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Beatriz Nicolau Soares Complicações de Catéteres Centrais em Recém-Nascidos internados numa UCIN de Nível III/ Complications of Central Lines in Neonates admitted to a Level III NICU

março, 2017





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Trabalho efetuado sob a Orientação de: Doutora Susana Maria Saraiva Pissarra da Silva

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Neonatologia

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Complications of Central Lines in Neonates admitted to a Level III NICU

ORIENTADOR

Susana Maria Saraiva Pissarra da Silva

COORIENTADOR (se aplicável)

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, N° MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	X
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	

Faculdade de Medicina da Universidade do Porto, <u>28 / 03 / 2017</u>

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Abstract

Objective: To investigate the incidence and risk factors for central line related complications in neonates.

Methods: A retrospective cohort study of infants who underwent central line (CL) placement, from 1 July 2014 to 31 June 2016, was conducted in Neonatal Intensive Care Unit of Centro Hospitalar de São João. Infants hospitalized more than two days and CLs placed for more than 24 hours were included. Patients' demographic characteristics, hospital data and information on CLs were collected. Indwelling complications were compared between infant groups and types of CL inserted. Results: A total of 400 CLs were inserted in 240 infants with a CL utilization ratio of 0.64. Overall CL complication rate was 29.6 per 1000 catheter days. Of all complications, central line-associated bloodstream infection had the highest incidence (12.4 per 1000 catheter days). Infiltration was the most reported mechanical complication. Non-umbilical catheters showed a significantly higher incidence of complications than umbilical ones. Low gestational age, low birth weight, prolonged catheter stay, long duration of total parenteral nutrition, and peripherally inserted central catheter placement were associated with a higher risk of indwelling complication. Conclusions: The implementation of measures to prevent catheter-related complications must be a priority in care of vulnerable neonates.

Keywords: Central line; Catheter related complication; Neonatal Intensive Care Unit.

Introduction

Central lines (CLs) are life-saving devices routinely used in Neonatal Intensive Care Units (NICUs), mainly in preterm neonates and neonates who have cardiorespiratory and gastrointestinal conditions that require surgical intervention [1-4]. They provide stable intravascular access for fluid, medication and parenteral nutrition administration, allowing the safe delivery of large volumes and hyperosmolar solutions [4-7].

There are several types of CLs. Umbilical Venous Catheters (UVC) and Umbilical Arterial Catheters (UAC), frequently the first choice in neonates, provide easy and fast access in the first days of life [2,8]. If continuous intravenous therapy or total parenteral nutrition

(TPN) are still needed, umbilical catheters shall be replaced by Peripherally Inserted Central Catheters (PICC) [3,9]. PICCs are inserted into a peripheral vein and are threaded until a central location using *Seldinger technique* [10,11]. Its length of stay should not exceed 2-4 weeks [11]. Alternatively, tunneled venous catheters, either Short Duration Venous Catheters (SDVCs) or Broviacs, implanted by venous dissection, require a surgical procedure for placement which allows a long permanence [2,3]. Broviac has a specific handling and removal protocol, justifying lower infection and migration/dislodgement risks [3,11].

Repeated peripheral intravenous insertions are inadvisable in the NICU population due to the progressively increasing difficulty accessing small and friable veins, especially in extremely preterm infants [5,7]. CL use allows avoidance of pain and handling underlying those procedures.

Despite its importance, central access is associated with significant morbidity and mortality [3,10]. Compared with adults, CLs used in children are narrower, predisposing to the development of complications such as obstruction and thrombosis. Mechanical complications are frequently related to insertion technique. The main non-mechanical complication is central line-associated bloodstream infection (CLABSI) [12]. After catheter insertion, a radiograph should be routinely obtained to verify the catheter tip position (CTP) and evaluate the need for repositioning or removing [5,7,13]. Often, suboptimal non-central CTP, with consequent shorter length of catheter stay and non-elective catheter removal, is associated with a higher incidence of complications [5,13].

The objective of this study was to access CL related complications in neonates in a level III NICU and to identify risk factors for the development of these complications. In addition, we also sought to test the hypothesis that longer duration of indwelling is associated with higher rate of complications.

Material and Methods

A register-based retrospective cohort of infants admitted to NICU of Centro Hospitalar de São João (CHSJ), Porto (Portugal), who had CLs placed between 1 July 2014 and 31 June 2016, was performed. This 17-bed NICU admits approximately 400 patients per year, including inborn and outborn neonates and infants, either preterm or with conditions that need early surgical intervention or close monitoring and care.

Neonates staying in NICU for less than three days or those with CLs inserted and removed in the same day were excluded from analysis.

Clinical data on patients' demographic characteristics (gender, gestational age (GA) at birth, birth weight (BW), birth place, delivery type and 1-minute and 5-minute Apgar score) were collected.

Gestational age (completed weeks) was determined by the time elapsed between the first day of the last normal menstrual period and the day of delivery, by ultrasound examination [14] or by the New Ballard Score [15]. According to the World Health Organization, patients were classified as extremely (GA <28 weeks), very (28 to <32 weeks) or moderate-to-late preterm (32 to <37 weeks) and term (\geq 37 weeks) and as low BW (LBW; <2500g) and very low BW (VLBW; <1500g).

