Joint Diseases and Related Surgery

Jt Dis Relat Surg
2024;35(1):105-111

ORIGINAL ARTICLE

# Do metastatic volumes measured in breast cancer patients with bone metastases correlate with the numbers of skeletal and extraskeletal events?

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Despite notable advancements in the diagnosis and treatment of breast cancer, it remains a significant public health concern, causing high incidence, morbidity, and mortality rates. In our country, efforts to address the issue include a national screening program that involves monthly breast self-examinations for women aged 20 to 40 years, annual clinic examinations, and mammography screening every two years for women aged 40 to 69 years.[1] Nonetheless, 8.4% of breast cancer patients in our country still receive diagnoses with distant metastases.[2] Bone metastases are most common in lung, breast, and prostate cancers, respectively.[3]

Received: July 22, 2023
Accepted: October 02, 2023
Published online: November 02, 2023

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Doi: 10.52312/jdrs.2023.1333

**Citation:** Yağar H, Aytekin MN, Şener Dede D, Şendur M.A.N., Öztürk R, Yalçın B. Do metastatic volumes measured in breast cancer patients with bone metastases correlate with the numbers of skeletal and extraskeletal events? Jt Dis Relat Surg 2024;35(1):105-111. doi: 10.52312/jdrs.2023.1333.



## ABSTRACT

**Objectives:** The study aimed to investigate the relationship between metastatic volume measurement, skeletal-related events, and survival in women diagnosed with breast cancer and bone metastases.

**Patients and methods:** This retrospective study was conducted with 82 female breast cancer patients (mean age: 53±14.3 years; range, 23 to 87 years) diagnosed, treated, and followed up between January 2005 and December 2019. The collected data included information on metastasis sites and the presence of skeletal-related events. Metastatic volume was measured in two ways: the number of metastases (high to low) and their localization (the first, second, and third groups). The first group consisted of vertebrae, ribs, sternum, and calvarial bones; the second group included scapula, clavicle, proximal humerus, and proximal femur regions; the third group consisted of femur and humerus diaphyseal and distal regions, as well as metastasis regions in other long bones.

**Results:** Sixty-three (76.8%) patients were diagnosed with ductal carcinoma. Half of the patients had bone metastases at the time of initial diagnosis, while 62 (75.6%) experienced skeletal-related events, with at least three events occurring in 30 (36.6%) patients. Bone pain was the most common skeletal-related event. No correlation was found between metastatic volume measurement based on the localization of bone metastases and the number of bones and the occurrence of skeletal-related events ($p>0.05$ for each). Patients' survival time spanned from one to 231 months (median: 56.8 months) from their first diagnosis. Patients with high metastatic volume, those in the third group, those whose pelvis and lung were involved, and elderly patients had a shorter survival time ($p<0.05$ for each).

**Conclusion:** The study indicates that measuring metastatic volume may be a critical factor in evaluating the survival of breast cancer patients with bone metastases. Future prospective and randomized controlled studies can explore the potential of this measurement to create practical clinical tools.

***Keywords:*** Bone metastasis, breast cancer, metastatic volume, skeletal related event.

The presence of distant metastases is a significant determinant of breast cancer prognosis. Breast cancer frequently spreads to the bones, with most metastases occurring in the axial skeleton.[4] Initially, approximately 5 to 6% of women diagnosed with breast cancer have bone metastases, with this percentage notably higher in those diagnosed at a metastatic stage. Research suggests that 70% of breast cancer fatalities in women are caused by bone metastases.[5]

Bone metastases and associated skeletal-related events notably deteriorate the prognosis of breast cancer patients, negatively impacting their quality of life and increasing healthcare expenditure through changes in treatment modalities.[6-8] Skeletal-related events stemming from bone metastases encompass pathological fractures, hypercalcemia, spinal cord compression, the requirement of radiotherapy or surgery, and bone pain.[9] Data indicate that around 50% of women with breast cancer and bone metastases experience skeletal-related events.[8,10,11]

The incidence of skeletal-related events in breast cancer patients diagnosed with bone metastases is a vital factor in developing appropriate treatment plans. Additionally, these factors aid in deciding whether to consider surgery and the type of surgery required for patients presenting with pathological or impending fractures.[12]

Since breast cancer is the most common cancer among women, the repercussions of bone metastases and associated skeletal-related events for patients, their families, and the healthcare system are significant. As a consequence, evaluating bone metastases and skeletal-related events in breast cancer patients is essential for accurate diagnosis, treatment, and long-term care. This study aims to investigate the relationship between metastatic volume measurement, skeletal-related events, and survival in women diagnosed with breast cancer and bone metastases.

