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Bone metastasis patterns in solid cancers at a tertiary cancer center

Patrones de metástasis ósea en cánceres sólidos en un centro oncológico terciario

Rosas LC,*,‡ García-Ortega DY,*,§ Clara-Altamirano MA,*,‡,¶ Martínez-Said H,*,‖ Villavicencio-Valencia V,*,§ Meléndez-Fernández AP,*,§ González-Prieto RE,*,‡ González-Álvarez C,*,‡ Cuellar-Hubbe M*,§

Instituto Nacional de Cancerología. Mexico City, Mexico.

ABSTRACT. Introduction: Metastatic Bone Cancer (MBC) is the most common malignancy affecting the skeletal system. The cancers that most frequently metastasize to bone include breast, prostate, lung, kidney, and thyroid cancers (comprising 70% of cases). Metastatic patterns are classified as lytic, blastic, or mixed lesions, often affecting the axial skeleton. **Materials and methods:** this retrospective cohort study included patients with MBC treated between January 1, 2012, and December 31, 2022. Patients over 17 years of age with a diagnosis of solid neoplasia and evidence of metastatic bone disease confirmed by plain radiographs, computed tomography, magnetic resonance imaging, or PET-CT were included. Patients who died from causes unrelated to cancer and those who discontinued follow-up were excluded. Statistical analysis: we performed a descriptive analysis of demographic variables and used a Cox regression model, incorporating variables adapted to the model. Overall Survival (OS) was evaluated using the Kaplan-Meier method. **Results:** we analyzed data from 902 patients with a median age of 61 years. The majority were male (54.4%). Multiple lesions (three or more) were found in 49% of cases, primarily in the axial skeleton. Prostate cancer was the most common primary cancer (32%), while lytic lesions were most often

RESUMEN. Introducción: el cáncer óseo metastásico (MBC) es la neoplasia maligna más frecuente que afecta al sistema esquelético. Los cánceres que con mayor frecuencia metastatizan en los huesos son los de mama, próstata, pulmón, riñón y tiroides (que representan 70% de los casos). Los patrones metastásicos se clasifican en lesiones líticas, blásticas o mixtas, que a menudo afectan al esqueleto axial. **Material y métodos:** este estudio de cohorte retrospectivo incluyó a pacientes con MBC tratados entre el 1 de enero de 2012 y el 31 de diciembre de 2022. Se incluyeron pacientes mayores de 17 años con diagnóstico de neoplasia sólida y evidencia de enfermedad ósea metastásica confirmada mediante radiografías simples, tomografía computada, resonancia magnética o PET-TC. Se excluyeron los pacientes que fallecieron por causas no relacionadas con el cáncer y a los que interrumpieron el seguimiento. Análisis estadístico: realizamos un análisis descriptivo de las variables demográficas y utilizamos un modelo de regresión de Cox, incorporando variables adaptadas al modelo. La supervivencia general (SG) se evaluó mediante el método de Kaplan-Meier. **Resultados:** analizamos los datos de 902 pacientes con una mediana de edad de 61 años. La mayoría eran hombres (54.4%). Se encontraron lesiones múltiples (tres o más) en 49% de los casos, principalmente

Level of evidence: II

* Instituto Nacional de Cancerología. Mexico City, Mexico.
‡ Orthopedic Oncologist. Skin, Soft Tissues and Bone Tumors.
§ Surgical Oncologist. Skin, Soft Tissues and Bone Tumors.
¶ ORCID: 0000-0002-2304-5389
‖ Deputy Director of Surgery at the National Cancer Institute.

Correspondence:
Miguel Angel Clara-Altamirano. M.D., MSc, PhD.
Skin, soft tissue and bone tumors department. National Cancer Institute, Mexico City. Av. San Fernando 22, Col. Seccion XVI. Tlalpan, 14080, Mexico City, Mexico.
E-mail: drmiguelclara@gmail.com

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associated with lung cancer (38%). Additionally, 153 patients (17%) had pathological fractures, 77% experienced pain secondary to Hypercalcemia of Malignancy (HCM), and 59% had metastases in organs other than bone. The median OS was 15 months. **Conclusions:** bone metastases are a poor prognostic factor in cancer patients and negatively impact quality of life. Identifying and understanding metastatic patterns is essential for developing effective therapeutic strategies and innovative treatments.

