

# Risk factors to port-a-cat damage/removal in patients in antineoplastic chemotherapy: a retrospective observational study

## Fatores de risco para danos ou retirada de port-a-cath em pacientes em quimioterapia antineoplásica: Um estudo observacional retrospectivo

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### Abstract

**Objective:** To identify the prevalence and risk factors for damage or removal of fully implanted long-term catheters from patients undergoing antineoplastic chemotherapy. **Methods:** This is an observational, cross-sectional study that evaluated medical records of patients undergoing placement of a fully implanted catheter for antineoplastic chemotherapy from January 2015 to December 2019. Clinical and sociodemographic data were collected that were associated with catheter survival using Log-Rank Mantel-Cox and Cox Regression tests (SPSS,  $p < 0.05$ ). **Results:** Of 58 devices evaluated, most patients were higher educated married females, younger than 60 years old. The most frequent side of catheter implantation was the right side, and the most prevalent implantation site was the internal jugular vein. Less than 1/3 of patients (29.3%) had port-a-cath loss due to complications with a five-year follow-up survival of  $35.73 \pm 3.76$  (95% CI = 28.35-43.11). Two patients (4.7%) needed removal due to device exposure, three (7.0%) due to obstruction, and 12 (27.9%) due to infection. Female patients ( $p = 0.019$ ) and patients with breast tumors ( $p = 0.049$ ) had a shorter mean survival time. The women showed port-a-cath survival 9.25 times (95% CI = 1.35-50.25) shorter in the multivariate analysis. **Conclusion:** port-a-cath catheter loss is around 30% and being female is a determining risk factor.

**Keywords:** Vascular Access Devices; Antineoplastic Agents; Complications. Peripherally Inserted Central Catheter; Risk Factors.

### Resumo

**Objetivo:** Identificar a prevalência e os fatores de risco para danos ou retirada de cateter de longa permanência totalmente implantado em pacientes submetidos à quimioterapia antineoplásica. **Metodos:** Trata-se de um estudo observacional transversal que avaliou prontuários de pacientes submetidos à colocação de cateter totalmente implantado para quimioterapia antineoplásica, no período de janeiro de 2015 a dezembro de 2019. Foram coletados dados clínicos e sociodemográficos associados à sobrevida do cateter por meio do Log-Rank testes de Mantel-Cox e Regressão de Cox (SPSS,  $p < 0,005$ ). **Resultados:** Dos 58 dispositivos avaliados, a maioria dos pacientes era mulheres casadas com nível superior de escolaridade e com idade inferior a 60 anos. O lado mais frequente de implantação do cateter foi o direito, e o local de implantação mais prevalente foi a veia jugular interna. Pouco menos de 1/3 dos pacientes (29,3%) tiveram perda de port-a-cath devido complicações com uma sobrevida de seguimento de cinco anos de  $35,73 \pm 3,76$  (IC 95% = 28,35-43,11). Dois pacientes (4,7%) necessitaram de remoção por exposição do dispositivo, três (7,0%) por obstrução e 12 (27,9%) por infecção. Pacientes do sexo feminino ( $p = 0,0019$ ) e pacientes com tumores de mama ( $p = 0,049$ ) apresentam menor tempo médio de sobrevida. As mulheres apresentaram sobrevida port-a-cath 9,25 vezes (IC 95% = 1,35-50,25) menor na análise multivariada. **Conclusão:** A perda do cateter port-a-cath foi de aproximadamente 30% e ser do sexo feminino foi um fator de risco importante.

**Palavras-chave:** Dispositivos de acesso vascular; Agente antineoplásico; Complicações; Cateter Central de Inserção Periférica; Fatores de risco.

### INTRODUCTION

Chemotherapy is performed mainly intravenously, using cytotoxic agents alone or in combination to treat malignant tumors. However, the practice commonly requires several venous punctures during treatment. In addition, the vesicant and/or irritant characteristics of many drugs can cause damage to the vascular wall, making access difficult and favoring drug extravasation<sup>1</sup>.

Venous catheters are technological resources used to assist in

intravenous drug therapy, with the peripheral venous catheter being one of the most commonly used. Still, there is also the option of central venous accesses, semi or fully-implantable. Venous catheters are technological resources used to assist in intravenous drug therapy, and the peripheral venous catheter is one of the most used. However, there is also the option of central venous access, semi or fully-implantable<sup>2</sup>.

