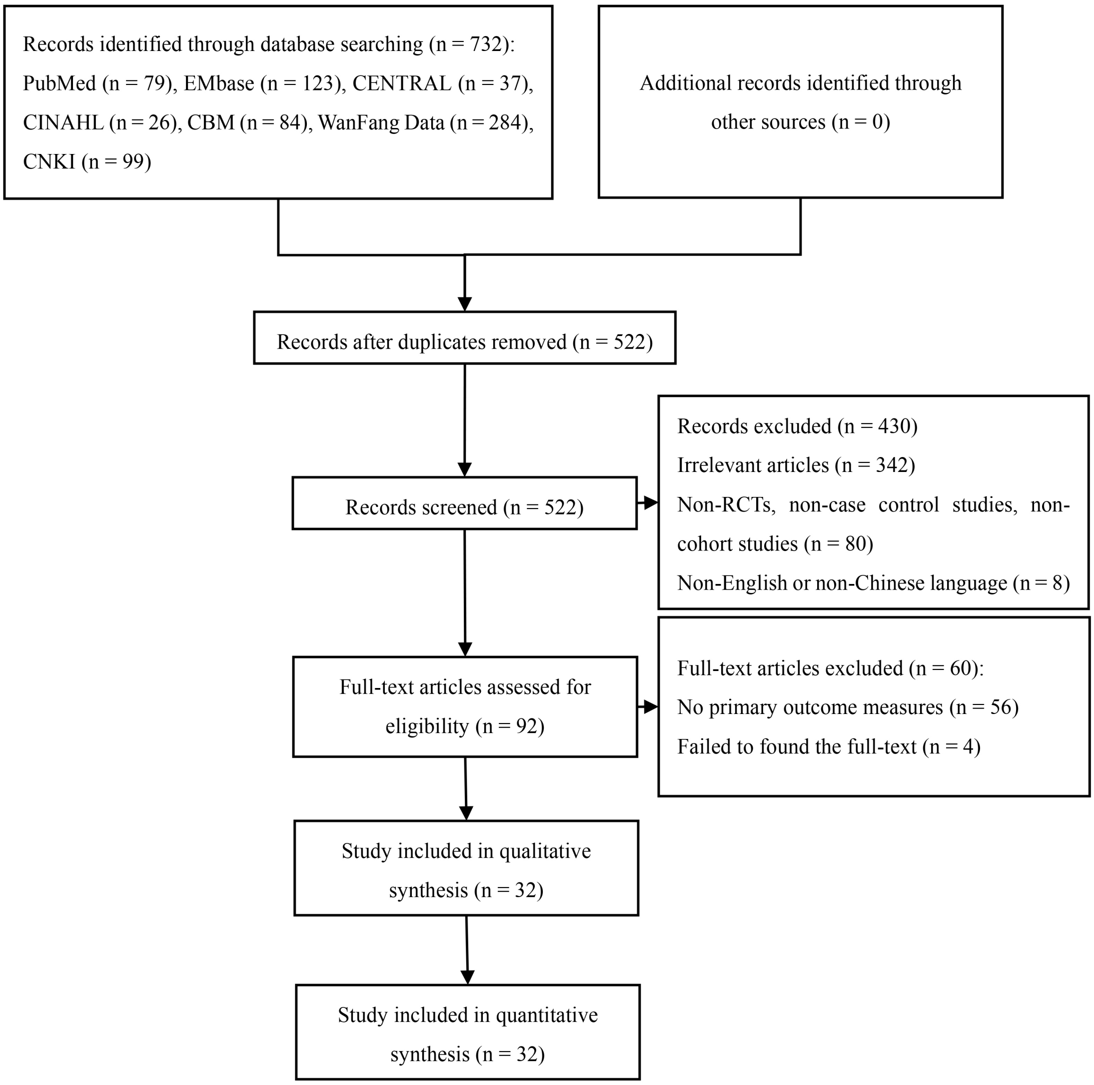

FIGURE 1. Literature screening process.

