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Sociodemographic, clinical and survival profile of adult metastatic patients

Perfil sociodemográfico, clínico e de sobrevida de pacientes adultos metastáticos

Perfil sociodemográfico, clínico y de supervivencia de pacientes adultos metastáticos

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ABSTRACT

Objective: To characterize the sociodemographic, clinical and survival profile of adult metastatic patients.

Method: Retrospective cross-sectional study, with secondary data from an oncology care unit, analyzed using logistic regression, Chi-Square test and Fisher's exact test, Kaplan-Meier and Log-Rank tests.

Results: From the 678 patients, male gender, mean age 59.54 years old and low education level prevailed. The mean time between diagnosis and initiation of treatment was 89.50 days (± 58.87). Increased risk of primary cancer in the digestive tract (OR 1.42). Prevalence of adenocarcinoma (OR 1.53) and metastasis to bone (OR 2.59), lymph nodes (OR 1.75), liver and peritoneum (OR 1.42). The mean overall survival was 4.16 months and a median of 3.0 months.

Conclusion: The main primary site was the digestive system, and the identification of metastases was predominantly unifocal liver in both genders. Overall patient survival was reduced by cancer progression.

Descriptors: Neoplasms. Neoplasm metastasis. Oncology nursing. Survival.

RESUMO

Objetivo: Caracterizar o perfil sociodemográfico, clínico e de sobrevida de pacientes adultos metastáticos.

Método: Estudo transversal retrospectivo, com dados secundários de uma unidade de assistência oncológica, analisados por: regressão logística, teste de Qui-Quadrado e testes exato de Fisher, Kaplan-Meier e Log-Rank.

Resultados: Dos 678 pacientes, prevaleceu o sexo masculino, a idade média 59,54 anos e a baixa escolaridade. A média entre o diagnóstico e o início de tratamento foi 89,50 dias (± 58,87). Maior risco de câncer primário no aparelho digestivo (OR 1,42). Prevalência do adenocarcinoma (OR 1,53) e metástase para o osso (OR 2,59), linfonodos (OR 1,75), fígado e peritônio (OR 1,42). A média de sobrevida global foi de 4,16meses e mediana de 3,0 meses.

Conclusão: O principal sítio primário foi o aparelho digestivo e a identificação das metástases foi prevalentemente hepática unifocal em ambos os sexos. A sobrevida global dos pacientes foi reduzida pelo avanço do câncer.

Descritores: Neoplasias. Metástase neoplásica. Enfermagem oncológica. Sobrevida.

RESUMEN

Objetivo: Caracterizar el perfil sociodemográfico, clínico y de supervivencia de pacientes adultos metastáticos.

Método: Estudio transversal retrospectivo, con datos secundarios de una unidad de atención oncológica, analizados por: regresión logística, prueba de Chi-Cuadrado y prueba exacta de Fisher, Kaplan-Meier y Log-Rank.

Resultados: De los 678 pacientes predominó el sexo masculino, edad media 59,54 años y baja escolaridad. El promedio entre el diagnóstico y el inicio del tratamiento fue de 89,50 días (± 58,87). Mayor riesgo de cáncer primario en el tracto digestivo (OR 1,42). Prevalencia de adenocarcinoma (OR 1,53) y metástasis en hueso (OR 2,59), ganglios linfáticos (OR 1,75), hígado y peritoneo (OR 1,42). La supervivencia global media fue de 4,16 meses y una mediana de 3,0 meses.

Conclusión: El principal sitio primario fue el tracto digestivo y la identificación de metástasis fue predominantemente hepática unifocal en ambos sexos. La supervivencia general del paciente se redujo por la progresión del cáncer.

Descriptores: Neoplasias. Metástasis de la neoplasia. Enfermería oncológica. Sobrevida.

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INTRODUCTION

Cancer is a serious public health issue and is characterized by the uncontrolled growth of cells[1]. Its ability for invasion and spread to nearby or distant organs is called metastasis, which can be unifocal or multifocal[1,2], and this characteristic is the main cause of death among oncology patients[3].

In 2020, there were 19.3 million new cases of cancer worldwide. In Brazil, for each year of the 2023-2025 triennium, it is estimated that there will be around 704 thousand new cases of cancer, the most frequent types of which will be breast cancer (10.5%) in women and prostate cancer (10.2%) in men[4].