## PATIENTS AND METHODS

The retrospective study evaluated the medical records of female breast cancer patients diagnosed, treated, and followed up at the medical oncology clinic of the Ankara Atatürk Training and Research Hospital between January 2005 and December 2019. The study comprised only patients diagnosed with breast cancer and bone metastases. A total of 957 medical records of breast cancer cases were analyzed, and 82 female patients (mean age: 53±14.3 years; range, 23 to 87 years) with bone metastasis were included in the study. To be eligible for the study, patients were required to have a confirmed tissue diagnosis, undergo regular follow-ups, and possess imaging/biopsy results.

The study's data were collected using an evaluation form created by the researchers. The patient data collected included age, breast cancer type, the date of initial breast cancer diagnosis, any history of bone and visceral metastases, the sites of the metastases, and the presence of any skeletal-related events, such as pain, pathological fracture, spinal cord compression, hypercalcemia, and whether bisphosphonate therapy was administered. The patients were separated into two groups according to age: those under 60 years and those over 60 years of age.

### Evaluation of metastases of patients and measurement of metastatic volume

To assess the diagnosis of metastatic breast cancer, all laboratory and imaging tests conducted within 30 days of the diagnosis were evaluated together. Metastatic lesions were evaluated independently, while any bone metastases that appeared after 30 days of diagnosis were not factored in for the analysis. Metastasis diagnosis in patients was conducted by a radiologist with expertise in musculoskeletal tumor detection. The diagnosis was made using a combination of whole-body bone scintigraphy, magnetic resonance imaging, or positron emission tomography and computed tomography scans.

Metastatic volume measurement was performed in two steps based on the number and sites of metastases. During the first stage, volume measurement was based on the number of metastatic bones, classified into high-volume and low-volume groups. A high volume of metastases was considered present when there were four or more metastatic bones, as well as one axial extraskeletal metastasis or visceral metastasis.[13] The second stage involved volume measurement according to the location of the metastatic bones, which were categorized into three groups: *(i)* vertebrae, ribs, sternum, and calvarial bones; *(ii)* scapula, clavicle, proximal humerus, and proximal femur regions; *(iii)* femur and humeral diaphyseal and distal regions, irrespective of other bone metastases, and other metastasis sites in long bones.

### Statistical analysis

The data were analyzed using SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics of the study group were reported in the

form of mean ± standard deviation (SD), median (min-max), or number and percentage. Data analysis was conducted using the chi-square test, and survival analysis was carried out using the Kaplan-Meier method. A *p*-value <0.05 was considered statistically significant.

## RESULTS

Sixty-three (76.8%) patients had a histopathological diagnosis of ductal carcinoma, and 41 (50%) had bone metastases identified at their initial diagnosis. Among the patients, 82.9% (n=68) were administered bisphosphonate therapy for bone metastases. The most commonly observed site for bone metastases was the vertebrae, while liver metastases were the most frequent visceral metastases observed among participants. Cancer types and metastasis characteristics of the study group are provided in Table I, while Table II presents information on the sites of metastases.

Among the study group, at least one skeletal-related event was experienced by 62 (75.6%) participants, with 30 (36.6%) of them experiencing at least three skeletal-related events. The most common skeletal-related event was bone pain (n=49, 33.8%; Table III). The occurrence of skeletal-related events was not found to have a correlation with the measurement of metastatic volume based on bone localization and bone number (Table IV).

The median survival time from the first diagnosis was 56.8 (1-231) months. Survival times of the patients are presented in Table V. Compared to bone number, patients over the age of 60 had a higher metastatic volume, and those in the third group and with lung involvement had a significantly shorter survival time (p<0.05 for each). Table VI presents the distribution of patient survival times according to certain variables.