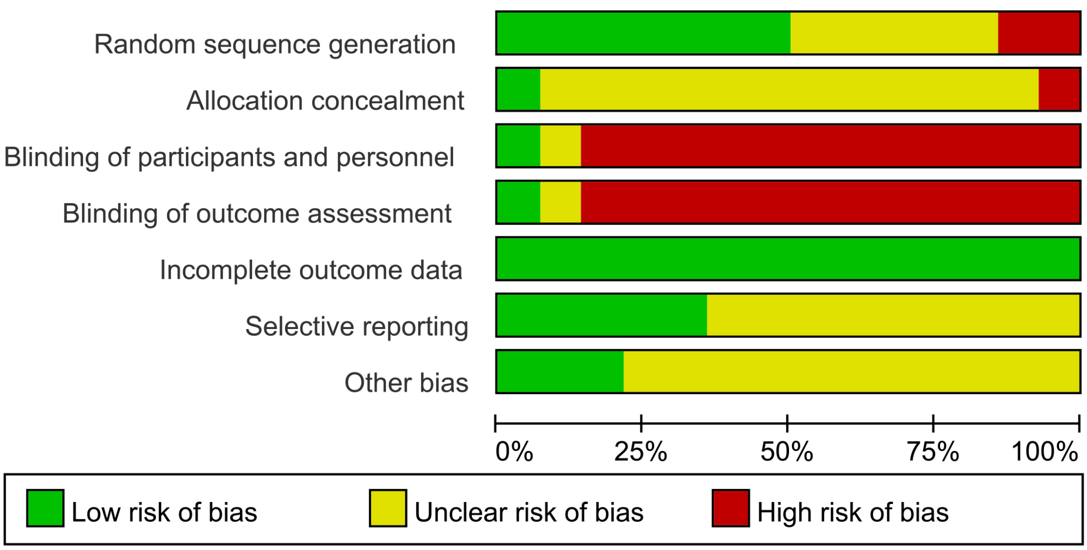

FIGURE 2. Risk bias assessment of included RCTs.

TABLE 1. Characteristics of included studies.

Studies	Country	Study design	Study group			Control			Influencing factors investigated*
			Gestational Age (w)	Body Weight (g)	Sample size	Gestational Age (w)	Body Weight (g)	Sample size	
Bashir 2016 [7]	Canada	Cohort	28.8 ± 3.2	1236 ± 520	593	28.9 ± 3.2	1227 ± 514	234	①
Konjevic 2015 [38]	Bosnia	Cohort	30.7 (28–34)	1220.8 (1050–1450)	12	28.1(25–33)	824.4 (670–990)	18	②
Ozkiraz 2013 [37]	Turkey	Cohort	29 (26–33)	1165 (1040–1500)	28	26 (24–31)	790 (580–990)	34	②
Callejas 2016 [8]	Canada	Cohort	35 (24–41)	2392 (505–110)	471	29 (23–42) 31 (23–42)	1331 (450–4240)	149/69	①
Cuiwei C 2018 [31]	China	RCT	NM	1210 ± 78.6	40	NM	1208 ± 80.5	40	④
Fang C 2018 [9]	China	RCT	207 ± 21 d	1530 ± 360	60	210 ± 18 d 212 ± 20 d	1630 ± 420 1640 ± 430	60/60	①
Liping C 2011 [33]	China	Cohort	≤32 w	≤1500 g	140	>32 w	>1500 g	60	⑤⑥
Yu C 2019 [34]	China	RCT	35.47 ± 2.46	1480 ± 260	53	34.63 ± 2.31	1320 ± 220	53	④
Li G 2013 [10]	China	RCT	28.59 ± 2.92	1040 ± 220	39	30.50 ± 2.26	1050 ± 270	40	①
Yin H 2019 [35]	China	Case control	NM	1203 ±197	16	NM	1203 ±197	134	③⑤⑥⑦⑧
Ailing J 2016 [30]	China	RCT	30.5 ± 3.8	2800 ± 1500	55	33.4 ± 2.7	2900 ± 1700	55	④
Li L 2014 [11]	China	RCT	32.0 ± 2.2	1600 ± 400	73	32.4 ± 2.1	1500 ± 700	92	①
Zhiying L 2016 [12]	China	Cohort	NM	NM	535	NM	NM	292/354/80/255	①
Lianshu L 2014 [13]	China	Cohort	30.42 ± 2.52	1290 ± 260	39	30.42 ± 2.52	1290 ± 260	98	①
Xiaofang L 2018 [14]	China	Cohort	NM	1458.7 ± 32.7	16	NM	1457.8 ± 32.3	13	①
Chunchou L 2013 [28]	China	RCT	30.4 ± 2.2 30.4 ± 2.0	1332.5 ± 123.9 1321.7 ± 151.3	60/60	30.3 ± 2.2	1309.5 ± 143.7	60	⑨
Yanyan L 2019 [29]	China	RCT	30.6 ± 3.9	NM	56	30.4 ± 3.6	NM	56	⑨
Jianping T 2018 [36]	China	RCT	NM	NM	35	NM	NM	35	⑨

TABLE 1. Continued.

