

# Indwelling-tunneled-central-venous-catheter-related early bacteremia and preoperative prophylaxis: a case and control study

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## ABSTRACT

**Introduction.** The indication of preoperative prophylaxis in the insertion of indwelling tunneled central venous catheters (ITCVC) has a low level of evidence. Our objective was to assess risk factors of ITCVC-related early bacteremia in oncological pediatric patients and to determine the need for preoperative prophylaxis.

**Materials and methods.** A univariate and multivariate retrospective analysis of patients in whom an ITCVC was placed from January 2020 to July 2023, according to whether they had ITCVC-related early bacteremia (EB) in the first 30 postoperative days, was carried out. Demographic variables, leukopenia, neutropenia, use of preoperative antibiotic prophylaxis, and history of central venous catheter (CVC) or bacteremia were collected. Calculations were carried out using the IBM SPSS29® software.

**Results.** 176 patients with a mean age of 7.6 years (SD: 4.82) were analyzed. 7 EB cases were identified, with a greater frequency of neutropenia ( $p=0.2$ ), history of CVC in the 48 hours before insertion ( $p=0.08$ ), and intraoperative CVC ( $p=0.04$ ). The presence of intraoperative CVC increased the risk of EB 9-fold [OR: 9.4 (95%CI: 1.288-69.712) ( $p=0.027$ )]. The lack of preoperative prophylaxis did not increase the risk of EB [OR: 2.2 (CI: 0.383-12.669) ( $p=0.3$ )]. The association with other variables was not significant.

**Conclusions.** The intraoperative presence of CVC was a risk factor of EB in our patients. Preoperative prophylaxis had no impact on the risk of EB, which in our view does not support its use. However, further studies with a larger sample size are required. Leukopenia or neutropenia at diagnosis were not associated with a greater prevalence of infection.

**KEY WORDS:** Central venous catheters; Surgical oncology; Pediatrics; Bacteremia; Antibiotic prophylaxis.

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## BACTERIEMIA PRECOZ ASOCIADA A CATÉTER VENOSO CENTRAL TUNELIZADO PERMANENTE Y PROFILAXIS PREOPERATORIA: ESTUDIO DE CASOS Y CONTROLES

### RESUMEN

**Introducción.** La indicación de profilaxis preoperatoria en la colocación de catéteres venosos centrales tunelizados permanentes (CVCTP) tiene bajo nivel de evidencia. Nuestro objetivo fue evaluar factores de riesgo de bacteriemia precoz asociada a CVCTP en pacientes pediátricos oncológicos y determinar la necesidad de profilaxis preoperatoria.

**Material y métodos.** Realizamos un análisis retrospectivo univariante y multivariante de los pacientes con colocación de CVCTP entre enero 2020 y julio 2023, en función de si presentaron bacteriemia precoz (BP) relacionada con CVCTP en los primeros 30 días postoperatorios. Recogimos variables demográficas y otras como: leucopenia, neutropenia, uso de profilaxis antibiótica preoperatoria y antecedente de catéter venoso central (CVC) o bacteriemia. Los cálculos se realizaron mediante el software IBM SPSS29®.

**Resultados.** Analizamos 176 pacientes, con edad media de 7,6 años (SD 4,82). Identificamos 7 casos de BP, que presentaron mayor frecuencia de neutropenia ( $p=0,2$ ) y antecedente de CVC las 48h previas a la colocación ( $p=0,08$ ) y CVC intraoperatorio ( $p=0,04$ ). La presencia de CVC intraoperatorio aumentó 9 veces el riesgo de BP [OR 9,4 (IC 95% de 1,288-69,712) ( $p=0,027$ )]. La falta de profilaxis prequirúrgica no aumentó el riesgo de BP [OR 2,2 (IC 0,383-12,669) ( $p=0,3$ )]. La relación con otras variables no fue significativa.

**Conclusiones.** La presencia intraoperatoria de CVC fue factor de riesgo de BP en nuestros pacientes. La profilaxis preoperatoria no influyó sobre el riesgo de BP, por lo que creemos que su empleo no está justificado, aunque se necesitarían más estudios con mayor tamaño muestral. La leucopenia o neutropenia al momento diagnóstico no se relacionaron con mayor prevalencia de infección.

**PALABRAS CLAVE:** Catéter venoso central; Oncología pediátrica; Bacteriemia; Profilaxis antibiótica.

## INTRODUCTION

Indwelling tunneled central venous catheters (ITCVC) are widely used in oncological patients requiring chemo-

therapy for long periods of time, allowing for an easy and safe access to the blood.

