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Original Article

Complications Following Umbilical Vein Catheterization in Preterm Neonates – Single-Center

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ABSTRACT

Background: Despite their widespread use, umbilical venous catheters (UVCs) are associated with various complications.

Methods: This single-center retrospective cohort study examined UVC-related complications in preterm neonates within a tertiary Neonatal Intensive Care Unit (NICU) from January 2020 to December 2022. The study aimed to analyze these complications in relation to UVC positioning.

Results: Over the course of three years, 146 preterm neonates underwent UVC insertion. The cohort's mean gestational age was 29.2 ± 3 weeks, with a median birth weight of 1110 g (817-1482 g). The median UVC placement duration was 8 days (6-10), totalling 1220 catheter days. Overall, 37% of the UVC placements were categorized as optimal, 35.6% as low-lying, 20.5% as high-lying, and 6.8% were categorized as malpositioned. The UVC-related complications occurred in 62 neonates (42.5%), with central line-associated bloodstream infection (CLABSI) in 8.2%, portal vein thrombosis (PVT) in 2.7%, pericardial effusion in 0.7%, and necrotizing enterocolitis (NEC) in 2.7% of neonates. The incidence of UVC-related complications was lowest with high-lying positions (23.3%), followed by optimal positioning (31.5%), low-lying (63.5%), and the highest in malpositioned UVCs (70%). UVC placement exceeding 8 days were significantly associated with increased complications.

Conclusion: The study highlights an elevated rate of complications associated with umbilical vein catheterization emphasizing the need for judicious use, especially in preterm neonates.

Keywords: Complications, Preterm neonate, Umbilical venous catheter

Introduction

Umbilical venous catheters (UVCs) are commonly used in neonatal intensive care units (NICUs). They offer efficient vascular access that is both immediate and painless in high-risk preterm neonates who require frequent blood sampling, intravenous administration of fluids, medications, and parenteral nutrition (1).

Despite its widespread use, UVCs have been associated with multiple complications. These include central line-associated bloodstream infections (CLABSIs), intestinal necrosis, portal vein thrombosis, as well as cardiac and hepatic complications. Mechanical complications such as leakage at the umbilical site, umbilical bleeding, and catheter blockage further contribute to the incidence of these complications (2–12).

Several studies have examined the relationship between UVC complications and the position of the catheter tip (12–16). The proper placement of the tip of the UVC (outside the heart, precisely at the junction of the inferior vena cava and the right atrium) is crucial in order to avoid the aforementioned complications (1).

This study aims to estimate the rate of UVC-

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related complications and conduct a comparative analysis based on the positions of the catheter tips.

Methods

We conducted a retrospective cohort study involving all preterm neonates who underwent UVC insertion after admission to the Neonatal Intensive Care Unit (NICU) at the Institute of Child and Youth Healthcare of Vojvodina, Novi Sad, Serbia, from January 2020 to December 2022. The research was reviewed and approved by our institutional ethics committee.

The study included neonates with a gestational age (GA) of less than 37 0/7 weeks who underwent umbilical vein catheterization. However, neonates with major congenital anomalies, fetal hydrops, prenatally diagnosed pericardial effusion, and ascites, as well as those without immediate radiographic conformation of the UVC positioning after insertion, were excluded from the study.

The demographic data included gender, gestational age (GA), birth weight (BW), and Apgar scores at the 1st and 5th minute. Additionally, we assessed the post-insertion catheter tip position on the thoracoabdominal radiograph (TAR), the duration of UVC placement, the administration of vasoactive drugs, and the duration of parenteral nutrition until the onset of UVC-related complications.

We defined UVC-related complications as any newly occurring complication resulting in catheter removal. These complications included central line-associated bloodstream infections (CLABSIs), venous thrombosis, pericardial effusion, necrotizing enterocolitis (NEC), periumbilical erythema, umbilical site leakage, bleeding, and catheter block. CLABSI was defined based on the Dutch Neonatal CLABSI Surveillance Criteria (SC) as a bloodstream infection occurring more than 72 hours after birth, associated with an indwelling central venous or arterial line, and confirmed by one or more positive blood cultures. The blood culture finding must not be linked to an infection at another site and it should meet one of the following criteria: 1. Identification of a bacterial or fungal pathogen from one or more blood cultures; 2. Presence of clinical symptoms of sepsis and 2A) isolation of a common commensal in two separate blood cultures or 2B) isolation of a common commensal from one blood culture, along with a C-reactive protein level above 10 mg/L in the first 36 h following blood culture collection (17). NEC was defined using the corrected Bell's staging system as stage II or III (18).