Studies	Country	Study design	Study group			Control			Influencing factors investigated*
			Gestational Age (w)	Body Weight (g)	Sample size	Gestational Age (w)	Body Weight (g)	Sample size	
Elmekkawi 2018 [15]	Canada	Cohort	30 (26, 35)	1246 (948, 2090)	138	32 (27, 37)	1460 (960, 2720)	227	①
Aiqing X 2016 [17]	China	Cohort	31.46 ± 2.15	1523 ± 431	236	31.28 ± 2.07 31.65 ± 2.22	1506 ± 402 1542 ± 423	48/22	①
Yuting X 2019 [18]	China	Cohort	34.45 ± 4.99	2460 ± 114	97	33.13 ± 3.31 35.23 ± 4.05	1960 ± 610 2440 ± 840	144/30	①
Collaborative 2018 [19]	China	Case control	29.97 ± 2.27	1309.09 ± 251.74	68	30.52 ± 3.22	1447.60 ± 534.55	526	①③⑦⑧
Hoang 2008 [20]	America	Cohort	28 (26, 30)	937 (760,135)	370	28 (25, 31)	946 (740, 1427)	107	①
Caiying X 2011 [32]	China	RCT	28~34	1350	23	28~35	1380	23	⑨
Xiaoyun X 2013 [21]	China	Cohort	30.36 ± 2.92	1210 ± 680	152	31.86 ± 3.75	1280 ± 630	82	①
Chunyan Y 2014 [26]	China	RCT	29.95 ± 1.87	1232.27 ± 198.98	44	30.00 ± 1.71	1289.77 ± 170.64	44	⑨
Cuifeng Z 2014 [22]	China	Cohort	30.78 ± 2.24	1300 ± 200	64	30.67 ± 1.41	1320 ± 130	62	①
Shuyun Z 2014 [27]	China	RCT	30.08 ± 1.05	1258 ± 128.4	90	30.20 ± 1.12	1320 ± 106.3	90	⑨
Huimin Z 2018 [23]	China	RCT	NM	2578 ± 104	8	NM	2718 ± 104	8	①
Wrightson 2013 [24]	America	Cohort	NM	1207 ± 718	374	NM	1232 ± 708	252	①
Ma 2015 [25]	America	Cohort	36 (35, 37)	2516 (2214, 2810)	89	37 (35, 37)	2540 (2220, 2842)	40	①
Hongrong W 2016 [16]	China	RCT	NM	1575 ± 51	42	NM	15603	50	①

Data are presented as mean ± SD, or median (interquartile range).
*NM—not mentioned, * ①puncture site (upper limb/lower limb/scalp), ②Birth weight (very low birth weight/extremely low birth weight), ③catheter malposition, ④innovative nursing interventions, ⑤catheter occlusion, ⑥gestational age(≤ 32 w/>32 w), ⑦sex(male/female), ⑧asphyxia,⑨dexamethasone solution to infiltrate the catheter.*

3.2 Quality assessment of the included studies

For the RCTs, seven studies (50.0%) reported random sequence generation methods. Only 1 study (6.7%) reported allocation concealment. Blinding was at an overall high risk of bias of participants and personnel, as only 1 study (6.7%) reported the blinding of participants and personnel. The same results were shown in the blinding of outcome assessors. All the included RCTs were considered to have a low risk of bias for incomplete outcome data. Five studies (35.7%) had a low risk of selective reporting. For the cohort and case-control studies, a total score range of 6–9 was reached, which indicated that the overall quality of these studies was relatively high. Detailed information about the risks of bias for the included studies is reported in Fig. 2 and Table 2 (Ref. [7, 8, 12–15, 17–22, 24, 25, 33, 35, 37, 38]).

3.3 Results of the Meta-analysis

The pooled results of 2 studies with a random-effects model showed that the incidence of PICC-related phlebitis was higher in the malpositioning group than in the correct positioning group (OR: 5.53, 95% CI: 1.22, 25.15, p = 0.03, Fig. 3).

The results of the fixed-effects model meta-analysis showed that catheter occlusion (OR: 7.18, 95% CI: 3.43, 14.56, $p <$ 0.00001, Fig. 4), and a gestational age $\leq$ 32 weeks (OR: 2.51, 95% CI: 1.35, 4.66, p = 0.003, Fig. 5) were risk factors for PICC phlebitis; innovative nursing interventions (OR: 0.17, 95% CI: 0.07, 0.42, p = 0.0001, Fig. 6) and using a dexamethasone solution to infiltrate catheters (OR: 0.26, 95% CI: 0.17, 0.41, $p <$ 0.00001, Fig. 7) were protective factors for PICC phlebitis; and sex (OR: 0.77, 95% CI: 0.49, 1.21, p = 0.25, Fig. 8), asphyxia (OR: 0.90, 95% CI: 0.50, 1.61, p = 0.72, Fig. 9), and birth weight (OR: 0.79, 95% CI: 0.10, 6.30, p = 0.82, Fig. 10) were not significantly associated with PICC-related phlebitis.

3.4 Results of the network meta-analysis

Neonatal PICC puncture sites contained upper limb, lower limb and scalp veins. The incidence of PICC-related phlebitis at the different puncture sites was compared using network meta-analysis.

