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# Risk of catheter-associated bloodstream infection by catheter type in a neonatal intensive care unit: a large cohort study of more than 1100 intravascular catheters

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SUMMARY

***Background:*** The aim of this study was to evaluate the risk of catheter-associated bloodstream infection (CABSI) among different catheter types using a large prospective database in the neonatal intensive care unit (NICU) of a tertiary care centre in Switzerland.

***Methods:*** We included all neonates admitted to the NICU with at least one central intravascular catheter inserted between January 2017 and December 2020. We used marginal Cox model to determine the risk of CABSI among different catheter types.

***Results:*** A total of 574 neonates and 1103 intravascular catheters were included in the study: 581 venous umbilical catheters, 198 arterial umbilical catheters and 324 peripherally inserted central catheters (PICCs). We identified 17, four and four CABSIs in neonates with venous umbilical catheters, arterial umbilical catheters and PICCs, respectively. The risk of CABSI increased after two days of umbilical catheter maintenance. Using univariable Cox models, and adjusting for sex and gestational age, we observed a similar CABSI risk between venous and arterial umbilical catheters (HR 0.57; 95% CI 0.16e2.08). Birth weight was associated with CABSI, with higher weight being protective (HR 0.37, 95% CI 0.16e0.81).

***Conclusions:*** Strategies aimed at reducing umbilical catheter dwell time, particularly in low and very low birth weight neonates, may be effective in decreasing the incidence of CABSI in this population.



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## Background

Neonates in the neonatal intensive care unit (NICU) are at high risk of developing healthcare-associated infections (HAIs). Immature immune system, fragile skin, frequent exposure to invasive procedures and medical devices, and a level of care requiring multiple contacts with healthcare workers [1] make them particularly vulnerable to HAIs, especially catheter-associated bloodstream infections (CABSIs), the leading cause of HAI in NICUs [2–4]. Up to 25% of very low-birth-weight preterm infants will develop at least one bloodstream infection (BSI) during their NICU stay [5,6]. CABSIs cause significant morbidity and mortality and are responsible for long-term neurodevelopmental sequelae [5,7,8].

Umbilical catheters are the universal early vascular access for neonates, inserted immediately at birth as they provide fast and painless vascular access in the neonatal setting due to the unobstructed umbilical vessels from the foetal circulation. Venous umbilical catheters are commonly used in the first days of life for intravenous administration of fluids, nutrition, and medications, and are usually replaced in the first week after birth with a peripherally inserted central catheter (PICC) for parenteral nutrition and medications. Despite its widespread use, data are lacking to estimate the risk associated with umbilical catheters and guide optimal management of vascular access in this high-risk population.

The aims of this study were (1) to describe CABSI by catheter type (venous and arterial umbilical catheters and PICCs) over a four-year period in a large NICU in Switzerland and (2) to investigate the risk factors for CABSI with umbilical catheters, focusing on dwell time.

## Methods

### *Study setting and design*

We conducted a prospective cohort study from 1st January 2017 to 31st December 2020, at the NICU of Geneva University Hospitals (Geneva, Switzerland), a 2100-bed university-affiliated tertiary care hospital. The NICU has 15 intensive care beds and 7 intermediate care beds. In 2001, a continuous prospective surveillance of neonatal BSI was established in our institution for neonates. All neonates admitted to the NICU with at least one central vascular catheter insertion were included in the surveillance. We used the European Centre for Diseases Prevention and Control (ECDC) criteria for CABSI definitions [9].

### *Definitions*

Each BSI episode was prospectively investigated by the infection control nurse and/or the infection control physician through manual chart review and discussion with the NICU team when necessary. BSI and CABSI were defined according to the ECDC specific entities for laboratory-confirmed neonatal BSI (NEO-LCBI) and laboratory-confirmed neonatal BSI with coagulase-negative staphylococci (NEO-CNSB). NEO-LCBI requires the following two conditions: (1) clinical criteria, and (2) a recognized pathogen other than a coagulase-negative staphylococci (CNS) cultured from blood. NEO-CNSB requires the following three conditions: (1) clinical criteria, (2) the presence of CNS cultured from blood or from the catheter tip, and (3) criteria for inflammatory blood biomarkers. CABSI was defined according to the ECDC CRI-3-CVC definition: a NEO-LCBI or a NEO-CNSB occurring 48 h before or after catheter removal (if any) and a quantitative central venous catheter (CVC) culture $\geq$1000 cfu/mL with the same micro-organism. A new BSI episode was considered if the same micro-organism was isolated from a blood culture >10 days after the first positive blood culture.