The Totally Implanted Central Venous Catheter (CVC-TI), also

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known as port-a-cath, is a device with a diameter of less than 10 French. It is implanted by puncturing or dissecting a peripheral or central vein after passing through a subcutaneous pathway<sup>3,4</sup>. CVC-TI is a safe option for adult patients on antineoplastic chemotherapy. The proposed treatment is with vesicant/irritant drug infusions of extended duration (greater than six months) or patients with a compromised venous network or challenging access<sup>5</sup>. Enabling the reduction of pain and discomfort of multiple peripheral punctures without restricting the patients' activities, port-a-cath catheters allow greater patient independence during infusion therapy and contribute to a better quality of life for these patients<sup>6</sup>.

Although the implantation of a central venous device, such as the port-a-cath, was initially considered safe, complications related to implantation or device handling are widely reported in the literature<sup>4,7</sup>. Complications can be classified as acute - when identified still in the preoperative period or at the post-implantation moment, before the first handling; and late - characterized by events detected after the first cycle of chemotherapy using the device<sup>8</sup>.

The most common complications, such as hematomas, edema, obstruction, or local infection, manifest later but are more easily detectable<sup>3,4,7</sup>. Some complications can be avoided or treated, and the management of catheter-related infections varies according to the type of catheter involved. Still, it is always possible to guarantee the preservation of the device, and the insertion of a new device is necessary, contributing to the delay in oncologic treatment<sup>9-11</sup>.

As the complications related to the CVC-TI in patients on antineoplastic therapy directly impact treatment, causing adverse events at a systemic level and delaying treatment, this study aims to identify the risk factors that lead to damage or removal of the fully implanted catheter of patients on antineoplastic chemotherapy.

## MATERIALS AND METHODS

### Study type and location

This observational, cross-sectional, retrospective and quantitative study proposed identifying the risk factors for patients' damage or removal of fully implanted catheters (CVC-TI) on antineoplastic chemotherapy guided by STROBE.

### Study population, sample selection, and inclusion and exclusion criteria

The sample population was composed of medical records of patients undergoing placement of a fully implanted catheter to perform chemotherapy treatment from January 2015 to December 2019, summing the last five years of the survey.

A survey was conducted through the Tasy system of long-term catheter installation or removal procedures from January 1,

2015, to December 31, 2019. From the number of surgical procedures, the Electronic Patient Records (EPR), a non-probabilistic sample with 144 records was surveyed. The records of patients that dealt with the insertion of the central venous catheter, catheter for hemodialysis, or that dealt only with the removal of the device at the institution were excluded. The records did not have the clinical information necessary for the evaluation of risk factors.

During the manual collection of information, based on the medical record number, the following sociodemographic variables were analyzed: gender; date of birth; marital status; education; social security status; occupation; who lives with; origin, and health insurance. Concerning the clinical-surgical variables, the data referring to the side and place of catheter implantation; history of radiotherapy at the implantation site; date of installation and removal of the catheter; reason for removal; primary tumor; as well as comorbidities (DM, HBP, DLP, among others); the outcome (discharge, transference, or death) and the date of the outcome were analyzed.

### Statistical Analysis

Data were tabulated in Microsoft Excel and exported to the Statistical Package for the Social Sciences (SPSS) software version 20.0 for Windows. The analyses were performed adopting a confidence level of 95%. The sociodemographic and clinical-surgical variables were expressed as absolute and percentage frequency, and the survival time of port-a-cath catheters was calculated using Kaplan-Meier curves. The curves were associated with the sociodemographic and clinical-surgical variables using the Mantel-Cox log-rank test (bivariate analysis) and Cox regression (multivariate analysis).

### Ethical aspects

The research was conducted within the standards required by the Declaration of Helsinki and approved by the Research Ethics Committee (CEP) of Hospital Haroldo Juaçaba and Plataforma Brasil, with approval number 4,394,412.

### Results

From the 144 electronic medical records analyzed, a total of 58 port-a-cath catheters were surveyed in five years. Most patients were female (53.4%), younger than 60 years old (53.4%), married (63.8%), with higher education (41.1%), with no social security status (51.7%), public employees (42.4%), living with their spouse and children (93.8%), from the state capital (74.1%). All were seen by the private service. High blood pressure (32.8%) was the most prevalent comorbidity (Table 1).