**TABLE I**
Cancer types and metastasis characteristics of the study group

| Characteristics | n | % |
|---|---|---|
| Age groups (year) | | |
| ≥60 age | 29 | 35.4 |
| <60 age | 53 | 64.6 |
| Breast cancer histopathological diagnosis | | |
| Ductal carcinoma | 63 | 76.8 |
| Lobular carcinoma | 8 | 9.8 |
| Mixed carcinoma | 7 | 8.5 |
| Other carcinomas | 4 | 4.9 |
| Bone metastasis at diagnosis | | |
| Present | 41 | 50 |
| Absent | 41 | 50 |
| Brain/visceral metastases at diagnosis | | |
| Present | 37 | 45.1 |
| Absent | 45 | 54.9 |
| Brain/visceral metastases in the disease process | 62 | 75.6 |
| Present | 20 | 24.4 |
| Absent | | |

**TABLE II**
Metastasis sites of the study group

| Metastasis sites | n* | %* |
|---|---|---|
| Distribution of bone metastases | | |
| Vertebra | 80 | 24.9 |
| Pelvis | 55 | 17.1 |
| Costa | 52 | 16.1 |
| Femur | 35 | 10.9 |
| Sternum | 28 | 8.7 |
| Calvarium | 23 | 7.1 |
| Humerus | 22 | 6.8 |
| Scapula | 16 | 5.0 |
| Clavicle | 8 | 2.5 |
| Other** | 3 | 0.9 |
| Sum | 322 | 100.0 |
| Visceral organ (during illness) | | |
| Lung | 37 | 38.9 |
| Liver | 39 | 41.1 |
| Brain | 13 | 13.7 |
| Other*** | 6 | 6.3 |
| Sum | 95 | 100.0 |

* Numbers and percentages are given over the number of metastases, not individuals; ** Tibia, fibula; *** Adrenal gland, skin.

**TABLE III**
Detected skeletal-related events

| Skeletal-related events | n | % |
|---|---|---|
| Bone pain | 49 | 33.8 |
| Need for radiotherapy | 46 | 31.7 |
| Pathological fracture | 32 | 22.1 |
| Hypercalcemia | 8 | 5.5 |
| Cord compression | 5 | 3.5 |
| Need for surgery | 5 | 3.4 |
| Sum | 145 | 100.0 |

* Numbers and percentages are given not on individuals, but on detected skeletal-related events.

**TABLE IV**
Distribution of metastatic volume measurement according to the incidence of skeletal-related events

| | | | Skeletal-related events | | | | |
|---|---|---|---|---|---|---|---|
| | | | Absent | | Present | | |
| | n | % | n | % | n | % | p |
| Metastatic volume (According to the number of bones) | | | | | | | 0.934 |
| Low | 24 | 29.3 | 6 | 25.0 | 18 | 75.0 | |
| High | 58 | 70.7 | 14 | 24.1 | 44 | 75.9 | |
| Metastatic volume* (According to bone localization) | | | | | | | 0.286 |
| Group 1 | 17 | 37.8 | 4 | 23.5 | 13 | 76.5 | |
| Group 2 | 21 | 46.7 | 6 | 28.6 | 15 | 71.4 | |
| Group 3 | 7 | 15.6 | 0 | 0.0 | 7 | 100.0 | |

* 37 patients with visceral metastases were not included in the metastatic volume measurement based on bone localization.

**TABLE V**
Survival times of patients

| | Median (month) | Min-Max |
|---|---|---|
| Overall survival | 56.8 | 1.0-231.1 |
| Time from breast cancer diagnosis to bone metastasis | 2.0 | 0.0-299.0 |
| Time from breast cancer diagnosis to brain or visceral metastasis | 21.0 | 0.0-299.0 |
| Time to death after metastasis | 29.5 | 1.0-159.0 |
| Time to death after bone metastasis | 27.5 | 1.0-159.0 |
| Time to death after a brain or visceral metastasis | 16.9 | 1.0-66.2 |

**TABLE VI**
Distribution of patients' survival times according to some variables

| | Overall survival time | | |
|---|---|---|---|
| | Median (month) | Min-Max | Statistical Analysis Log Rank |
| Age group (year) | | | 0.026 |
| ≥60 age | 24.7 | 5.4-43.9 | |
| <60 age | 76.8 | 50.9-102.6 | |
| Metastatic volume (According to the number of bones) | | | 0.017 |
| Low | 89.9 | 31.1-148.6 | |
| High | 47.3 | 24.1-70.6 | |
| Metastatic volume (According to bone localization) | | | 0.008 |
| Group 1 | 165.6 | 26.6-304.7 | |
| Group 2 | 71.4 | 24.7-118.1 | |
| Group 3 | 38.3 | 0.0-97.5 | |
| Absent | 66.2 | 39.6-92.8 | |
| Lung metastasis | | | 0.044 |
| Present | 38.3 | 28.9-47.7 | |
| Absent | 77.8 | 46.8-108.8 | |
| Absent | 73.4 | 34.7-112.1 | |
| Skeletal-related events | | | 0.034 |
| Present | 63.3 | 1.0-231.1 | |
| Absent | 21.6 | 3.3-129.5 | |

## DISCUSSION

Understanding the characteristics of bone metastases and skeletal-related events in breast cancer patients is crucial. This study aimed to investigate how metastatic volume measurement affects skeletal-related events in women with breast cancer who have bone metastases. The study's defined classifications of metastatic volume did not display any significant correlation with skeletal-related events.