Hospital data (age and diagnosis at admission, length of hospital stay and the postadmission outcome), number and type of catheters inserted, administration of TPN, anatomical site of line placement (umbilical vessel, external jugular vein, internal jugular vein, lower limb or upper limb vein, or epicranial vein), radiologic CTP, length of catheter stay, removal reason and complications, if any, were also extracted and analyzed.

Central venous catheters (UVC, PICC, Broviac and SDVC) were defined as central if the tip was located at superior vena cava (SVC), inferior vena cava (IVC) or at SVC/IVCright atrium junction and non-central if located elsewhere. For UAC, *high placement* and *low* *placement* were considered if CTP was above the diaphragm (at the level of T6-T9) and at the level L3-L4, respectively. We considered the radiograph obtained after the last repositioning for CTP evaluation.

Length of catheter stay was defined as the number of days the line stayed in the patient. CL utilization ratio was calculated by dividing the number of catheter-days by the number of patient-days. Types of complications were divided into three categories: mechanical, infectious and thromboembolic. Mechanical complications included occlusion, breakage, external leaking, infiltration, vasospasm, bleeding, phlebitis, exteriorization, pneumothorax, pericardial and pleural effusion and cardiac tamponade, whereas infectious complications included CLABSI. Catheter-related thromboembolism refers to catheter occlusion due to the presence of a thrombus and was confirmed by echocardiography or ultrasonography.

Occlusion referred to inability to infuse through a line or inability to flush it. External leaking was considered when there was a collection of intravenous fluid under the catheter dressing. Infiltration was defined as fluid extravasation into soft tissues and diagnosed by the inability to infuse fluid associated with swelling in the region of the catheter tip. Phlebitis was defined as inflammation tracking along the path of a non-occluded venous catheter expressed as tenderness, erythema and/or induration at the surrounding area of the insertion site. Exteriorization was defined as the migration of the catheter until its tip surfaces. Pleural or pericardial effusion was defined as the escape of fluid from blood vessels and its collection, respectively, in pleural or pericardial space; the latter may lead to cardiac tamponade, a lethal complication (mortality rate of 30-50%) with a reported prevalence of 1-3% [16].

We defined CLABSI according to Centers for Disease Control and Preventions' (CDC) National Healthcare Safety Network criteria, used for surveillance purposes, as a primary bloodstream infection in a patient with a CL at the time or within 48-hour period before the onset of sepsis clinical signs, without another identifiable infection source [17,18] and with a positive blood culture, collected when possible from CL. Line days to infection was defined as the number of days from line placement to onset of sepsis signs.

A death was considered CL-related in cases whose autopsy report referred to it.

CL was removed due to elective (end of therapy, discharge or death) or non-elective reasons. Catheter removal because of CLABSI is only required if clinical deterioration after starting antibiotherapy or persisting or relapsing bacteremia [19]. In this case, CL removal is followed by tip culture.

This study was approved by CHSJ Ethics Committee.

Data analysis was performed using SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY) and statistical software package R, version 3.3.2.

Continuous variables were reported as median (percentile 5-percentile 95); categorical variables were reported as absolute or relative frequencies.

The infants were compared per indwelling complication. CLs were compared per CL type.

For comparison of distributions between groups, Mann-Whitney and Kruskal Wallis tests were used for continuous variables. Pearson Chi-Square was used for all other variables, reporting the 95% confidence interval (CI95%). Risk ratio was also calculated for some categorical variables, with respective CI95%. P-values <0.05 were considered statistically significant.

Results

Characteristics of Study Population and Risk Factors for CL-related complications

During the study period, of 763 admitted to CHSJ-NICU, 251 infants had a CL inserted, 240 of which met the eligibility criteria -128 (53.3%) male and 112 (46.7%) female. Mean patient age at admission was 3.1 days (range 1 to 52 days).

Patients' demographic and CL related profile in complicated and uncomplicated indwelling groups are shown in Table 1. There was no statistically significant difference in gender (p=0.252), delivery type (p=0.058) and 1-minute (p=0.266) or 5-minute (p=0.067) Apgar score between groups. Median age at admission revealed no significant difference between groups (Mann-Whitney U, p=0.186). Risk ratio of indwelling complication for inborn compared to outborn infants was 1.828 (IC95%=[1.220;2.741]). A partial correlation was run to evaluate relationship between indwelling complication and birth place, controlling for GA, BW, and diagnosis at admission. Birth place lost significant correlation to indwelling complication after removing confounding variables effects.

The mortality rate of analyzed population was 10.4%, with no differences between infants with or without indwelling complication (p=0.076). Of deceased infants, 14 had an indwelling complication and 21.4% of deaths were CL-related.

PICC showed a significant relation with indwelling complication. Risk ratio of CL-related complications for infants with a PICC compared to those without it was 1.878 (IC95%=[1.272;2.774]).