The most frequent side of catheter implantation was the right side (75.9%), and the most prevalent implantation site was the internal jugular vein (82.8%). Only four (6.9%) patients had a history of radiotherapy at the catheter site, and among the most prevalent reasons for catheter removal, the end of treatment

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(60.5%) was the most prevalent. The most frequent tumor associated with port-a-cath installation was breast (36.2%), followed by colorectal (19.0%) and lymphomas (15.5%) (Table 1).

**Table 1.** Sociodemographic profile of patients about a Port-a-cath catheter implant for treatment with antineoplastic chemotherapy at the Hospital Haroldo Juaçaba, Instituto do Câncer do Ceará from 01.01.2015 to 12.31.2019.

| Variables                 | n (%)      |
|---------------------------|------------|
| Total                     | 58 (100.0) |
| Sex                       |            |
| Feminine                  | 31 (53.4)  |
| Masculine                 | 27 (46.6)  |
| Age                       |            |
| <60                       | 31 (53.4)  |
| 60+                       | 27 (46.6)  |
| Marital Status            |            |
| Married                   | 37 (63.8)  |
| Divorced                  | 6 (10.3)   |
| Widower                   | 3 (5.2)    |
| Single                    | 12 (20.7)  |
| Education                 |            |
| Can read and write        | 1 (1.8)    |
| Elementary School         | 11 (19.6)  |
| High School               | 21 (37.5)  |
| Higher Education          | 23 (41.1)  |
| Social security situation |            |
| Absent                    | 30 (51.7)  |
| In Activity               | 19 (32.8)  |
| Retiree                   | 9 (15.5)   |
| Occupation                |            |
| From Home                 | 1 (3.0)    |
| Autonomous                | 13 (39.4)  |
| Func. Publico             | 14 (42.4)  |
| Aposentado                | 5 (15.2)   |
| Who lives                 |            |
| Spouse and children       | 30 (93.8)  |
| Sons                      | 2 (6.3)    |
| Source                    |            |
| Metropolitan Area         | 43 (74.1)  |
| Countryside               | 15 (25.9)  |
| Conventional risk factors |            |
| Diabetes Mellitus         | 9 (15.8)   |
| Arterial hypertension     | 19 (32.8)  |
| Obesity                   | 8 (13.8)   |
| Others                    | 11 (19.0)  |
| Smoking                   | 10 (17.2)  |
| Alcoholism                | 7 (12.1)   |

Data expressed as absolute and percentage frequency

**Table 2.** Clinical profile of patients undergoing implantation of Port-a-cath catheters for treatment with antineoplastic chemotherapy at the Hospital Haroldo Juaçaba, Instituto do Câncer do Ceará from 01.01.2015 to 12.31.2019.

| Variables                      | n (%)     |
|--------------------------------|-----------|
| Implant side                   |           |
| Right                          | 44 (75.9) |
| Left                           | 14 (24.1) |
| Implant Site                   |           |
| Internal jugular vein          | 48 (82.8) |
| Subclavian Vein                | 9 (15.5)  |
| Femoral Vein                   | 1 (1.7)   |
| Catheter-site radiotherapy     | 4 (6.9)   |
| Reason for removal             |           |
| End of treatment               | 26 (60.5) |
| Catheter exposure              | 2 (4.7)   |
| Obstruction                    | 3 (7.0)   |
| Catheter infection             | 12 (27.9) |
| Lost catheter                  | 17 (29.3) |
| Death                          | 7 (12.1)  |
| Reason for death               |           |
| Sepsis                         | 4 (57.1)  |
| Accute breathing insufficiency | 2 (28.6)  |
| Disease progression            | 1 (14.3)  |
| Tumor under treatment          |           |
| Mama                           | 21 (36.2) |
| Colon                          | 11 (19.0) |
| Lymphom                        | 9 (15.5)  |
| Gastric                        | 3 (5.2)   |
| Bladder                        | 2 (3.4)   |
| Uterine                        | 2 (3.4)   |
| Lung                           | 2 (3.4)   |
| Sarcomas                       | 2 (3.4)   |
| Head and Neck                  | 1 (1.7)   |
| Kidney                         | 1 (1.7)   |
| Testicle                       | 1 (1.7)   |
| Thymus                         | 1 (1.7)   |
| Neuroendocrine Tumor           | 1 (1.7)   |
| Unknown                        | 1 (1.7)   |