Keywords: metastatic bone cancer, overall survival, mortality, bone metastasis.

en el esqueleto axial. El cáncer de próstata fue el cáncer primario más frecuente (32%), mientras que las lesiones líticas se asociaron con mayor frecuencia al cáncer de pulmón (38%). Además, 153 pacientes (17%) presentaban fracturas patológicas, 77% experimentaba dolor secundario a hipercalcemia maligna (HCM) y 59% presentaba metástasis en órganos distintos de los huesos. La mediana de la SG fue de 15 meses. **Conclusiones:** las metástasis óseas son un factor de mal pronóstico en pacientes con cáncer y afectan negativamente a su calidad de vida. Identificar y comprender los patrones metastásicos es esencial para desarrollar estrategias terapéuticas eficaces y tratamientos innovadores.

Palabras clave: cáncer óseo metastásico, supervivencia general, mortalidad, metástasis ósea.

Abbreviations:
MBC = Metastatic Bone Cancer
OS = Overall Survival

Introduction

Metastatic Bone Cancer (MBC) is the most common malignant neoplastic condition affecting the skeletal system.[1,2] The five most common histologies associated with MBC are breast, prostate, lung, kidney, and thyroid cancers, accounting for up to 70% of all patients with metastatic disease.[1,2,3] Neoplasms of hematopoietic origin and soft tissue sarcomas are less frequently associated with bone metastases.[4]

Globally, more than 18 million cancer cases are diagnosed each year, with over 50% progressing to metastatic disease.[5,6] An estimated 19.3 million new cancer cases and 10 million cancer-related deaths were reported in 2020 alone.[6]

Different reports in the literature consistently show that MBC most frequently affects the spine, ribs, pelvis, and proximal long bones.[3,7,8,9,10,11] MBC can present as lytic, blastic, or mixed lesions, which are visible in plain radiographs, computed tomography, and magnetic resonance imaging.[11,12,13] In lytic bone lesions, bone resorption exceeds bone formation. In blastic lesions, however, the opposite occurs.[3,13] These three patterns of metastasis lead to bone fragility and a greater predisposition to pathological fractures.[13]

Osteolytic lesions are typically associated with bone metastases in triple-negative breast cancer, renal adenocarcinoma, and small-cell lung cancer.[13,14,15,16,17] In contrast, osteoblastic metastases are more common in prostate cancer.[4,18,19]

MBC is associated with a poor prognosis in most cancer patients, representing an advanced and aggressive stage of the disease,[20] and is currently the leading cause of disability among cancer patients.[2,10,21,22] This study aims to identify and evaluate the biological behavior of different bone metastatic patterns in malignant solid neoplasms to develop therapeutic strategies to extend overall survival and improve quality of life.

Material and methods

We conducted a retrospective cohort study including the records of patients diagnosed with metastatic bone cancer (MBC) from January 1, 2012, to December 31, 2022. Patients over 17 years of age who were assessed in the oncology orthopedics clinic with a confirmed diagnosis of solid neoplasia and radiographic evidence of bone metastatic disease from any of the following imaging modalities were included: plain radiographs, computed tomography, magnetic resonance imaging, or PET-CT. Patients who died from causes unrelated to cancer and those who discontinued follow-up were excluded.

The main clinical, radiological, and pathological variables were documented, including the location of metastases, involvement of the axial or appendicular skeleton, type of primary neoplasia, number of bones affected, biological behavior patterns of bone metastases (lytic, blastic, or mixed), Overall Survival (OS) in months, and mortality.

Statistical analysis

A descriptive analysis of demographic variables was conducted, with central tendency measures (mean, median) and dispersion (standard deviation and ranges) calculated based on the normality of the variables, evaluated using the Kolmogorov-Smirnov test.

For the analysis of qualitative variables, the χ^2 test or Fisher's exact test was used, as appropriate. The Student's t-test or Mann-Whitney U test was employed for quantitative variables, as applicable. A Cox regression model was subsequently performed, incorporating variables that best

fit the model. Kaplan-Meier analysis was conducted to evaluate OS. Statistical analysis was performed using SPSS version 29.

Results

A total of 902 patients were analyzed, with a median age at diagnosis of 61 years (range: 17-91 years). MBC was more prevalent in male patients (491 [54.4%]), while 411 patients (45.6%) were female. At diagnosis, 856 patients (94.9%) had metastases, and 46 patients (5.1%) showed disease progression. The main demographic characteristics of the cohort are summarized in *Table 1*.

