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# The incidence and mortality rate of catheter-related neonatal pericardial effusion
## A meta-analysis

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**Abstract**

**Backgroud:** Neonatal pericardial effusion (PCE) is one of the most severe complications of central catheters in neonates with its rapid progression and high mortality. We aim to estimate the overall incidence and mortality of catheter-related neonatal PCE, more importantly, to identify possible predictors for clinical reference.

**Methods:** We searched MEDLINE, Embase, Cochrane Library, Web of Science, china national knowledge infrastructure, Wanfang Data, and Sinomed databases for subject words "central catheter," "neonate," "pericardial effusion" and their random words till June 8, 2020. This meta-analysis is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Possible predictors of occurrences and deaths were extracted and assessed cooperatively. The pooled incidence rate of catheter-related neonatal PCE was calculated using a random effects model.

**Results:** Twenty-one cohort studies and 99 cases were eligible. Pooled incidence is 3·8‰[2.2‰, 6.7‰]. Polyurethane catheters generate significantly more neonatal PCE than silicone counterparts ($P < .01$). 27% of the patients die. The mortality of patients with bradycardia is higher than others ($P < .05$). Catheters with a guidewire result in more deaths than umbilical venous catheter (UVC) and peripherally inserted central catheters (PICC) ($P < .05$). Without pericardiocentesis, mortality increases ($P < .01$). The difference of deaths between reposition and removing the catheter is insignificant ($P > .05$).

**Conclusion:** Central catheters in Seldinger Technique (with a guidewire) put neonates at greater risk of PCE and consequent death. Silicone catheters excel at avoiding deadly catheter-related PCE, which could be a better choice in neonatal intensive care units (NICU). When catheter-related PCE occurs, timely diagnosis and pericardiocentesis save lives.

**Abbreviations:** CT = cardiac tamponade, CVC = central venous catheter, FDA = food and drug administration, NICU = neonatal intensive care units, PCE = pericardial effusion, PICC = peripherally inserted central catheters, PN = parenteral nutrition, UVC = umbilical venous catheter.

**Keywords:** neonate; pericardial effusion; cardiac tamponade; central venous catheter

### 1. Introduction

In 1972, Daly Walker reported a rare case: a 1540g newborn had an umbilical venous catheter (UVC) in the right atrium. Three days later, the patient suddenly appeared dyspneic. Radiography showed apparently larger heart size, and a pericardial effusion (PCE) was diagnosed.[1] This is the first reported case of central venous catheter (CVC)-related neonatal PCE. It has been reported repeatedly since then. The reported incidence and mortality of this complication varied due to differences in catheter selection and placement operation.

There are 4 types of neonatal CVC: peripherally inserted central catheters (PICC), UVC, CVC with a guidewire (Seldinger technique) and surgically inserted CVC.[2] For some newborns, preterm mainly, CVCs are their precious lifeline to receive long-term total parenteral nutrition (PN) and sustain growth.

Neonatal myocardium is relatively thin, thus vulnerable to mechanical and osmotic injury, under the risk of PCE[3] (shown

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*Ethics Committee of The First Affiliated Hospital of Hainan Medical University approved this research.*

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in Fig. 1, by JW). The U.S. Food and Drug Administration (FDA) recommended that the catheter tip stays outside the cardiac silhouette to avoid cardiac tamponade (CT) in 1989,[4] while some researchers argued that FDA was too cautious about this risk and the right atrium placement does not increase risk of CT.[5] The problem is that their research includes adults and older children as well, not just neonates. A great deal of literature has pointed out that ultrasound is superior to X-ray in localizing catheter tip position.[6,7] Our guidelines need updates.

Normally, about 5 mL fluid is present in the neonatal pericardial cavity. When the fluid exceeds certain amount, it leads to CT and cardiac shock. The faster the accumulation, the less accumulation it needs to generate CT.[8] Following classification of PCE has been applied to all age groups, including neonates: mild 5 to 10 mm (100–250 mL), moderate 10 to 20 mm (250–500 mL), severe > 20 mm (>500 mL).[9] When the volume of PCE is less than 250 mL, the heart size on X-ray can be normal; when that exceeds 250 mL, the heart size widens.


**Figure 1.** Illustration of pericardial effusion secondary to central venous catheters. (A) Tip of the catheter in close contact with the myocardial wall. (B) Mechanical or osmotic injury of endocardium and myocardium. (C) Perforation of myocardium causes pericardial effusion and cardiac tamponade eventually.

In this meta-analysis, we hope to identify some more risk factors of catheter-related neonatal PCE (other than the well-known one of intracardiac tip position) and the predictors of mortality as well.

## 2. Methods

This meta-analysis is based on the PRISMA statement (Preferred reporting items for systematic reviews and meta-analysis, http://www.prisma-statement.org). Subject words——“Central venous catheter,” “neonate,” “pericardial effusion” and their free words were searched in MEDLINE, Embase, Cochrane Library, Web of Science, china national knowledge infrastructure, Wanfang Data, and Sinomed databases by June 8, 2020. To include as many studies and cases qualified as possible, no restriction was attached to language or publication time.

Registration number of this meta-analysis: INPLASY202030014.

We retrieved 399 records. After duplication removal, abstract screening, 173 were qualified for full-text evaluation. For literature in neither English nor Chinese, translators were invited to help interpret the full text. In the end, 21 retrospective cohort studies[2,6,7,10–27] and 99 cases (from 75 case reports and case series) were found eligible.