Data expressed as absolute and percentage frequency

Almost one-third of patients (29.3%) had port-a-cath loss due to complications with a median port-a-cath survival time was  $35.73 \pm 3.76$  (95% CI = 28.35-43.11) months showing a 70.7% success rate at the end of five years of follow up. Of the patients who needed early removal of port-a-cath catheters,

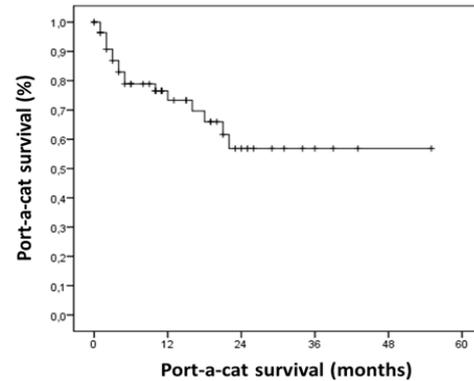
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two patients (4.7%) needed removal due to device exposure, three (7.0%) due to obstruction, and 12 (27.9%) due to infection (Figure 1).

Female patients ( $p=0.019$ ) and patients with breast tumors ( $p=0.049$ ) had a shorter mean port-a-cath survival time (Table 3). In multivariate analysis, female patients had 9.25 (95% CI = 1.35-50.25) times shorter mean port-a-cath survival time than men ( $p=0.022$ ) (Table 3).

The overall survival of patients was 46.58 (95%CI = 40.38-52.79) months, and losing (20.76, 95%CI = 18.42-23.11 months) or not losing (45.78, 95%CI = 38.88-52.68 months) did not significantly influence this outcome ( $p=0.559$ ).

**Figure 1.** Kaplan-Meier survival curve for port-a-cat catheters in patients undergoing antineoplastic chemotherapy at the Hospital Haroldo Juaçaba, Instituto do Câncer do Ceará from



**Table 3.** Influence of sociodemographic and clinical-surgical variables on the survival of Port-a-cath catheters in patients undergoing antineoplastic chemotherapy at the Hospital Haroldo Juaçaba, Instituto do Câncer do Ceará from 01.01.2015 to 12.31.2019.

| Variables                        | Port-a-cath survival (months) |                          | HR adjusted          |                   |                      |
|----------------------------------|-------------------------------|--------------------------|----------------------|-------------------|----------------------|
|                                  | n (%)                         | Mean±SEM (CI 95%)        | p-Value <sup>a</sup> | (CI 95%)          | p-Value <sup>b</sup> |
| <b>Sex</b>                       |                               |                          |                      |                   |                      |
| Feminine                         | 18 (58.1)                     | 26.69±5.27 (16.36-37.03) | 0,019                | 8,25 (1,35-50,25) | 0,022                |
| Masculine                        | 23 (85.2)                     | 36.30±3.06 (30.30-42.29) |                      |                   |                      |
| <b>Age</b>                       |                               |                          |                      |                   |                      |
| <60                              | 21 (67.7)                     | 25.23±3.42 (18.53-31.93) | 0,446                | 1,21 (0,35-4,15)  | 0,758                |
| 60+                              | 20 (74.1)                     | 37.69±5.35 (27.21-48.18) |                      |                   |                      |
| <b>Married Marital Status</b>    |                               |                          |                      |                   |                      |
| Not                              | 15 (71.4)                     | 33.31±6.39 (20.79-45.83) | 0,906                | 4,31 (0,76-24,40) | 0,098                |
| Yes                              | 26 (70.3)                     | 29.99±3.24 (23.64-36.34) |                      |                   |                      |
| <b>Education</b>                 |                               |                          |                      |                   |                      |
| Even High School                 | 21 (63.6)                     | 25.37±3.69 (18.14-32.60) | 0,234                | 2,86 (0,75-10,87) | 0,123                |
| University Education             | 20 (80.0)                     | 42.15±5.06 (32.23-52.07) |                      |                   |                      |
| <b>Social Security Situation</b> |                               |                          |                      |                   |                      |
| Absent                           | 23 (76.7)                     | 35.09±5.94 (23.45-46.74) | 0,466                | 0,40 (0,10-1,70)  | 0,215                |
| Gift                             | 18 (64.3)                     | 27.90±3.75 (20.54-35.25) |                      |                   |                      |
| <b>Origin</b>                    |                               |                          |                      |                   |                      |
| Capital                          | 29 (67.4)                     | 33.26±4.50 (24.44-42.08) | 0,476                | 2,21 (0,26-18,96) | 0,468                |
| Interior                         | 12 (80.0)                     | 33.50±4.81 (24.08-42.92) |                      |                   |                      |
| <b>Diabetes Mellitus</b>         |                               |                          |                      |                   |                      |
| Not                              | 33 (68.8)                     | 34.96±4.12 (26.88-43.04) | 0,467                | 2,05 (0,26-16,21) | 0,496                |
| Yes                              | 7 (77.8)                      | 32.29±5.99 (20.55-44.02) |                      |                   |                      |
| <b>Arterial hypertension</b>     |                               |                          |                      |                   |                      |
| Not                              | 26 (66.7)                     | 33.29±4.62 (24.23-42.36) | 0,351                | 2,30 (0,40-13,21) | 0,352                |
| Yes                              | 15 (78.9)                     | 32.53±4.53 (23.66-41.41) |                      |                   |                      |
| <b>Obesity</b>                   |                               |                          |                      |                   |                      |
| Not                              | 36 (72.0)                     | 36.59±4.03 (28.68-44.49) | 0,701                | 0,72 (0,07-7,49)  | 0,786                |
| Yes                              | 5 (62.5)                      | 20.86±4.63 (11.78-29.93) |                      |                   |                      |