Epidemiological data on metastatic patterns are scarce, studies generally focus on metastatic tumors from a single primary tumor, on clinical trials of new target molecules, but do not address the profile of metastases[5].

Furthermore, cancer records rarely document metastases[5]. A Swedish study, with 179,581 patients, described the metastatic pathways to 12 sites. In men, colorectal cancer was the main source of lung, peritoneal and liver metastases. Among women, breast cancer was the dominant origin of most metastatic sites, except for the peritoneum, which had the ovary as its primary site[5].

Metastasis is an aggressive condition that limits the good prognosis and the evolution of anticancer treatment[6]. This condition generates a devastating burden of physical, emotional and psychological symptoms that negatively impact individuals' quality of life. Such damage leads to recurrent hospitalization due to worsening symptoms and/or an active death process, demanding specific care and more time from nursing professionals, and also generating an increase in costs for healthcare institutions[7].

According to Brazilian studies, metastatic patients have a significant reduction in overall survival time, characterized as the time that the individual remains alive after their diagnosis[6,8].

Clinical trials have evolved extensively to translate the biological factors of cancer and its vulnerabilities into therapeutic opportunities[9], however metastasis remains largely incurable due to its high phenotypic complexity in the formation cascade[10].

Therefore, epidemiologically, it is important to know the main areas of metastasis and its correlation with the type of primary cancer, so that there is better tracking of metastatic lesions and planning of early detection actions[8]. In this sense, this study aims to characterize the sociodemographic, clinical and survival profile of metastatic adult patients.

METHOD

This is a retrospective cross-sectional study that complied with the recommendations from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [11]. The study was conducted in a High Complexity Oncology Care Unit (*Unidade de Assistência de Alta Complexidade em Oncologia* – UNACON) intended for adult patients, linked to a university hospital of the Unified Health System (*Sistema Único de Saúde* – SUS), located in Belém, Pará, Brazil. This unit is intended to provide services to the adult population and offers oncological surgery, chemotherapy, radiotherapy, and palliative care services.

Data collection was conducted in October 2020, by two researchers, in digital media, with double checking, using secondary data from the institution's Hospital Cancer Registry (*Sistema de informação Registro Hospitalar de Câncer* – SisRHC) information system, specifically through the Tumor Registration Form (*Ficha de Registro de Tumor* – FRT), standardized by the José Alencar Gomes da Silva National Cancer Institute (INCA).

Data from adult oncology patients were included, with metastases confirmed at the time of cancer diagnosis or during annual follow-up, for five years, regardless of the primary site, treated from January 2012 to December 2019 (covering the first seven years of service). Patient information with incomplete identification data was excluded. At SisRHC, data from 4,397 oncology patients were identified. Of these, 678 met the established criteria. Exclusions were due to the absence of metastasis (n= 3,716) and incomplete identification data (n=03), without further losses.

In the FRT, the following variables were collected: sociodemographic data (gender, age and education level), categorization of the age group into over and under 60 years and clinical characteristics (tumor primary site, histological type of the primary tumor, date of diagnosis, first treatment performed at UNACON, date of first treatment, distant metastasis site, disease status at the end of the first treatment and death from cancer).

The collected data were tabulated using Microsoft Excel® software version 2019 and compiled for analysis in the statistical software Statistical Package for Social Sciences (SPSS) version 25.0. A descriptive analysis of sociodemographic and clinical characteristics was conducted using measures of central tendency (mean) and dispersion (standard deviation), after preliminary test of data normality. Categorical variables were described by frequencies and percentages. Logistic regression analyses were performed to estimate Odds Ratios (OR) and their 95% confidence intervals (CI).

In these analyses, the independent variables were gender and age group, and the dependent variables were clinical-pathological data (topography, histological type, metastasis, and survival).

The Chi-Square test and Fisher's exact test were used to investigate the relationship between the occurrence of primary cancer and metastasis sites, to identify preferential sites. To represent the relationship better graphically between primary cancer and the preference of organs to metastasize, a Circos Plot was performed using the Circlize package. Positive associations were represented in blue, and the negative ones, in red.