Central-venous-catheter-related bacteremia (CVCRB) is one of the ITCVC complications associated with greater costs and morbidity. To prevent early CVCRB associated with catheter insertion, the use of empirical preoperative antibiotic prophylaxis based on blood test immunosuppression parameters such as leukopenia and neutropenia has become widespread in many hospitals<sup>(1,2)</sup>.

In recent years, scientific publications have suggested that antibiotic prophylaxis has no impact on the risk of CVCRB<sup>(3-7)</sup>, but the level of evidence is low<sup>(8)</sup>. In Spain, the use of antibiotic prophylaxis varies as it may fit into hospital protocols or be at the surgeon's discretion.

Our objective was to assess the risk factors of ITCVC-related early bacteremia in oncological pediatric patients and to determine the need for preoperative prophylaxis in our environment.

## MATERIALS AND METHODS

A retrospective review of the medical records of pediatric patients undergoing ITCVC insertion in our institution from January 2020 to July 2023 was carried out. Patient ID data was codified in the data collection notebook to ensure confidentiality. Patients with no surgical report available in digital medical records were excluded. Variables such as age, sex, diagnosis, leukopenia, neutropenia, previous chemotherapy, previous central venous catheters and CVC location, history of bacteremia, at-surgery factors –such as the use of antibiotic prophylaxis, catheter laterality, and excessive manipulation due to technical difficulty–, and post-surgery factors –such as first date of device use and infection date– were collected.

Leukopenia and neutropenia were established based on preoperative blood test levels.

History of previous CVC was defined as the presence of a central venous access device at any given location in the last 30 days before surgery.

History of bacteremia was defined as the presence of a positive blood culture in the last 30 days before surgery.

The ITCVC was placed in the operating room under general anesthesia and in sterile conditions in all cases. Central catheterization was ultrasound-guided and performed by pediatric anesthesiologists. When the catheterization technique proved uneasy and required various puncture attempts, it was regarded as excessive manipulation. The catheter was introduced and the device was implanted by oncological pediatric surgeons. In all cases, the proper functioning of the device was checked for, and the system was heparinized.

Antibiotic prophylaxis was defined as any given antibiotic administered 1 hour before surgery or during anes-

thetic induction. The indication of prophylaxis was at the head surgeon's discretion.

CVCRB diagnosis was defined as the presence of a positive blood culture. Postoperative CVCRB was characterized as any given CVCRB occurring in the first 7 days following surgery, whereas early bacteremia (EB) was described as any given bacteremia recorded in the first 30 days postoperatively.

The case group was made up of EB patients. It was compared with the control group, which consisted of patients who did not develop EB.

A descriptive analysis of the sample was carried out, and variables potentially associated with a higher risk of EB occurrence were identified. Subsequently, a univariate and multivariate analysis was conducted to identify CVCRB-associated risk factors.

The comparative analysis of quantitative variables such as age, neutropenia, leukopenia, and days to infection was performed through Mann-Whitney U test, whereas qualitative variables, such as the presence of EB or the administration of antibiotic prophylaxis, were compared using the chi-squared test. Missing data due to the absence of specific records for any given variable in patient medical histories was isolated and omitted from the statistical analysis. Calculations were carried out using the IBM SPSS software, version 29.

## RESULTS

The sample consisted of 176 patients (102 boys and 74 girls) with a mean age at surgery of 7.6 years (range: 1 month-17.6 years).

The data gathered in the descriptive analysis of the total sample is featured in Table 1. Within this data, the prevalence of certain preoperative factors, such as baseline condition (52.8% solid organ tumor, 39.2% malignant blood disease, and 8% benign blood disease), leukopenia (31.3%) and neutropenia (23.9%) at surgery, history of carrying a CVC in the last 30 days (20.5%), in the last 48 hours (9.7%), and at surgery (8%), and history of bacteremia in the last 30 days (5.7%), was reported.

In addition, 80 patients (45.5%) received intravenous antibiotic prophylaxis, 76 of whom were given cefazolin. 4 patients received prophylaxis with another antibiotic –amoxicillin-clavulanic acid in 2 cases (1 case due to concomitant soft tissue cellulitis in the upper limb, and 1 case as a result of gastrostomy button placement in the same surgery), cefuroxime and metronidazole in 1 case (owing to an abdominal procedure in the same surgery), and gentamicin in 1 case (reason not specified in the medical record).