Inclusion criteria: Patients in neonatal intensive care units (NICU), including preterm infants and term neonates; Studies with an exact number of catheters placed and cases of catheter-related neonatal PCE. Exclusion criteria: Neonates with cancer, cardiomyopathy, inherited metabolic disorder, and those who have undergone dialysis, for these neonates might have impaired cardiac function; Older patients, for they might differ from neonates in the maturity of the myocardium.[28]

The primary outcome of this paper is the estimation of the occurrence of catheter-related neonatal PCE, with the data extracted from 21 cohort studies, and the secondary outcome is the estimation of the death rate of this complication with the data extracted from 99 cases. The case report belongs to the least significant source of evidence based on its small size and potential publication bias. Nevertheless, for a rare condition of catheter-related neonatal PCE with few relevant studies, aggregated findings of these cases might represent the best evidence available.

*R*-3.6.3 was used for statistical analysis. Due to possible heterogeneity from catheter selection and placement operation among different ages and regions, we chose the random effect model to pool the overall incidence. $I^2$ statistic was calculated to assess heterogeneity. We define $50\% < I^2 < 75\%$ as moderate heterogeneity, $I^2 < 75\%$ as high heterogeneity. A funnel plot was made to decide whether obvious publication bias was present.

To further analyze the incidence and mortality of this complication, we quantified the statistics data of patients, catheters, study period, symptoms, treatments, etc. For count data, if sample size $n \geq 40$, theoretical number $T \geq 5$, Pearson chi-square test was applied to analyze the data; If $n \geq 40$, $1 \leq T \leq 5$, Pearson’s chi-square test with Yates’ continuity correction was applied; If $T < 1$ or $n < 40$, or *P* value approached the level of significance $\alpha$, Fisher’s exact test was applied.

For quantitative data like gestational age and effusion volume, they were divided into 2 groups—death group and survival group, to analyze their relationship with death. If normality test and homogeneity test for variance were not significant, *t* test was used; If the data met the homogeneous variance assumption, but violated normal distribution, t’-test was used; otherwise Wilcoxon signed-rank test was used.

## 3. Results

By random effect model, the pooled incidence is 3·8‰ [2.2‰, 6.7‰]. That means approximately 3.8 neonates suffer from this complication every 1000 CVC placed. Some studies with zero events are present, partially because these NICUs are well aware of the severity of this complication and reformed the placement operation, such as Gupta 2016.[24] The inclusion of these events helps mirror the true incidence.

Publication bias was not significant, judging from the symmetrical distribution of the funnel plot. Due to the rarity of this complication, Freeman-Tukey double arcsine conversion was used to bring out the funnel plot with transformed proportion and the stand error. The majority of studies that have a large sample size and high precision, lie at the upper central part of the plot. Cartwright DW reported only 1 case of non-lethal catheter-related PCE in 2186 catheters placed.[29] As the only study outside the left pseudo 95% confidential interval, it applied silicone catheters for all insertions which could explain its low incidence. On the contrary, Oh et al reported a relatively higher incidence with a small sample size—12 catheters in total. They concluded that these catheters in Seldinger technique with a hard guidewire could injure the myocardium.[26] Due to its small sample size and low precision, this study is scattered at the bottom of the plot.

The characteristics of the 21 studies are listed in Table 1. The quantified data on risk factors like catheter type, material, path (via superior vena cava or inferior vena cava), study period and newborn weight extracted from those studies are displayed in Figure 2. The details of the 99 included cases are summarized in Table 2, and the quantified data related to death extracted from these cases are displayed in Figure 3.

Among all those cases of catheter-related PCE, 91 were diagnosed with CT. The median birth weight of patients was 1180g. The median time from catheter placement to effusion onset was 3 days. 14 cases were complicated with pleural effusion, 1 case was complicated with ascites.

Sixty-two cases reported that the means to confirm tip position was X-ray, the other 37 cases did not specify the means. None of them chose ultrasound. Among the 99 cases, there was evidence of the catheter tip inside the cardiac chambers in 61 cases. Twelve catheter tips were lodged in the myocardial wall, 11 perforated the myocardium, 9 coiled, 4 curled, 3 angulated and 1 broke.

Forty-six cases showed bradycardia, 45 cyanosis, 33 hypotension, 21 cardiac arrest, 21 dyspnea, 19 distant heart sounds, 18 acidosis, 16 enlarged heart size on X-ray, 14 frequent apnea, 14 tachycardia, 11 grayish or pale skin, 7 white lungs, 6 mottled skin, 6 delayed capillary refill, 4 hyperglycemia, 3 low voltage in the electrocardiogram, 2 dilated pupils, 2 oliguria, 1 hyperkalemia and 1 hyponatremia.

All tamponades relieved immediately after pericardiocenteses (72 cases) and pericardiotomy (1 case). The mean drainage was 24.5 mL ± 18.0 mL. Thirty-eight cases of drainage underwent biochemical analysis and was proved to be PN. Effusion absorption took 1 day to 3 weeks for those without pericardiocentesis.

Twenty-seven neonates died. The mean duration between PCE onset to death was less than 24 hours, ranging from 4 hours to 5 days. Seventeen cases underwent autopsy, among which 15 confirmed the fluid in the pericardial cavities to be PN.

By statistical analysis of quantified data, we find that polyurethane catheters are prone to induce PCE in neonates ($P < .01$). This finding accords with material property (see details in discussion).[30] UVC tend to cause more PCE than PICC ($P < .05$), however, central catheters via inferior vena cava (including UVC and PICC from lower limbs inserted together) have a lower incidence of PCE than PICC inserted from upper extremity with an insignificant difference ($P > .05$). This implies that UVC's higher PCE risk originates from its thick straight short route (see details in discussion). Very low birth weight infants (birth weight < 1500g) are probably more vulnerable than heavier neonates ($P > .05$). The incidence of this complication slightly decreased after 2004 ($P > .05$).

