

## Bone metastases and skeleton-related events in people subjected to radiotherapy: characterization and survival

*Metástases ósseas e eventos relacionados ao esqueleto em pessoas submetidas a radioterapia: caracterização e sobrevivência*

*Metástasis óseas y eventos relacionados con el esqueleto en personas sometidas a radioterapia: caracterización y sobrevida*

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### Abstract

**Objective:** To characterize bone metastases and skeleton-related events associating them with survival time in people subjected to radiotherapy. **Methods:** This is a retrospective, descriptive and cross-sectional study. It was conducted in a High-Complexity Oncology Center with medical records of people diagnosed with bone metastases. **Results:** A total of 122 medical records were analyzed and most of the patients were female (59.02%), with a mean age of 58.86 years old ( $\pm 14.54$ ). The most incident primary sites were breast (43.44%) and prostate (30.33%). The mean number of bones or bone groups affected was 3.09 ( $\pm 2.14$ ). The spine was the most affected area (80.33%). This region was also the most irradiated in the radiotherapy treatments (55.74%). Most of the patients (70.49%) underwent 10 radiotherapy sessions, with a mean of 9.05 ( $\pm 2.89$ ). With regard to the skeleton-related events, 100% of the patients reported pain, 32.78% suffered pathological fractures with a survival time of 32.53 months, and 10.65% presented spine compression with a mean survival of 41.52 months. **Conclusion:** Bone metastases were more common in the spine. All the patients presented bone pain records, and pathological fractures were associated with lower survival among the individuals.

**Descriptors:** Neoplasm Metastasis; Bone and Bones; Radiotherapy; Nursing.

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### Whats is already known on this?

The changes caused by bone metastases result in complications concerning Skeleton-Related Events such as pain, pathological fractures and spine compression. These complications exert a significant impact on the patients' survival.

### What this study adds?

People with bone metastases subjected to radiotherapy had the spine as the most affected area. Bone pain, pathological fractures (associated with lower survival) and spine compression were described.



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### Resumo

**Objetivo:** Caracterizar as metástases ósseas e os eventos relacionados ao esqueleto associando-os ao tempo de sobrevida em pessoas submetidas a radioterapia. **Métodos:** Trata-se de um estudo retrospectivo, descritivo e transversal. Foi realizado em um Centro de Alta Complexidade em Oncologia, com prontuários de pessoas diagnosticadas com metástases ósseas. **Resultados:** Foram analisados 122 prontuários, a maioria dos pacientes era do sexo feminino (59,02%), com média de idade de 58,86 anos ( $\pm 14,54$ ). Os sítios primários mais incidentes foram a mama (43,44%) e a próstata (30,33%). O número de osso ou grupo de ossos atingidos foi, em média, de 3,09 ( $\pm 2,14$ ). A coluna vertebral foi a mais acometida (80,33%). Esta região também foi a mais irradiada no tratamento radioterápico (55,74%). A maioria dos pacientes recebeu 10 sessões de radioterapia (70,49%), em média 9,05 ( $\pm 2,89$ ). Quanto aos eventos relacionados ao esqueleto, 100% dos pacientes apresentavam registros de dor óssea, 32,78% sofreram fratura patológica, com tempo de sobrevida de 32,53 meses, e 10,65% apresentaram compressão medular, com sobrevida média de 41,52 meses. **Conclusão:** As metástases ósseas foram mais comuns na coluna vertebral. Todos os pacientes apresentaram registros de dor óssea, e a fratura patológica foi associada à menor sobrevida dos indivíduos.

**Descritores:** Metástase Neoplásica; Osso e Ossos; Radioterapia; Enfermagem.

### Resumen

**Objetivo:** Caracterizar las metástasis óseas y los eventos relacionados con el esqueleto asociándolos al tiempo de sobrevida en personas sometidas a radioterapia. **Métodos:** Estudio retrospectivo, descriptivo y transversal. Se realizó en un Centro de Alta Complejidad en Oncología con historias clínicas de personas diagnosticadas con metástasis óseas. **Resultados:** Se analizaron 122 historias clínicas; la mayoría de los pacientes era del sexo femenino (59,02%) y la media de edad fue 58,86 años ( $\pm 14,54$ ). Los sitios primarios con mayor incidencia fueron las mamas (43,44%) y la próstata (30,33%). La cantidad media de huesos o grupos óseos afectados fue de 3,09 ( $\pm 2,14$ ). La columna vertebral fue el área más afectada (80,33%). Esta región también fue la más irradiada en el tratamiento de radioterapia (55,74%). La mayoría de los pacientes recibió 10 sesiones de radioterapia (70,49%), con una media de 9,05 ( $\pm 2,89$ ). En cuanto a los eventos relacionados con el esqueleto, el 100% de los pacientes presentaron registros de dolor en los huesos, el 32,78% sufrieron fracturas patológicas con 32,53 meses de tiempo de sobrevida, y el 10,65% presentó compresión medular con una sobrevida media de 41,52 meses. **Conclusión:** Las metástasis óseas fueron más comunes en la columna vertebral. Todos los pacientes presentaron registros de dolor en los huesos, y las fracturas patológicas estuvieron asociadas a menor sobrevida de los individuos.