In our NICU, UVCs are inserted by trained physicians, and the catheter tip's position is confirmed with a thoracoabdominal radiograph (TAR). The final position of the UVC tip is assessed relative to the vertebral body and the cardiac silhouette. The optimal position is achieved when the UVC tip lies between the upper border of the eighth thoracic vertebral body (T8), and the lower border of the tenth thoracic vertebral body (T10) on the anteroposterior TAR, outside the cardiac silhouette. The tips positioned above the upper border of T8 were classified as high-lying UVCs. The tips positioned below the lower border of T10 were classified as low-lying UVCs and malpositioned catheters were classified as those deviating laterally into the portal vein system. Immediate readjustment was performed for high-lying or malpositioned UVCs. Cardiac point-of-care ultrasound was used to check and adjust high-lying UVCs in real time. The decision to use a low-lying UVC was at the physician's discretion, based on the infant's condition and the feasibility of alternative venous access. Contrary to the existing recommendations, we did not routinely repeat radiographs after catheter placement (19). The insertion site of the catheter was typically secured with a sterile adhesive tape while suturing of the umbilical cord was performed only in exceptional cases.

Furthermore, the study group was stratified based on the presence of UVC-related complications (patients with and without complications) and the catheter tip position at the initial insertion (optimal, high-lying, low-lying, and malpositioned UVCs).

Statistical analyses were conducted using IBM SPSS Statistics software, version 23. Data were presented as either mean with standard deviation (SD) or median with interquartile range (P25-P75), depending on the normality of the distribution as determined by the Shapiro-Wilk test ($p > 0.05$). Categorical variables were represented as frequencies, and their corresponding percentages (n %). Differences between the two groups of parametric data were assessed using the Independent Samples t-test or Mann-Whitney U test, while differences between categorical variables were determined using the Chi-square test, and Fisher's exact test. The Kruskal-Wallis test was used to evaluate the differences in the initial position of the UVC at the moment of insertion.

Ethical approval

Institute of Child and Youth Healthcare of

Vojvodina Ethics Committee decision number: 763-6

Results

During the study period, 539 preterm neonates (GA < 37 GW) were admitted to the NICU, of which 146 (27.1%) required UVC insertion. The mean gestational age of the study cohort was 29.2 ± 3 weeks, with a median birth weight of 1110 g (817-1482 g). The median duration of UVC placement was 8 days (6-10), accumulating to a total of 1220 catheter days. Regarding UVC positioning, 54 (37%) were classified as optimal, 52 (35.6%) as low-lying, 30 (20.5%) as high-lying, and 10 UVC placements (6.8%) were classified as malpositioned.

Demographic characteristics of patients based on the catheter tip position are summarized in Table 1. No statistically significant difference was found in gestational age across the initial positions of the UVC post-insertion (F = 1.259; p = 0.291). The highest birth weight was observed in neonates with low-lying UVCs (1200 g; 945-1720), and the lowest in those with malpositioned UVCs (1060 g; 838-1683). A significant difference in median birth weight (p < 0.001) was noted among low-lying UVCs. However, variations were observed in UVC placement duration. The longest duration was seen in optimally positioned UVCs (10 days; 8-13), shorter in high-lying positions, and the shortest in low-lying UVCs (6 days; 7-10). The Kruskal-Wallis test revealed no statistically significant differences in birth weight ($\chi2$ = 2.938; df = 3; p = 0.401), but there was a significant difference among the three groups in terms of UVC placement duration ($\chi2$ = 30.135; df = 3; p = 0.000).

A total of 62 neonates (42.5%) developed UVC-related complications resulting in earlier catheter removal, while 84 (57.5%) did not. Neonates with UVC-related complications had a significantly lower birth weight (Z = 4.068; P = 0.000), lower gestational age ($t_{(144)}$ =-3.486; P = 0.001), and longer duration of UVC-placement (Z = -4.204; P = 0.000) compared to those without complications. Furthermore, UVC-related complications were associated with UVC placements exceeding 8 days. Vasoactive support was significantly more common in neonates with complications (χ^2 = 50.658; df = 1; P = 0.000) (Table 2).