Table 1: Demographic variables in 902 patients with bone metastases.

Variables	Total n (%)
Age (years), median [range]	61 [17–91]
Sex	
Male	491 (54.4)
Female	411 (45.6)
Location	
Axial	448 (49.7)
Appendicular	77 (8.5)
Both	377 (41.8)
Number of bones affected	
One bone	87 (9.6)
Two bones	64 (7.1)
> 3 bones	751 (83.3)
Metastasis to other organs	
Yes	367 (40.7)
No	535 (59.3)
Type of metastasis	
Lytic	345 (38.3)
Blastic	270 (29.9)
Mixed	287 (31.8)
Pain	
Yes	696 (77.2)
No	206 (22.8)
Presence of fracture	
Yes	154 (17.1)
No	748 (82.1)
Type of cancer	
Prostate	290 (32.2)
Lung	251 (27.8)
Breast	243 (26.9)
Kidney	39 (4.3)
Others	79 (8.8)
Overall survival (months), median [range]	15 [1-180]
Death from disease	
Yes	783 (86.8)
No	119 (13.2)

Most metastatic lesions were multiple, involving three or more bones in 751 patients (83.3%). Single metastases were found in 87 patients (9.6%), and two bones were affected in 64 patients (7.1%). The axial skeleton was the most frequent site of metastasis, seen in 448 patients (49.7%), followed by both axial and appendicular skeleton involvement in 377 patients (41.8%), and the appendicular skeleton alone in 77 patients (8.5%) *(Table 1, Figure 1)*.

The most common primary cancer was prostate cancer (290 patients, 32.2%), followed by lung cancer (251 patients, 27.8%), breast cancer (243 patients, 26.9%), and kidney cancer (39 patients, 4.3%). Other histologies, including sarcomas, colon cancer, and thyroid cancer, were categorized as «other primary tumors», representing 8.8% of the cohort *(Table 1)*. Demographic variables by cancer type are shown in *Table 2*.

Regarding bone destruction by histology, a higher percentage of blastic lesions were seen in prostate cancer patients (198 [68.3%]), lytic lesions in lung cancer patients (184 [73.3%]), and mixed lesions primarily in breast and prostate cancer patients (87 [35.8%] and 84 [29%], respectively) *(Table 1, Figure 2)*.

Among the 902 cases in the cohort, 153 patients (17%) had pathological fractures in previously damaged bones. Pain secondary to bone metastases was reported by 696 patients (77.2%).

Bone-only metastases were present in 367 patients (40.7%), while 535 patients (59.3%) had metastases to other organs *(Table 1)*. During follow-up, 783 patients (86.8%) died, with a median OS of 15 months (range: 1-180 months). OS by histology is detailed in *Table 3*. Among breast cancer patients (n = 243), 41% (101 patients) were alive at one year, and 6% (15 patients) at five years. In lung cancer (n = 251), 29% (72 patients) were alive at one year, and 4% (10 patients) at five years. Among renal cancer patients (n = 39),

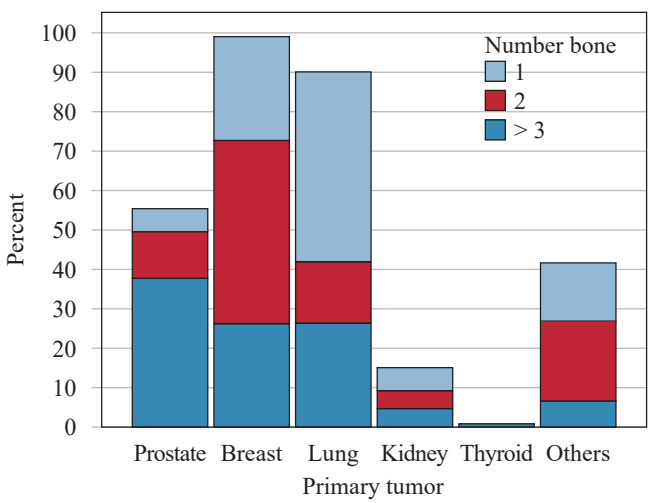

Figure 1: Number of bone lesions observed in the cohort depends on the type of cancer.

Table 2: Distribution of variables based on type of cancer.