**Descritores:** Metástasis de la Neoplasia; Hueso y Huesos; Radioterapia; Enfermería.

## INTRODUCTION

The invasion and dissemination capacity is a remarkable feature of cancer known as metastasis.<sup>(1)</sup> Bones are one of the most common target organs, especially in advanced cancer.<sup>(2-4)</sup> Bone metastasis occurs in 65-80% of the patients with prostate or breast cancer, in 40-50% of those with lung cancer, and in less than 10% of those with gastrointestinal cancer.<sup>(5)</sup> This phenomenon is the leading cause of death for more than 90% of the cancer patients.<sup>(1)</sup>

When they reach a bone, metastases can be classified as follows: 1) Osteolytic: when there is greater stimulus to osteoclast formation and activation intensifying bone destruction; 2) Osteoblastic: characterized by increased proliferation and differentiation of osteoblasts; and 3) Mixed: where there is an increase both in the lytic and blastic components.<sup>(3,4)</sup>

Changes in the bone microenvironment result in complications referred to as Skeleton-Related Events (SREs), including pain, pathological fractures, spine compression and hypercalcemia.<sup>(3,6)</sup> These complications exert a significant impact on cancer patients' survival and quality of life, increasing hospital costs and mortality risks.<sup>(7,8)</sup>

Radiotherapy is fundamental in the management of bone metastasis, primarily for palliative, analgesic or decompressive purposes, and should be performed as early as possible.<sup>(9)</sup> In this context, nurses provide patient education on the disease and interact with the multiprofessional team by coordinating the provision of optimal patient care.<sup>(6)</sup> They also play a vital role in the treatment plans for patients with bone metastasis by implementing interventions that prevent complications.<sup>(10)</sup>

In 2020 there were 19.3 million new cancer cases in the world. For the 2023-2025 triennium in Brazil, there is an estimation of nearly 704,000 new cancer cases, whose most common types will be breast (10.5%) in women and prostate (10.2%) in men.<sup>(11)</sup> These latter being very susceptible to metastases.<sup>(12)</sup>

Although bone metastasis is very common in the clinical practice, only one Brazilian study was conducted on the theme in the Southeast region, focusing on SREs and survival time, whose result related poor prognosis with a specific subtype of lung cancer.<sup>(13)</sup> Consequently, there is scarcity of studies showing the clinical epidemiological profile or manuals that dictate the appropriate/standardized clinical protocol,<sup>(14)</sup> thus making it difficult to define an assertive approach for nurses and proper monitoring of the patients.

Therefore, it is necessary to conduct research studies about the profile of these patients to boost intervention studies and/or for the development of future care protocols.

The main hypothesis to be tested is to analyze if pathological fractures, spine compression and the sociodemographic and clinical pathological data are associated with death. In order to test this hypothesis, the dependent variable considered was death and the independent variables corresponded to pathological fractures, spine compression and the sociodemographic and clinical pathological data.

Therefore, this research aimed at characterizing bone metastases and SREs (pain, pathological fractures and spine compression), associating them with survival time in people subjected to radiotherapy.

## METHODS

This is a retrospective, descriptive and cross-sectional study that followed the recommendations set forth in STrengthening the Reporting of OBservational studies in Epidemiology (STROBE).<sup>(15)</sup> It was conducted in a High-Complexity Oncology Center (*Centro de Alta Complexidade em Oncologia, CACON*) located in Belém-PA, Brazil.

The documentary research took place with the objective of outlining the profile of the patients treated in the health institution. The data sources consisted of handwritten medical records of patients with bone metastasis who underwent radiotherapy in the Radiotherapy Service from the beginning of its operation up to conception of the research project (from June 2016 to June 2021, respectively). A total of 408 patients classified as with bone metastasis were treated during this period.

The following parameters were considered for sample size calculation: 90% confidence level; 5% significance level; and a finite population of 408 patients, according to the Radiotherapy Service database. These data were calculated in Microsoft Excel, version 2019, resulting in 122 patients. 40% related to sample losses was added.