A forward stepwise Wald logistic regression was performed to ascertain the effects of gender, GA, BW, 5-minute Apgar score, birth place, length of catheter stay, total number and catheter type, and duration of TPN on the likelihood of having an indwelling complication. The model was statistically significant, $\chi^2(3) = 58.253$, p<0.001, explaining 29.5% (Nagelkerke R2) of the variance in indwelling complication and correctly classified 73.8% of cases. The presence of Broviac, SDVC and PICC was associated with an increased likelihood of CL-related complication (Exp(B)=5.62, 3.13, and 6.16, respectively).

CL outcomes

A total of 400 CLs were inserted (4160 catheter days) with a CL utilization ratio of 0.64. An average of 1.67 CL per patient was recorded. The most common anatomical site for line insertion was upper limb (177 (67.8%) out of the 261 non-umbilical CL).

Overall CL complication rate was 29.6/1000 catheter days. As a whole, mechanical complications had the highest incidence, although CLABSI was the most common complication.

Major mechanical complications occurred in 4 CLs with 2 pleural effusions (1 PICC and 1 SDVC), 1 pericardial effusion (with a UVC placed) and 1 non-lethal cardiac tamponade (1 SDVC). All CLs that developed these complications presented a non-central CTP on radiograph.

Other mechanical complications comprised 11 (2.8%) external leaking, 9 (2.3%) occlusions, 8 (2.0%) exteriorizations, 4 (1.0%) breakages, 3 (0.8%) phlebitis and 2 (0.5%) vasospasms (with UAC inserted). There was no reference to thromboembolic complications.

Infectious complications occurred in 48 (20.0%) patients (CLABSI rate of 12.4/1000 catheter days). There were 51 (12.8%) CLABSI episodes with a positive blood culture obtained in 35 (68.6% of infected CLs). The most common organism isolated was *Staphylococcus epidermidis* (65.7%, n=23) followed by *Staphylococcus aureus*, *Staphylococcus haemolyticus* and *Candida parapsilosis* (5.7%, n=2 for each).

CLABSI episodes were significantly associated with higher length of catheter stay (median of days to infection of 14 (2-94) vs 5 (2-30) for CLABSI versus non-CLABSI group) and with TPN (median length of days to infection, of only catheters with TPN, of 14 (2-82) vs 5 (1-26)); Mann-Whitney U, p<0.001 for both comparisons.

In most cases the removal of CL was elective (n=263, 73.3%). 41 neonates were transferred with a CL in place.

Comparative analysis of CL types

45 (81.8%) UACs revealed a *high placement*, 5 (9.1%) a *low placement* and the remaining other CTP (1 (1.8%) at T4 and 4 (7.3%) at T11 level). The relation between indwelling complication and CTP of UAC was not significant (p=0.604).

The comparative analysis of CL types is in Table 2. The relation between CTP and CL type was significant for venous catheters, but only Broviac revealed statistically significant difference from other CL types (p=0.003). Risk ratio of a Broviac being inserted in a non-central position was 0.303 compared to other CL types (IC95%=[0.106;0.869]).

The incidence of complications differed significantly between umbilical and nonumbilical catheters (p<0.001), with a risk ratio of 2.743 (IC95%=[1.780;4.227]) for nonumbilical catheters compared to other ones.

As for individual complication types, there was no statistically significant difference between CL types (p=0.816). However, PICCs and Broviacs significantly differed from other CL types (p=0.003), but not from each other, concerning the occurrence of infiltration. Additionally, the comparison of CLs with mechanical complication and all others, per CL type, shows significant differences (p=0.001), due to the differences between umbilical and non-umbilical types (mainly Broviacs and PICCs); the risk of a non-umbilical CL having a mechanical complication was 2.953 compared to umbilical CL (IC95%=[1.608;5.425]).

Ascending order of length of catheter stay was: UAC=UVC<SDV=PICC<Broviac. Broviac had significantly higher length of catheter stay for non-elective removal than umbilical catheters and PICC, and a tendency for higher than SDVC was found (Mann-Whitney U, p<0.001 and p=0.053, respectively).

There was significant relation between administration of TPN and indwelling complication (p<0.001). Risk ratio of CL-related complications for infants receiving TPN compared to those without TPN was 2.748 (IC95%=[1.552;4.864]). No significant difference was found between administration of TPN and CLABSI (p=0.032).

Discussion

Studies involving several types of CL and assessing their complications in NICUs are uncommon. This is understandable due to differences regarding postnatal age at the time of insertion and vascular access itself, which hampers adequate CL comparison. Nevertheless, assessment of overall incidence of CL-related complications and comparison of different CL types can be quite informative, aiding neonatologists in cost-effective decisions and improving care of vulnerable neonates by development of measures to reduce CL complications, mortality rate and health care costs.

As expected, both GA and BW were associated with CL-related complication with extremely preterm and VLBW infants more vulnerable to it. Prematurity was a risk factor for indwelling complication. Contrarily, admission due to hypoxic-ischemic encephalopathy revealed to be a protective factor for indwelling complication. This might be explained by differences in CL type and length of catheter stay between the two groups. We found higher length of catheter stay to be associated with higher complication incidence [Table 1] and non-umbilical catheters showed higher length of catheter stay and complication rate [Table 2]. As Arnts IJ et al. [9] reported in their comparative study of UVCs and PICCs, a prolonged PICC stay is associated with higher incidence of complications. Comparison of these two diagnostic groups showed that the prematurity group had higher length of catheter stay (14 (2–109) vs 10

(4–28), Mann-Whitney U, p=0.002). Additionally, preterm patients had significantly more non-umbilical catheters, mainly PICCs (89.6% vs 16.1%, p<0.001). Infants with hypoxic-ischemic encephalopathy also had lower length of hospital stay (8 (3–28) vs 27 (3–115), Mann-Whitney U, p<0.001), which justifies less need for non-umbilical catheters.