The final tests and charts were conducted using the R statistical environment (version 4.0.2). Survival curves were calculated based on the date of first diagnosis and date of death using the Kaplan-Meier method, and the Log-Rank test was used for comparisons. For all statistical tests, probability (p-value) was considered significant when ≤ 0.05.

All ethical precepts that guide research involving human beings, established in Resolution No. 466/2012 of the National Health Council, were followed.

The research was approved by the Research Ethics Committee (REC) of the *Hospital Universitário João de Barros Barreto*, under Opinion No.3,910,555, in March 2020. Since this involved secondary data collection, the REC granted permission to waive the requirement for the Informed Consent Form (ICF) and instead presented the Data Use Commitment Form (DUCF).

RESULTS

Among the 678 metastatic patients, 347 (51.2%) were male and 331 (48.8%) were female, with a mean age of 59.54 (±14.213). Regarding education level, 80 (11.80%) were illiterate; 425 (62.68%) had primary education; 155 (22.86%), high school; and only 18 (2.65%) had higher education.

Regarding oncological treatment (chemotherapy, radiotherapy and/or surgery), 485 (71.5%) underwent these therapeutic modalities and 193 (28.5%) were referred to exclusive palliative care.

The mean time between diagnosis and the start of treatment for patients was 89.50 days (± 58.87), with 246 (36.3%) taking more than 180 days; 297 (43.8%), between 61 and 180 days; followed by 135 (19.9%), from 30 to 60 days.

From the total sample, 507 (74.8%) patients presented unifocal metastasis; 163 (24%), multifocal; and 8 (1.2%), without identification regarding the type of metastasis. When an active search for patients followed up over a 5-year period was made, 454 (67%) of them had died and 224 (33%) remained alive.

Table 1 describes the Odds Ratio (OR) of the association between gender and clinical-pathological data of metastatic patients using the logistic regression model.

Table 2 describes the Odds Ratio (OR) of the association between age group (≤60 and >60 years) and topography of the primary cancer of metastatic patients, using the logistic regression model. Considering the age group >60 years as the reference category, individuals >60 years had a 2.76 higher risk of developing urological cancer (p: <0.001; CI: 1.588 – 4.815) than those ≤60 years old.

The Circos Plot graph (Figure 1) shows a positive association between primary cancer and metastatic sites, highlighting the blue coloring for the most frequent events, such as (I) digestive system cancer (AD) with metastasis to the digestive organs, with emphasis on liver metastasis; (II) head and neck cancer (CEP) for nearby locations and lymph nodes; (III) gynecological cancer (GIN) with metastasis to the bladder, rectum and peritoneum; (IV) breast cancer (MA) with metastasis to the brain, bone and lung; (V) mediastinal and pleural cancer (MED and PLE) with metastasis to the lung; (VI) skin cancer (PEL – Melanoma) with metastasis to the lung; (VII) lung cancer (PUL) with metastasis to the brain, bone and pleura; and (VIII) urological cancer (URO) with metastasis to the bone. Fisher's exact test identified a p-value = 2.2 e-16.

Figure 2 describes the overall survival curve of metastatic patients, in which was observed a mean overall survival prevalence of 4.166 months and a median of 3.0 months.

Figure 3 describes the overall survival curve for the variable gender and most prevalent metastasis site, estimated using the Kaplan-Mie method and Log-Rank test. Regarding the variable gender and survival, the median for both genders was 3 months. The Log-Rank test did not show a significant difference between the genders (p-value = 0.678).

In the survival curve according to the most prevalent metastasis sites (liver, bone, peritoneum and other sites), the curves indicated lower values for patients who had metastasis to the liver. The median survival for liver metastasis was 2 months; for the peritoneum, it was 4 months; and for the bone and other sites, it was 3 months. The curves indicated that patients who had metastases to the liver had a higher risk of death, however statistical analyses did not show any statistical difference. Log-Rank test (p-value =0.118).