Catheter insertion and removal dates were prospectively recorded in the electronic health record by the neonatal nurses caring for the neonates. Catheter-days were defined as the total number of days of exposure to each central line by a neonate (e.g., if a patient had two central lines on a single day, two central-line days are counted). We included the following types of central lines: venous and arterial umbilical catheters and PICCs. Tunnelled catheters (e.g., Broviac), fully implanted catheters and other central venous catheters (femoral, internal jugular, subclavian) were excluded. Because PICCs were rarely cultured, we focused most of our analyses on umbilical catheters.

### *Variables routinely collected*

From the NICU electronic database, we automatically extracted the following variables: demographic characteristics (gender, date of birth, birth weight and prematurity), catheter type and catheter-days. From the infection control program surveillance database, we extracted the following variables: characteristics of the BSI episode (date of infection onset, type of catheter, type of CABSI according to the ECDC criteria) and microbiological data (micro-organisms isolated from the blood culture and from the catheter tip culture). The two databases were merged by unique neonatal identifier and by date.

### *Statistical analysis*

First, we described CABSI according to the catheter types (venous umbilical catheter, arterial umbilical catheter and PICC) during the catheter maintenance. Continuous variables were summarized as means and medians and were compared using the Student's *t*-test or the Wilcoxon rank sum test, as appropriate. Second, we graphically described the daily risk of CABSI in umbilical catheters using the hazard rate function from right-censored data using kernel-based methods. Third, we investigated the risk factors for CABSI in umbilical catheters using an univariable marginal Cox model for clustered data (PROC PHREG of SAS), to account for a possible clustering effect of multiple catheters per neonate. This model accounts for the censored nature of the data and possible intra-cluster dependence using a robust sandwich covariate estimation. A hazard risk (HR) greater than one indicates an increased risk of CABSI. Fourth, we tested the association between catheter type (venous vs umbilical catheter) in a multivariable marginal Cox model adjusting for possible confounders (sex and birth weight). Fifth, we examined the association between selected risk factors and CABSI using similar models. The proportionality of hazard risks for catheter type was tested using Martingale residuals. Tests were two-tailed, with $P<0.05$ being considered significant. Analyses were performed with SAS (version 9.4; SAS Institute, Cary, NC, USA) and R (version 4.0.3).

### Ethics

This prospective surveillance was conducted as part of the routine quality improvement activities of our infection control programme, and therefore institutional review board approval was not required for the current analysis.

## Results

Of the 575 neonates included, 323 (56.3%) were low birth weight (<2500 g) and 55 (9.6%) were extremely low birth weight (<1000 g). In total, 388 neonates (67.6%) were born preterm, of which 101 (17.6%) were extremely preterm, 170 (29.6%) were very preterm and 117 (20.4%) were moderate to late preterm. A total of 264 were female (46%). A total of 1159 CVC were inserted in neonates from 1st January 2017 to 31st December 2020. Of these, 24 tunnelled catheter (Broviac) and 32 other CVC were excluded. A total of 1103 catheters (581 venous umbilical catheters, 198 arterial umbilical catheters, and 324 PICCs) were included in the analysis. The median dwell-time was two (interquartile range (IQR): 0; 4), three (IQR: 2; 5) and six days (IQR: 4; 13) for venous umbilical catheter, arterial umbilical catheter and PICCs, respectively.