A total of 19 studies were eligible for the network meta-analysis. The network relationship plot is shown in Fig. 11. The results of the network meta-analysis showed that there was a statistically significant difference in the occurrence of PICC-related phlebitis for lower limb venipuncture compared with scalp vein (OR: 3.57, 95% CI: 1.39, 10.18) and upper limb vein (OR: 1.89, 95% CI: 1.08, 3.37) venipuncture, and there was no statistically significant difference in the occurrence of phlebitis between scalp vein puncture and upper limb vein puncture (Table 3).

Nodal analysis showed a $p >$ 0.05, suggesting that there was no significant inconsistency between the results of the direct and indirect comparisons. The GeMTC ranking results showed that the PICC puncture of lower limb veins was most likely to lead to phlebitis, followed by upper limb vein puncture, followed by scalp vein puncture (Fig. 12).

4. Discussion

4.1 Relationship between birth weight and PICC-related phlebitis in neonates

Two studies enrolled in this review compared the incidence of PICC-related phlebitis between very low birth weight neonates and extremely low birth weight neonates, which showed that there was no significant difference [37, 38]. However, other studies that were not enrolled in the meta-analysis due to grouping by birth weight showed different results. The results of Liping's research showed that there was a statistically significant difference in the incidence of PICC-related phlebitis between neonates with a birth weight $\leq$ 1500 g and those with a birth weight $>$1500 g [33]. Ying's research showed that there was a statistically significant difference in the incidence of PICC-related phlebitis between neonates with a birth weight $<$1200 g and those with a birth weight $\geq$ 1200 g [35]. A case-control study showed that the birth weights of neonates in the phlebitis group were significantly lower than the birth weights of neonates in the control group [19]. The above 3 studies included a total sample of 944 neonates and showed that the lower the birth weight was, the higher the risk of PICC-related phlebitis, which was inconsistent with the meta-analysis results. Due to the small sample sizes of the 2 studies included in the meta-analysis (30 and 62 neonates, respectively), the results might have the possibility of bias.

4.2 Other neonatal influencing factors for PICC-related phlebitis

In addition to the factors that were included in the meta-analysis, some factors that have been shown to be associated with the development of PICC-related phlebitis were not included, as only one study analyzed the relationship between these factors and PICC-related phlebitis, including the following: the weight at placement, number of puncture attempts, catheter retention time, length of catheter placement, irritation from bleeding, and delivery method. A case-control study showed that newborns in the phlebitis group had lower birth weights than those in the control group, with a statistically significant difference (t = –0.3.027, p = 0.003) [19]. Ying's case-control study showed that more than 2 puncture attempts, a catheter retention for more than 2 weeks, and irritation from bleeding were risk factors for PICC-related phlebitis (OR $>$1, $p <$ 0.05) [35]. Qi's study showed that retaining the appropriate length of protective film when trimming the catheter to avoid its exposure, cooperating with an assistant after a successful puncture, gradually tearing the film while delivering the catheter, and avoiding glove contact with the catheter could effectively reduce the incidence of phlebitis (t = 14.328, $p <$ 0.001) [39]. The above factors, although not included in the meta-analysis, have been shown to be associated with neonatal PICC-related phlebitis and should also be considered when assessing risk factors related to PICC phlebitis.

TABLE 2. Risk bias assessment of included case control and cohort studies.

Studies	Study design	Selection				Comparability	Exposure			Total score
		I*	II*	III*	IV*	V*	VI*	VII*	VIII*	
Bashir 2016 [7]	Cohort	1	1	1	1	1	1	1	1	8
Konjevic 2015 [38]	Cohort	1	1	1	1	2	1	1	1	9
Ozkiraz 2013 [37]	Cohort	1	1	1	1	2	1	1	0	8
Callejas 2016 [8]	Cohort	1	1	1	0	1	1	1	1	7
Lingping C 2011 [33]	Cohort	1	1	1	0	1	1	0	1	6
Zhiying L 2016 [12]	Cohort	1	1	1	1	0	1	0	1	6
Lianshu L 2014 [13]	Cohort	1	1	1	0	1	1	0	1	6
Xiaofang L 2018 [14]	Cohort	1	1	1	0	1	1	0	1	6
Elmekkawi 2018 [15]	Cohort	1	1	1	0	1	1	1	1	7
Aiqing X 2016 [17]	Cohort	1	1	1	0	2	1	0	1	7
Yuting X 2019 [18]	Cohort	1	1	1	0	2	1	0	1	7
Hoang 2008 [20]	Cohort	1	1	1	1	2	1	1	1	9
Xiaoyun X 2013 [21]	Cohort	1	1	1	0	2	1	0	1	7
Cuifeng Z 2014 [22]	Cohort	1	1	1	0	2	1	0	1	7
Wrightson 2013 [24]	Cohort	1	1	1	0	2	1	1	1	8
Ma 2015 [25]	Cohort	1	1	1	0	2	1	1	1	8
Yin H 2019 [35]	Case control	1	0	1	1	2	1	1	1	8
Collaborative 2018 [19]	Case control	1	1	1	1	2	1	1	1	9