Additionally, we compared UVC-related complication rates with the UVC tip positions (Table 3). 12 neonates (8.2%) developed CLABSI resulting in a CLABSI rate of 9.83 per 1.000 catheter days. The UVCs in these cases were positioned either optimally or in low-lying positions, with no statistically significant differences between these groups. The primary pathogen identified was the Coagulase-negative Staphylococcus (CONS; n = 9), followed by Enterobacter cloacae (E. cloacae; n = 2), and Escherichia coli (E. coli; n = 1). Tragically, one patient died due to sepsis caused by E. cloacae. In all infants with proven CLABSI, the umbilical venous catheters were immediately removed without retrieving the catheter tips for culture. Regarding other complications, one patient

Table 1. Comparison of characteristics between four UVC positions

	Optimal[a] (n=54)	Low-lying[b] (n=52)	High[c] (n=30)	Malpositioned[d] (n=10)	Total (n=146)
Gestational age (wk) ‡	29.2 (3)	29.7 (3.1)	28.6 (2.6)	28.3 (3.2)	29.2 (3)
Birth weight (g)†	1080 (850-1555)	1200 (945-1720)	1115 (857-1420)	1060 (838-1683)	1110 (817-1482)
Gender male#	30 (55. 6)	29 (55.8)	15 (50)	3 (30)	77 (52.7)
Duration of UVC days†	10 (8-13)	6 (7-10)&a,c	9.5 (6-9)	8 (6-10)	8 (6-10)

N (%): Chi-square test;†Median (P25-P75): Mann-Whitney U test; ‡Mean (SD): t-test; IQR-Interquartile Range; SD-Standard deviation; UVC-Umbilical venous catheter; Bolded values are statistically significant; wk-week; &p<0,001

Table 2. Comparison of demographic and clinical characteristics depending on the presence of UVC-related complication

	With UVC-related complications	Without UVC-related complications	Total	P
N#	62 (42.5)	84 (57.5)	146 (100)	0.069
Gender male#	30 (48.4)	47 (56)	77 (52.7)	0.461
Birth weight (g)†	970 (815-1200)	1295 (1050-1705)	1110 (817-1482)	**<0.001**
Gestational age (wk)‡	28.2 (2.9)	29.9 (2.8)	29.2 (3)	**0.001**
Length of parenteral nutrition days†	10.5 (7-16)	10 (7-15)	10 (7-15)	0.163
Vasoactive support yes #	16 (25.8)	14 (16.7)	30 (20.5)	**<0.001**
Duration of UVC days†	7 (5-9)	9 (7-12)	8 (6-10)	**<0.001**

N (%): Chi-square test;†Median (P25-P75): Mann-Whitney U; ‡Mean (SD): t-test; IQR-Interquartile Range; SD-Standard deviation; UVC-Umbilical venous catheter; p: Significance; Bolded values are statistically significant;

Table 3. Comparison of UVC-related complications based on catheter tip position; and (%)

Complications	Optimal (N=54)	Low-lying (N=52)	High-lying (N=30)	Malposition (N=10)	Total (N=146)
Any complication resulted with an early catheter removal	17 (31.5)	31 (63.5)	7 (23.3)	7 (70)	62 (42.5)
CLABSI	6 (11.1)	6 (11.5)	-	-	12 (8.2)
Catheter blockage	1 (1.9)	5 (9.6)	5 (16.7)	6 (60)	17 (11.6)
Umbilical site leak	6 (11.1)	12 (23.1)	-	-	18 (12.3)
PVT	2 (3.7)	-	1 (3.3)	1 (10)	4 (2.7)
Pericardial effusion	-	-	1 (3.3)	-	1 (0.7)
Umbilical bleeding	2 (3.7)	1 (5.8)	-	-	3 (2.1)
Periumbilical erythema	-	3 (5.8)	-	-	3 (2.1)
NEC	-	4 (7.7)	-	-	4 (2.7)
Without complications	37 (68.5)	21 (40.4)	23 (76.7)	3 (30)	84 (57.5)

UVC-Umbilical venous catheter; NEC- necrotizing enterocolitis; PVT- portal vein thrombosis

developed pericardial effusion, three patients had periumbilical erythema and umbilical bleeding, and four neonates with low-lying UVCs developed clinical and radiological signs of stage II NEC, as defined by the corrected Bell's staging system. All four of these neonates were treated conservatively, had a GA of 29 weeks with a mean birth weight of 995 g (range 760 -1140 g), and the mean onset of NEC was 9.25 days (range 7 - 11) after UVC insertion. Three newborns were fed pasteurized donor breast milk, achieving an enteral volume intake of up to 120 ml/kg/day. Meanwhile, the smallest baby received minimal enteral nutrition at the time of NEC onset. Portal vein thrombosis occurred almost equally in patients with optimally positioned UVCs, high-lying, and malpositioned UVCs (n = 2; n = 1; n = 1 respectively). However, mechanical complications such as catheter site blockage and leakage, were more frequent in the low-lying UVC.