As stated before, inborn infants had higher risk of indwelling complication than outborns. We found that the inborn group had a higher proportion of infants with low GA, low BW, prematurity and PICC (78.5% vs 31.7%, p<0.001); hypoxic-ischemic encephalopathy and congenital malformation admissions and UVC insertion (45.1% vs 29.7%, p=0.018) were more common in outborns. However, there was no influence of birth place on the complication incidence when adjusted for GA, BW, admission diagnosis and CL type. This suggests that other factors are involved.

As umbilical catheters had a lower length of catheter stay, we performed a partial correlation to evaluate the association between UVC and PICC types and indwelling complication, controlling for length of catheter stay. It revealed that PICC remains positively and UVC negatively correlated with indwelling complication. Probably other factors related to insertion technique, insertion site, sequential use of PICCs after UVC removal, CL manipulation and antibiotic exposure during line use are involved and should be included in future analysis. In our study, most PICCs were inserted at upper limb (95.6%). However, the small sample size precluded the association analysis between insertion site and complication incidence for PICCs. In the literature, upper limb as PICC's insertion site was associated with a non-central CTP [5,20], probably due to considerable CTP changes with arm movements [10,11] and to higher rate of non-infectious complications of CL inserted [21].

Broviac was the CL type more often located at a central position, probably because its anatomical insertion site allows a straighter course to SVC. Moreover, it had the longest duration of TPN and the highest length of catheter stay associated with non-elective removal. Most studies describe CLABSI as the most common complication of CLs, with multicenter studies [3,22], reporting the lowest CLABSI rates. Our CLABSI rate of 12.4/1000 catheter days was the same as that reported in a comparative study involving umbilical and central venous catheters [9], when a CLABSI definition based on clinical signs was considered. A study analyzing a total of 369 CLs of the same type we studied, described a similar CLABSI rate (18.1 infections/1000 catheter-days), based on adjusted CDC criteria before 2008 [18]. However, unlike that study, we reported that non-umbilical catheters had a 2.485 (IC95%=[1.247;4.955]) higher infection rate than umbilical ones, similarly to De Brito et al. [23]. This may be explained by the high prevalence of antibiotic use given the possibility of maternal infection, during the first days of life, when UVC is inserted [9]. CLABSI rate was also related to prolonged catheter stay. Despite best efforts, CLABSI rate in our study period was higher than that described previously in our NICU (10.4/1000 catheter days) [24]. Similarly to our study, no differences in CLABSI rate among CL types were reported by some authors [8,25] while others reported higher risks (6-23/1000 catheter-days) with the use of PICCs [23,26].

Coagulase-negative Staphylococcus (CoNS) was the main isolated causative agent (71.4%), as stated in the literature [5,9,18,23]. CLABSI incidence was independent of CTP, as described by Jain A et al. [5]. We found duration of TPN to be significantly associated with CLABSI rate unlike other studies [18].

We used a CLABSI definition based only in sepsis clinical signs which, in practice, are frequently enough to start antibiotherapy. Probably, the consequence was an overestimation of CLABSI rate. However, a definition based on laboratory criteria may not be appropriate since the blood volume for blood culture usually obtained in infants is frequently insufficient for sensitive detection of bacteremia [10].

There are some limitations to our study. First, its retrospective character precluding collection and control for all factors that might have contributed to the CL-related complications. Second, catheter tip cultures upon removal were not routinely performed, which may have resulted in an overestimated CLABSI rate. Thus, further studies of infection rate effectively related to the CL are required. Third, as we considered the radiograph obtained after the last repositioning for CTP evaluation we were unable to account for potential migration of catheters before the development of complications. Fourth, CLs analyzed are inserted by different health care professional groups, which change regularly and whose different skills may influence the complication incidence. Finally, this is a single center study with a relatively small sample size.

Conclusion

This study adds new perspectives for clinical practice because of the limited number of studies comparing several types of CLs. The knowledge of the incidence of CL-related complications is important in the care of vulnerable infants. We believe the evidence generated by this study may help clinicians to perform a more informed risk-benefit analysis.

Despite the measures implemented to prevent nosocomial sepsis, the incidence of CLABSI is still high. The prevention of catheter-related complications by accurate evaluation of the CTP, routine monitoring, and compliance with bundles for CL insertion, maintenance and CLABSI prevention must be important goals in the daily care of infants in NICUs.

Declaration of interest

The authors declare no conflict of interest.