Table 1 – Logistic regression analysis of the association between gender and clinical data of metastatic patients treated at the High Complexity Oncology Care Unit. Belém, Pará, Brazil, 2012-2019

Clinical data	Gender		p-value	OddsRatio	95% CI
	Female n (%)	Male n (%)			
Cancer topography					
Digestive System	138 (66.7)	197 (58.6)	0.001	1.428	1.148 –1.775
Lung	52 (25.1)	62 (18.5)	0.350	1.192	0.825 – 1.724
Head and neck	8 (3.8)	13 (3.9)	0.280	1.625	0.674 – 3.921
Urological	5 (2.4)	59 (17.6)	<0.001	11.800	4.736 – 29.400
Skin	3 (1.5)	3 (0.8)	1	1	0.202 – 4.955
Mediastinum	1 (0.5)	2 (0.6)	0.571	2	0.181–22.056
Histological type					
Carcinoma	232 (71)	198 (58)	0.101	0.853	0.706 – 1.032
Adenocarcinoma	91 (27.8)	140 (41)	0.001	1.538	1.182 – 2.003
Melanoma	4 (1.2)	4 (1.1)	1	1	0.250 – 3.998
Metastasis					
Liver	72 (22.1)	101 (29.4)	0.028	1.403	1.037 – 1.898
Peritoneum	46 (14.1)	36 (10.5)	0.271	0.783	0.506 – 1.210
Lung	33 (10.1)	17 (4.9)	0.026	0.515	0.287 – 0.925
Bone	27 (8.3)	70 (20.3)	< 0.001	2.593	1.663 – 4.042
Pleura	19 (5.8)	16 (4.7)	0.613	0.842	0.433 – 1.638
Brain	16 (4.9)	2 (0.6)	0.006	0.125	0.029 – 0.544
Liver and Peritoneum	14 (4.3)	20 (5.8)	0.306	1.429	0.722 – 2.828
Lymph Nodes	12 (3.7)	21 (6.1)	0.122	1.750	0.861 – 3.557
Liver and Lung	12 (3.7)	6 (1.7)	0.166	0.500	0.188 – 1.332
Liver and Bone	12 (3.7)	4 (1.2)	0.057	0.333	0.108 – 1.034
Others	63 (19.3)	51 (14.8)	0.262	0.810	0.560 – 1.171

Source: Prepared by the authors, 2021.
*CI – 95% confidence interval (Odds Ratio scale). The reference category is male. Unspecified data were excluded for statistical analysis.

