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# COMPLICATIONS WITH THE USE OF CENTRAL VENOUS ACCESS IN PEDIATRIC ONCOLOGY PATIENTS

## Central venous catheter: pediatric oncology patients

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**Abstract**

**Objective**: Central venous access is an essential strategy when treating oncology patients due to the frequent need to administer chemotherapy or collect blood specimens. However, there is a considerable risk of complications. The aim of this research was to observe the nature and incidence of complications associated with central venous access and fully implanted catheters in pediatric oncology patients, as well as their association with clinical and laboratory findings.

**Methodology:** In this observational, retrospective and descriptive study, the data was collected from medical records of patients aged 0 to 14 years in a referral hospital in the extreme south of Santa Catarina and were analysed using the SPSS platform.

**Results:** From a total of 145 central catheters, 90 (62,06%) complications were identified, 21 (14,5%) infections, where 15 (25,4%) occurred in leukopenic patients ($p$= 0,016) and 18 (27,7%) in patients with thrombocytopenia ($p$<0,001). Six patients (4,1%) developed hematomas at the injection site, all of which occurred in thrombocytopenic patients ($p$=0,008). Among mechanical complications related to placement, 2 patients (1,4%) developed pneumothorax, 14 (9,7%) hemorrhages, 2 (1,4%) catheter breaks and 5 (3,4%) catheter malpositioning.

**Conclusion:** In this study it was observed that the most frequent complications are of a mechanical and infectious nature. A positive correlation was found between infection, leukopenia, and thrombocytopenia. Also, it is worth mentioning how a significant number of thrombocytopenic patients developed hematomas.

Keywords: Central venous catheters, medical oncology, peroperative complications, leukopenia, thrombocytopenia

## INTRODUCTION

Central venous access is important in the management of pediatric oncology patients as it minimizes the discomfort associated with frequent venipuncture required for blood collection and infusions while also providing access to central veins, allowing safe infusion of vesicant chemotherapeutic agents[1]. Unfortunately, venous accesses are also associated with several early and late complications[1]. Perioperative complications – such as pneumothorax or hemorrhage – are usually related to the technique during insertion or anatomy. Later complications, such as infection, dysfunction, or thrombosis are often related to patient illness or maintaining access[1].

There is a wide variety of devices used to facilitate venous access and infusion of drugs through a central line. Some devices are external while others are implanted in the subcutaneous tissue[2]. The increased use of such devices has been advocated for since it facilitates medication administration, improves quality of treatment, reduces discomfort and anxiety caused by repeated venipuncture pain, and it increases patient's quality of life[3].

The present study is justified due to the abundant use of venous access in cancer patients and the serious consequences complications of its use can generate. With this, we seek to identify the most prevalent complications, noted in the studied medical records, aiming at increasing staff preparedness for preventing complications that could impact patient health. Also, the awareness of what patients are at highest risk to develop these types of complications is of scientific relevance to the researched hospital, which receives citizens from all surrounding metropolitan regions of Criciúma-SC. Therefore, the main objective was to observe the nature and incidence of complications with the use of central venous access and a fully implanted catheter in pediatric oncology patients in a hospital in the extreme south of Santa Catarina and verifying if there is a correlation between these complications and the clinical an laboratory situations of the patients. It was then verified, studied and described with data from said medical records and successfully achieved.

## METHODS

The present study consists of an observational, retrospective, and descriptive analysis of secondary data and a quantitative approach.

This study included children and adolescents admitted and treated in a hospital in the extreme south of Santa Catarina. The inclusion criteria were defined as follows:

pediatric oncology patients aged 0-14 of both genders, subjected to central venous catheter (CVC) placement during their stay, between January 2014 and December 2019.

Cases in which the CVC placement did not occur at this hospital, as well as cases lacking sufficient information for the purposes of this study were both excluded from this analysis.

The population to be sampled was n (236); and n refers to the minimum sample size which resulted in 145 cases who were equally distributed in collections of 29 cases per year within the 5 years. The minimum sample size was reached, the number of cases evaluated was 145.