Variables	Total N = 902 n (%)	Prostate N = 290 N (%)	Lung N = 251 n (%)	Breast N = 243 n (%)	Kidney N = 39 n (%)	Others N = 79 n (%)	*p*
Sex							0.001
Male	491 (54.4)	0 (0.0)	136 (54.2)	2 (0.8)	20 (51.3)	43 (54.4)	
Female	411 (45.6)	290 (100.0)	115 (45.8)	241 (99.2)	19 (48.7)	36 (45.6)	
Location							0.001
Axial	448 (49.7)	136 (46.9)	109 (43.4)	143 (58.9)	28 (71.8)	32 (40.5)	
Appendicular	77 (8.5)	8 (2.8)	45 (17.9)	10 (4.1)	3 (7.7)	11 (13.9)	
Both	377 (41.8)	146 (50.3)	97 (38.7)	90 (37.0)	8 (20.5)	36 (45.6)	
Number of bones affected							0.001
One bone	87 (9.6)	5 (1.7)	42 (16.7)	23 (9.5)	4 (10.3)	13 (16.5)	
Two bones	64 (7.1)	8 (2.8)	10 (4.0)	30 (12.3)	3 (7.7)	13 (16.5)	
>3 bones	751 (83.3)	277 (95.5)	199 (79.3)	190 (78.2)	32 (82)	53 (67.0)	
Metastasis to other organs							0.001
Yes	367 (40.7)	21 (7.2)	155 (61.8)	145 (59.7)	8 (20.5)	38 (51.9)	
No	535 (59.3)	269 (92.8)	96 (38.2)	98 (40.3)	31 (79.5)	41 (48.1)	
Type of metastasis							0.001
Lytic	345 (38.3)	8 (2.7)	184 (73.3)	107 (44.0)	12 (30.8)	34 (43.0)	
Blastic	270 (29.9)	198 (68.3)	20 (8.0)	49 (20.2)	0 (0.0)	3 (3.8)	
Mixed	287 (31.8)	84 (29.0)	47 (18.7)	87 (35.8)	27 (69.2)	42 (53.2)	
Pain							0.043
Yes	696 (77.2)	233 (80.3)	185 (73.7)	180 (74.1)	36 (92.3)	62 (78.5)	
No	206 (22.8)	57 (19.7)	66 (26.3)	63 (25.9)	3 (7.7)	17 (21.5)	
Presence of fracture							0.001
Yes	154 (17.1)	48 (16.6)	23 (9.2)	59 (24.3)	6 (15.4)	18 (22.8)	
No	748 (82.1)	242 (83.4)	228 (90.8)	184 (75.7)	33 (84.6)	61 (77.2)	
Death from disease							0.001
Yes	783 (86.8)	259 (89.3)	235 (93.6)	190 (78.2)	36 (92.3)	63 (79.8)	
No	119 (13.2)	31 (10.7)	16 (6.4)	53 (21.8)	3 (7.7)	16 (20.2)	

13% (five patients) were alive at one year, and 8% (three patients) at five years.

The number of affected bones correlated with survival: patients with one affected bone had a median survival of 26.5 months, two affected bones had a median survival of 31.3 months, and three or more affected bones had a median OS of 27.3 months with no statistically significant differences between the groups.

Based on the pattern of bone destruction (lytic, blastic, or mixed lesions), the median OS was 12, 15, and 21 months, respectively. This difference was statistically significant (p = 0.001), although no association was found between the different lesion types and mortality *(Figure 3)*.

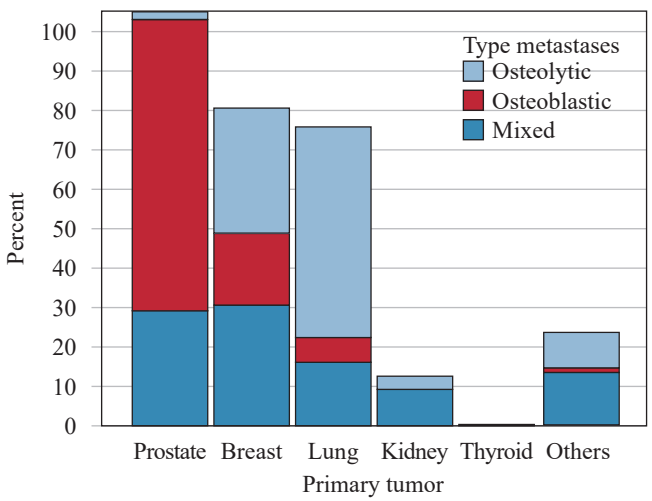

Figure 2: Biological behavior of metastatic bone lesions according to their histological type.