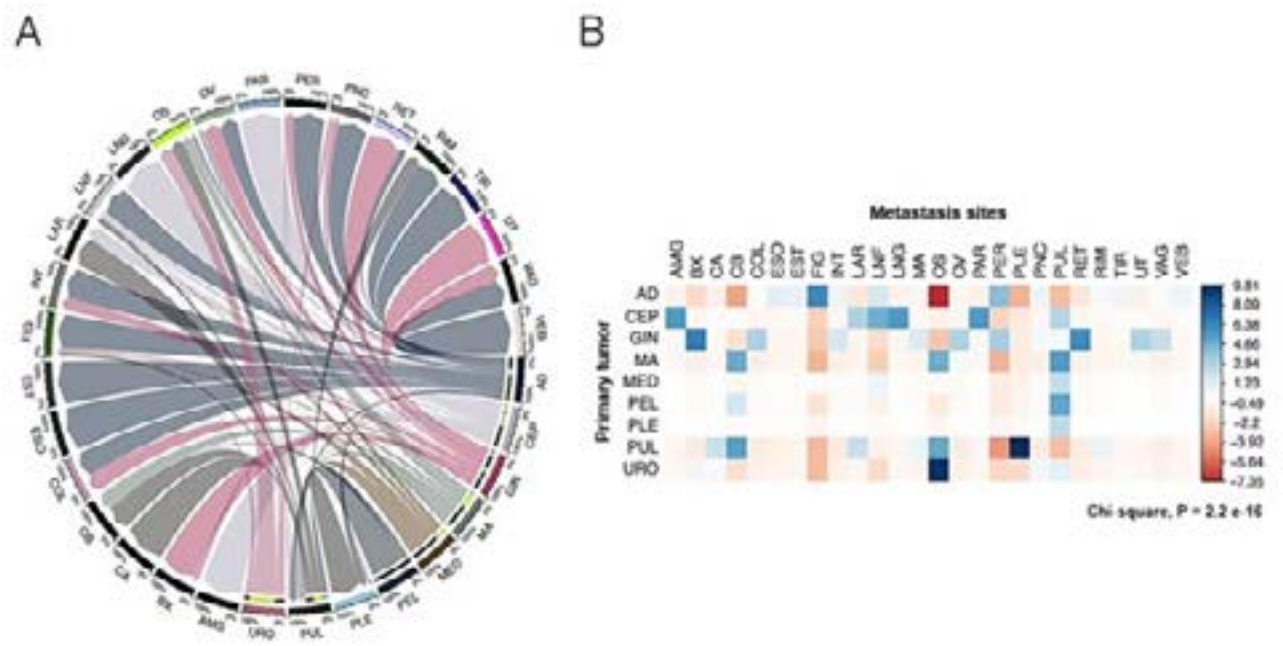

Figure 1 – Relationship between topography of the primary cancer and the most frequent site of metastasis in metastatic patients treated at the High Complexity Oncology Care Unit. Belém, Pará, Brazil, 2012-2019

Source: Prepared by the authors, 2021.

Legend: Primary Tumor: AD – Digestive System; CEP – Head and Neck; GIN – Gynecological; MA- Breast; MED – Mediastinum; PEL – Skin; PLE – Pleura; PUL – Lung; URO – Urological. Metastasis Sites: AMG – Tonsil; BX – Bladder; CA – Anal Canal; CB – Brain; COL – Uterine Cervix; ESO – Esophagus; EST – Stomach; FIG – Liver; INT – Intestine; LAR – Larynx; LINF – Lymph nodes; LING – Tongue; MA – Breast; OS – Bone; OV – Ovary; PAR – Parathyroid; PNC – Pancreas; PER – Peritoneum; PLE – Pleura; PUL – Lung; RET – Rectum; TIR – Thyroid; UT – Uterus; VAG – Vagina; VEB – Gallbladder.

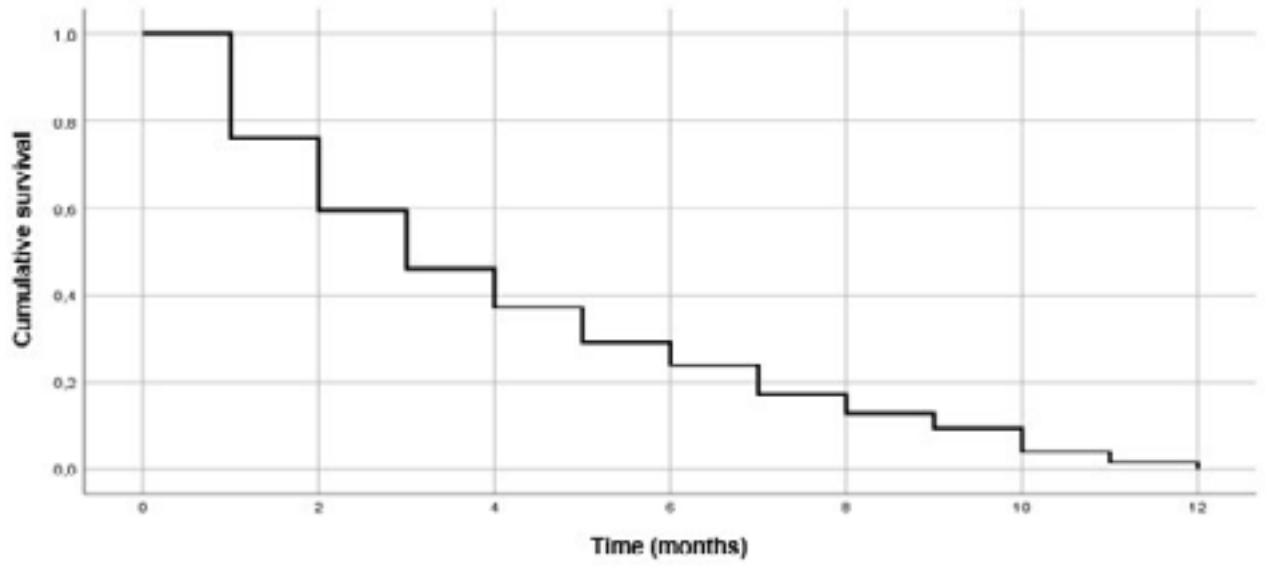

Figure 2 – Overall survival curve of metastatic patients treated at the High Complexity Oncology Care Unit. Belém, Pará, Brazil, 2012-2019

Source: Prepared by the authors, 2020.