**Assessed variables**

Patient's age (years), sex (male or female), type of catheter (dual lumen catheter, Totally Implanted Venous Access Device or TIVAD and PICC), white blood cell (WBC) count (4000-11000/µL), platelet count (150.000 – 400.000/µL), infection (catheter tip culture), broken catheter, thrombosis, pneumothorax, hemorrhage, malpositioning, and other non-specified complications.

**Statistical analysis**

The data was directly collected from the patient's charts using the collection instrument and transferred to the IBM Statistical Package for the Social Sciences (SPSS) software version 21.0 for statistical analysis.

The inferential analysis was made with a significance level $\alpha = 0,05$ or 95% confidence. The investigation of normality was reached with the Kolmogorov-Smirnov test. The homogeneity of the quantitative variables was evaluated through the Levene test. To verify the association between qualitative variables the Pearson's chi-squared test was used. The mean of the variables was compared using the Student's T-test.

The project was approved by the Research and Ethics committee of the HSJ (process no. 26647219.0.3001.5364) on 24/06/2020. Data collection started only after approval by the referred committees following the norms of Ordinance 466/12 of the National Health Council.

As it is a retrospective study with an investigation of medical records of the patients, there is a risk of a minimal loss of information due to loss of confidentiality of the data. Participants' privacy was respected, and the data obtained was only used for scientific purposes.

## RESULTS

The medical records of 236 patients treated by two pediatric oncologists from the same hospital were analyzed. Among those, 186 were excluded based on the exclusion criteria and only 50 were selected. The data for each venous access used by these patients was analyzed, with the final "n" amounting in 145 central accesses.

The mean age resulted in 4 years, and the patients' age ranged between 0,3 and 13 years old. 26 (52%) were female and 24 (48%) were male.

**Table 01. Complications by type of catheter**

| | Type of catheter, n (%) | | | |
|---|---|---|---|---|
| | TIVAD n = 46 | Dual lumen catheter n = 91 | Picc n = 8 | *p*¥ |
| Infection | | | | |
| Yes | 8 (17,4) | 12 (13,2) | 1 (12,5) | 0,798 |
| No | 38 (82,6) | 79 (86,8) | 7 (87,5) | |
| Thrombosis | | | | |
| Yes | 2 (4,3) | - | - | 0,098 |
| No | 44 (95,7) | 91 (100) | 8 (100) | |
| Pneumothorax | | | | |
| Yes | 1 (2,2) | 1 (1,1) | - | 0,794 |
| No | 45 (97,8) | 90 (98,9) | 8 (100) | |
| Hemorrhage | | | | |
| Yes | 5 (10,9) | 7 (7,7) | 2 (25,0) | 0,354 |
| No | 41 (89,1) | 84 (92,3) | 6 (75,0) | |
| Hematoma | | | | |
| Yes | 2 (4,3) | 3 (3,3) | 1 (12,5) | 0,573 |
| No | 44 (95,7) | 88 (96,7) | 7 (87,5) | |
| Catheter malpositioning | | | | |
| Yes | - | 5 (5,5) | - | 0,092 |
| No | 46 (100) | 86 (94,5) | 8 (100) | |
| Broken catheter | | | | |
| Yes | 1 (2,2) | 1 (1,1) | - | 0,794 |
| No | 45 (97,8) | 90 (98,9) | 8 (100) | |
| Non-specified complication | | | | |
| No | 40 (87,0) | 62 (68,1) | 5 (62,5) | 0,150 |
| No progression | - | - | 1 (12,5) | |
| Obstruction | 3 (6,5) | 7 (7,7) | 1 (12,5) | |
| Phlogistic signs | 2 (4,3) | 15 (16,5) | 1 (12,5) | |
| Pulled out | - | 4 (4,4) | - | |
| Extravasation | 1 (2,2) | 2 (2,2) | - | |
| Carotid puncture | - | 1 (1,1) | - | |

¥Values obtained after applying the likelihood ratio test; Source: Research data, 2020.