We identified 17, four and four CABSIs for venous umbilical catheters, arterial umbilical catheters and PICCs, respectively. For umbilical catheters (venous and arterial) CABSI were mostly observed after two days of catheter maintenance (Figure 1). Among umbilical catheters ($N = 779$), the instantaneous hazard of CABSI among umbilical catheters was low in the first two days of catheter maintenance and, thereafter, increased rapidly (Supplementary Figure S1). Using univariable marginal Cox models, we observed a similar risk of CABSI between venous and arterial umbilical catheters (HR 1.09, 95% CI: 0.38–3.08, Table I). Moreover, birth term category and birth weight were associated with CABSI risk. After adjustment for sex and birth weight, we still observed a similar risk of CABSI comparing venous with umbilical catheters in multivariable

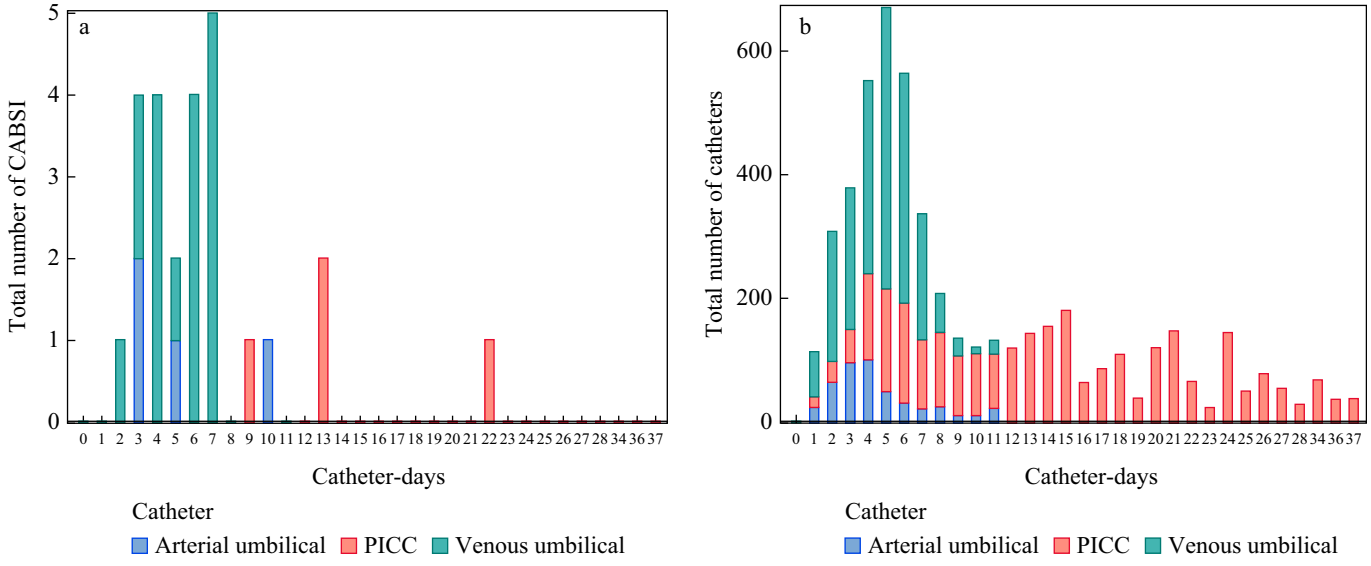


**Figure 1.** Number of catheter-associated bloodstream infections (CABSIs) during catheter maintenance, stratified by catheter-type (a) and number of catheters by catheter-days (b). PICC, peripherally inserted central catheter.

**Table I**
Univariable marginal Cox models – risk for catheter-associated bloodstream infection (CABSI) among arterial and venous umbilical catheters

| | Without CABSI | CABSI | HR | 95% CI | *P* |
|---|---|---|---|---|---|
| **Type of catheter** | | | | | |
| Arterial umbilical catheter, *N* (%) | 194 (25.6) | 4 (19) | 1.087 | (0.38–3.08) | 0.87 |
| Venous umbilical catheter, *N* (%) | 564 (74.4) | 17 (81) | | | |
| **Category of term** | | | | | |
| Term, *N* (%) | 219 (28.9) | 0 (0) | 0.000 | (0–0) | <0.01 |
| Moderate to late preterm, *N* (%) | 127 (16.8) | 1 (4.8) | 0.223 | (0.03–1.9) | |
| Very preterm, *N* (%) | 210 (27.7) | 13 (61.9) | 1.507 | (0.61–3.74) | |
| Extremely preterm, *N* (%) | 202 (26.6) | 7 (33.3) | | | |
| **Gender**, female, *N* (%) | 346 (45.6) | 10 (47.6) | 0.970 | (0.42–2.22) | 0.94 |
| **Birth** weight, median (IQR) | 1.5 (0.9; 2.9) | 0.9 (0.7; 1.2) | 0.369 | (0.17–0.82) | 0.01 |

CI, confidence interval; HR, hazard risk; IQR, interquartile range.