Around 27% of patients of this complication die. Pericardiocentesis can adequately prevent death in these patients ($P < .01$). As for disposal of the catheter after the event, reposition or withdrawing it to serve as a peripheral 1 do not increase the risk of death compared to removing catheter ($P > .05$).

The mortality of catheter-related PCE differs in the choice of the catheter ($P < .05$). Cases with CVC in Seldinger technique (e.g., catheters inserted from internal/external jugular vein, subclavian vein and femoral vein) have a higher risk of death than UVC and PICC ($P < .05$). This can be attributed to the potential injury to the myocardium by the hard guidewire of the Seldinger technique for the most part. Besides, the relatively short route renders more migration as compared to PICC. Cases with UVC have slightly more deaths than PICC, but that is not significant ($P > .05$).

The mortality of patients presented with bradycardia is higher than those without this sign ($P < .05$). There seem to be more deaths with females and with smaller gestational age ($P > .05$). Drainage volume is irrelevant to death, we reckon that timely drainage makes that difference. The rescue success rate has increased from 61% (before 2003) to 77% (after 2004).

## 4. Discussion

To our knowledge, this is the first review to synthesize cohort studies on catheter-related neonatal PCE. Previous incidence and mortality of this complication were estimated from single center studies with relatively limited size. Besides, we are the first to report a significant difference in its incidence and mortality with different catheter types.

The U.S. FDA advocated an extra-cardiac position of central catheter tips in 1989,[4] which has been confirmed to be an independent risk factor of CT.[31] Among 99 cases included, 61 have reported migration of catheter into heart chambers for at least once. Although most agree that the intra-cardiac tip position is not appropriate, some disagree.[5] The reason probably lies in the patient group. Studies that support intra-cardiac positions are mostly targeted at all age groups including older children and adults.

It would be dangerous to equate neonatal patients to those from other age groups. Neonatal myocardium is immature structurally as well as functionally. The thin myocardium of neonates is more prone to damage than that from an older heart, with the myocardium usually absent in some sections of the atrial wall, only epicardium and endocardium present.[3] The immature myocardium of newborns, especially preterm infants, has less contractile elements, higher water content, higher baseline microvascular blood flow, a greater surface to volume ratio, and an under-developed sarcoplasmic reticulum.[28] Bensley et al found reduced cardiomyocyte proliferation of preterm infants, which adversely impact upon the final number of cardiomyocytes, decrease cardiac functional reserve, and impair the reparative capacity of the myocardium.[32]

Among cases included in our study, neonates weigh less have a higher tendency to develop catheter-related PCE and die. However, the difference is not significant enough ($P > .05$).

The conventional method of X-ray to confirm the tip position is flawed. Be it vertebra, rib, carina of the trachea,[33] tracheobronchial angle,[34] 1 cm above diagram level or heart silhouette, landmarks on X-ray do not provide a safe, accurate extra-cardiac tip position but rather an anatomical proximity to pericardial reflection, let alone potential projection bias of 2-dimensional image. A catheter tip at T3-T4 vertebral level, carina level, tracheobronchial angle level from superior vena cava, or at T7-T9 vertebral level, 1 cm above diagram level from inferior vena cava, or at heart silhouette on X-ray could already sit inside heart chambers, or not.