An investigation of the WBC count of patients requiring double lumen central lines, TIVADs and PICC was also performed. The WBC count upon the date of

insertion of double lumen lines was considered since these are limited to use during maximum of 14 days. Therefore, WBC count of patients with TIVADs in place longer than 14 days was considered upon the date of initial signs of complication. Of the analyzed cases 59 (42,1%) had leukopenia at the time of placement (or complication), 65 (46,4%) presented WBC within the reference values and 16 (11,4%) had leukocytosis.

The platelet count was also analyzed, 65 (46,1%) presenting thrombocytopenia, 68 (48,2%) cases within the reference values and 8 (5,7%) presenting thrombocytosis.

**Table 02. Complications vs WBC count**

| | WBC count, n (%) | | | |
|---|---|---|---|---|
| | Leukopenia n = 59 | Normal n = 65 | Leukocytosis n = 16 | $p^{¥}$ |
| Infection | | | | |
| Yes | **15 (25,4)[b]** | 5 (7,7) | 1 (6,3) | **0,016** |
| No | 44 (74,6) | 60 (92,3) | 15 (93,8) | |
| Thrombosis | | | | |
| Yes | 1 (1,5) | 1 (1,7) | - | 0,781 |
| No | 64 (98,5) | 58 (98,3) | 16 (100) | |
| Pneumothorax | | | | |
| Yes | - | - | **2 (12,5)[b]** | **0,012** |
| No | 65 (100) | 59 (100) | 14 (87,5) | |
| Hemorrhage | | | | |
| Yes | 7 (10,8) | 6 (10,2) | 1 (6,3) | 0,849 |
| No | 58 (89,2) | 53 (89,8) | 15 (93,8) | |
| Hematoma | | | | |
| Yes | 3 (4,6) | 3 (5,1) | - | 0,471 |
| No | 62 (95,4) | 56 (94,9) | 16 (100) | |
| Unspecified complications | | | | |
| No | 54 (83,1) | 36 (61,0) | 12 (75,0) | 0,318 |
| No progression | - | 1 (1,7) | - | |
| Obstruction | 3 (4,6) | 6 (10,2) | 2 (12,5) | |
| Phlogistic signs | 5 (7,7) | 12 (20,3) | 1 (6,3) | |
| Pulled out | 2 (3,1) | 1 (1,7) | 1 (6,3) | |
| Extravasation | 1 (1,5) | 2 (3,4) | - | |
| Carotid puncture | - | 1 (1,7) | - | |

[¥]Value obtained after applying the likelihood ratio test.; [b]Letter indicating statistically significant value after residual analysis; Source: Research data, 2020

**Table 03. Complications vs Platelet count**

| Platelet count, n (%) |
|---|

| | Thrombocytopenia<br>n = 65 | Normal<br>n = 68 | Thrombocytosis<br>n = 8 | Valor-p[¥] |
|---|---|---|---|---|
| Infection | | | | |
| Yes | **18 (27,7)[b]** | 3 (4,4) | - | **<0,001** |
| No | 47 (72,3) | 65 (95,6) | 8 (100) | |
| Thrombosis | | | | |
| Yes | 1 (1,5) | 1 (1,5) | - | 0,889 |
| No | 64 (98,5) | 67 (98,5) | 8 (100) | |
| Pneumothorax | | | | |
| Yes | - | 1 (1,5) | 1 (12,5) | 0,103 |
| No | 65 (100) | 67 (98,5) | 7 (87,5) | |
| Hemorrhage | | | | |
| Yes | 9 (13,) | 5 (7,4) | - | 0,199 |
| No | 56 (86,2) | 63 (92,6) | 8 (100) | |
| Hematoma | | | | |
| Yes | **6 (9,2)[b]** | - | - | **0,008** |
| No | 59 (90,8) | 68 (100) | 8 (100) | |
| Unspecified complications | | | | |
| No | 37 (56,9) | 59 (86,8) | 7 (87,5) | **0,010** |
| No progression | 1 (1,5) | - | - | |
| Obstruction | 8 (12,3) | 3 (4,4) | - | |
| Phlogistic signs | **14 (21,5)[b]** | 4 (5,9) | - | |
| Pulled out | 1 (1,5) | 2 (3,1) | 1 (12,5) | |
| Extravasation | 3 (4,6) | - | - | |
| Carotid puncture | - | 1 (1,5) | - | |