7 CVCRB cases were identified in the first 30 days, 2 of which occurred in the first postoperative week –which means they were early CVCRB. Mean time from ITCVC

**Table 1. Descriptive analysis**

		<i>Total</i>
Sex	Male	102 (58%)
	Female	74 (42%)
Age		7.6 (0.1-17.6 / 4.82)
Diagnosis	Solid tumor	93 (52.8%)
	Malignant blood disease	69 (39.2%)
	Benign blood disease	14 (8%)
Chemotherapy initiation before reservoir insertion	Yes	59 (33.5%)
	No	117 (66.5%)
Tumor relapse or progression	Yes	22 (12.5%)
	No	154 (87.5%)
Leukopenia	Yes	55 (31.3%)
	No	121 (68.8%)
Neutropenia	Yes	42 (24%)
	No	133 (76%)
Days to first use		0 (0-33 / 5.3)
Use in the first 48 hours following insertion	Yes	133 (76.4%)
	No	41 (23.6%)
Previous CVC (< 30 days)	Yes	36 (20.5%)
	No	140 (79.5%)
Previous CVC (< 48 hours)	Yes	17 (9.7%)
	No	159 (90.3%)
CVC at surgery	Yes	14 (8%)
	No	160 (92%)
Ipsilateral CVC	Yes	32 (18.5%)
	No	141 (81.5%)
Re-catheterization at surgery	Yes	3 (1.7%)
	No	171 (98.3%)
Excessive manipulation at surgery	Yes	4 (2.3%)
	No	172 (97.7%)
Bacteremia (< 30 days)	Yes	10 (5.7%)
	No	166 (94.3%)
Antibiotic prophylaxis	Yes	80 (45.5%)
	No	96 (54.5%)
Insertion site	RIJV	161 (91.5%)
	LIJV	15 (8.5%)

insertion to infection was 14.29 days (range: 2-26 days). Isolated germs at blood culture included two cases of *Staphylococcus aureus*, one case of *Staphylococcus hominis*, one case of *Escherichia coli*, one case of *Streptococcus epidermidis*, one case of *Pseudomonas aeruginosa*, and one case of *Streptococcus oralis* + *Candida krusei*. In the last three cases, the device had to be removed.

In the comparative analysis (Table 2) according to whether CVCRB occurred or not, patients from the CVCRB group were younger [5.2 years (range: 0.9-12.3 years) vs. 7.7 years (range: 0.1-17.6 years) ( $p=0.179$ )], with 42.9% of them being under 3 years old ( $p=0.195$ ). In

this group, a greater percentage of leukopenia ( $p=0.499$ ) and neutropenia ( $p=0.233$ ), as well as a larger proportion of previous CVC, were noted, with CVC in the last 48 hours [28.6% vs. 8.9% ( $p=0.084$ )] and CVC at surgery [28.6% vs. 7.2% ( $p=0.042$ )] standing out. In the CVCRB group, there was greater manipulation at surgery (14.3% vs. 1.8%) ( $p=0.034$ ). As for the use of antibiotic prophylaxis, there were no significant differences (42.9% vs. 45.6%) ( $p=0.888$ ).

In the multivariate analysis (Table 3), the risk of CVCRB in the first 30 days increased 9.4-fold in patients who carried a CVC at surgery [OR: 9.4 (95%CI: 1.288-