Discussion

Cancer is one of the leading causes of mortality worldwide and is the first or second leading cause of death in people under 70 years of age in 112 of 183 countries.[6] Consequently, cancer must be considered a priority in public health policies focused on prevention, early diagnosis, and treatment of the primary disease and its complications, such as metastatic bone disease.

We describe the histological types of cancer most frequently associated with bone metastases in an oncology center, as well as the primary patterns of bone destruction (lytic, blastic, or mixed), their locations, and the number of bone lesions. This information is crucial for preventing skeletal complications, which have a direct impact on patients' quality of life.[2]

While similar studies have been conducted globally,[8,21,22] our study represents the most extensive series in Latin

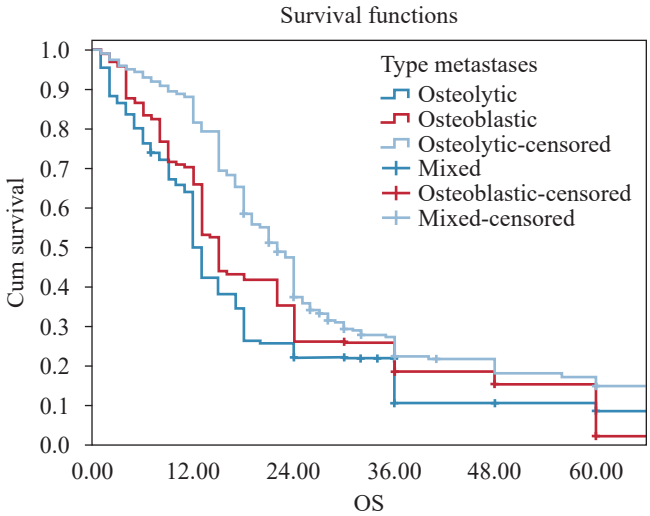

Figure 3: Overall survival and biological behavior of metastatic cancer to bone.

Table 3: Overall survival by type of cancer at one and five years.

Type of cancer	Total	OS at one year (n)	OS at five years (n)
All types	902	–	–
Prostate	290	–	–
Lung	251	72	10
Breast	243	101	15
Kidney	39	5	3
Other types	79	–	–

America regarding the patterns of bone metastasis in patients with Hypercalcemia of Malignancy (HCM). This is significant because bone fragility increases the likelihood of fractures and pain.[2,12,23,24,25] In our cohort, 77.2% (696 patients) experienced bone pain related to MBC, and 17.1% (154 patients) suffered fractures in previously damaged bones. Therefore, the onset of musculoskeletal pain in an oncology patient without a history of trauma should raise suspicion of MBC.[2]

The findings of our study regarding the most commonly affected sites in MBC are consistent with those in the literature.[1,5,10,20,26] In particular, the association between metastases to the axial skeleton and increased mortality (HR 1.1, CI95% 1.05-1.16, p = 0.04) was significant and should be considered a prognostic factor in treatment planning.

The high mortality observed in this study reflects the severity and complexity of MBC, regardless of cancer type, as 783 out of 902 patients (86.8%) died during follow-up. The overall survival by cancer type is shown in *Figure 4*.

The relationship between the biological behavior of MBC and histological subtypes can be seen in prostate cancer. In our series, 290 patients had prostate cancer, accounting for 32.2% of the sample. Of these, 198 patients (68.3%) had blastic lesions, 84 patients (29%) had mixed lesions, and only eight patients (2.7%) had lytic lesions.

Among the 243 breast cancer patients analyzed, 41.6% (101 patients) were alive at one year, and 6.2% (15 patients) were alive at five years. A similar survival pattern was observed in lung and kidney cancers *(Table 3, Figure 4)*. All patients with lung adenocarcinoma in this study had the small-cell subtype, and bone was a primary site of metastasis in these patients. The OS for this group is low, as reported in the literature. In our study, 184 of the 251 lung adenocarcinoma patients (73.3%) had lytic bone lesions (p = 0.01), 199 patients (79.3%) had lesions in three or more bones (p = 0.001), and 155 patients (61.8%) had metastases to other organs (p = 0.001), which explains the high mortality in this group.