|                         |           |                          |       |                     |       |
|-------------------------|-----------|--------------------------|-------|---------------------|-------|
| Others                  |           |                          |       |                     |       |
| Not                     | 33 (70.2) | 34.49±4.34 (25.99-43.00) | 0,630 | 0,49 (0,10-2,34)    | 0,369 |
| Yes                     | 8 (72.7)  | 28.93±4.86 (19.41-38.45) |       |                     |       |
| Smoking                 |           |                          |       |                     |       |
| Not                     | 32 (66.7) | 33.44±4.16 (25.29-41.59) | 0,205 | 1,78 (0,12-26,78)   | 0,676 |
| Yes                     | 9 (90.0)  | 38.56±4.19 (30.34-46.77) |       |                     |       |
| Alcoholism              |           |                          |       |                     |       |
| Not                     | 34 (66.7) | -                        | 0,066 | 9,78 (0,09-18,97)   | 0,978 |
| Yes                     | 7 (100.0) | -                        |       |                     |       |
| Implant Side            |           |                          |       |                     |       |
| Right                   | 31 (70.5) | 35.62±4.30 (27.20-44.05) | 0,966 | 1,45 (0,23-9,12)    | 0,692 |
| Left                    | 10 (71.4) | 29.76±5.37 (19.23-40.30) |       |                     |       |
| Implant Site            |           |                          |       |                     |       |
| internal jugular vein   | 32 (66.7) | 33.61±4.11 (25.56-41.66) | 0,203 | 11,83 (0,77-182,43) | 0,077 |
| Subclavian/femoral vein | 9 (90.0)  | 35.11±3.67 (27.92-42.30) |       |                     |       |
| RTx no local do cateter |           |                          |       |                     |       |
| Not                     | 37 (68.5) | -                        | 0,321 | 3,56 (0,03-13,57)   | 0,988 |
| Yes                     | 4 (100.0) | -                        |       |                     |       |
| Tumor Under Treatment   |           |                          |       |                     |       |
| Mama                    | 11 (52.4) | 25.47±6.14 (13.44-37.51) | 0,049 | 1,47 (0,26-8,44)    | 0,664 |
| Rectal Cervix           | 10 (90.9) | 28.40±2.47 (23.57-33.23) |       |                     |       |
| Others                  | 20 (76.9) | 31.38±3.93 (23.67-39.08) |       |                     |       |

\*p<0.05; aLog-Rank Mantel-Cox Test; bCox regression; SEM = standard error of the mean; HR = hazard risk; 95%CI = adjusted HR confidence interval.

## DISCUSSION

CVC-TIs have been used since 1983 for the administration of antineoplastic drugs and are crucial to the quality of life of cancer patients. The implantation of CVC-TI allows for reducing the anxiety associated with repeated punctures, thus improving their quality of life. The main advantage of the CVC-TI concerning other types of venous access is that it is a totally subcutaneous system, which contributes to the reduction of infection and greater durability<sup>12</sup>.