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	Complicated indwelling	Uncomplicated indwelling	Total	D 1
	(<i>n</i> =95; 39.6%)	(<i>n</i> =145; 60.4%)	(<i>n</i> =240)	P value
Diagnosis on admission, <i>n</i> (%)				
Prematurity and associated complications	57 (60.0)	58 (40.0)	115 (47.9)	0.002ª
Congenital malformation	28 (29.5)	37 (25.5)	65 (27.1)	0.502ª
Hypoxic-ischemic encephalopathy	5 (5.3)	26 (17.9)	31 (12.9)	0.004^{a}
Necrotizing enterocolitis in term infants	1 (1.1)	3 (2.1)	4 (1.7)	NA
Infection	1 (1.1)	2 (1.4)	3 (1.3)	NA
Age at admission (days), median (min-max)	1 (1–23)	1 (1–52)	1 (1–52)	0.186*
Place of birth, n (%)				
Inborn	74 (77.9)	84 (57.9)	158 (65.8)	0.001ª
Outborn	21 (22.1)	61 (42.1)	82 (34.2)	0.001ª
Gestational age at birth (weeks), median (min-max)	33 (24-42)	36 (25-41)	34.5 (24-42)	0.001*
Extremely preterm (< 28 weeks), n (%)	13 (13.7)	8 (5.5)	21 (8.8)	0.029ª
Very preterm (28 – $<$ 32 weeks), n (%)	22 (23.2)	26 (17.9)	48 (20.0)	0.322ª
Moderate-to-late preterm $(32 - <37 \text{ weeks}), n (\%)$	34 (35.8)	49 (33.8)	83 (34.6)	0.752ª
Term (\geq 37 weeks), <i>n</i> (%)	26 (27.4)	62 (42.8)	88 (36.7)	0.016 ^a
Birth weight (g), median (min-max)	1720.0 (580.0–3975.0)	2390.0 (630.0-4200.0)	2107.5 (580.0-4200.0)	0.006*
Very low birth weight (< 1500 g), n (%)	38 (40.0)	37 (25.5)	75 (31.3)	0.018^{a}
Low birth weight (1500 – 2499 g), <i>n</i> (%)	28 (29.5)	38 (26.2)	66 (27.5)	0.578^{a}
Normal birth weight (≥ 2500 g), <i>n</i> (%)	29 (30.5)	70 (48.3)	99 (41.3)	0.006^{a}
Length of hospital stay (days), median (min-max)	26 (4-115)	15 (3–88)	20 (3-115)	< 0.001*
Length of hospital stay (days), total	3371	3089	6460	NA
Central-lines, n (%)				
UAC	20 (21.1)	35 (24.1)	55 (22.9)	0.578^{a}
UVC	28 (29.5)	56 (38.6)	84 (35.0)	0.146ª
BROVIAC	13 (13.7)	9 (6.2)	22 (9.2)	0.050^{a}
SDVC	26 (27.4)	28 (19.3)	54 (22.5)	0.144 ^a
PICC	72 (75.8)	78 (53.8)	150 (62.5)	0.001^{a}
Number of central-lines, median (min-max)	2 (1-8)	1 (1–4)	1 (1-8)	< 0.001*
Length of catheter stay, median (min-max)	18 (2–109)	11 (2–70)	13 (2–109)	< 0.001*
Parenteral nutrition, n (%)	93 (97.9)	133 (91.7)	226 (94.2)	0.046ª
Duration of parenteral nutrition, median (min-max)	15 (0-88)	10 (0–70)	11 (0-88)	<0.001*

NA, not applicable

^a Pearson Chi-Square test

* Mann Whitney U-test

Table 2. Comparison of catheter characteristics and outcomes

	UAC (n=55; 13.75%)	UVC (n=84; 21.0%)	Broviac (n=22;	SDVC (n=57;	PICC (n=182;	Total (n=400;	P value
Catheter tip position evaluated by radiograph	13.75%) NA	21.0%) 84 (100.0)	5.5%) 21 (95.5)	14.25%) 57 (100.0)	45.5%) 179 (98.4)	100%) 341 (85.3)	0.007ª
Central	NA	37 (44.0)	18 (85.7)	33 (57.9)	99 (55.3)	187 (54.8)	
Non-central	NA	47 (56.0)	3 (14.3)	24 (42.1)	80 (44.7)	154 (45.2)	
Type of complications, <i>n</i> (%)							
All	8 (14.5)	12 (14.3)	10 (45.5)	18 (31.6)	75 (41.2)	123 (30.8)	<0.001ª
Mechanical	5 (9.1)	6 (7.1)	7 (31.8)	9 (15.8)	45 (24.7)	72 (18.0)	0.816ª
Infiltration	0 (0)	0 (0)	2 (9.1)	1 (1.8)	28 (15.4)	31 (7.8)	0.003ª
Infectious	3 (5.5)	6 (7.1)	3 (13.6)	9 (15.8)	30 (16.5)	51 (12.8)	0.816 ^a
Length of catheter stay, median (min-max)	6 (2–28)	5 (2–18)	16 (4–94)	11 (2–37)	10 (2-46)	8 (2–94)	$<\!\!0.001^{\dagger}$
Parenteral nutrition, n (%)	0 (0.0)	66 (78.6)	20 (90.9)	50 (87.7)	179 (98.4)	315 (78.8)	<0.001ª
Duration of parental nutrition, median (min-max)	NA	5 (0–18)	14 (0-82)	7 (0–37)	9 (0-46)	7 (0-82)	$<\!\!0.001^{\dagger}$
Rate of non-elective removals, <i>n</i> (%)	7 (13.0)	9 (11.7)	7 (46.7)	11 (19.6)	62 (39.5)	96 (26.7)	<0.001ª
Length of catheter stay for nonelective removals (days), median (min–max)	18 (8-55)	14 (3–52)	37 (11–100)	19 (4–83)	7 (2–100)	10 (2–100)	0.005^{\dagger}