Access to sampling was processed by convenience, according to the availability of medical records in the Medical and Statistics File Department (*Departamento de Arquivo Médico e Estatística, DAME*). The collection procedure was conducted in a room reserved for this purpose.

The inclusion criteria applied corresponded to the medical records of patients with bone metastasis, regardless of gender, age or primary cancer site, and who concluded radiotherapy from June 2016 to June 2021, concomitantly or not with other cancer treatment in the hospital selected for the study. The exclusion criteria corresponded to medical records with unintelligible and/or incomplete identification data.

Data collection was conducted by applying a collection instrument comprised by six items: 1) The participants' characterization data (gender, age, schooling level, marital status and family income); 2) Personal disease history and treatment history (primary site, diagnosis date, life habits, comorbidities, chemotherapy treatment, hormone therapy and previous surgery); 3) Characterization of bone metastasis and radiotherapy (classification, diagnosis date, skeleton area affected, bone(s) affected, number of fractions, and dose per fraction); 4) Complementary treatment (use of bisphosphonates); 5) Skeleton-Related Events (bone pain: location, intensity, assessment scale used, improvement in pain after RT; pathological fractures: location, history of falls and when they occurred; spine compression: location, signs and symptoms, when it occurred and whether the patient underwent any surgical procedure); and 6) End of treatment (treatment conclusion, outcome, death and date of death).

It was necessary to create this instrument, as there was no validated tool encompassing the objectives of this study. Once created, it was evaluated by a focus group comprised by specialists (Radiotherapy nurses) to consider necessary adjustments.

The following classification was adopted regarding the number of bones or bone groups affected: axial skeleton (skull, jaw, spine, sternum, costal arches, sacrum and coccyx); appendicular skeleton (clavicle, scapula, humerus, ulna/radius, carpus/metacarpus/phalanges, ilium, femur, patella, tibia/fibula and tarsus/metatarsus/phalanges). This division respected the anatomical limits and sought to standardize the analysis. Only the bones affected were described in the results.<sup>(16)</sup>

Referring to the Skeleton-Related Events, the following were standardized: (1) Pain: date of the first evolution, recorded by a health professional (physician or nurse), with report of bone pain after the metastasis diagnosis; (2) Pathological fractures; and (3) Spine compression: date of the imaging test that confirmed the event, such as magnetic resonance imaging or computed tomography (recorded on the medical chart) and/or accurate description of the aforementioned test, made by a health professional. The

“hypercalcemia” event was not assessed because the hematological tests were not available in the medical records (only in the system), which precluded collecting this datum.

Data consolidation was performed by preparing a database in the Epi info program, version 7.3.2.1, which was subjected to double-checking to avoid errors while transcribing the information. Subsequently, the data were exported to Microsoft Excel 2019 spreadsheets.

The continuous variables were expressed as mean and Standard Deviation (SD), whereas the categorical ones, as absolute numbers and percentages. In order to calculate the prevalence rates corresponding to the Skeleton-Related Events (SREs) (pathological fractures and spine compression), the following formula was used: (Number of adverse events / Total number of medical records analyzed) x 100. The prevalence rate for pain was not evaluated, as it affected all the participants.

This study also analyzed the time interval in months between diagnosis of the underlying disease (confirmed by a histopathological test) and the metastasis diagnosis (confirmed by bone scintigraphy, magnetic resonance or computed tomography),<sup>(17)</sup> associated with the death outcome.

The statistical analyses were performed via the Python programming language, in the Jupyter Notebook platform. Kaplan Meier graphs were generated by using this tool, in order to analyze the impact of the events (pathological fractures and spine compression) on the patients' survival.

In addition, the Logistic Regression Test was used to assess dependence of the “death” variable on the “pathological fractures” and “spine compression” covariates. In order to measure the association between the “death” variable and other sociodemographic and clinical variables, the Chi-Square Test was used. In all the analyses, the significance level considered was  $p=0.05$ .

This study was developed according to the National Health Council (Conselho Nacional de Saúde, CNS) ethical precepts, observing Resolution No. 466 of December 12th, 2012. The Data Use Commitment Form (DUCF) was signed, ensuring physical integrity of the medical records and confidentiality of the data collected. This research was submitted to evaluation by the Research Ethics Committee, obtaining due approval under Opinion No. 5,338,142.

## RESULTS

A total of 174 medical records were analyzed, of which 122 were eligible and selected for the study, according to the inclusion criteria. Fifty-two were excluded. Of these, 42.31% due to lack of confirmed metastasis diagnoses, 30.76% for resenting incomplete data, and 26.93% because only radiotherapy planning was conducted.