The 39 patients with clear cell renal cell carcinoma metastatic to the bone had a prognosis similar to those with breast and lung cancer. Only five patients (12.8%) were alive at one year, and three patients (7.7%) were alive at five years. Most of these patients had mixed lesions (27 patients, 69.2%), multiple lesions (32 patients, 82%), and axial skeleton involvement (28 patients, 71.8%). Given these findings, focusing treatment on palliative care that allows short-term functional recovery without interrupting oncological treatment is essential. A multidisciplinary approach is crucial for managing these patients.

One limitation of our study is its retrospective nature, which carries biases inherent to this research design. Additionally, the sample's heterogeneity, due to the various cancer types included, could affect the findings. However, this diversity also allows us to observe the behavior of MBC across different cancer types and compare their characteristics and impact on overall survival.

Analyzing the biological and epidemiological behavior of MBC in various solid neoplasms helps understand the prognosis and the potential to refer these patients to specialists experienced in managing MBC. This may lead

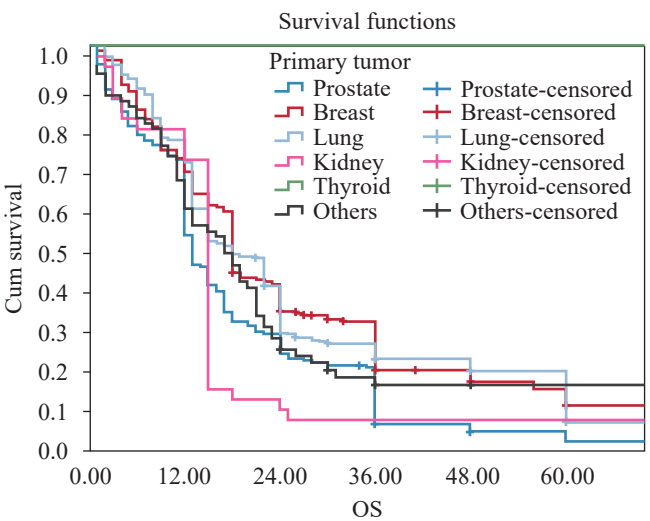

Figure 4: Overall survival of different types of cancer with bone metastasis.

to the development of diagnostic and treatment algorithms for each type of MBC, ultimately improving oncological outcomes for our patients.

Conclusion

Metastatic bone cancer is a marker of poor prognosis in cancer patients, representing an advanced and aggressive stage of the disease. The spread of cancer to the skeleton not only worsens the disease's severity but also negatively impacts the patient's quality of life. Identifying and understanding these metastatic patterns is essential for developing effective therapeutic strategies. This study represents one of the largest collections of metastatic bone cancer cases. The results highlight the need to promote research to develop early detection protocols and innovative treatments that can improve the quality of life for patients with MBC.