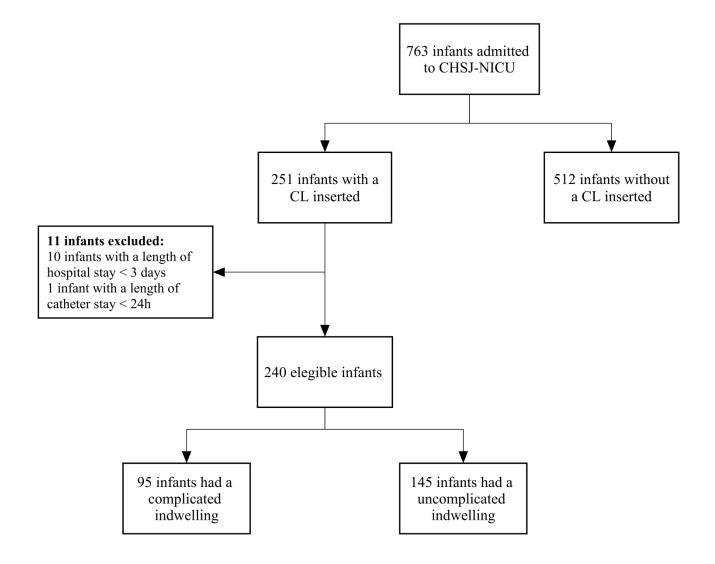
NA, not applicable

^a Pearson Chi-Square test

[†]Kruskal-Wallis Rank test

Apêndices

Appendix 1. Flowchart for study population of Neonatal Intensive Care Unit of Centro Hospitalar de São João (CHSJ-NICU) from 1st July 2014 to 31st June 2016.

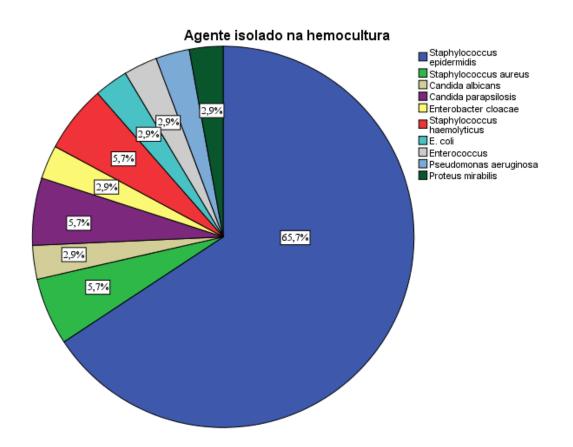


CL, central line.

	UAC (<i>n</i> =2)	UVC (<i>n</i> =4)	Broviac (n=2)	SDVC (<i>n</i> =5)	PICC (<i>n</i> =22)	Total (<i>n</i> =35)
Coagulase-negative Staphylococcus	1 (50.0)	2 (50.0)	1 (50.0)	4 (80.0)	17 (77.3)	25 (71.4)
Staphylococcus epidermidis	1 (50.0)	0 (0.0)	1 (50.0)	4 (80.0)	17 (77.3)	23 (65.7)
Staphylococcus haemolyticus	0 (0.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.7)
Staphylococcus aureus	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (4.5)	2 (5.7)
Candida albicans	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
Candida parapsilosis	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	1 (4.5)	2 (5.7)
Escherichia coli	0 (0.0)	1 (30.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
Enterococcus sp.	0 (0.0)	1 (30.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.9)
Enterobacter cloacae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	1 (2.9)
Proteus mirabilis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	1 (2.9)
Pseudomonas aeruginosa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	1 (2.9)

Appendix 2. Pathogens isolated from infants with Central Line-Associated Bloodstream Infection (CLABSI), per central line type

Appendix 3. Pie chart representing pathogens isolated from infants with Central Line-Associated Bloodstream Infection (CLABSI)



COMPLICAÇÕES DE CATÉTERES CENTRAIS EM RN INTERNADOS NA UCIN DO CHSJ (ENTRE 1 JULHO 2014 – 31 JUNHO 2016)