Discussion

While umbilical vein catheterization remains the preferred venous access in newborns treated in Neonatal Intensive Care Units (NICUs), malpositioned UVCs pose a significant risk, potentially leading to life-threatening complications. According to the literature, among all neonates undergoing umbilical vessel catheterization, UVC-related complications develop in 5% to 19% of cases due to mechanical causes, 5% to 26% due to infectious causes, and 2% to 26% due to thrombosis (20). Malposition and low-lying UVCs have been noted to be more frequently associated with complications (13–15).

We observed a high incidence of UVC-related complications (62 or 42.5%) in the study. CLABSI occurred in 8.2% of these cases, portal vein thrombosis (PVT) in 2.7%, pericardial effusion in 0.7%, and NEC in 2.7% of neonates. Fortunately, apart from the aforementioned, most of the complications were minor (periumbilical erythema, umbilical site leakage, bleeding, and catheter blockage).

The incidence of CLABSI varies between NICUs, ranging from 1.16 to 18.1 per 1,000 central line days (21–24). In our study, the umbilical CLABSI rate was 9.83 per 1,000 catheter days (8.2%), comparable to previously published studies. The Canadian Neonatal Network study in 2015 reported a CLABSI rate of 7.8 per 1,000 catheter days in contrast to the peripherally inserted central catheter (PICC) lines, which had a much lower incidence of catheter-related infections (25). Additionally, a recently published retrospective cohort study in the Netherlands revealed that the mean 9-year CLABSI incidence was 14.3 per 1,000 central-line days among preterm infants (GA < 32 weeks), with no significant difference between annual rates (26).

Although UVCs have been used for over 60 years, there is high heterogeneity in practices surrounding their insertion, assessment, and monitoring of tip position, securement, management, and dwell time across the NICUs (13, 14, 27).

Optimal UVC position and minimal use duration are crucial to avoid severe complications. Few studies have assessed UVC complications related to the catheter tip position. In 2014, a survey of the 72 neonatal units in the United Kingdom showed that 52% of units kept the UVCs for ≤ 7 days, 24% for 8 – 10 days, 21% for 14 days, and 3% of the units stated no upper limit. The authors found that most respondent units accepted low-lying UVCs for either routine use (44%) or limited use (48%). Of these units, 76% removed low-lying UVCs effectively within 7 days (with approximately two-thirds removed within three days) and 11% within 14 days. Only 3% of the units placed no maximum time limit for the removal of the low-lying UVCs (28). A

retrospective cohort study examining UVC position in 1638 infants with a GA < 32 weeks found that a low-lying position was associated with higher incidences of catheter-related systemic blood infections and extravasation, especially when UVC placement exceeded 7 days (14). Butler-O'Hara et al., in a 2012 study compared UVCs with dwell times ≤ 7 vs. > 7 days and found a higher rate of CLABSI in the latter group (1/1,000 catheter days in the ≤ 7 days group vs. 4/1,000 catheter days in the > 7 days group with a *P* value of 0.001)) (29). Similarly, Leveillee et al. reported a higher infection rate in low-lying UVCs compared to the high-lying UVCs group (17.31/1000 catheter days vs. 11.49/1000 catheter days) (30). In contrast, two recent studies found no significant difference in infection rates between optimal and low-lying UVCs (15, 16). Current recommendations suggest limiting UVC placement to 7 to 10 days to reduce the risk of infections and thrombotic complications (31).

In our study, the UVC-related complications were lowest in the high-lying positions (23.3%), followed by the optimal positions (31.5%), and low-lying UVCs (63.5%), with the highest incidence in malpositioned UVCs (70%).

Our unit strategy accepts low-lying UVC for routine use. The mean duration of their placement in this cohort study was 6 days (range 2 – 11 days). We concluded that the low-lying position was not associated with a higher incidence of CLABSI compared with the optimal position, nor with extravasations (no cases). However, we observed a statistically significant increase in the risk of CLABSI with longer UVC placement exceeding 7 days (83.3% of newborns with CLABSI; $\chi^2 = 5.333$; df = 1; P = 0.021).

In our study, all four patients with NEC had low-lying UVCs. These findings align with the prospective cohort study by Selemanji et al. which revealed a significant association between malpositioned and low-lying UVCs, and an increased incidence of NEC in preterm infants. UVC-induced ductus venous occlusion may play a potential role in the development of NEC in preterm infants, similar to UVC passing through an anomalous patent vitellointestinal duct in the case of intestinal perforation (4, 32). Goh et al. also showed two neonates with UVC-related gastrointestinal perforation who had UVC malposition and thrombosis, suggesting vascular compromise as a possible pathophysiological mechanism (33).