Previous research on women with breast cancer and bone metastases conducted in two separate studies showed mean ages of 48 and 54 years.[14,15] In the current study, the majority of patients were under the age of 60, with a mean age of 53 years. A Turkish study reported a median age of 44.5 years.[16] Due to differences in life expectancy and variations in screening and diagnostic opportunities between countries, different demographic and developmental characteristics can influence study outcomes.

There are many studies that evaluate the relationship between breast cancer and age, and many cut-off values have been used for the age range. A threshold value of 60 was determined in our study to evaluate the young and old population. The current study revealed that patients who were over 60 years old had shorter survival times. El Saghir et al.[17] found that survival times were reduced for patients under 35 years and over 50 years of age. One possible explanation for these results is that younger patients may not consider themselves at risk, leading to a later diagnosis, different cancer histopathology, and a lack of participation in screening programs. Shen et al.[18] reported that increasing age was the most significant predictor of poor survival. Additionally, a study by Malmgren et al.[19] found that patients aged 70 and over had poorer survival rates for metastatic breast cancer.

The current study found that the vertebra was the most frequent site of bone involvement, with approximately 70% of patients having a high metastatic volume. The first group of patients, who had only the vertebrae, ribs, sternum, and calvarial bones affected with low metastatic volume, had longer survival times. Peterson et al.[20] reported that over half of the patients had more than 10 bone lesions, and overall survival was longer in those with less than five lesions. Koizumi et al.[21] found that the majority of patients had multiple bone metastases, with the most frequent site being the vertebrae or sternum for solitary metastases, and survival was worse for those with multiple metastases. Similar to this study, van der Pol et al.[22] assessed bone metastases by scoring regions and found that patients with widespread bone metastases (high score) had poorer survival. Ahn et al.[23] demonstrated that patients with multiple bone lesions had lower overall survival times.

Metastasis development is a key factor that restricts survival time. Largillier et al.[24] reported a median total survival time of 23 months in patients after metastasis. The study by Rezaianzadeh et al.[25] found that the probability of poor survival in patients with bone metastases was roughly two-fold higher, while those with lung metastases were three times more likely to undergo poor survival. However, Idota et al.[26] reported no difference in overall survival between patients with only bone metastases and those with visceral metastases. Consequently, the number and region of metastases, as well as the treatment method used, can influence survival outcomes.

The current study found that 75% of patients experienced at least one skeletal-related event, with 37% suffering three or more events.[27] The most prevalent events were bone pain, the need for radiotherapy, and pathological fracture, and no connection was found between metastatic volume measurement and the occurrence of skeletal-related events. In Domchek et al.'s[28] study, at least one skeletal-related event was found in 51% of patients, with over 25% having three or more events. The most common event was radiotherapy, followed by hypercalcemia and surgery. Skeletal-related events were reported in 81% of patients with only bone metastases, 60% with bone and other locations, and 21% in patients with extraskeletal metastases, with no difference in event type between groups.[28] Sathiakumar et al.[29] reported that 46% of patients with bone metastases experienced skeletal-related events, with radiotherapy, pathological fracture, and spinal cord compression being the most prevalent events.

Although the current study found no notable difference in survival time for patients who experienced skeletal-related events, it may be due to the small sample size. However, a population-based study in the USA reported that having a bone metastasis, as indicated by Medicare claims, was associated strongly with mortality among women with breast cancer. This association was stronger for bone metastasis complicated by skeletal-related events compared to bone metastasis without a skeletal-related event.[29]

A study carried out in Massachusetts found that the median life expectancy decreased in patients with skeletal-related events.[28] Nevertheless, the reason for the diverse outcomes in our study may be that the risk of skeletal-related events increases as life expectancy prolongs.

The main shortcomings of the present study were its retrospective design and the limited number of patients studied. In addition, the information in the patient files was evaluated for pain, which is a skeletal-related event criteria in our study; however, secondary events, such as avascular necrosis, may have been included in this group and may cause bias in the evaluation of skeletal-related events.