	חעט	DADOS DEMOGRÁFICOS			
Data de nascimento / / Sexo $F_{(0)}$ $M_{(1)}$ Idade gestacional	20	<u>S DEWOGR</u>			
Comprimento ao nascimento Perímetro cefálico ao nascim Peso ao nascimento	ento cm				
LIG (PN < P ₁₀ curvas de Fento LIG simétrico (P, C e PC < P ₁₀) RCIU		S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎	Desconhecido ₍₂₎ [
Outborn ₍₀₎ Inborn ₍₁₎ Inborn ₍₁₎					
		GESTAÇÃO			
Idade da mãe: anos					
Fumadora	N ₍₀₎	S ₍₁₎			
Gestações prévias Partos prévios Gestação múltipla	N ₍₀₎ [] N ₍₀₎ [] N ₍₀₎ []	S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎	N° N° N° gémeos		
Durante a gravidez: Corticoterapia Betametasona Dexametasona Sulfato de magnésio	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	$ \begin{array}{c} S_{(1)} \\ S_{(1)} \\ S_{(1)} \\ S_{(1)} \\ S_{(1)} \\ \end{array} $	Ciclo completo (2 tomas = compl (4 tomas = compl		S ₍₁₎
Infeção Medicamentos	N ₍₀₎ [] N ₍₀₎ []	S ₍₁₎ S ₍₁₎	Especificar Especificar		
Rastreio SGB Resultado:	Não realizado ₍₀₎ [] Negativo ₍₀₎ []			esconhecido ₍₂₎ [] lão aplicável ₍₂₎ []	
Doenças auto-imunes DM materna Diabetes gestacional HTA materna (crónica) Pré-eclâmpsia Eclâmpsia Síndrome HELLP Descolamento da placenta	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	$\begin{array}{c} S_{(1)} \\ \end{array}$	Qual(ais)?		
Transfusões materno-fetais Transfusões feto-fetais	N ₍₀₎	S ₍₁₎ S ₍₁₎			
<u>Ecografia</u> : Alteração do fluxo umbilical	N ₍₀₎	S ₍₁₎			

	PARTO		
Tipo: Eutócico ₍₀₎] Instrumentado(1)	Cesariana ₍₂₎	Desconhecido(10)
Na presença de trabalho de parto (TP)	N ₍₀₎	S ₍₁₎	
Rotura das membranas: horas ante RPM > 18h $N_{(0)}$ \Box $S_{(1)}$ \Box	es do parto		
Antibioterapia intraparto Corioamniotite clínica	$ \begin{array}{c c} N_{(0)} \square & & S_{(1)} \square \\ N_{(0)} \square & & S_{(1)} \square \end{array} $		
Índice de Apgar (1°, 5° e 10° minutos): _	//		
Necessidade de reanimação Oxigénio Tubo endotraqueal (TET) Máscara facial Adrenalina Compressões cardíacas	$\begin{array}{c c} N_{(0)} & & S_{(1)} \\ \hline \end{array}$		

PERÍODO NEONATAL: INTERNAMENTO EM UCIN

Motivo de internamento			
Diagnósticos			
Nº total de catéteres			
Duração do internamento <u>DESTINO</u> :	dias		
Alta para domicílio Transferência			
Com catéter	N ₍₀₎	S ₍₁₎	Ao fim de dias após colocação
Autópsia	N ₍₀₎	S ₍₁₎	Diagnóstico

CATÉTERES CENTRAIS						
1. CATÉTER ARTERIAL						
Tipo de catéter Local da colocação catéter Local anatómico de inserção		BO ₍₀₎]		
Posição da ponta do catéter Posição alta (T6-T9) Posição baixa (L3-L4) Mal posicionado / Fals			<mark>ı ecografia)</mark> (se	CAU):		
<u>Motivo de colocação do caté</u>	<u>eter</u> :	Prematuridade Nutrição parentérica Administração de fluid Administração de fárn Monitorização invasiv Avaliação de parâmete Outro(s)	nacos a da PA	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	$\begin{array}{c} S_{(1)} \\ \\ S_{(1)} \\ \\ S_{(1)} \\ \\ \\ S_{(1)} \\ \\ \\ \\ S_{(1)} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	Duração dias Duração dias Duração dias Duração dias Duração dias Qual(ais)?
Duração da cateterização	dias					
Complicações Na Qual(ais):	(0)	S ₍₁₎ □ Sinais de infeção PCR (mg/L) ↑ Sépsis Hemocultura +	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	$S_{(1)}$ $S_{($	Agente	
 Obstrução Infiltração Extravasamento pelo I Fratura Trombose Embolização Hemorragia Vasospasmo 	local de	inserção	Choque	pleural pericárdico v/deslocação ração		
<u>Tratamento farmacológia</u> Qual?		mplicação Qual?	N ₍₀₎	S ₍₁₎		Não aplicável ₍₂₎
Motivo da remoção do catét	er					🗌 Não removido
Complicação	Inf Ob Inf Tro He Va Ari De Ext Ou	strução iltração ombose morragia sospasmo ritmia rrame pleural rrame pericárdico eriorização tra	Agente Qual?			
Cumprimento do ob Alta Morte Desconhecido Outro	-	e colocação do catéter al?				