Hepatic complications due to umbilical vein catheterization are frequent and well-documented (9, 11, 34). Abdominal ultrasound is the gold standard for the diagnosing and monitoring of hepatic complications. The most common ultrasound findings are air in the portal vein system (20.1%), liver parenchyma lesions (7.4%), and thrombosis of the left portal vein (6.1%) (11). UVC-induced injury can be mechanical or chemical (use of parenteral nutrition, hypertonic solutions, or inotropes), leading to the damage of the vessel`s endothelium, leakage into the liver parenchyma, and the development of abscess, necrosis, and softening of the hepatic parenchyma. The first systematic review and meta-analysis of 16 studies from 1980 to 2020, showed that the use of UVCs is significantly associated with portal vein thrombosis in newborns with UVCs up to 3 months of postnatal age. Therefore, the use of UVCs requires a high index of suspicion for hepatic complications, and prospective studies are needed to evaluate the optimal prevention strategies of UVC-induced vascular thrombosis (5).

In our cohort, we identified four cases of portal vein thrombosis, distributed almost equally in patients with optimal-lying UVC (n=2), high-lying (n=1), and malpositioned UVC (n = 1). Due to its retrospective nature, a follow-up ultrasound assessment was not performed in all newborns.

Complications associated with high-lying UVCs are frequently reported, and they include arrhythmias, pleural and pericardial effusion, and tamponade. In our study, one case of pericardial effusion was observed in a 1030 g (10^{th} percentile) male baby with a GA of 30 weeks who underwent umbilical vein catheterization with a 4 French UVC at the 5^{th} hour of life. The initial high-lying position of the UVC tip on TAR was followed by subsequent readjustment. On the 7^{th} day of life, due to repeated episodes of bradycardia, echocardiography was performed and it revealed a pericardial effusion with a catheter tip located in the right atrium. As post-readjustment TAR has not been performed, several potential explanations exist, including inadequate position evaluation, inadequate repositioning, or migration.

Over the past few years, ultrasonography (US) has been suggested as the gold standard for initial placement and ongoing monitoring of the catheter tip position. Compared to anteroposterior chest radiography, the US provides a clearer view of the vein and the catheter. Notably, two large studies confirmed the higher accuracy of intraprocedural US compared to postprocedural radiographic confirmation. with up to 25% of UVCs requiring readjustment after US evaluation, despite

radiographic confirmation as correct (35, 36). A prospective cohort study by Akar et al. indicates that radiography is not a sufficiently reliable method for determining the UVC position (guided by the Shukla formula [(3 x PTM in kg + 9) / 2]), as evidenced by the discrepancies discovered after echocardiographic evaluations. During the evaluation, 80% of the cases were found to be adequately positioned. All the cases (100%) that were classified as high-lying, and 33% of cases that were defined as low-lying, were actually found to be intracardiac after the evaluation.37 The two most widely used methods, the Shukla-Ferrara formula and Dunn shoulder-umbilicus length method have not been validated in extremely preterm and very low birth weight neonates (38). Furthermore, even with an ideal UVC position, the tip migration can occur in 50% to 90% of the cases (35, 39–41). This is commonly attributed to the drying of the Wharton jelly and the secondary shortening of the umbilical cord remnant. The risk of tip migration strongly advocates for adopting ultrasound-based catheter tip location verification. Apart from it being a more precise evaluation method, it can be conveniently performed at the bedside and safely repeated, even daily (42).

The primary limitation of our study is its retrospective nature, which may influence the strength of the results. Nevertheless, we assume the findings provide valuable insight into the most frequent complications following umbilical vein catheterization in preterm neonates.

Conclusion

Despite the longstanding use of UVC, significant heterogeneity in practices remains across neonatal units. To the best of our knowledge, this study represents the first such review of UVC use and its complications in Serbia. While our study revealed a higher rate of UVC-related complications than what is reported in existing literature, fortunately, most were of lesser severity. We conclude that the most effective strategy to minimize UVC-related complications is to place and maintain the UVC in an optimal position for the shortest duration possible. In this context, we advocate for the use of real-time ultrasound both for initial guidance and for the ongoing monitoring of the UVC tip location in preterm neonates. Furthermore, we suggest a maximum retention period of eight days for UVC, except in specific circumstances. Given the potential for life-threatening complications, any clinical deterioration in preterm neonates with an inserted UVC should prompt an immediate heightened level of clinical suspicion.

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None.

Conflicts of interest

The authors declare there is no conflict of interest.

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