**For Cohort study: I—representativeness of the exposed cohort, II—selection of the non-exposed cohort, III—ascertainment of exposure, IV—demonstration that outcome of interest was not present at start of study, V—comparability of cohorts on the basis of the design or analysis, VI—assessment of outcome, VII—was follow-up long enough for outcomes to occur, VIII—adequacy of follow up of cohorts; For Case control study: I—is the case definition adequate? II—representativeness of the cases, III—selection of controls, IV—definition of controls, V—comparability of cases and controls on the basis of the design or analysis, VI—ascertainment of exposure, VII—same method of ascertainment for cases and controls, VIII—non-response rate.*

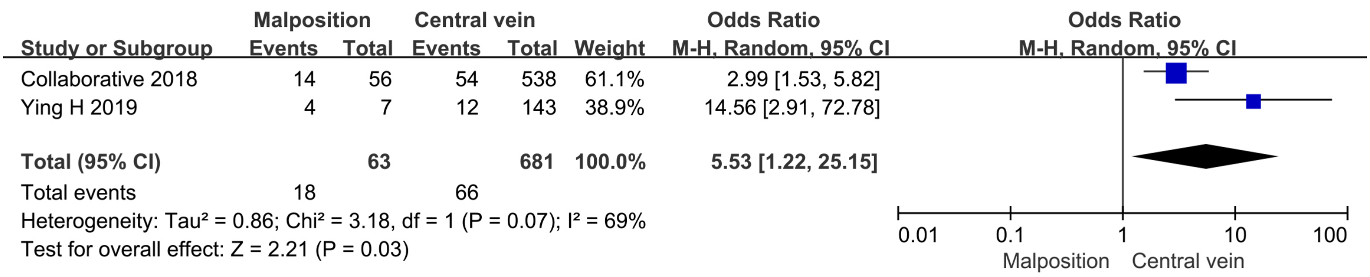

FIGURE 3. Correlation of catheter malposition and PICC-related phlebitis in neonates.

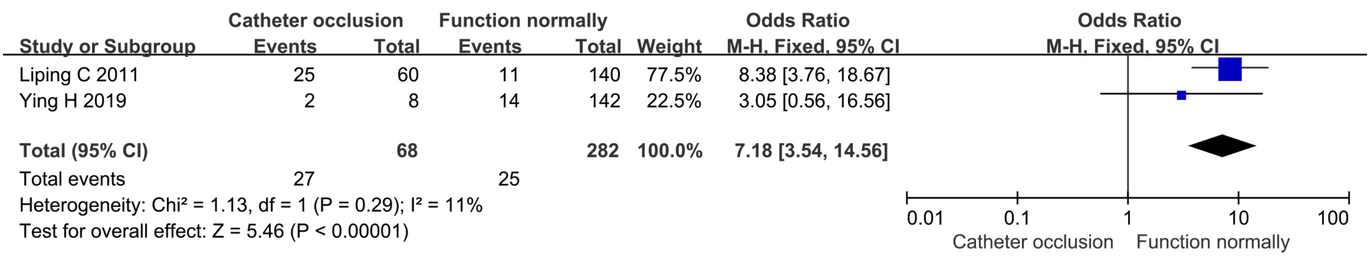

FIGURE 4. Correlation of catheter occlusion and PICC-related phlebitis in neonates.

4.3 Selection of the neonatal PICC puncture site

Clinical selection of the puncture site for a PICC should consider not only the incidence of phlebitis but also the incidence of other complications, the difficulty of placement, clinical comfort, *etc*. A meta-analysis by Xiuwen *et al*. [40] showed

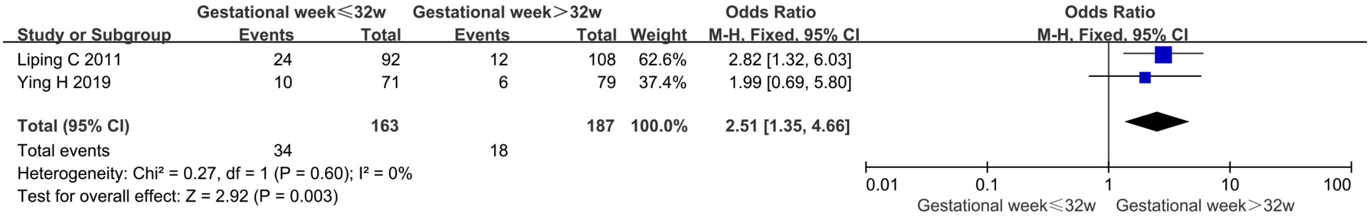

FIGURE 5. Correlation of gestational age and PICC-related phlebitis in neonates.