2. CATÉTER VENOSO]
Tipo de catéter					
Local da colocação catéter			l l		
Local anatómico de inserção do catéte			_		
Posição da ponta do catéter (confirm Bem posicionado (central) Mal posicionado / Falso trajeto Periférico Intracardíaco Intra-hepático		<u>ecografia)</u> :			
	Prematuridade Nutrição parentérica Administração de fluid Administração de fárm Monitorização invasiva Avaliação de parâmetr Outro(s)	nacos a da PA	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	$\begin{array}{c c} S_{(1)} & \square \\ \end{array}$	Duração dias Duração dias Duração dias Duração dias Duração dias Qual(ais)?
Duração da cateterização dias					
	S ₍₁₎ Sinais de infeção PCR (mg/L) ↑ Sépsis Hemocultura +	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎	Agente .	
 Obstrução Infiltração Extravasamento pelo local de ir Fratura Trombose Embolização Hemorragia Vasospasmo 	nserção	Choque Migração/ Exterioriza	pleural pericárdico /deslocação ação		
Tratamento farmacológico da con	nplicação	N ₍₀₎	S ₍₁₎		Não aplicável ₍₂₎
Qual? Antibiótico Trombolítico Outro	Qual?				
Motivo da remoção do catéter					🔲 Não removido
Complicação	strução Itração mbose norragia ospasmo itmia rame pleural rame pericárdico eriorização	Agente Qual?			
Cumprimento do objetivo de Alta Morte Desconhecido					

3. CATÉTER EPICUTÂNEO				
Tipo de catéter Local da colocação catéter Local anatómico de inserção de	BO ₍₀₎] UCIN ₍₁₎]	
Posição da ponta do catéter (c Bem posicionado (centra Mal posicionado Periférico Intracardíaco Intra-hepático		ia ou ecografia):		
Motivo de colocação do catéte	er: Prematuridade Nutrição parentér Administração de Administração de Monitorização inv Avaliação de parâ Outro(s)	fluidos fármacos asiva da PA	$ \begin{array}{c c} N_{(0)} & & & S_{(1)} \\ \end{array} $] Duração dias] Duração dias] Duração dias] Duração dias] Duração dias
Duração da cateterização	_ dias			
Complicações N ₍₀₎ Qual(ais): ☐ Infeção	Sinais de infeção PCR (mg/L) ↑ Sépsis Hemocultura +	N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎ N ₍₀₎	S ₍₁₎ S ₍₁₎ S ₍₁₎ S ₍₁₎ Age	nte
 Obstrução Infiltração Extravasamento pelo los Fratura Trombose Embolização Hemorragia Vasospasmo 	cal de inserção	Choque	pleural pericárdico /deslocação :ação	
Tratamento farmacológico Qual?	o da complicação Qual?	N ₍₀₎	S ₍₁₎	Não aplicável ₍₂₎ 🔲
Motivo da remoção do catéte	<u>r</u>			🗌 Não removido
Cumprimonto do obio	 Infeção Obstrução Infiltração Trombose Hemorragia Vasospasmo Arritmia Derrame pleural Derrame pericárdico Exteriorização Outra 	Qual?		
Cumprimento do obje	tivo de colocação do caté Qual?	ter		

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We recommend that you use our <u>templates</u> to prepare your article, but if you prefer not to use templates this guide will help you prepare your article for review.

If your article is accepted for publication, the manuscript will be copyedited and typeset in the correct style for the journal.

Font: Times New Roman, 12 point, double-line spaced. Use margins of at least 2.5 cm (or 1 inch). Guidance on how to insert special characters, accents and diacritics is available <u>here</u>.

Title: Use bold for your article title, with an initial capital letter for any proper nouns.

Abstract: Indicate the abstract paragraph with a heading or by reducing the font size. Check whether the journal requires a structured abstract or graphical abstract by reading the Instructions for Authors. The Instructions for Authors may also give word limits for your abstract. Advice on writing abstracts is available <u>here</u>.

Keywords: Please provide keywords to help readers find your article. If the Instructions for Authors do not give a number of keywords to provide, please give five or six. Advice on selecting suitable keywords is available <u>here</u>.

Headings: Please indicate the level of the section headings in your article:

- First-level headings (e.g. Introduction, Conclusion) should be in bold, with an initial capital letter for any proper nouns.
- Second-level headings should be in bold italics, with an initial capital letter for any proper nouns.
- Third-level headings should be in italics, with an initial capital letter for any proper nouns.
- Fourth-level headings should be in bold italics, at the beginning of a paragraph. The text follows immediately after a full stop (full point) or other punctuation mark.
- Fifth-level headings should be in italics, at the beginning of a paragraph. The text follows immediately after a full stop (full point) or other punctuation mark.

Tables and figures: Indicate in the text where the tables and figures should appear, for example by inserting [Table 1 near here]. The actual tables should be supplied either at the end of the text or in a separate file. The actual figures should be supplied as separate files. The journal Editor's preference will be detailed in the Instructions for Authors or in the guidance on the submission system. Ensure you have permission to use any tables or figures you are reproducing from another source.

- Advice on obtaining permission for third party material is available <u>here</u>.
- Advice on preparation of artwork is available <u>here</u>.
- Advice on tables is available <u>here</u>.

Running heads and received dates are not required when submitting a manuscript for review; they will be added during the production process.

Spelling and punctuation: Each journal will have a preference for spelling and punctuation, which is detailed in the Instructions for Authors. Please ensure whichever spelling and punctuation style you use is applied consistently.

If you have any queries...

If you need further advice, please contact us at <u>authorqueries@tandf.co.uk</u> giving the full title of the journal to which you are planning to submit, or see our <u>Author Services website</u>.