In conclusion, measuring metastatic volume may be a critical factor in evaluating the survival of breast cancer patients with bone metastases. Prospective multicenter studies with a larger patient population using different scoring methods are needed to gain further understanding of the prognosis and treatment alternatives for individuals with metastatic breast cancer.

**Ethics Committee Approval:** The study protocol was approved by the Yıldırım Beyazıt University Faculty of Medicine Clinical Research Ethics Committee (date: 09.05.2019, no: 63). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Data collection and/or processing, writing the article, literature review, references: H.Y.; Idea/concept, data collection and/or processing: M.N.A.; Analysis and/or interpretation, critical review: D.Ş.D.; Design: M.A.N.Ş.; Critical review: R.Ö.; Idea/concept, design: B.Y. All authors approved the final version of this manuscript.

**Conflict of Interest:** The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

**Funding:** The authors received no financial support for the research and/or authorship of this article.

## REFERENCES

1. T.C. Ministry of Health, General Directorate of Public Health, Cancer Department, Breast Cancer Screening Program National Standards. 2019 Available at: https://hsgm.saglik.gov.tr/tr/kanser-tarama-standartlari/listesi/485-meme-kanseri-tarama- program%C4%B1-ulusal-standartlar%C4%B1.html. [Accessed: 20.07.2023].
2. Gültekin M, Boztaş G. Türkiye cancer statistics. Ministry of Health, Public Health Institution of Türkiye; 2014.
3. Ulucaköy C, Yapar A, Şeyhoğlu MC, Tokgöz MA, Atalay İB, Güngör BŞ. Demographic features of metastatic bone tumors. Acta Oncologica Turcica 2021;54:98-102.
4. Batson OV. The function of the vertebral veins and their role in the spread of metastases. Ann Surg 1940;112:138-49. doi: 10.1097/00000658-194007000-00016.
5. Awolaran O, Brooks SA, Lavender V. Breast cancer osteomimicry and its role in bone specific metastasis; an integrative, systematic review of preclinical evidence. Breast 2016;30:156-71. doi: 10.1016/j.breast.2016.09.017.
6. Weinfurt KP, Li Y, Castel LD, Saad F, Timbie JW, Glendenning GA, et al. The significance of skeletal-related events for the health-related quality of life of patients with metastatic prostate cancer. Ann Oncol 2005;16:579-84. doi: 10.1093/annonc/mdi122.
7. Yong M, Jensen AÖ, Jacobsen JB, Nørgaard M, Fryzek JP, Sørensen HT. Survival in breast cancer patients with bone metastases and skeletal-related events: A population-based cohort study in Denmark (1999-2007). Breast Cancer Res Treat 2011;129:495-503. doi: 10.1007/s10549-011-1475-5.
8. Zhang H, Zhu W, Biskup E, Yang W, Yang Z, Wang H, et al. Incidence, risk factors and prognostic characteristics of bone metastases and skeletal-related events (SREs) in breast cancer patients: A systematic review of the real world data. J Bone Oncol 2018;11:38-50. doi: 10.1016/j.jbo.2018.01.004.
9. LoRusso P. Analysis of skeletal-related events in breast cancer and response to therapy. Semin Oncol 2001;28(4 Suppl 11):22-7. doi: 10.1016/s0093-7754(01)90228-3.
10. Lipton A, Steger GG, Figueroa J, Alvarado C, Solal-Celigny P, Body JJ, et al. Randomized active-controlled phase II study of denosumab efficacy and safety in patients with breast cancer-related bone metastases. J Clin Oncol 2007;25:4431-7. doi: 10.1200/JCO.2007.11.8604.
11. Stopeck AT, Lipton A, Body JJ, Steger GG, Tonkin K, de Boer RH, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: A randomized, double-blind study. J Clin Oncol 2010;28:5132-9. doi: 10.1200/JCO.2010.29.7101.
12. Ruggieri P, Mavrogenis AF, Casadei R, Errani C, Angelini A, Calabrò T, et al. Protocol of surgical treatment of long bone pathological fractures. Injury 2010;41:1161-7. doi: 10.1016/j.injury.2010.09.018.
13. Sweeney CJ, Chen YH, Carducci M, Liu G, Jarrard DF, Eisenberger M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med 2015;373:737-46. doi: 10.1056/NEJMoa1503747.
14. Lüftner D, Lorusso V, Duran I, Hechmati G, Garzon-Rodriguez C, Ashcroft J, et al. Health resource utilization associated with skeletal-related events in patients with advanced breast cancer: Results from a prospective, multinational observational study. Springerplus 2014;3:328. doi: 10.1186/2193-1801-3-328.
15. Tanaka R, Yonemori K, Hirakawa A, Kinoshita F, Takahashi N, Hashimoto J, et al. Risk factors for developing skeletal-related events in breast cancer patients with bone metastases undergoing treatment with bone-modifying agents. Oncologist 2016;21:508-13. doi: 10.1634/theoncologist.2015-0377.
16. Sakin A, Sakalar T, Sahin S, Yasar N, Demir C, Geredeli C, et al. Factors affecting survival and treatment efficacy in breast cancer patients with bone marrow metastasis. Breast J 2020;26:815-8. doi: 10.1111/tbj.13647.