**Table 2. Bivariate inferential comparative analysis.**

		Infection YES	Infection NO	Total	p
Sex	Male	3 (42.9%)	99 (58.6%)	102 (58%)	0.409
	Female	4 (57.1%)	70 (41.4%)	74 (42%)	
Age		5.2 (0.9-12.3 / 5.21)	7.7 (0.1-17.6 / 4.84)	7.6 (0.1-17.6 / 4.82)	0.179
3 years old	< 3 years old	3 (42.9%)	37 (21.9%)	40 (22.7%)	0.195
	> 3 years old	4 (57.1%)	132 (78.1%)	136 (77.3%)	
Diagnosis	Solid tumor	3 (42.9%)	90 (53.5%)	93 (52.8%)	0.518
	Malignant blood disease	4 (57.1%)	65 (38.5%)	69 (39.2%)	
	Benign blood disease	0 (0%)	14 (8.3%)	14 (8%)	
Chemotherapy	Yes	1 (14.3%)	58 (34.3%)	59 (33.5%)	0.271
	No	6 (85.7%)	111 (65.7%)	117 (66.5%)	
Tumor relapse or progression	Yes	1 (14.3%)	21 (12.4%)	22 (12.5%)	0.884
	No	6 (85.7%)	148 (87.6%)	154 (87.5%)	
Leukopenia	Yes	3 (42.9%)	52 (30.8%)	55 (31.3%)	0.499
	No	4 (57.1%)	117 (69.2%)	121 (68.8%)	
Neutropenia	Yes	3 (42.9%)	39 (23.2%)	42 (24%)	0.233
	No	4 (57.1%)	129 (76.8%)	133 (76%)	
Use in the first 48 hours following insertion	Yes	6 (85.7%)	127 (76%)	133 (76.4%)	0.478
	No	1 (14.3%)	40 (24%)	41 (23.6%)	
Previous CVC (< 30 days)	Yes	2 (28.6%)	34 (20.1%)	36 (20.5%)	0.438
	No	5 (71.4%)	135 (79.9%)	140 (79.5%)	
Previous CVC (< 48 hours)	Yes	2 (28.6%)	15 (8.9%)	17 (9.7%)	0.084
	No	5 (71.4%)	154 (91.1%)	159 (90.3%)	
CVC at surgery	Yes	2 (28.6%)	12 (7.2%)	14 (8%)	0.042
	No	5 (71.4%)	155 (92.8%)	160 (92%)	
Excessive manipulation at surgery	Yes	1 (14.3%)	3 (1.8%)	4 (2.3%)	0.034
	No	6 (85.7%)	166 (98.2%)	172 (97.7%)	
Bacteremia (< 30 days)	Yes	0 (0%)	10 (5.9%)	10 (5.7%)	0.508
	No	7 (100%)	159 (94.1%)	166 (94.3%)	
Antibiotic prophylaxis	Yes	3 (42.9%)	77 (45.6%)	80 (45.5%)	0.888
	No	4 (57.1%)	92 (54.4%)	96 (54.5%)	
Insertion site	RIJV	6 (85.7%)	155 (91.7%)	161 (91.5%)	0.577
	LIJV	1 (14.3%)	14 (8.3%)	15 (8.5%)	

69.712) ( $p=0.027$ ), and 20-fold in case of excessive manipulation during the procedure [OR: 20.6 (95%CI: 1.328-320.174) ( $p=0.031$ )]. The use of antibiotic prophylaxis had no impact on the risk of CVCRB [OR: 2.2 (95%CI: 0.383-12.669) ( $p=0.376$ )].

## DISCUSSION

According to the latest Cochrane review, the administration of antibiotic prophylaxis in ITCVC insertion does not reduce the risk of CVCRB in adults or children, with a moderate level of evidence<sup>(8)</sup>, but in hospitals worldwide,

there is no consensus regarding this<sup>(2,3,7,8)</sup>. Some institutions advocate the use of antibiotic prophylaxis as a result of the potential risk of infection that immunosuppressed patients who are ready for chemotherapy have, as posited by R. Bamba<sup>(2)</sup> or V. Taveira groups<sup>(1)</sup>. However, studies such as D. Tölle's<sup>(9)</sup> or W. Cher's<sup>(10)</sup> suggest neither antibiotic prophylaxis nor at-surgery leukocyte and neutrophil count have an impact on the risk of CVCRB. The results from our study are consistent with the latter, since the presence of leukopenia ( $p=0.499$ ) and neutropenia ( $p=0.233$ ) at surgery was not statistically significant, and the use of antibiotic prophylaxis did not impact the risk of CVCRB [OR: 2.2 (95%CI: 0.383-12.669) ( $p=0.376$ )].

**Table 3. Multivariate comparative analysis.**

	<i>B</i>	<i>SE</i>	<i>p</i>	<i>OR</i>	<i>95%CI (OR)</i> <i>(low ; high)</i>
Carrying a CVC at surgery	2.249	1.018	0.027	9.477	(1.288 ; 69.712)
Younger age at surgery	-0.149	0.098	0.130	0.861	(0.710 ; 1.045)
Excessive manipulation at surgery	3.026	1.399	0.031	20.623	(1.328 ; 320.174)
No antibiotic prophylaxis used	0.790	0.893	0.376	2.203	(0.383 ; 12.669)
Constant	-3.033	1.675	0.019		