References

1. Mundy GR. Metastasis to bone: Causes, consequences and therapeutic opportunities. *Nat Rev Cancer.* 2002; 2(8): 584-93.
2. Kirkinis MN, Lyne CJ, Wilson MD, Choong PFM. Metastatic bone disease: a review of survival, prognostic factors, and outcomes following surgical treatment of the appendicular skeleton. *Eur J Surg Oncol*. 2016; 42(12): 1787-97. doi: 10.1016/j.ejso.2016.03.036
3. Coleman RE, Roodman, Smith, Body, Suva, Vessella. Clinical features of metastatic bone disease and risk of skeletal morbidity. *Clin Cancer Res*. 2006; 12(20 Pt 2): 6243s-6249s.
4. Jehn CF, Diel IJ, Overkamp F, Kurth A, Schaefer R, Miller K, et al. Management of metastatic bone disease algorithms for diagnostics and treatment. *Anticancer Res*. 2016; 36(6): 2631-7.
5. Coleman RE, Croucher PI, Padhani AR, Clézardin P, Chow E, Fallon M, et al. Bone metastases. *Nat Rev Dis Primers*. 2020; 6(1): 83.
6. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021; 71(3): 209-49.
7. Ashford RU, Pendlebury S, Stalley PD. Management of metastatic disease of the appendicular skeleton. *Curr Orthop*. 2006; 20(4): 299-315. doi: 10.1016/j.cuor.2006.03.005.
8. Li S, Peng Y, Weinhandl ED, Blaes AH, Cetin K, Chia VM, et al. Estimated number of prevalent cases of metastatic bone disease in the U.S. adult population. *Clin Epidemiol*. 2012; 4: 87-93.
9. Coleman RE, Croucher PI, Padhani AR, Clézardin P, Chow E, Fallon M, et al. Bone metastases. *Nat Rev Dis Primers*. 2020; 6(1): 83.
10. Jiang W, Rixiati Y, Zhao B, Li Y, Tang C, Liu J. Incidence, prevalence, and outcomes of systemic malignancy with bone metastases. *J Orthop Surg (Honk Kong)*. 2020; 28(2): 2309499020915989.
11. Fornetti J, Welm AL, Stewart SA. Understanding the bone in cancer metastasis. *J Bone Miner Res*. 2018; 33(12): 2099-113.
12. Weilbaecher KN, Guise TA, McCauley LK. Cancer to bone: a fatal attraction. *Nat Rev Cancer*. 2011; 11(6): 411-25. doi: 10.1038/nrc3055
13. Hamaoka T, Madewell JE, Podoloff DA, Hortobagyi GN, Ueno NT. Bone imaging in metastatic breast cancer. *J Clin Oncol*. 2004; 22(14): 2942-53.
14. Sathiakumar N, Delzell E, Morrisey MA, Falkson C, Yong M, Chia V, et al. Mortality following bone metastasis and skeletal-related events among women with breast cancer: a population-based analysis of U.S. Medicare beneficiaries, 1999-2006. *Breast Cancer Res Treat*. 2012; 131(1): 231-8.
15. Zulauf N, Brüggmann D, Groneberg D, Oremek GM. Expressiveness of bone markers in breast cancer with bone metastases. *Oncology*. 2019; 97(4): 236-44.
16. Riihimaki M, Hemminki A, Fallah M, Thomsen H, Sundquist K, Sundquist J, et al. Metastatic sites and survival in lung cancer. *Lung Cancer*. 2014; 86(1): 78-84. doi: 10.1016/j.lungcan.2014.07.020.
17. Dudani S, De Velasco G, Wells JC, Gan CL, Donskov F, Porta C, et al. Evaluation of clear cell, papillary, and chromophobe renal cell carcinoma metastasis sites and association with survival. *JAMA Netw Open*. 2021; 4(1): 1-11.
18. Logothetis C, Morris MJ, Den R, Coleman RE. Current perspectives on bone metastases in castrate-resistant prostate cancer. *Cancer Metastasis Rev*. 2018; 37(1): 189-96.
19. Kang J, La Manna F, Bonollo F, Sampson N, Alberts IL, Mingels C, et al. Tumor microenvironment mechanisms and bone metastatic disease progression of prostate cancer. *Cancer Lett*. 2022; 530: 156-69. doi: 10.1016/j.canlet.2022.01.015.
20. Clara-Altamirano MA, Garcia-Ortega DY, Martinez-Said H, Caro-Sánchez CHS, Herrera-Gomez A, Cuellar-Hubbe M. Surgical treatment in bone metastases in the appendicular skeleton. *Rev Esp Cir Ortop Traumatol (Engl Ed)*. 2018; 62(3): 185-9. doi: 10.1016/j.recote.2017.12.011.
21. Hernandez RK, Wade SW, Reich A, Pirolli M, Liede A, Lyman GH. Incidence of bone metastases in patients with solid tumors: Analysis of oncology electronic medical records in the United States. *BMC Cancer*. 2018; 18(1): 44
22. Gartrell BA, Saad F. Managing bone metastases and reducing skeletal-related events in prostate cancer. *Nat Rev Clin Oncol*. 2014; 11(6): 335-45.
23. Hiraga T. Bone metastasis: interaction between cancer cells and bone microenvironment. *J Oral Biosci*. 2019; 61(2): 95-8. doi: 10.1016/j.job.2019.02.002.
24. Levin BM, Vaughn DJ, Malkowicz BS. Metastatic prostate cancer: optimal management strategies. *Am J Cancer*. 2003; 2(2): 87-94.
25. Sathiakumar N, Delzell E, Morrisey MA, Falkson C, Yong M, Chia V, et al. Mortality following bone metastasis and skeletal-related events among men with prostate cancer: a population-based analysis of U.S. Medicare beneficiaries, 1999-2006. *Prostate Cancer Prostatic Dis*. 2011; 14(2): 177-83. doi: 10.1038/pcan.2011.7.
26. Pereira J, Body JJ, Gunther O, Sleeboom H, Hechmati G, Maniadakis N, et al. Cost of skeletal complications from bone metastases in six European countries. *J Med Econ*. 2016; 19(6): 611-8.

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