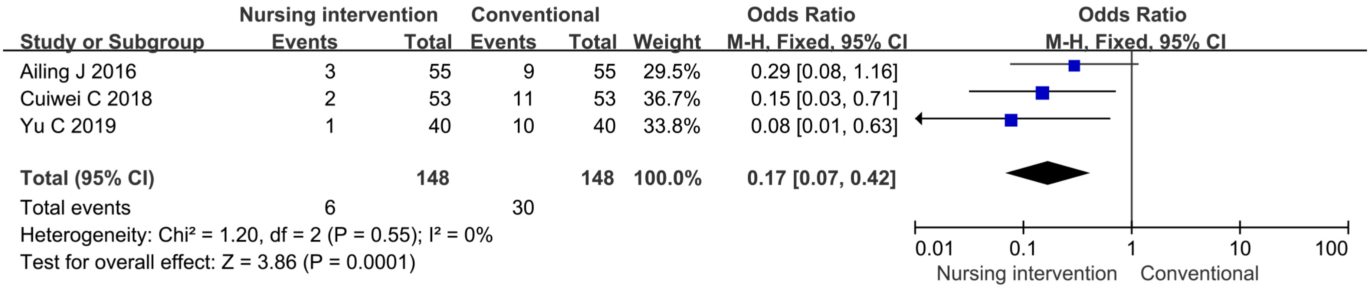

FIGURE 6. Correlation of innovative nursing interventions and PICC-related phlebitis in neonates.

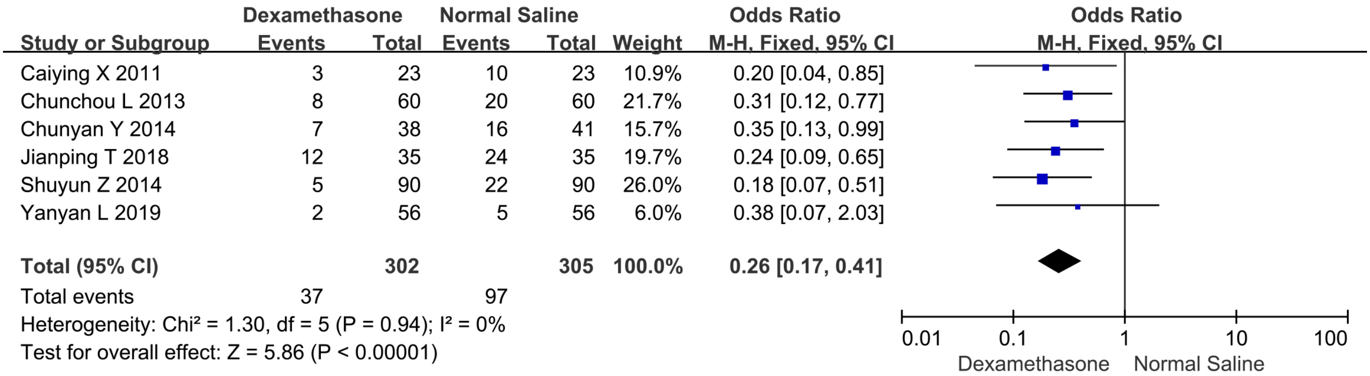

FIGURE 7. Correlation of dexamethasone solution to infiltrate the catheter and PICC-related phlebitis in neonates.

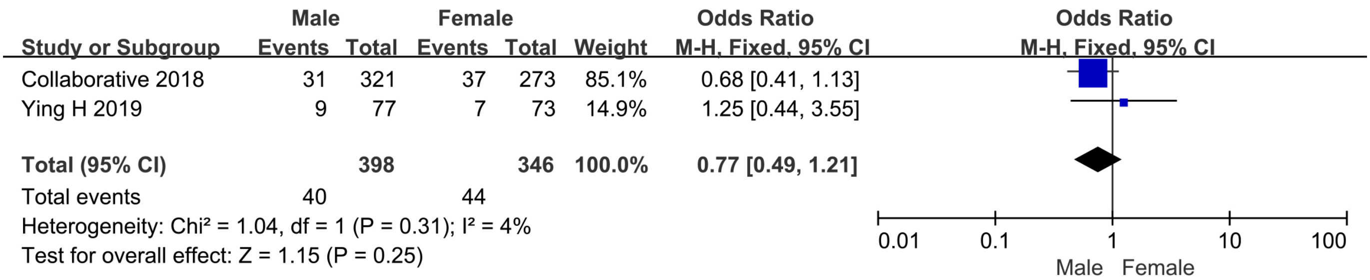

FIGURE 8. Correlation of sex and PICC-related phlebitis in neonates.

TABLE 3. Network meta-analysis of different puncture sites and PICC-related phlebitis in neonates.