[¥]Value obtained after applying the likelihood ratio test.; [b]Letter indicating statistically significant value after residual analysis; Source: Research data, 2020

Regarding the type of catheter utilized 46 (31,47%) were TIVAD, 91 (62,8%) were dual lumen catheters and 8 (5,5%) were PICC.

In relation to the insertion site 62 (42,8%) were placed in the right subclavian vein, 48 (33,1%) in the left subclavian vein, 19 (13,1%) in the right internal jugular vein, 13(9%) in the left internal jugular vein, 1 (0,7%) in the left axillary vein and 2(1,4%) in the right basilic vein.

When analyzing complications, there were 2 (1,4%) cases of broken catheters, 5 (3,4%) malpositioned catheters, 2 (1,4%) catheter thrombosis, 2(1,4%) pneumothoraces, 14 (9,7%) hemorrhages, 6 (4,1%) hematomas and 21 (14,5%) infections.

Among the unspecified complications 27 (19,28%) cases were registered the most frequent of which were phlogistic signs with 18 cases, 4 patients pulled the

catheter out, in 3 cases there was leakage or extravasation, 11 catheter obstructions and in 1 case the catheter did not progress through the vein.

The frequency of complications by type of catheter was similar for each device (Table 1)

Table 2 shows the number of complications versus the WBC count, with more incidence of infection in cases where there was pre-existing leukopenia and more pneumothorax in patients with leukocytosis. In table 3 the same data were compared with platelet counts, resulting in more infection, hematomas and phlogistic signs in patients with thrombocytopenia.

In table 4, complications by catheter site were analyzed, resulting in one statistically significant result ($p$=0,018) related to hematoma in axillary accesses. Pneumothorax cases only happened in subclavian sites.

The types of pathogens in catheter tip cultures were analyzed, resulting in the presence of 8 cases of coagulase negative staphylococcus, 4 *Klebsiella ozaenae*, 4 *Candida non albicans*, 2 *Staphylococcus aureus*, 1 *Pseudomonas aeruginosa*, 1 *Escherichia coli* and 1 *Klebsiella pneumoniae*.

In leukopenic patients' cultures resulted in 5 (8,5%) cases of coagulase negative staphylococcus, 3 (5,1%) *Candida non albicans*, 2 (3,4%) *S. aureus*, 2 (3,4%) *K. ozaenae*, 1 (1,7%) *P. aeruginosa*, 1 (1,7*) E. coli* and 1 (1,7%) *K. pneumoniae.*

In patients with thrombocytopenia, cultures resulted in 7 (10,8%) cases of coagulase negative staphylococcus, 3(4,6%) *K. ozanae*, 3 (4,6%) non-*albicans Candida*, 2 (3,1%) *S. aureus*, 1 (1,5%) *P. aeruginosa*, 1 (1,5%) E. *coli* and 1 (1,5%) *K. pneumoniae.*

## DISCUSSION

The study's objective was to assess the complications relater to central venous access through a retrospective multivariate analysis based on data from medical records.

Mechanical complications[4] (hemorrhage, pneumothorax, broken catheter, malpositioning) occurred in 15,86% of cases. Previous studies indicate variable frequencies of mechanical complications between 1,1 to 18,8%[5,6]. This result could relate to the increased risk of developing post-surgical complications in this patient population[7].