**Table 1**

**Characteristics of 21 eligible cohort studies.**

| Author, yr | Country | Study period | Catheters placed (n) | Catheter characteristics | Main viewpoint |
|---|---|---|---|---|---|
| Adriana 2017 | Brazil | 2012.04–2013.09 | 168 | All UVC | "Anteroposterior chest radiography is not reliable in identifying the exact anatomical location of the distal end of the UVC. " |
| Barreiros 2018 | Brazil | 2014.07–2016.12 | 194 | All PICC | "Bedside ultrasonography demonstrated its importance in shocks of uncertain etiology and neonates with sudden onset hemodynamic instability who are using central venous access." |
| Cartwright 2004 | Australia | 1984.01–2002.12 | 2186 | All PICC; all silicone | "This is the largest series of percutaneously inserted silicone central venous catheters reported with only 1 case of pericardial effusion." |
| Gupta 2015 | USA | 2010.12–2011.06 | 104 | 41 UVC,63 PICC | "The incidence of UVC and PICC tip migration into the cardiothymic silhouette is 36 and 23% of UVCs and 23 and 11% of PICCs at 1 and 24 hours,respectively." |
| Haase 2011 | Germany | 1999.01–2008.06 | 142 | All UVC | "Severe complications can occur also in catheters with previous correct position." |
| Huang 2020 | China | 2015.08–2017.08 | 144 | All UVC | "Bedside ultrasound is worth of adoption and promotion in neonate ward." |
| Kulkarni 1981 | USA | 1976.07–1978.07 | 130 | NA | "We suggest that the venogram through the central venous catheter should be obtained in infants on prolonged TPN once every 2-3 wk." |
| Leipälä 2001 | Finland | 1997.01–1999.01 | 100 | All PICC; 40 silicone, 60 polyurethane | "Proper visualization of the PCVC and vigilant attention to its location is required to prevent these rare but potentially fatal complications." |
| Li 2019 | China | 2017.01–2018.12 | 693 | NA | "Immediate bedside echocardiography should be performed to any patient with UVC/PICC indwelling, who develops sudden unexplained cardiorespiratory instability." |
| Lloreda-García 2015 | Spain | 2009.03–2015.02 | 604 | 347 UVC, 193 PICC, 34 femoral venous line; all polyurethane | "The incorrect location of the tip was associated with more mechanical complications." |
| Nadroo 2001 | USA | 2 yrs | 390 | All PICC | "The tip of the PICC should not be placed in the right atrium." |
| Newberry 2014 | USA | 2010.04–2011.03 | 80 | All PICC via SVC | "The incidence of overall complications was not statistically different whether standardizing upper extremity positioning or not." |
| Oh 2016 | Korea | 2014.05–2015.10 | 12 | All internal jugular venous line | "It is suspected that deep insertion of the 0.018 inch guidewire directly injured the heart." |
| Ohki 2013 | Japan | 2005.02–2017.03 | 946 | All PICC; 439 via SVC, 507 via IVC | "It is important to investigate the detailed circumstances associated with this complication, and to determine the relevant risk factors." |
| Pet 2019 | USA | 2012.01–2015.06 | 1234 | All PICC; 307 silicone, 845 polyurethane; 524 via SVC, 710 via IVC | "In our cohort, there was 1 case of fatal cardiac tamponade, which occurred in an infant with a polyurethane line." |
| Pezzati 2004 | Italy | 1996.01–2003.12 | 280 | All PICC; 232 silicone, 48 polyurethane; 219 via SVC, 61 via IVC | "Our experience shows that even preterm infants with cardiac tamponade can be successfully resuscitated by timely pericardiocentesis in most cases." |
| Sertic 2018 | Canada | 2004.01–2014.08 | 3454 | All PICC | "Cases with pericardial effusion were more likely to be female patients with lower weight at PICC insertion compared with controls." |
| Srinivasan 2013 | USA | 2010.01–2011.03 | 100 | All PICC; all polyurethane; 95 via SVC, 5 via IVC | "After controlling for arm position, 47% of PICCs placed in the upper limb migrated at 24 hours postinsertion with 32.6% migrating toward the heart." |
| Sterniste 1994 | Germany | 9 mo | 114 | All PICC | "The aim was to study the complications of peripheral percutaneous Silastic-catheters. No pericardial tamponade was found." |
| Storme 1999 | France | 1994.12–1995.12 | 108 | All UVC; 52 polyvinyl chloride; 56 polyurethane | "A hydropericardium was observed which required a cardiac puncture." |
| Tiran-Rajaofera 2001 | France | 1997.09–2000.01 | 352 | All PICC; all polyurethane | " A pericardial effusion was diagnosed in two cases." |

IVC = inferior vena cava, PICC = peripherally inserted central catheter, SVC = superior vena cava, UVC = umbilical venous catheter.

Overdoing it also costs. Since catheter placement is an aseptic technique, catheters can only be withdrawn outwards. Neonates grow fast, with the catheter tip migrating outwards naturally. Some recommend a T2 vertebral level or 1 cm below diagram level for tip placement,[35] where the tip inevitably leaves the heart, but prompts distal migration, leading to other complications of extravasation like a liver injury.

Some centers estimate the length of the catheter by vertebra (0.5 cm per vertebra) when withdrawing the catheter. This empirical operation has not taken individual differences into account. Without recheck after adjustment with an appropriate method, these tips can still be intra-cardiac.[36]

Electrocardiogram-guided catheter placement has emerged for a while. Just like catheters in Seldinger technique, a guidewire

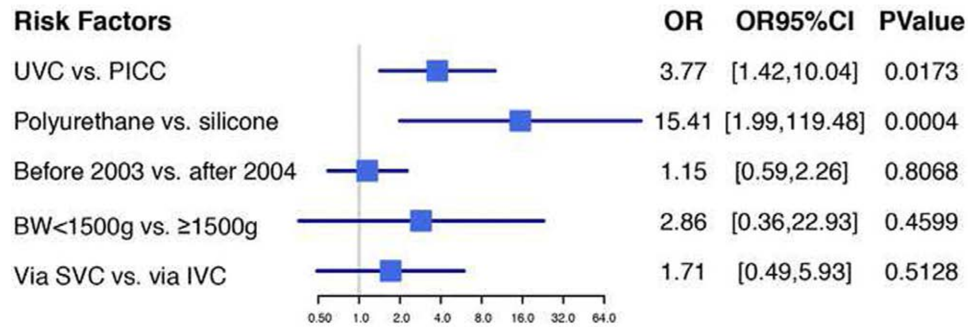


**Figure 2.** Risk factors of catheter-related pericardial effusion occurrence in neonates. BW = birth weight, IVC = inferior vena cava, OR = odds ratio, PCE = pericardial effusion, PICC = peripherally inserted central catheters, SVC = superior vena cava, UVC = umbilical venous catheters.

is introduced as well in this operation, which could bring equally higher risk in occurrences and deaths of cardiac effusion. Why we take all the trouble, when the solution is handy? Ultrasound is capable of locating the catheter exactly outside the entrance of the right atrium. A large number of scholars now recognize ultrasound as a superior method for tip evaluation to X-ray.[6,7] Even small-sized 1.9Fr catheters, still have a diameter larger than 1mm, which can be easily tracked by experienced sonographers. Flushing line with 2 mL normal saline and tracking the flow of the microbubbles helps to locate the tip.[37] Ultrasound is safe and accurate without radiation or guidewire, suitable for repeated evaluations. However, X-ray is still the "gold standard" in almost all clinical guidelines for locating catheter tips. We can do better by updating guidelines and training sonographers.

Nevertheless, X-ray has its unique value since catheter curvature, looping,[38] angulation and enlarged cardiac silhouette in a short time are known to be associated with PCE. In 99 cases included, 9 catheter tips coiled, 4 curled, 3 angulated. Timely intervention may alter the clinical course.