Table 2 – Logistic regression analysis of the association between age groups (≤60 and >60 years) and tumor topography of metastatic patients treated at the High Complexity Oncology Care Unit. Belém, Pará, Brazil, 2012-2019

Clinical data	Age group (years)		p-value	OddsRatio	95% CI
	≤60 n (%)	>60 n (%)			
Cancer topography					
Digestive system	169 (53.3)	166 (50.5)	0.870	0.982	0.793 – 1.217
Breast	34 (10.7)	24 (7.3)	0.191	0.706	0.419 – 1.190
Lung	55 (17.3)	59 (17.9)	0.708	1.073	0.743 – 1.549
Gynecological	33 (10.4)	21 (6.4)	0.105	0.636	0.368 – 1.100
Urological	17 (5.4)	47 (14.3)	< 0.001	2.765	1.588 – 4.815
Head and neck	9 (2.8)	12 (3.5)	0.514	1.333	0.562 – 3.164

Source: Prepared by the authors, 2021.
*95% CI – confidence interval (OddsRatio scale). The reference category is the age group >60 years old. Unspecified data were excluded for statistical analysis.

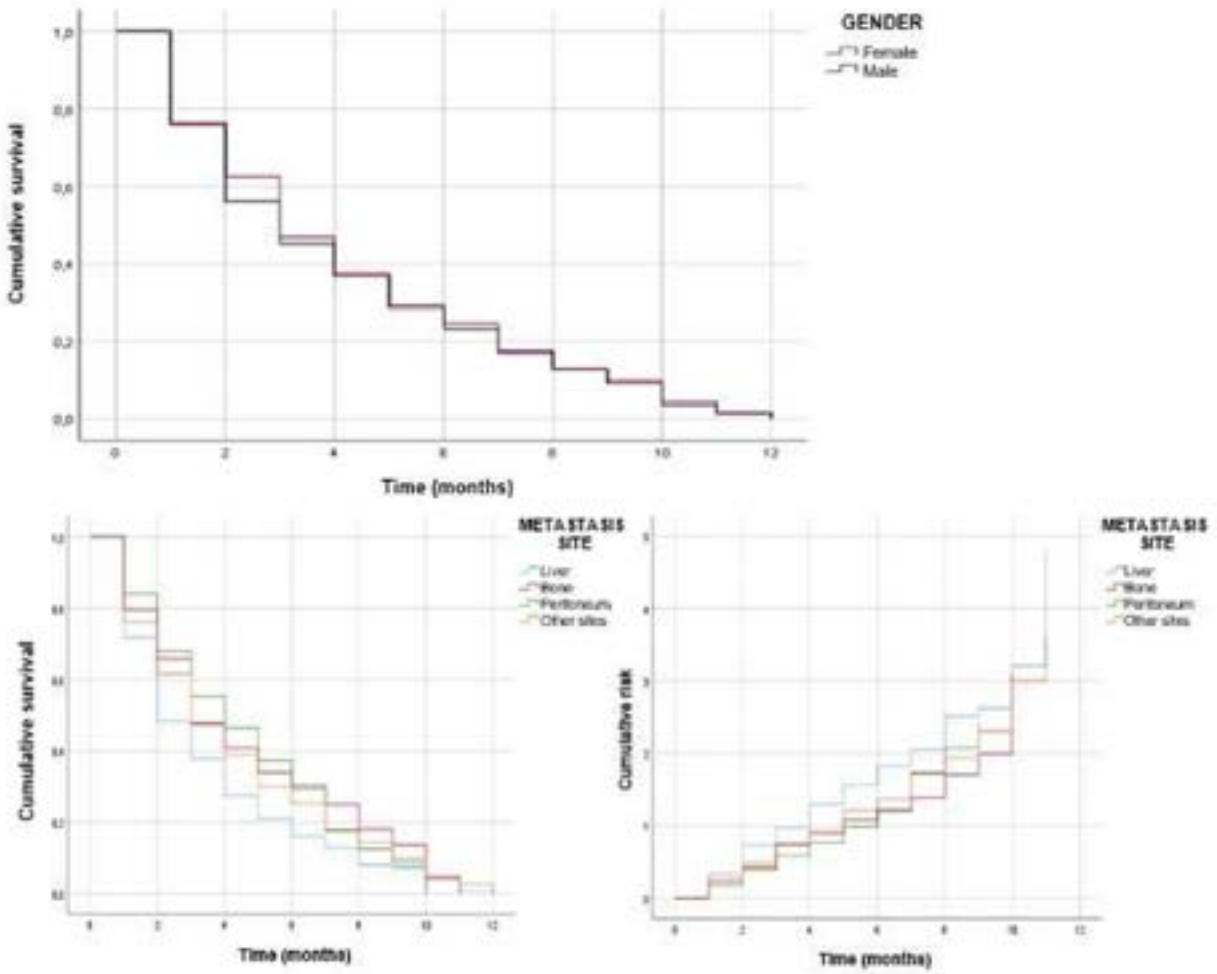

Figure 3 – Survival curve for the variable gender and most prevalent metastasis site, estimated using the Kaplan-Mie method and Log-Rank test.
Source: Prepared by the authors, 2020.

DISCUSSION

The study showed a prevalence of males, with a mean age of 59.54 years. This corresponds to the Brazilian cancer estimate for 2023, which indicates a 17% higher incidence of cancer in men than in women, excluding non-melanoma skin cancer[4]. The findings also corroborate a German study[12] with 1,008 metastatic patients, in which 57% of patients were male, and the mean age was 64 years.

The observation of individuals aged over 60 years confirms the justification that the increase in life expectancy is an influential factor in maintaining the cancer incidence and mortality, since physiological changes occur resulting from the aging process and the decline in organic functions[13].

Here it was observed that the prevalence of patients with a lower education level became a worrying fact due to the difficulty in understanding the various orientation regarding healthcare and specific treatments, also associating this lack of understanding with worse standards of health care, in addition to relate it to cancer diagnoses at more advanced stages and higher mortality[14,15]. This reinforces the need for continuous care until the end of life, especially for the most vulnerable population[16].