Central venous catheter use is a frequent cause of treatment-related morbidity and mortality in patients with malignancies, mainly due to infectious complications,

which are responsible for 10-15% of all nosocomial infections in the USA[7]. Within this study, infectious complications were present in 14.5% of catheters, this statistic proves to be relevant, after all, it approaches the sum of all mechanical complications.

The articles that analyze the complications with central venous accesses generally address different the insertion sites and type of catheters[5,6,8,9] utilized, which in this study had limited significance, after large hospitals have policies and procedures which already address complications resulting from these variables by avoiding insertion at the femoral site and opting for PICC lines. As well as avoiding mechanical complications using bedside ultrasound.

While considering individual complications, there was no predominance between external or totally implanted catheters (as shown in table 1), consistent with what was observed in other studies[1]. This suggests that the choice of the device should be based on the individual's treatment needs and the comfort of each patient.

Among the insertion sites analyzed, there was one significant correlation ($p$=0,018), the occurrence of hematoma in the axillary access (Table 4). Other studies that analyzed peripherally inserted catheters[10] did not observe the same correlation. This can be explained by the reduced "n" in this research. Regarding pneumothorax, only two cases were found – both occurring in the subclavian site- however there is no statistical significance as observed in large studies[5]. No other significant data related to the insertion sites was found, and this outcome is compatible with larger studies[5,8,9,11,12].

Comparing complications with patients' WBC count, 15 (25,4%) cases of infection occurred in leukopenic patients ($p$=0,016) (table 2). Retrospective studies observing the same variables also reported more local and systemic infections in these populations[1], supporting the hypotheses raised prior to data collection, especially since leukopenic patients are more susceptible to opportunistic infectious diseases due to their immunological fragility. In this analysis, 2 (12,5%) cases of pneumothorax were registered in patients with leukocytosis ($p$=0,012).

Observing complications in relation to platelet count, there is evidence of more infection[13], hematomas[14] and phlogistic signs in thrombocytopenic patients ($p$>0,05) (table 3). The decrease in platelet count affects primary coagulation, predisposing the formation of hematomas and/or minor hemorrhages, thus, the increase in hematomas was already predicted in the hypotheses for these patients. However, recent studies[13] also relate thrombocytopenia as an independent risk factor for

infectious processes. This research affirms this correlation, as infections in patients with thrombocytopenia had the lowest p-value in the study ($p$<0,001).

The infections were analyzed by means of catheter tip culture, therefore it was possible to ascertain and order the pathogens according to their frequency of involvement. Coagulase negative Staphylococcus being the most frequent pathogen, present 8 times, followed by *Klebsiella ozanae* occurring 4 times and *Streptococcus aureus*, 2 times. Other articles have observed the presence of the same bacteria, although not in the same proportion[1,15], this can due to a variance of pathogens and strains from region and hospital locations. The fungal infections that occurred, were caused by the Candida species, which is reaffirmed in other studies[15,16], this is due to the fact that this pathogen originates in the mucous membrane flora of a large part of the human population[17], causing infections when there is immunologic compromise or immunosuppression, as is seen in the patients present in this study.

## LIMITATIONS

This study had some limitations. First, a retrospective analysis of medical records was performed, so each chart contained documentation from different professionals, and some complications were charted by professionals who were not doctors. In addition, there was no designated section in the medical records for reporting a catheter complication, consequently the researchers needed to collect data throughout the patients' documented progression.

The diagnosis of central venous catheter infection was considered by means of catheter tip culture, as there was no other form of diagnosis in the medical records.

## CONCLUSION

The analysis carried out in this study suggests that the patient with hematological alterations has a higher risk of complications with the use of central venous catheters, therefore it would be necessary to be aware of laboratory changes in patients using these devices, in order to predict or even prevent such complications.

We hope this study will lead the way for larger studies that can include other populations, and scientifically prove if there really is correlation between the hematological alterations and the complications observed in this study.

## CONFLICT OF INTEREST

All authors declared there was no conflict of interest.

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