Lower limb	-	-
3.57 (1.39, 10.18)	Scalp	-
1.89 (1.08, 3.37)	0.53 (0.20, 1.26)	Upper limb

that the incidence of infection, catheter malposition, extravasation/infiltration, and unplanned catheter removal were significantly lower in neonates with a PICC placement via lower limb veins than in neonates with placement via upper limb veins, and the one-time puncture success rate of PICC placement via lower limb veins was higher than that of upper limb veins [40]. PICC puncture via the upper limb veins reduced the incidence of PICC-related phlebitis but increased the incidence of other complications. In addition, based on our clinical puncture experience, it was relatively difficult to achieve successful puncture with catheter placement through the upper limb veins. The puncture site should be decided by taking a neonate's clinical situation into account.

Study or Subgroup	Asphyxia Events	Asphyxia Total	No asphyxia Events	No asphyxia Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Collaborative 2018	11	105	57	489	73.7%	0.89 [0.45, 1.76]
Ying H 2019	5	49	11	101	26.3%	0.93 [0.30, 2.84]
Total (95% CI)		**154**		**590**	**100.0%**	**0.90 [0.50, 1.61]**
Total events	16		68			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.36 (P = 0.72)

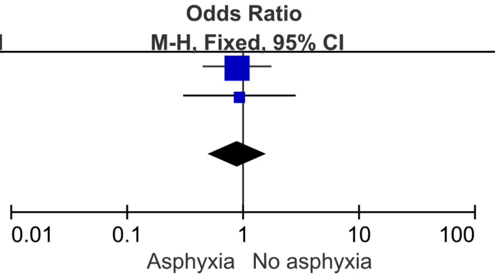

FIGURE 9. Correlation of asphyxia and PICC-related phlebitis in neonates.

Study or Subgroup	VLBW Events	VLBW Total	ELBW Events	ELBW Total	Weight	Odds Ratio M-H, Fixed, 95% CI
KONJEVIĆ 2015	0	12	1	18	57.4%	0.47 [0.02, 12.43]
Ozkiraz 2013	1	28	1	34	42.6%	1.22 [0.07, 20.47]
Total (95% CI)		**40**		**52**	**100.0%**	**0.79 [0.10, 6.30]**
Total events	1		2			

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 0.22 (P = 0.82)

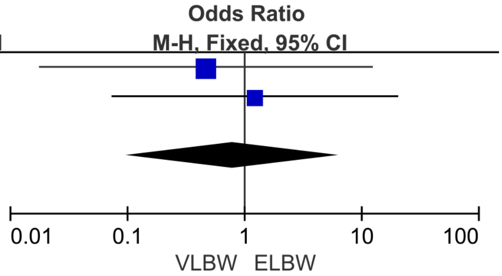

FIGURE 10. Correlation of birth weight and PICC-related phlebitis in neonates.

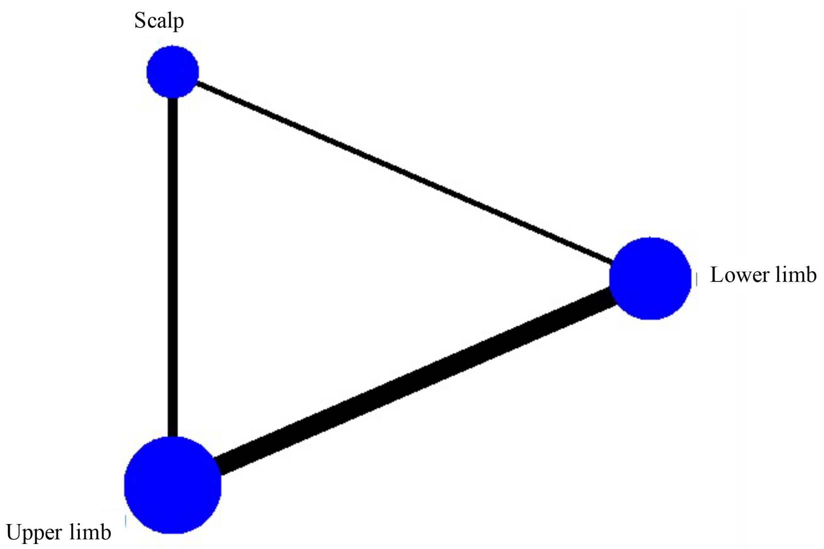

FIGURE 11. Network plot of relevant studies for phlebitis caused by different puncture sites of neonatal PICC.