Cox marginal modelling (HR 0.56, 95% CI 0.16—1.91, supplementary Table S1). Using a multivariable Cox model without forcing catheter type, we observed that neonates with higher birth weight had a decreased risk of umbilical CABSI (HR 0.37, 95% CI 0.16—0.82, Supplementary Table S2). Coagulase-negative staphylococci were the most frequently identified micro-organisms in umbilical CABSI (Supplementary Table S3).

## Discussion

Using a large prospective database including more than 1000 catheters in an NICU, our study provides three main findings. First, the risk of CABSI increased from the third day of maintenance for both venous and arterial umbilical catheters. Second, we observed no difference in the risk of CABSI between arterial and venous umbilical catheters. Finally, neonates with the lowest birth weight had the highest risk of umbilical catheter-related BSI.

Of all catheter types in newborns, umbilical catheters had the highest infection rate. However, there is still a lack of strong evidence on appropriate management [4]. Updated CDC guidelines recommend removal of venous and arterial umbilical catheters in NICU patients as soon as possible and when no longer needed, but this recommendation has a very low level of confidence due to imprecision [10,11]. Previous studies have reported conflicting results regarding the risk of CABSI and the optimal duration of umbilical catheters [12]. Only one previous randomized trial, published in 2006, has been conducted and found no difference in infections between long-term use of venous umbilical catheters (up to 28 days) and systematic removal and replacement by PICC at day 7—10. However, both groups had relatively high CABSI incidence densities and the number of catheters included (<110 in both groups) may have been too small to detect a difference in infection rate. Conversely, a large observational study reported a higher adjusted intravascular catheter infection risk after controlling for dwell time, suggesting early replacement by day 4 [13]. Similarly, a retrospective cohort study found an increased infection rate with prolonged umbilical catheter dwell-time [4]. Few studies have shown that the use of a care bundle can prevent CABSI in the neonatal setting [14,15]. In a prospective interventional study, the use of a bundle resulted in a shorter duration of catheterization and a reduction in venous umbilical catheter-associated BSI [14]. From our high-quality, prospective database, we have shown that most umbilical catheter-associated BSIs were observed after the second day of catheter maintenance leading to the recommendation to systematically remove umbilical catheters at day 3.

There is little published data on the risk of infection associated with arterial umbilical catheters. Arterial umbilical catheters are often removed earlier than venous umbilical catheters because there is less need to maintain an arterial access and because of the risk of non-infectious complications such as thrombo-embolic event. CDC guidelines recommend removal of arterial umbilical catheters at or before seven days of dwell time in NICU patients, but with very limited evidence to support this recommendation. In light of our findings, we recommend that any intervention focused on umbilical catheters should encompass both arterial and venous catheters. As shown in previous studies and observed in our study, a higher risk of infection is observed in neonates with low or very low birth weight [1,4,6] and infection prevention intervention should therefore target this specific population as a priority.

The strengths of our study include its large sample size and the prospective collection of standardized outcomes within our surveillance system. This study has some limitations. First, we used the ECDC criteria which could potentially lead to an underestimation of the CABSI incidence in the neonatal population, as recently pointed out by some experts [16]. In this context and since ECDC definitions may underestimate the number of CABSI in PICCs, we focused on umbilical catheters only. Second, the number of CABSIs in each catheter group was relatively small, which limits the interpretation of the results from multivariable models. Finally, several process indicators at catheter insertion and during maintenance (e.g., antiseptic procedure for insertion, number of manipulations of the catheter after insertion) that could influence the infection risk were not routinely extracted.

In conclusion, our study supports the elective removal of venous and arterial umbilical catheters prior to day 4, particularly among low-birth-weight neonates. Our study highlights the urgent need for a randomized trial comparing different catheter management strategies in this population such as systematic early venous umbilical catheter removal and replacement by PICC versus later individualized venous umbilical catheter removal.

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**Conflict of interest statement**
All authors have no conflict of interest to declare.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2023.06.011.

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