Regarding the eligible cases, most of the patients were female (59.02%), with mean age of 58.86 (SD  $\pm 14.54$ ) years old. It was identified that 59.84% of the patients only had Complete Elementary School, that 55.74% were married, and that 73.77% earned family incomes of up to 1 minimum wage (Table 1).

In relation to the comorbidities, 12.30% had diabetes and 24.59% had hypertension. Concerning life habits, 32.79% of the patients were identified as drinkers and 39.34% as smokers. The primary cancer site was breast for 43.44% of the patients, followed by prostate for 30.33%. In relation to previous treatments, 59.02% of the patients underwent chemotherapy, 63.93% hormone therapy, and 60.66% were subjected to surgical procedures (Table 1).

Nearly 57.38% of the patients made use of bisphosphonates, including zoledronic acid (38.52%) and clodronic acid (11.48%), and 7.38% used both during their bone metastasis treatment (Table 1).

**Table 1.** Sociodemographic, clinical pathological and historical profile corresponding to the patients' treatments, correlated to death. Belém, Pará, Brazil, 2022.

Characteristics	Values	p-value*
<b>Gender - n (%)</b>		0.765
Male	50 (40.98)	
Female	72 (59.02)	
<b>Age - Mean (Min-Max) <math>\pm</math> SD</b>	58.86 (25-96) $\pm$ 14.54	0.921
<b>Schooling - n (%)</b>		0.339
Illiterate	13 (10.66)	
Elementary School	73 (59.84)	
High School	28 (22.95)	
Higher Education	8 (6.56)	

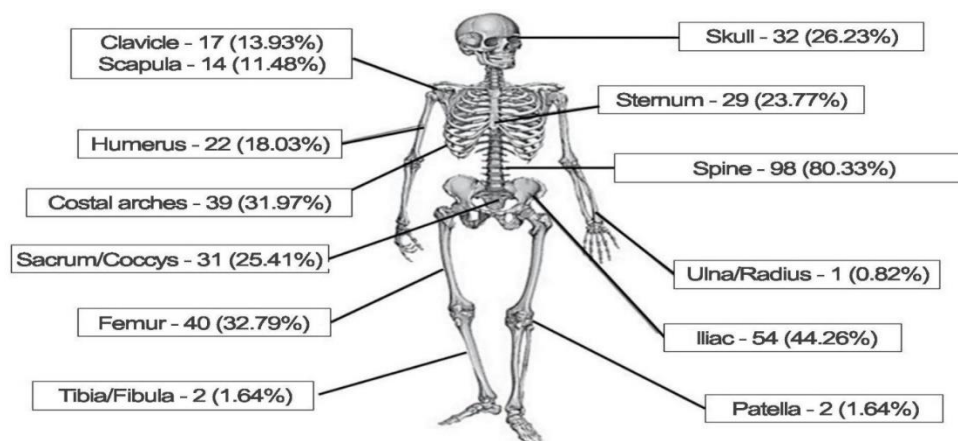
<b>Marital status - n (%)</b>		0.159
Single	38 (31.15)	
Married	68 (55.74)	
Divorced	6 (4.92)	
Widowed	10 (8.20)	
<b>Income (Minimum wages) - n (%)</b>		0.927
Up to 1	90 (73.77)	
Up to 2	32 (26.23)	
<b>Primary site affected - n (%)</b>		0.210
Breast	53 (43.44)	
Prostate	37 (30.33)	
Cervix	9 (7.38)	
Kidney	6 (4.92)	
Lung	3 (2.46)	
Colon/Rectum	4 (3.28)	
Others	10 (8.20)	
<b>Chemotherapy treatment - n (%)</b>		0.617
Not performed	46 (37.70)	
Previous	72 (59.02)	
Associated with RT	4 (3.28)	
<b>Hormone therapy - n (%)</b>		0.717
Yes	44 (36.07)	
No	78 (63.93)	
<b>Surgery - n (%)</b>		0.117
Yes	74 (60.66)	
No	48 (39.34)	
<b>Use of bisphosphonates</b>		0.581
None	52 (42.62)	
Clodronic acid	14 (11.48)	
Zoledronic acid	47 (38.52)	
Zoledronic acid and clodronic acid	9 (7.38)	
<b>Total - n (%)</b>	122 (100.00)	

Source: The authors, 2022.

\*Chi-Square Test

The time elapsed from the cancer diagnosis to bone metastasis confirmation varied from 0 to 198 months, with a mean of 20.55 (SD  $\pm$ 30.93), which obtained  $p=0.04$  when compared to the death outcome. Figure 1 shows the number of bones or bone groups affected by metastases. The spine stood out as the most affected site, accounting for 80.33% of the metastases.