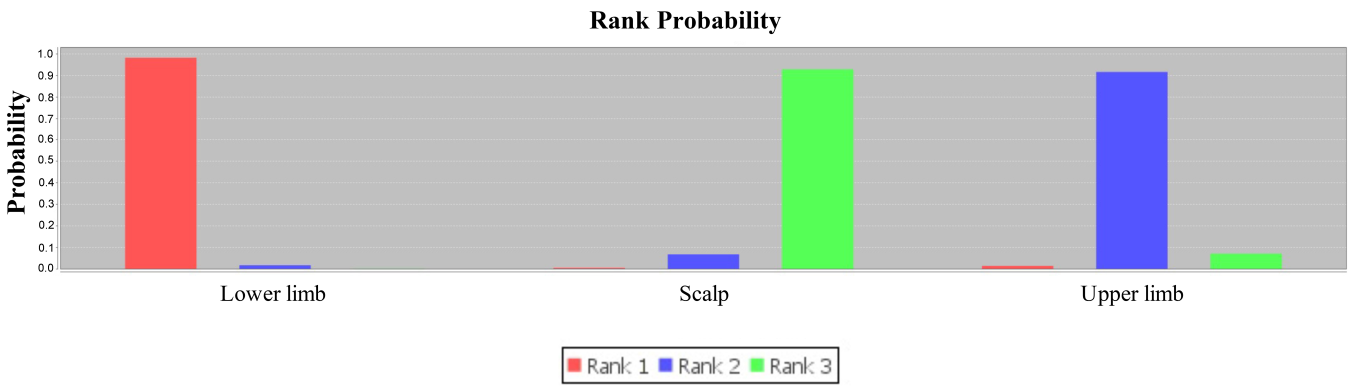

FIGURE 12. Rank of probability of PICC-related phlebitis via different puncture sites in neonates.

4.4 Prevention of PICC-related phlebitis in neonates

We found that innovative nursing interventions and using a dexamethasone solution to infiltrate catheters are effective measures to prevent PICC-related phlebitis in neonates through meta-analysis. For innovative nursing interventions, all 3 included studies presented a bundle of interventions to reduce the incidence of PICC-related phlebitis [30, 31, 34], including the selection and prioritization of puncture sites, the placement by an operator experienced in catheter placement, comforting the child, applying moist warm heat to the punctured vessel prior to puncture, adjusting the body position during puncture, summarizing the puncture experience in time, and making quality improvements for specific problems. For using a dexamethasone solution to infiltrate catheters, the 6 included studies showed different concentrations of dexamethasone and infiltration times [26–29, 32, 36]. The concentration of dexamethasone used to infiltrate the catheters was 0.05–0.5 mg/mL, and the infiltration time was generally 5 min [26–28, 32], with one study recommending 20–30 min of infiltration [29]. Based on the results of the literature review, the recommended measures to prevent PICC-related phlebitis are as follows: (a) calm the child down to avoid vasoconstriction and spasm, in order to reduce venous irritation; (b) proceed evenly and slowly when placing the catheter, and apply moist warm compresses to the skin where the vein runs before puncture to stretch the blood vessels; (c) improve puncture proficiency and try to puncture successfully one time to reduce vascular irritation; (d) keep the corresponding length of protective film when trimming the catheter, and gradually tear the film while delivering the catheter after successful puncture to avoid gloves touching the catheter; (e) use powder-free sterile gloves to avoid irritation of powder to the vein; (f) use dexamethasone solution to infiltrate the catheter before puncturing the vein; (g) apply Hirudoid® along the direction of the punctured vein; and (h) use a hydrocolloid dressing along the direction of the punctured vein.

4.5 Limitations of the study

In this meta-analysis, we included RCTs, case-control studies, and cohort studies. Only one of the 14 included RCTs had a low risk of bias in all 7 dimensions of the Cochrane risk of bias assessment tool. The overall quality of the original study was relatively low. In addition, for the network meta-analysis of the relationship between puncture site and the occurrence of phlebitis, the results of the RCT, case-control, and cohort studies were integrated because of the small number of included RCTs (only 5 RCTs) and the absence of high-quality RCT studies. Moreover, with 75% (24/32) of the included studies originating from China, there may be a regional bias, and the results should be considered with caution. Last, there are other variables that may influence the incidence of PICC-related phlebitis, such as the type of lipid emulsion used in parenteral nutrition. Due to the lack of original experimental studies on these topics, we failed to perform the analysis.

5. Conclusion

Catheter malposition, catheter occlusion and a gestational age $\leq$ 32 weeks were risk factors for PICC-related phlebitis, while using a dexamethasone solution to infiltrate catheters and innovative nursing interventions were protective factors for PICC-related phlebitis. Venipuncture of the lower limbs is the most likely location to cause PICC-related phlebitis. Due to the relatively low quality of the included RCTs, the meta-analysis results should be considered carefully. High-quality RCTs are needed to explore the best way to avoid PICC-related phlebitis.

AUTHOR CONTRIBUTIONS

XL—contributed to the study conceptions and design, literature research, study selection, data extraction, risk of bias assessment, data analysis and drafting of the manuscript; XG—made substantial contributions to the study selection, data extraction, and risk of bias assessment; XW—as the corresponding author, made substantial contributions to the study conception and design, the data extraction, risk of bias assessment, and revision of the manuscript; YH—contributes to the study conception and design and revision of the manuscript, all authors have read and approved the final version of the manuscript and agree the order of the presentation of the author.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1501840803342761984/attachment/Supplementary%20material.docx.

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