Another important element was the limited access to Health Care Networks (HCN), which directly reflects the longer time between diagnosis and the start of treatment, as well as diagnosis at an advanced stage. The findings were in line with a Brazilian study [17] conducted in a public hospital, with 222 cancer patients, in which a time >60 days was identified for the start of treatment for 46.9% of participants.

Shortened times to treatment can lead to increased survival and reduced mortality. However, if the period between the initial consultation and treatment is prolonged, patients may experience tumor progression and clinical staging, which impacts the therapeutic schedule, negatively affecting the prognosis[18].

Regarding the topography of primary cancer, men had greater risk of developing cancers in the digestive system, lung cancer, head and neck cancer and urological cancer, with adenocarcinoma being the most significant histological type, in line with literature[19].

According to the 2020 global statistics on cancer, the most common types of cancer in men are lung, prostate, colon and rectum, stomach and liver cancer[1]. Additionally, for 2023 national estimates, the most frequent cancers in men, except for non-melanoma skin cancer, will be prostate, colon and rectum, lung, stomach, and oral cavity.

Urological cancer stood out, which was 11,800 times more likely to occur in males, aged <60 years (OR= 2.765), and can be characterized by the high rate of prostate cancer, which stood out as the second most prevalent cancer in men, second only to non-melanoma skin cancer[20]. Furthermore, regarding risk factors for prostate cancer, age presented a certain consensus in previously conducted studies, with a prevalence among the elderly[21].

A research that characterized the profile of 124 adult cancer patients undergoing palliative therapy in a reference hospital for oncology care in Paraná identified an incidence of males, with metastatic sites in the lymph nodes (48.4%), lung (45.2%), liver/pancreas (26.6%), bone (41.1%) and brain (25.8%) as the most affected sites[21]. Another study conducted in a hospital in the north of Rio Grande do Sul evaluated the profile of 244 patients, with a predominance of males, and identified the presence of metastasis in 53.7% (n=131), with an incidence for the bone, 15.2%; liver, 14.3%; and lung, 11.1%[6].