**Figure 1.** Bones or bone groups affected by metastases, Belém, Pará, Brazil, 2022.



Source: Adapted from Oliveira *et al.* 2018<sup>(17)</sup>

Key: [-]: Number of patients affected; [()]: Percentages in relation to the total number of 122 patients were considered, as several bone areas were affected in most of the cases.

Referring to characterization of the metastases, 36.89% were classified as osteoblastic; and 56.56% of the metastases affected both skeletons (axial and appendicular). With regard to the bones irradiated, there was also predominance of the spine (55.74%). Most of the patients underwent 10 RT sessions (70.49%), with a mean of 9.05 (SD  $\pm$ 2.89) and a daily dose of 300 cGy (73.77%) (Table 2).

**Table 2.** Characterization of the bone metastases and of the radiotherapy treatment. Belém, Pará, Brazil, 2022.

Characteristics	Values
<b>Metastasis Classification - n (%)</b>	
Osteolytic	35 (28.69)
Osteoblastic	45 (36.89)
Both	29 (23.77)
Not described	13 (10.66)
<b>Skeleton affected - n (%)</b>	
Axial	41 (33.61)
Appendicular	12 (9.84)
Both	69 (56.56)
<b>Bones targeted by radiotherapy - n (%)</b>	
Skull	3 (2.46)
Spine	68 (55.74)
Spine and other bones	11 (9.02)
Clavicle/Scapula	3 (2.46)
Sternum	3 (2.46)
Costal arches	3 (2.46)
Humerus	5 (4.10)
Ilium	5 (4.10)
Ilium and sacrum	8 (6.56)
Sacrum	3 (2.46)
Femur	9 (7.38)
Patella	1 (0.82)
<b>Number of RT fractions</b>	
1	2 (1.64)
4	1 (0.82)
5	25 (20.49)
7	2 (1.64)
10	86 (70.49)
16	5 (4.10)
20	1 (0.82)
<b>Dose per fraction</b>	
250 cGy	6 (4.92)
300 cGy	90 (73.77)
400 cGy	26 (21.31)
<b>Total - n (%)</b>	<b>122 (100.00)</b>

Source: The authors, 2022.

Key: cGy: centiGrays

The “bone pain” SRE was evaluated and all 122 medical charts included reports of this event. In 68.85% of the cases, it was located in the spine. In 94.26% of the medical records, there was no description of pain intensity or of pain measuring scales. Improvement in pain was only recorded in 44.26% of the cases after the radiotherapy treatment (Table 3).

There were 40 cases of pathological fractures, with 32.78% prevalence. In 55% of the cases, the fractures were located in the spine. Only 7.5% of the patients had a history of falls. In 57.5% of the cases, the event took place before radiotherapy. Thirteen spine compression cases were identified, with 10.65% prevalence. With regard to the signs and symptoms, the most frequent was low back pain (84.62%). Asthenia was reported in 23.08% of the cases. Sensory loss/Paraplegia was only described in 15.38% of the events. In 53.85% of the cases, the need to perform a surgical procedure (laminectomy) for decompression was reported. It was observed that most of the events (84.62%) occurred before the radiotherapy treatment (Table 3).