In 2001, the U.S. Centers for Disease Control and Prevention pointed out that catheters made of polyvinyl chloride and polyethylene generate more thromboses and infections than those made of polyurethane and silicone.[29] Therefore, only limited NICUs still use polyvinyl chloride and polyethylene catheters; polyurethane and silicone ones are the main trends.

The association between polyurethane and neonatal PCE has raised some suspicion over the years. Goutail-Flaud et al doubted polyurethane could be the reason for 1 catheter-related neonatal PCE. Since then, their NICU stopped using polyurethane catheters.[39] McGee et al thought silicone catheters were exceptions to perforation complication.[35] Pezzati et al considered silicone catheters to be more flexible and less traumatic. They only chose relatively hard but small polyurethane catheters when the insertion of silicone ones failed.[27] Bouissou et al stated that their NICU preferred silicone catheters unless insertion did not go well, or the patient weighed less than 800g.[40]

Hereby, we simply conclude the difference between polyurethane and silicone catheters from Enrico in *Peripherally Inserted Central venous catheters*: Silicone catheters are softer and more flexible, can bend and recover more efficiently, and are not permanently deformed as easily as polyurethane catheters. Silicone catheters are less prone to stress cracking, and more resistant to attack by common antiseptic and cleaning preparations than polyurethane catheters because it is cross-linked. Silicone catheters are more resistant to solvents; therefore, do not break in most solvents because their hydrophobicity limits the attack by water. Silicone catheters have lower burst strength (the pressure applied to a catheter lumen of a closed catheter that causes it to leak). This implies the danger of force flush. Silicone catheters with same internal diameters have greater wall thickness.[30]

Gupta et al found out that 36% of UVC and 23% of PICC migrated into cardiac chambers 1 hour after catheter insertion. Among these, 28% of upper limb inserted PICC migrated, and 21% of lower limb inserted ones migrated. 24 hours after insertion, migration of UVC still outnumbered PICC, while at this time, lower limb inserted PICC did not migrate any further.[39] Though the accuracy of X-ray in examining those tip positions is questionable, their data helps explain the higher incidence of PCE in UVC and relatively higher incidence of that in upper limb inserted PICC as compared to lower limb inserted PICC. To reduce migration, more NICUs choose lower limb for PICC insertion routinely.

## 5. Limits

This meta-analysis may possibly underestimate the real incidence of this complication. Etiological diagnosis of catheter-related neonatal PCE needs a timely ultrasound, thorough clinical thinking, and objective judgment. Not all cases of neonatal PCE undergo pericardiocentesis and subsequent biochemical analysis of drainage. The cause might be covered up. Besides, some neonates can progress so rapidly and die in a short time. Without an autopsy, the reason for their deaths could stay a mystery. To illuminate the clinical practice of neonatal central catheters, further relevant studies are still needed on this rare complication.

## 6. Conclusions

Our study suggests that CVC in Seldinger Technique (with a guidewire) put neonates at greater risk of PCE and consequent death; while silicone catheters excel at avoiding deadly catheter-related PCE, which could be a better choice in NICU. A safe tip position nips this complication in the bud.

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## Author contributions

JYW, JCD and QW contributed equally to this meta-analysis by designing this study, searching the literature, plotting figures, processing data and writing the draft. YXL helped the search process by settling disagreements of the two authors above. ZBL helped process data by settling disagreements of this process and revising the draft. MUJ evaluated the bias risk of included studies and corrected grammatical errors of the draft. JXP evaluated bias risk of studies and examined the statistical methods applied.

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**Data curation:** Jingyi Wang, Qing Wang, Jichang Du.
**Formal analysis:** Jianxiong Peng.
**Funding acquisition:** Qing Wang, Jichang Du.