In this study, it was possible to observe that of the 58 port-a-cath catheters, 53.4% were implanted in female patients and that the most frequent tumor associated with the installation of port-a-cath was breast (36.2%), followed by colorectal (19.0%) and lymphomas (15.5%). This fact may be associated with the oncologic therapy of choice for breast cancer, the administration of cyclophosphamide with doxorubicin, vesicant chemotherapy, and an extended treatment time, with a mean of 6 months on average. As this tumor is the most prevalent among women, these therapeutic characteristics tend to choose the implantation of these devices<sup>1,4</sup>.

Another critical tumor associated with catheters was colorectal tumor. Besides being the third most common type of cancer in

Brazil, approximately 80% of patients diagnosed with CRC receive some sort of chemotherapy, either after receiving surgical treatment with curative intent (adjuvant chemotherapy), pre-surgical (neoadjuvant), or palliative. Neoadjuvant to adjuvant chemotherapy regimens last around six months, so port-a-cath catheters are essential during treatment<sup>13</sup>. These intravenous infusion regimens for breast and Colorectal Cancer are primarily administered with CVC-TI systems due to the difficulty of providing intravenous access<sup>14</sup>.

Xu et al.<sup>15</sup> describe that the insertion of fully implantable venous access ports in the upper arm is feasible and safe for patients with early breast cancer, with low complication rates, being a good alternative to central venous ports. Thus, the most commonly used site in our sample was the internal jugular vein. Interestingly, in the present study, female patients had a mean port-a-cath survival time 9.25 times shorter than males, regardless of the other variables studied. The increasing use of fully implantable arm vascular access devices for breast cancer patients requiring chemotherapy has led to a higher risk of complications and failures and, in particular, upper limb deep vein thrombosis, reducing the average survival of these catheters<sup>16</sup>. This fact corroborates the findings of the present

study.

Catheter-related bloodstream infection is an ever-present danger for patients who require venous access and particularly for those who need long-term medication. Implementing more rigorous care packages and greater adherence to aseptic techniques have substantially reduced infection rates<sup>17</sup>. Moreover, the peripherally inserted central catheter-PORT is a safe vascular device for chemotherapy administration that achieves similar clinical outcomes to traditional long-term vascular access devices<sup>16</sup>.

Despite port-a-cath catheters presenting a lower risk of complications when compared to those of short-stay catheters, the safety of the technique does not entirely eliminate the occurrence of complications, which can cause an increase in morbidity and mortality of patients with a clinical condition already impaired by the underlying disease and hospital costs<sup>18</sup>. Among the known complications that culminate in the removal of the port-a-cath catheter are the infectious complications, with emphasis on store infections and bloodstream infection (BSI), and non-infectious, such as deep vein thrombosis (DVT), malfunction, reservoir rotation, reservoir extrusion, catheter embolization, and even material failures<sup>19</sup>. In the present study, regarding complications, there were cases of removal due to problems related to device exposure (4.7%), and catheter obstruction (7.0%), with catheter infection (27.9%) being the most prevalent.

Access and flushing with heparin at regular intervals are

essential to maintain function and minimize complications such as thrombosis and infection. However, little is known about the appropriate flushing interval for CVC-TI. Manufacturers recommend flushing every four weeks. The European Society of Medical Oncology (ESMO) guidelines also recommend access with normal saline and flushing with heparin every four weeks, preventing catheter occlusion and minimizing the risk of catheter-associated infection<sup>4,15</sup>. Access and heparin flushing is considered the most critical interventions to maintain catheter patency<sup>4</sup>.

The major limitation of this study is its retrospective nature, which limits a more accurate investigation of the determining factors for early loss of port-a-cath catheters. However, this study exposes essential risk factors for the loss of these devices, allowing the structuring of preventive clinical conduct for the risk groups identified in this study. Moreover, cohort studies, preferably prospective, are needed to evaluate the influence of different chemotherapy regimens on the loss of long-term catheters.

## CONCLUSION

In the present study, the rate of port-a-cath catheter loss was less than 40%, and infection was the most commonly described reason. Female gender and systemic treatment for breast cancer proved to be the most critical risk factors for the reduced longevity of this device.

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