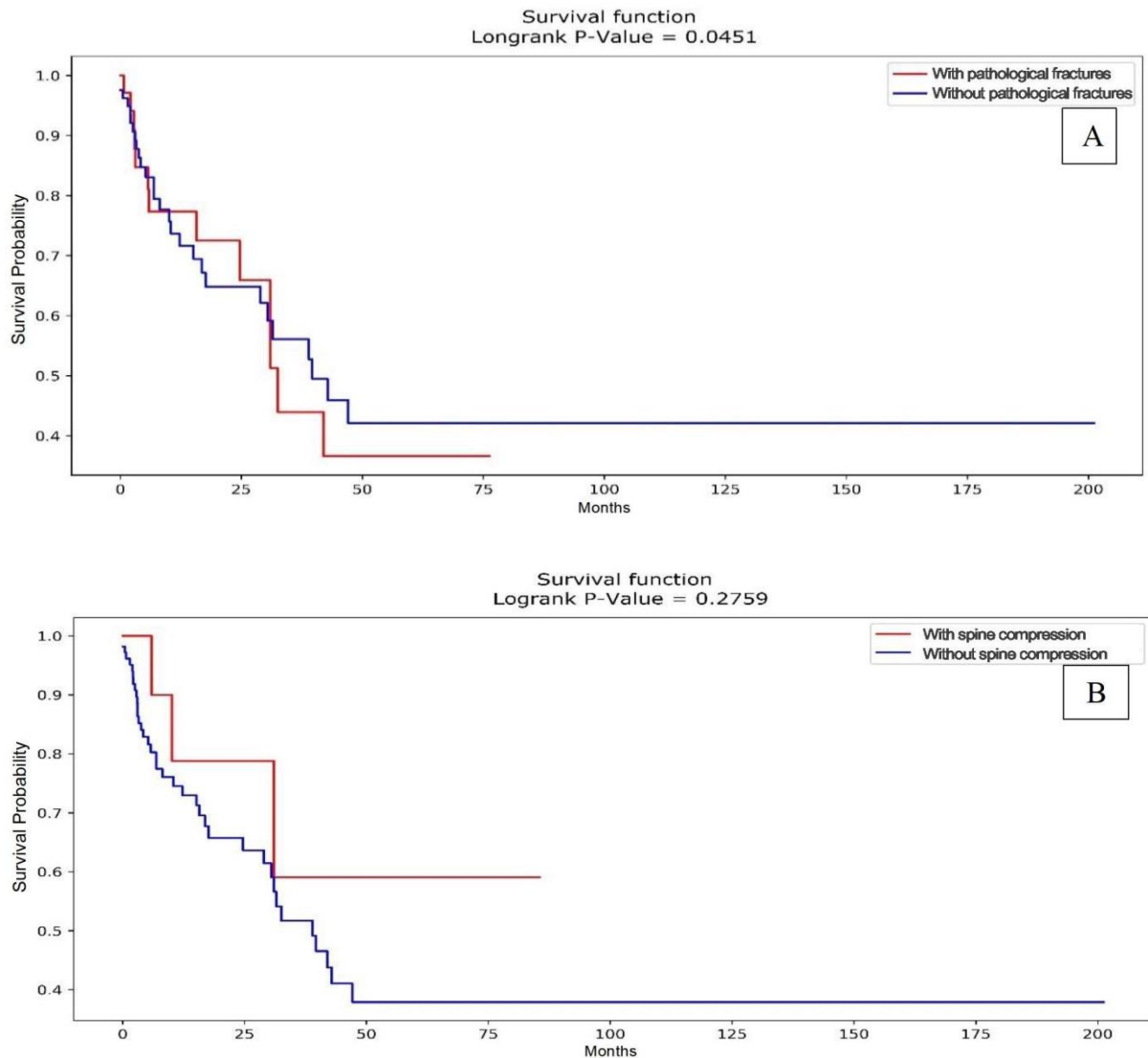
**Table 3.** Characterization of the Skeleton-Related Events: bone pain, pathological fractures and spine compression. Belém, Pará, Brazil, 2022.

Characteristics	Values - n (%)
<b>Bone pain</b>	
No	0 (0)
Yes	122 (100)
<b>Pain location</b>	
Skull	1 (0.82)
Spine	84 (68.85)
Spine and another region	6 (4.92)
Thorax	9 (7.38)
Humerus	4 (3.28)
Pelvis	5 (4.10)
Sacrum	3 (2.46)
Femur	10 (8.20)
<b>Pain intensity</b>	
Not described	115 (94.26)
Moderate	2 (1.64)
Strong	2 (1.64)
Intense	1 (0.82)
Accentuated	1 (0.82)
High	1 (0.82)
<b>Improvement in pain after RT</b>	
Yes	54 (44.26)
Not described	68 (55.74)
<b>Total - n (%)</b>	<b>122 (100.00)</b>
<b>Pathological fractures</b>	
<b>Fracture site</b>	
Spine	22 (55)
Humerus	6 (15)
Ilium	1 (2.5)
Femur	11 (27.5)
<b>History of falls</b>	
Yes	3 (7.5)
Not described	37 (92.5)
<b>The event took place</b>	
Before RT	23 (57.5)
During or after RT	2 (5)
After RT	15 (37.5)
<b>Total - n (%)</b>	<b>40 (100.00)</b>
<b>Spine compression</b>	
<b>Signs and symptoms</b>	
<b>Low back pain</b>	
Yes	11 (84.62)
No	2 (15.38)
<b>Asthenia</b>	
Yes	3 (23.08)
No	10 (76.92)
<b>Sensory loss/Paraplegia</b>	
Yes	2 (15.38)
No	11 (84.62)
<b>Surgical procedure performed (laminectomy)</b>	
Yes	7 (53.85)
Not described	6 (46.15)
<b>The event took place</b>	
Before RT	2 (15.38)
After RT	11 (84.62)
<b>Total - n (%)</b>	<b>13 (100.00)</b>

Source: The authors.