**Table 2**

**Characteristics of 99 cases reported.**

| Author, yr | Country | Gestational Ag (wks) | Sex | Birth weight (g) | CT | Time from line insertion to PCE onset | Effusion volume by ultrasound | Pericardio-centesis and volume of drainage | Drainage proved to be PN | Removal of catheter after PCE | Outcome | Type and material of catheter |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Abdellatif 2012 | Oman | 38 | Male | 2400 | Yes | 2 d | Huge; 40 mL | Yes | Yes | Yes | Alive | UVC; silicone |
| Abiramalatha 2016 | India | 34 | Female | 1500 | Yes | 3 d | 1 mm | Yes; 40 mL | Yes | Yes | Alive | UVC |
| Abu-dalu 1984 | Israel | 36 | Male | 1600 | Yes | 24 h | NA | Yes | NA | NA | Alive | Right subclavian vein |
| Aiken 1992 | New Zealand | 25 | Male | 790 | Yes | 17 h | NA | Yes; 8 mL | Yes | Yes | Alive | UVC; silicone |
| Akbay 2019 | Turkey | 28 | Female | 1070 | Yes | 7 d | Large | Yes; 16 mL | No | Yes | Alive | PICC |
| Aktaş 2016 | Turkey | 28 | Male | 670 | Yes | 5 d | Large; 9 mm | Yes; 51 mL | Yes | NA | Alive | PICC; polyurethane |
| Al Nemri 2006 | Turkey | 32 | Female | 1620 | Yes | 1 d | NA | NA | NA | NA | Dead | UVC |
| Al Nemri 2006 | Turkey | NA | Female | 2975 | Yes | 1 d | Large; 10–15 mm | Yes | Yes | Yes | Alive | UVC; polyvinyl chloride |
| Alabsi 2010 | Germany | 29 | Male | 1235 | Yes | 2 d | NA | Yes | NA | Yes | Alive | UVC; polyurethane |
| Almasri 2012 | USA | 24 | Female | 580 | Yes | <15 h | NA | Yes | Yes | NA | Dead | UVC |
| Arya 2009 | USA | 37+ | Male | 2520 | Yes | 4 d | NA | Yes; 9 mL | NA | Yes | Alive | UVC |
| Atmawidjaja 2016 | Malaysia | 33 | Male | 1360 | Yes | 7 d | Large | Yes; 25 mL | Yes | NA | Dead | NA |
| Bagtharia 2001 | UK | 28 | Male | NA | Yes | 80 h | Massive | Yes; 22 mL | NA | Yes | Alive | UVC |
| Bagtharia 2001 | UK | 25 | Female | NA | Yes | 48 h | NA | Yes; 20 mL | Yes | NA | Alive | PICC; silicone |
| Bar-Joseph 1983 | USA | NA | Male | 2500 | Yes | 3 d | NA | NA | NA | No | Dead | Internal jugular vein; silicone |
| Beattie 1993 | New Zealand | 27 | Female | 1040 | No | 4 d | NA | Yes; 5 mL | Yes | Yes | Alive | PICC; silicone |
| Cade 1997 | UK | 30 | Female | 1240 | Yes | 8 d | NA | Yes; 23 mL | Yes | NA | Alive | PICC; polyurethane |
| Carles 2012 | France | 35 | Female | 1525 | Yes | 40 h | Moderate | NA | NA | NA | Dead | UVC |
| Chen 2018 | China | 30 + 2 | Male | 1320 | Yes | 1 d | NA | NA | NA | Yes | Alive | UVC |
| Cherng 1994 | China | 37+ | Male | 2994 | Yes | 3 h | NA | Yes; 12 mL | Yes | No | Alive | Internal jugular vein |
| Chioukh 2016 | Tunisia | 27 | Female | 970 | Yes | 3 d | NA | Yes; 20 mL | NA | NA | Alive | UVC |
| Desai 2017 | India | 28 | Male | 980 | Yes | 2 d | NA | Yes; 9 mL | NA | NA | Alive | PICC |
| Dhanasekaran 2014 | India | NA | Female | 2200 | Yes | Immediately | NA | NA | NA | Yes | Alive | Left internal jugular vein |
| Dornaus 2011 | Brazil | 30 + 2 | Male | 1290 | Yes | 5 d | Marked | Yes; 25 mL | Yes | No | Alive | PICC |
| Elbatreek 2019 | Saudi Arabia | 31 | Male | 1300 | Yes | 8 h | NA | Yes; 15 mL | NA | Yes | Alive | UVC |
| Fusco 2008 | Italy | 26 | Female | 695 | Yes | 11 h | NA | NA | NA | NA | Dead | PICC |
| Fusco 2008 | Italy | 25 | Female | 720 | Yes | 24 h | NA | Yes; 15 mL | NA | NA | Alive | PICC |
| Fusco 2008 | Italy | 26 | Female | 850 | No | 10 d | NA | NA | NA | Yes | Alive | PICC |
| Gálvez-Cancino 2015 | Mexico | 35 | Male | 2180 | Yes | 2 d | NA | Yes; 40 l | NA | NA | Alive | UVC |
| Giacoia 1991 | USA | 26 | Male | 960 | Yes | 4 d | NA | Yes; 15 mL | NA | NA | Alive | PICC |
| Giacoia 1991 | USA | 28 | Female | 870 | Yes | 3 d | NA | NA | NA | NA | Dead | PICC |
| Gunay 2016 | Turkey | 36 | Male | 3600 | Yes | 36 h | NA | Yes | Yes | Yes | Alive | UVC; polyvinyl chloride |
| Guo 2018 | China | 38 + 5 | Male | 3260 | No | 8 d | 6.5 mm | Yes; 35 mL | NA | Yes | Alive | Right subclavian vein |
| Haass 2009 | Italy | 25 | Female | 630 | Yes | 26 d | NA | Yes; 6 mL | Yes | NA | Alive | PICC; polyurethane |
| Iyer 2014 | India | 29 | Female | NA | Yes | 2 d | NA | Yes; 15 mL | Yes | Yes | Alive | PICC |
| Kabra 2001 | Australia | 26 | Female | 774 | Yes | 3 h | Large | Yes; 3.5 mL | Yes | NA | Alive | PICC; silicone |

(*Continued*)