When the most prevalent metastasis sites were associated to the topography of the primary cancer, there was a frequency of primary cancer of the digestive system, with metastasis to the digestive organs. When performing Fisher's exact test, a value of $p = 2.2$ e-16 was identified, that is, primary cancers have a higher prevalence of metastasizing to certain specific organs[22].

The liver, due to its high vascularization, is the organ most affected remotely, especially from cancers of the gastrointestinal tract, remaining an important barrier for successful treatment, as it directly affects the prognosis, causing, on average, 2/3 of deaths related to metastasis[23]. This information justifies the findings of this study, since there was a prevalence of primary cancer of the digestive system and consequently, a higher prevalence of metastasis to this organ.

On the other hand, breast cancer exhibits a distinct metastatic pattern, but it can also show a tendency to metastasize to the liver, however the most common sites are bone, lung and brain, similar to the data from this study[24].

Bone is the third most common site of metastasis for a wide range of solid tumors, with 70% of patients with prostate and breast cancer showing bone metastasis[23]. Remarkably, the lung, liver and bone represent the most common sites of distal metastasis for all types of cancer[25].

A Korean study evaluated a national database with 1,849 patients diagnosed with bone metastases during or after diagnosis of primary cancer, in which the most common primary sites were the breast (18.8%), prostate (17.5%) and the lung (13.7%)[26].

The German study already mentioned evaluated the patterns of metastatic progression in 16 main types of cancer and identified that breast cancer tends to metastasize to the liver (80%), bones (79%), non-regional lymph nodes (60%), lung (54%) and pleura (52%), while prostate cancer is predominantly associated with metastatic spread to the

bone (91%), and, at very low frequencies (<50%), to others anatomical sites. Lung cancer was frequently associated with metastatic spread to the distal lymph nodes (61%), liver (60%), pleura (49%), and bone (47%)[12].

In this context, it is evident that primary cancer has specific predilection sites for tumor spread, which is probably attributed to the anatomical structure of the vessels and blood flow. This logic suggests that, in general, the prevalence of metastases to an organ is governed by two parameters: the frequency with which metastasizing cells are physically attached to an organ and the ease with which they can adapt to the microenvironment of that organ, colonizing it[12].

Regarding the overall survival curve, it was observed that one of the factors that strongly influenced survival was the disease staging at the time of diagnosis[8], characterizing low survival rate in the study, since all patients had metastasis and more than half progressed to death.

A study conducted in the INCA database evaluated the survival of 165 patients with malignant pleural effusion secondary to cancer and identified a survival rate of 21 months for ovarian cancer, 6 months for breast cancer and 4 months for lung cancer[27]. According to an international research, the median survival for patients with liver, lung, bone and brain metastases was 38,6, 9 and 2 months, respectively[28], demonstrating that the mean survival in the present study was lower than what has been found in national and international literature.

This research may contribute to the generation of knowledge about the profile of individuals with metastasis, highlighting the need for investment in more in-depth studies on the subject, with the purpose of understanding this reality and enhancing the quality of management of these individuals with this clinical diagnosis.

As a contribution to oncology nursing, this study may support nursing care, since nurses are the professionals who spend the most time in contact with patients, especially when hospitalized, playing an important role in comprehensive care, supporting action planning for comprehensive care, thus being able to look for early clinical signs of metastasis in patients with primary cancer, allowing for accurate diagnosis and treatment of the disease.

The limitation of the study was the use of secondary data, which restricted the analysis of variables due to the absence of information.

CONCLUSION

The majority of patients were male, with a mean age of 59.54 years. The main primary site was the digestive system and the identification of metastases was predominantly unifocal hepatic in both genders. The overall survival of patients was reduced by the progression of the cancer, with no significant difference between the genders, with a median of 3 months. However, survival for liver metastasis was 2 months; and for the peritoneum, it was 4 months.

These findings have contributed to understand metastatic patterns according to the primary site. Furthermore, they favor the structuring of services, resource management and planning for more appropriate management of oncology patients. Finally, this study highlights the need for the creation of a database for metastatic diseases.

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