17. El Saghir NS, Seoud M, Khalil MK, Charafeddine M, Salem ZK, Geara FB, et al. Effects of young age at presentation on survival in breast cancer. BMC Cancer 2006;6:194. doi: 10.1186/1471-2407-6-194.
18. Shen K, Yao L, Wei J, Luo Z, Yu W, Zhai H, et al. Worse characteristics can predict survival effectively in bilateral primary breast cancer: A competing risk nomogram using the SEER database. Cancer Med 2019;8:7890-902. doi: 10.1002/cam4.2662.
19. Malmgren JA, Calip GS, Atwood MK, Mayer M, Kaplan HG. Metastatic breast cancer survival improvement restricted by regional disparity: Surveillance, Epidemiology, and End Results and institutional analysis: 1990 to 2011. Cancer 2020;126:390-9. doi: 10.1002/cncr.32531.
20. Peterson LM, O'Sullivan J, Wu QV, Novakova-Jiresova A, Jenkins I, Lee JH, et al. Prospective study of serial 18F-FDG PET and 18F-Fluoride PET to predict time to skeletal-related events, time to progression, and survival in patients with bone-dominant metastatic breast cancer. J Nucl Med 2018;59:1823-30. doi: 10.2967/jnumed.118.211102.
21. Koizumi M, Yoshimoto M, Kasumi F, Ogata E. Comparison between solitary and multiple skeletal metastatic lesions of breast cancer patients. Ann Oncol 2003;14:1234-40. doi: 10.1093/annonc/mdg348.
22. van der Pol CB, Schweitzer ME, Di Primio G, Sampaio ML, Kielar A, Clemons M, et al. Breast cancer and bone metastases: The association of axial skeleton MRI findings with skeletal-related events and survival. Breast Cancer Res Treat 2014;146:583-9. doi: 10.1007/s10549-014-3046-z.
23. Ahn SG, Lee HM, Cho SH, Lee SA, Hwang SH, Jeong J, et al. Prognostic factors for patients with bone-only metastasis in breast cancer. Yonsei Med J 2013;54:1168-77. doi: 10.3349/ymj.2013.54.5.1168.
24. Largillier R, Ferrero JM, Doyen J, Barriere J, Namer M, Mari V, et al. Prognostic factors in 1,038 women with metastatic breast cancer. Ann Oncol 2008;19:2012-9. doi: 10.1093/annonc/mdn424.
25. Rezaianzadeh A, Peacock J, Reidpath D, Talei A, Hosseini SV, Mehrabani D. Survival analysis of 1148 women diagnosed with breast cancer in Southern Iran. BMC Cancer 2009;9:168. doi: 10.1186/1471-2407-9-168.
26. Idota A, Sawaki M, Yoshimura A, Hattori M, Inaba Y, Oze I, et al. Bone Scan Index predicts skeletal-related events in patients with metastatic breast cancer. Springerplus 2016;5:1095. doi: 10.1186/s40064-016-2741-0.
27. Atik OŞ. Which articles do the editors prefer to publish? Jt Dis Relat Surg 2022;33:1-2. doi: 10.52312/jdrs.2022.57903.
28. Domchek SM, Younger J, Finkelstein DM, Seiden MV. Predictors of skeletal complications in patients with metastatic breast carcinoma. Cancer 2000;89:363-8. doi: 10.1002/1097-0142(20000715)89:2<363::aid-cncr22>3.0.co;2-3.
29. 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;131:231-8. doi: 10.1007/s10549-011-1721-x.