**Table 2**
**(*Continued*)**

| Author, yr | Country | Gestational Ag (wks) | Sex | Birth weight (g) | CT | Time from line insertion to PCE onset | Effusion volume by ultrasound | Pericardio-centesis and volume of drainage | Drainage proved to be PN | Removal of catheter after PCE | Outcome | Type and material of catheter |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kaluarachchi 2015 | Germany | 31 + 1 | Male | 1730 | Yes | NA | Large | Yes; 6 mL | NA | No | Alive | PICC; polyurethane |
| Kugelman 2005 | Israel | NA | Male | 3050 | Yes | 2 d | NA | Yes; 40 mL | NA | NA | Alive | UVC |
| Kulkarni 1981 | USA | 26 | Female | 780 | Yes | 17 d | NA | Yes; 50 mL | Yes | Yes | Alive | Silicone |
| Leipala 2001 | Finland | 23 + 5 | NA | 685 | Yes | 14 d | Marked | NA | NA | No | Dead | PICC; polyurethane |
| Lemus-Varela 2004 | Mexico | NA | Male | 2960 | Yes | 2 d | Massive | Yes; 11 mL | Yes | NA | Dead | UVC; polyethylene |
| Lemus-Varela 2004 | Mexico | 29 | Male | 970 | Yes | 5 d | Significant | Yes; 27 mL | Yes | No | Alive | PICC; silicone |
| Lemus-Varela 2004 | Mexico | 36 | Male | 2175 | Yes | 3 d | NA | Yes; 26 mL | NA | NA | Alive | External jugular vein; polyethylene |
| Lemus-Varela 2004 | Mexico | 29 | Female | 1080 | Yes | 7 d | NA | Yes; 23 mL | Yes | NA | Dead | Right external jugular vein; silicone |
| Lemus-Varela 2004 | Mexico | 32 | Female | 1450 | Yes | 12 d | large; 6 mm | Yes; 18 mL | Yes | NA | Alive | PICC; silicone |
| Little 2004 | USA | 28 | NA | 1037 | Yes | 6 d | NA | Yes; 25 mL | NA | Yes | Alive | PICC; silicone |
| Liz 2020 | Portugal | 26 | Female | 690 | Yes | 11 d | NA | No | | NA | Alive | PICC |
| Megha 2011 | India | 38 | NA | 3350 | Yes | 2 h | Massive | Yes; 20 mL | Yes | Yes | Alive | UVC; silicone |
| Modelli 2014 | Brazil | NA | Male | NA | Yes | Immediately | NA | NA | NA | NA | Dead | Right internal jugular vein |
| Monteiro 2008 | Brazil | 37 | NA | 3450 | Yes | 5 d | Massive | Yes; 50 mL | NA | NA | Alive | UVC; polyurethane |
| Monteiro 2008 | Brazil | 38 | NA | 3725 | Yes | 48 h | Massive | Yes; 60 mL | Yes | NA | Alive | UVC; polyurethane |
| Morini 2006 | Italy | 29 | Female | 1150 | Yes | 1 d | NA | Yes | NA | NA | Dead | PICC |
| Mukerji 2016 | Canada | 25 | Female | NA | Yes | 24 h | Massive | Yes; 5 mL | NA | NA | Alive | PICC |
| Mukerji 2016 | Canada | 37 | Female | NA | Yes | 5 d | NA | Yes | NA | NA | Alive | UVC |
| Mukerji 2016 | Canada | 25 | Female | NA | Yes | 2 d | NA | Yes; 5 mL | NA | NA | Alive | PICC |
| Nadroo 2001 | USA | 34 | Female | NA | Yes | 4 d | NA | NA | NA | NA | Dead | PICC |
| Nadroo 2001 | USA | 26 | Female | 610 | Yes | 6 d | Very large | NA | NA | NA | Dead | PICC |
| Nicholls 1993 | UK | 34 | Male | 2200 | Yes | 4 d | NA | No | NA | NA | Dead | Internal jugular vein; polyurethane |
| Onal 2004 | Turkey | 39 | Male | 3450 | Yes | 60 h | NA | Yes; 80 mL | Yes | Yes | Alive | UVC; polyvinyl chloride |
| Pesce 1999 | Italy | 36 | Male | 2300 | Yes | 20 d | Massive | NA | NA | NA | Dead | Internal jugular vein; polyurethane |
| Pignotti 2004 | Italy | 29 | Female | 840 | Yes | 4 d | NA | No | NA | NA | Alive | Silicone |
| Pizzuti 2010 | Italy | 25 | Female | 620 | Yes | 17 d | Large | Yes; 2 mL | Yes | NA | Alive | PICC; polyurethane |
| Rajpal 2013 | USA | 34 | Male | NA | Yes | 4 d | NA | NA | NA | NA | Dead | Left subclavian vein |
| Ş Kayalı 2016 | Germany | 27 | Male | 1120 | Yes | 19 d | NA | Yes; 15 mL | Yes | NA | Alive | PICC |
| Ş Kayalı 2016 | Germany | 28 | Male | 895 | Yes | 14 d | NA | Yes; 20 mL | Yes | NA | Alive | NA |
| Scharf 1990 | Germany | NA | Male | 1210 | Yes | 24 h | NA | Yes | NA | NA | Alive | PICC; silicone |
| Scharf 1990 | Germany | NA | NA | NA | Yes | 7 d | NA | Yes; 19 mL | Yes | NA | Alive | PICC; silicone |
| Schlapbach 2009 | Switzer-land | 25 | NA | 590 | No | 2 d | NA | NA | NA | NA | Alive | UVC; polyurethane |
| Schulman 2002 | USA | 27 | NA | 984 | Yes | 8 d | NA | Yes; 25 mL | NA | Yes | Alive | Right external jugular vein; silicone |
| Schulman 2002 | USA | 28 | NA | 1080 | Yes | 15.5 h | NA | Yes; 30 mL | NA | NA | Alive | NA |
| Sehgal 2007 | Canada | 28 | Male | 580 | No | 9 d | NA | Yes; 11 mL | Yes | Yes | Alive | UVC |
| Shannon 2014 | USA | 27 + 1 | Male | 840 | Yes | 11 h | Massive | Yes; 6 mL | NA | NA | Alive | PICC; silicone |
| Shenoy 2009 | USA | 28 | NA | NA | Yes | 3 d | NA | Yes; 30 mL | Yes | Yes | Alive | PICC |
| Shivalli 2017 | India | 33 | Male | 1600 | Yes | 7 d | NA | Yes | Yes | Yes | Alive | UVC |
| Singh 2018 | India | 29 + 4 | Female | 1100 | Yes | 3 d | Large | Yes; 12 mL | NA | NA | Dead | UVC |