In our study, the presence of a CVC at another location at surgery increased the risk of CVCRB up to nearly 10-fold [OR: 9.4 (95%CI: 1.288-69.712) ( $p= 0.027$ )]. CVCs are known to entail a risk of colonization that surges with catheter days<sup>(6,11)</sup>, so it seems reasonable to believe that CVCs at another location may be colonized in a latent fashion, thus favoring colonization of the new one. In the bibliographic review carried out, no references to this as a potential risk factor of ITCVC infection in pediatric patients were found, so we believe this can be valuable information for clinical practice. Today, there are various techniques and dressings intended to prevent CVCRB in non-tunneled CVCs<sup>(11)</sup>. However, the risk of CVCRB is not fully removed, which explains why, in our institution, we try to remove the CVC at least 48 hours before surgery, and always subject to patient condition.

The primary potential limitation of this study lies in its retrospective nature, with data being collected and analyzed from medical records. In addition, the diagnosis of catheter-related bacteremia was based on a positive blood culture, with no differential cultures available in certain cases, which led to the assumption that infection in these patients had a central origin as a result of their history of CVC. The small number of CVCRB cases in our study is a positive result for patients and clinical practice, but further studies with a larger sample size are required to extrapolate results to the remaining population.

In conclusion, the use of preoperative antibiotic prophylaxis had no impact on the risk of EB in our study, which in our view does not support its use. However, further studies with a larger sample size are required. The presence of another intraoperative CVC as well as excessive manipulation were EB-independent risk factors in our patients. Leukopenia or neutropenia at diagnosis were not associated with a higher prevalence of infection.

## REFERENCES

- Viana Taveira MR, Lima LS, de Araújo CC, de Mello MJG. Risk factors for central line-associated bloodstream infection in pediatric oncology patients with a totally implantable venous access port: A cohort study. *Pediatr Blood Cancer*. 2017; 64(2): 336-42.
- Bamba R, Lorenz JM, Lale AJ, Funaki BS, Zangan SM. Clinical predictors of port infections within the first 30 days of placement. *J Vasc Interv Radiol*. 2014; 25(3): 419-23.
- Choksi A, Finnegan K, Etezadi V. Does systemic antibiotic prophylaxis prior to the placement of totally implantable venous access devices reduce early infection? A retrospective study of 1,485 cases at a large academic institution. *Am J Infect Control*. 2020; 48(1): 95-9.
- Akbar S, Qudsia Z, Ashraf M, Tarar M, Qazi A. Prophylactic antibiotics for reducing central line-associated blood stream infection in children with totally implantable venous access devices. *J Coll Physicians Surg Pak*. 2020; 30(03): 304-8.
- Cher WQ, Lee V, Wang R, Cheah SM, Lee YT, Saffari SE, et al. Postoperative rather than preoperative neutropenia is associated with early catheter-related bloodstream infections in newly diagnosed pediatric cancer patients. *Pediatr Infect Dis J*. 2022; 41(2): 133-9.
- Zakhour R, Chaftari AM, Raad II. Catheter-related infections in patients with haematological malignancies: novel preventive and therapeutic strategies. *Lancet Infect Dis*. 2016; 16(11): e241-50.
- Gallart E, Delicado M, Nuvials X. Actualización de las recomendaciones del Proyecto Bacteriemia Zero. *Enferm Intensiva*. 2022; 33: S31-9.
- Van den Bosch CH, van Woensel J, van de Wetering MD. Prophylactic antibiotics for preventing gram-positive infections associated with long-term central venous catheters in adults and children receiving treatment for cancer. *Cochrane Database Syst Rev*. 2021; (10): CD00329510.
- Tölle D, Hentrich M, Pelzer BW, Kremer P, Einhell S, Schulz S, et al. Impact of neutropenia on central venous catheter-related bloodstream infections in patients with hematological malignancies at the time of central venous catheter insertion: A matched-pair analysis. *Infect Control Hosp Epidemiol*. 2019; 40(10): 1204-6.
- Cher WQ, Lee V, Wang R, Cheah SM, Lee YT, Saffari SE, et al. Postoperative rather than preoperative neutropenia is associated with early catheter-related bloodstream infections in newly diagnosed pediatric cancer patients. *Pediatr Infect Dis J*. 2022; 41(2): 133-9.
- Xu H, Hyun A, Mihala G, Rickard CM, Cooke ML, Lin F, et al. The effectiveness of dressings and securement devices to prevent central venous catheter-associated complications: A systematic review and meta-analysis. *Int J Nurs Stud*. 2024; 149: 104620.