The mean survival times of the patients with and without pathological fractures were 32.53 and 39.67 months, respectively ( $p=0.04$ ) (Graph 1A), whereas the mean survival times of the patients with and without spine compression were 41.52 and 38.93 months, respectively ( $p=0.27$ ) (Graph 1B).

**Graph 1.** Kaplan-Meier survival curves considering the following skeleton-related events: (a) pathological fractures; and (b) spine compression, in patients with bone metastases. Belém, Pará, Brazil, 2022.



**Source:** The authors.

Nearly 95.08% (116) of the patients finished their treatment, of which 66.39% (81) were discharged and 33.61% (41) evolved to death after radiotherapy. Considering the bivariate logistic regression related to the death outcome and to the SREs,  $\beta=-0.02$  ( $p=0.96$ ) was obtained for pathological fractures and  $\beta=-0.57$  ( $p=0.40$ ) for spine compression.

## DISCUSSION

This study analyzed medical records of patients with bone metastasis subjected to radiotherapy. There was a prevalence of the female gender, with a mean age of 54.74 years old. The most frequent primary sites were breast and prostate, which corresponds to the highest estimates for women and men for the 2023-2025 triennium. These data corroborate those found in a study conducted in São Paulo, Brazil,<sup>(12)</sup> which analyzed a database including 131 patients with bone metastasis, of which 55% were female, with mean age of 58.5 years old and breast as the most incident primary site (22.9%).



The results obtained diverge from those of a Korean study<sup>(5)</sup> conducted in a national database that investigated 1,849 patients with bone metastases, where most of them were male (53.05%) and aged from 60 to 69 years old (27.9%). However, given the population and epidemiological differences, there was similarity between the most incident sites: breast (18.8%) and prostate (17.5%).

With regard to the characterization of the bone metastases, in an African study<sup>(18)</sup> conducted with 234 patients subjected to palliative RT the most frequent location was the axial skeleton (30.2%), differently from the findings herein reported, where 56.56% of the metastases affected both skeletons (axial and appendicular).

In relation to bone impairment, the findings of this study point to the spine as the most affected by metastases (80.33% of the cases), with the literature reporting a preference for the axial skeleton specifically for this region, which reflects the distribution of the so-called red bone marrow, a highly vascular tissue that contains hematopoietic stem cells and an active microenvironment that promotes cell growth<sup>(2,4)</sup>. These data corroborate those from another analysis<sup>(17)</sup> where this was the predominant location in 32.1% of the 407 patients analyzed. Even so, another study<sup>(12)</sup> found that the most affected bone was the femur (49.6%), followed by the spine (25.2%).

In the current documentary analysis, the mean time elapsed from the cancer diagnosis to bone metastasis confirmation was 20.55 months (SD  $\pm 30.93$ ), presenting statistical significance ( $p=0.04$ ) referring to its impact on the patients' death outcome. In a Korean study,<sup>(5)</sup> this time was even shorter: 18.9 months.

In the complementary treatment, bisphosphonates were frequently used by the study patients. These medications are selective osteoclastic bone resorption inhibitors known for reducing and delaying morbidity of the metastatic bone disease.<sup>(8)</sup> Bisphosphonates are also known for their potential to control pain, characterized as one of the most incident SRE and mainly caused by the destruction of bone structure due to proliferation of cancer cells, leading to periosteal irritation and nerve damage.<sup>(5,19)</sup>

A study characterized pain in 84 patients with bone metastasis who were treated with bisphosphonates. Self-reported pain was 91.6%, with 34.5% of the patients reporting severe pain (score of 7-10).<sup>(19)</sup> In the current study, 100% of the medical charts included bone pain records. However, 94.26% of them did not describe pain intensity. This finding reflects the incipience of pain management assessment and control in these patients.

With regard to pain assessment and control, a multicenter randomized study evaluated 354 patients subjected to radiotherapy for bone metastases. In this study, the effect of personalized nurse-led education on pain was compared to that of usual care. In the end, 70% of the patients from the Intervention Group had their pain controlled. In the Control Group, only 40% of the patients reported improvements in pain ( $p=0.013$ ).<sup>(20)</sup>

A Brazilian study conducted in Aracaju (PE), Brazil,<sup>(21)</sup> evaluated 30 patients with painful bone metastases before and after radiotherapy treatment using the Visual Analog Scale (VAS). These patients were subjected to a mean of 5.72 RT fractions (SD  $\pm 3.37$ ), with a total dose of 2,000 cGy (38%). In the end, 86% reported improvements in pain after RT. Here, the patients received a mean of 9.05 RT fractions (SD  $\pm 2.89$ ), with a total dose of 3,000 cGy (68.85%). In 44.26% of the cases, there were reports of improvements in pain after the treatment, but no measuring scales were used, reflecting the absence of standardized clinical protocols.