(*Continued*)

**Table 2**

**(*Continued*)**

| Author, yr | Country | Gestational Ag (wks) | Sex | Birth weight (g) | CT | Time from line insertion to PCE onset | Effusion volume by ultrasound | Pericardio-centesis and volume of drainage | Drainage proved to be PN | Removal of catheter after PCE | Outcome | Type and material of catheter |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Soleimani 2019 | Iran | 27 + 5 | Male | 780 | Yes | 14 d | Large | Yes; 5 mL | NA | Yes | Alive | PICC |
| Stanek 1993 | USA | 24 | Male | 665 | Yes | <1 d | NA | NA | NA | NA | Dead | UVC |
| Sullivan 1987 | USA | 29 | Female | 850 | Yes | 48 h | Massive | NA | NA | NA | Dead | Right internal jugular vein; silicone |
| Suresh 2007 | India | 37+ | Male | 3500 | Yes | 72 h | NA | Yes; 18 mL | Yes | NA | Alive | Right femoral vein |
| Sutcliffe 1995 | UK | 26 | Female | 780 | Yes | 5 d | NA | Yes; 24 mL | NA | Yes | Dead | Right internal jugular vein |
| Tang 2019 | China | 29 + 4 | Female | 1500 | No | 3 d | NA | NA | NA | Yes | Alive | UVC |
| Tang 2019 | China | 31 + 1 | Male | 1640 | No | 2 d | Massive | NA | NA | Yes | Alive | UVC |
| Thomson 2010 | USA | 35 + 4 | Female | NA | No | 6 d | Very large | Yes; 70 mL | NA | NA | Alive | UVC |
| Törer 2009 | Turkey | 27 | Male | 910 | Yes | 10 d | NA | Yes | Yes | Yes | Alive | PICC; polyurethane |
| Traen 2005 | Belgium | 32 | Female | 1470 | Yes | 4 d | NA | Yes; 25 mL | Yes | NA | Alive | UVC; polyurethane |
| Traen 2005 | Belgium | 33 | Female | 1800 | Yes | 3 d | NA | Yes; 35 mL | Yes | Yes | Alive | NA |
| Traen 2005 | Belgium | 34 | Female | 1380 | Yes | 2 d | NA | Yes; 10 mL | NA | NA | Alive | NA |
| Tseng 2016 | China | 31 | Male | 1510 | Yes | 5 d | NA | Yes; 50 mL | Yes | Yes | Alive | PICC |
| Unal 2017 | Turkey | 29 | Male | 865 | Yes | 3 d | NA | Yes; 25 mL | NA | Yes | Alive | UVC |
| Van Ditzhuyzen 1996 | France | 35 | Male | 2300 | Yes | 4 h | NA | Yes; 10.5 mL | Yes | Yes | Alive | Right internal jugular vein; polyurethane |
| Van Niekerk 1998 | South Africa | 37+ | Female | NA | Yes | 1 d | 1.5 cm | NA | NA | NA | Dead | Right femoral vein; polyurethane |
| Walker 1972 | NA | NA | Female | 1540 | Yes | 2 d | Severe | Yes; 80 mL | NA | No | Alive | UVC |
| Warren 2013 | USA | 25 + 2 | Female | 580 | Yes | 10 d | NA | NA | NA | NA | Dead | UVC |
| Warren 2013 | USA | 26 | Male | 860 | Yes | 11 d | NA | NA | NA | NA | Dead | UVC |
| Warren 2013 | USA | 24 | Male | 580 | Yes | NA | Huge | NA | NA | NA | Dead | Right femoral vein |
| Warren 2013 | USA | 26 + 4 | Male | 671 | Yes | 3 d | NA | NA | NA | NA | Dead | UVC |
| Warren 2013 | USA | 41 | Male | 3142 | Yes | Immediately | NA | Yes | NA | NA | Dead | PICC |
| Wirrell 1993 | Canada | 26–28 | Female | 740 | Yes | 32 d | NA | Yes; 23 mL | Yes | Yes | Alive | PICC; silicone |
| Zou 2015 | China | 32 | Male | 1460 | Yes | 71 d | NA | Pericardiotomy | NA | NA | Alive | PICC |

CT = cardiac tamponade, PCE = pericardial effusion, PN = parenteral nutrition.

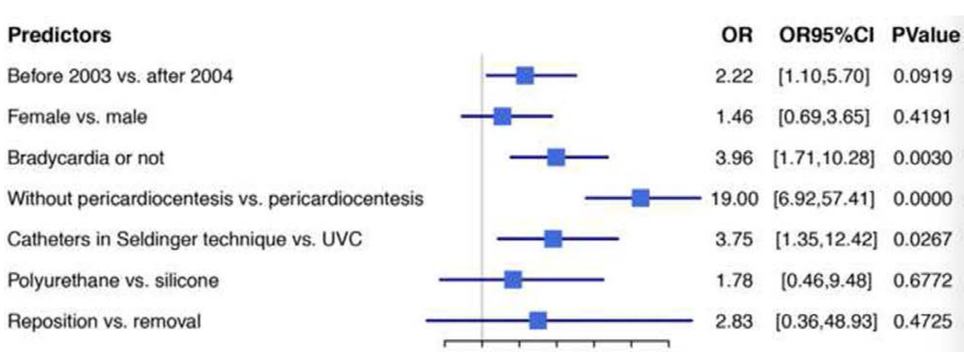


**Figure 3.** Predictors of death in neonatal catheter-related pericardial effusion. CI = confidential interval, OR = odds ratio, UVC = umbilical venous catheters.

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