The data found in the studies cited on pain<sup>(19-21)</sup> reinforce that the implementation of a successful treatment for pain requires assessment, characterization and quantification. The emergence of other SREs exerts a significant impact on pain. A research study included 5,543 randomized patients in relation to the presence or absence of SREs. It was observed that the proportion of patients with moderate/intense pain was increased in the six months preceding an SRE and remained high after its occurrence.<sup>(22)</sup>

With regard to pathological fractures, the prevalence in 122 patients was 32.78% here. In 55% of them, the trauma was located in the spine. In turn, another study<sup>(17)</sup> conducted with 407 patients with lung carcinoma found 19.1% prevalence and that the most affected bone was the humerus (36.4%). Another analysis<sup>(23)</sup>, with 3,731 patients with breast cancer that metastasized to the bones, identified that 28.1% of them had pathological fractures.

In relation to the survival analysis, this study showed that the "pathological fractures" event exerts a significant impact on survival ( $p=0.04$ ), as the patients with this event lived a mean of 7.14 fewer months, findings consistent with those of another study<sup>(17)</sup> in which the patients had a mean survival time of 2 months after the event.

With regard to spine compression, its prevalence was 10.65% here. Although this SRE is considered rare, its prevalence fluctuated in the studies analyzed. A retrospective cohort study<sup>(13)</sup> involving 245 patients with lung cancer and bone metastases identified that 21.2% suffered from spine compression. The already cited Korean study<sup>(5)</sup> presented even lower incidence: 3.4%.

The most frequent treatment for spine compression is radiotherapy alone, although associated decompressive surgery is suggested in some cases, depending on the patients' clinical condition, prognosis, primary site and the characteristics of the compression.<sup>(24)</sup> In this study, 53.85% of the medical records reported that this procedure was performed.

In this context, the survival of patients with spine compression was higher than that of those who did not experience this event, which may be justified by the reduced number of cases. Another study<sup>(13)</sup> also did not find any relationship between this event and increased risk of death.

In the bivariate logistic regression analysis, pathological fractures and spine compression were not significantly associated with the death outcome. However, it was also possible to identify that the p-value for compression was much lower than the one for fractures. Therefore, it was verified that compression might exert more influence on the patients' death outcome if the sample was larger.

In view of all the analyses, it is important to highlight nurses' role in caring for patients with bone metastases subjected to radiotherapy. One of the main courses of actions by these professionals is health education, with a focus on prevention.<sup>(14)</sup> Therefore, the basis of their knowledge should be broad enough to clearly explain the effects of radiotherapy and the profile of the main SREs.<sup>(6,10)</sup>

The limitations of this study are mainly related to gaps in the reports made by the professionals with regard to monitoring of the patients, as well as to the impossibility of analyzing the hypercalcemia SRE. With regard to the contributions, it is worth mentioning the possibility of improving Nursing care and management of patients with bone metastases subjected to radiotherapy, by means of their characterization, including associated skeleton-related events (pain, pathological fractures and spine compression).

## CONCLUSION

This study allowed characterizing patients with bone metastases subjected to radiotherapy, as well as the associated SREs and their influence on patients' survival. Most of the patients were female, with a mean age of 58.86 (SD  $\pm$ 14.54) years old. The most incident primary sites were breast (43.44%) and prostate (30.33%).

There was a significant inference ( $p=0.04$ ) regarding the correlation between time from the cancer diagnosis to bone metastasis confirmation referring to the impact on the patients' death outcome. Concerning the SREs, 100% of the patients presented bone pain records, 32.78% suffered pathological fractures with a mean survival time of 33.53 months, and 10.65% presented spine compression with a survival time of 41.52 months.

It is noted that no similar studies were found with data from the Brazilian Northern region. These data are expected to support new research studies on this little studied theme, in order to optimize the quality of the Nursing assistance provided to patients with these problems, by preventing complications and monitoring the SREs.

## CONTRIBUTIONS

Contributed to the conception or design of the study/research: Sagica TP, Oliveira SSS, Ramos AMPCR. Contributed to data collection: Sagica TP, Oliveira SSS. Contributed to the analysis and/or interpretation of data: Sagica TP, Vilhena DI, Pereira OV, Silva MRB, Vilhena FDM. Contributed to article writing or critical review: Sagica TP, Oliveira SSS, Vilhena DI, Pereira OV, Silva MRB, Vilhena FDM, Ramos AMPCR. Final approval of the version to be published: Sagica TP, Ramos AMPCR.

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