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RESEARCH ARTICLE

# The Epidemiological Trends of Primary Benign and Malignant Bone Tumors in Iran

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## Abstract

**Background & objective:** The incidence of various tumors is strongly influenced by racial characteristics, and therefore the distribution of benign and malignant lesions follows different epidemiological and pathophysiological patterns in the societies. This study aimed to evaluate the epidemiological trend of primary benign and malignant bone tumors in the Iranian population. **Methods:** In this cross-sectional study, epidemiological and pathological information related to cases of benign and malignant primary bone tumors registered in the data registry of pathology laboratory of Imam Khomeini Complex hospital in Iran between 2017 and 2022 were assessed. Including criteria was all patient with established pathology diagnosis of bone tumors and excluding criteria was patients with incomplete data. **Results:** In total, 617 primary bone tumors (233 benign lesions and 384 malignant lesions) were assessed within 5 years between 2017 and 2022. The average age of patients in benign and malignant lesions subgroups was 29.50±16.95 years and 35.30±19.70 years respectively with the highest incidence in the second and third decades of life in both lesion types. Overall, 52.8% of benign tumors and 58.9% of malignant tumors were found in men. The most frequent benign tumors reported in the study periods including osteochondroma found in 30.5%, and enchondroma in 29.2%. Of malignant bone tumors, osteosarcoma was the most prevalent type with an overall prevalence of 32.6% followed by chondrosarcoma (20.8%) and Ewing sarcoma (16.7%). In the case of benign tumors, a decrease in the trend during the last four years was showed, while the trend of malignant tumors was completely upward in the last four years. **Conclusion:** The epidemiological distribution of primary benign and malignant bone tumors in Iran is similar to global statistics, but with a downward trend in benign masses and vice versa, an increasing trend in malignant tumors in recent years.

**Keywords:** Bone tumors- benign- malignant

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## Introduction

Although bone tissue is a common target for all types of cancers, primary bone malignancies are much rarer and account for only 0.2% of all malignancies [1]. Despite being rare, the outcome of such bone malignancies is significant, and the overall survival rate and recurrence-free survival in these malignancies are low. The progress of imaging modalities and molecular techniques regarding the identification of early bone points involved with the tumor has led to the early identification of such lesions, however, in many cases, because the lesion remains asymptomatic until the advanced stages, it is not possible to detect these tumors early in many cases [2, 3]. Additionally, community-based evaluations in various communities have indicated a high variant in the epidemiologic characteristics of primary benign and malignant bone tumors. In developed countries like the United States and the United Kingdom, primary malignant bone tumors are the third leading osteogenic cancer-related

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death followed by hematopoietic malignancies in different age groups especially among young adults [4, 5]. Even in developed countries, a downward trend in the incidence of these types of tumors can be revealed. In a recent data registry-based study in China, the incidence of primary bone tumors declined by 2.2% in men and 4.8% in women per year, and the rates in urban areas were lower than those in rural areas [6]. Unfortunately, there is very little information about the state of bone tumors in developing countries or the third world, which is due to the lack of a comprehensive data registry system to record cases of bone tumors and the lack of proper follow-up of patient's prognosis. In a study on the Iranian population, it was found an increasing trend in the incidence of bone sarcomas from 8.59 in 2007 to 11.37 per million person-year in 2015 [7] indicates the increase in the incidence of this type of malignancy during the last decade, despite the modification of scientific instructions for their prevention and treatment.

The best approach to reduce the incidence of various types of cancers is to obtain a clear and comprehensive view of the epidemic characteristics as well as the physiopathological indicators related to them. This issue can only be made possible through the design and management of community-based data registries in large referral centers in the countries for such patients. Also, such a tool provides the possibility of checking the trend of changes in the incidence of various cancers during different years. What we discussed in this study was the evaluation of the epidemiological situation of primary benign and malignant bone tumors and the evaluation of the changes in these characteristics during the last six years.

## Materials and Methods

Imam Khomeini Complex hospital in Tehran, as the largest diagnostic and treatment complex in the country, is considered the largest reference for cancer patients throughout Iran. This diagnostic and treatment center has the most comprehensive data registry regarding the registration and follow-up of all types of cancers, especially bone cancers. In the present study, the aim was to collect epidemiological and pathological information related to cases of benign and malignant primary bone tumors registered in the data registry of this complex between 2017 and 2022. Including criteria was all patient with established pathology diagnosis of bone tumors and excluding criteria was patients with incomplete data. What was focused on in the present studies was, first of all, the evaluation of the demographic characteristics of patients with benign and malignant bone tumors and the site of involvement in these tumors. Then, the change in these parameters during the six years of the study was also evaluated.

Descriptive data were described based on frequency and percentage for qualitative variables and mean and standard deviation for quantitative parameters. Qualitative variables were compared using the Chi-square test and quantitative variables using independent t-tests. The SPSS software version 26.0) was used for data analysis. A p-value < 0.05 was considered significant.

## Results

In total, 617 primary bone tumors (233 benign lesions and 384 malignant lesions) were assessed within 5 years between 2017 and 2022. The demographic characteristics of these tumor lesions are summarized in (Table 1). The average age of patients in benign and malignant lesions subgroups was 29.50±16.95 years (ranged 1 to 79 years) and 35.30±19.70 years (ranged 1 to 91 years) respectively. Regarding age distribution, the age distribution was completely asymmetric, and involvement in both categories of benign and malignant tumors was related to the second and third decades of life (Figure 1). Concerning sex distribution, 52.8% of benign tumors and 58.9% of malignant tumors were found in men. Overall, the most frequent site involved by benign tumors included the femur (19.3%) followed by fingers (18.5%) and tibia (13.7%), while malignant bone lesions were prominently revealed in the femur (31.8%) followed by the shoulder (11.2%), humerus (10.9%) and hip (10.7%) (Table 1). Regarding the side of involvement, both groups of lesions mainly involved the right side (54.1% of benign tumors and 59.6% of malignant tumors). The different types of benign and malignant tumors are presented in (Figure 2). The most frequent benign tumors reported in the study periods included osteochondroma found in 30.5%, and enchondroma in 29.2%. Of malignant bone tumors, osteosarcoma was the most prevalent type with an overall prevalence of 32.6% followed by chondrosarcoma (20.8%) and Ewing sarcoma (16.7%). Comparing benign

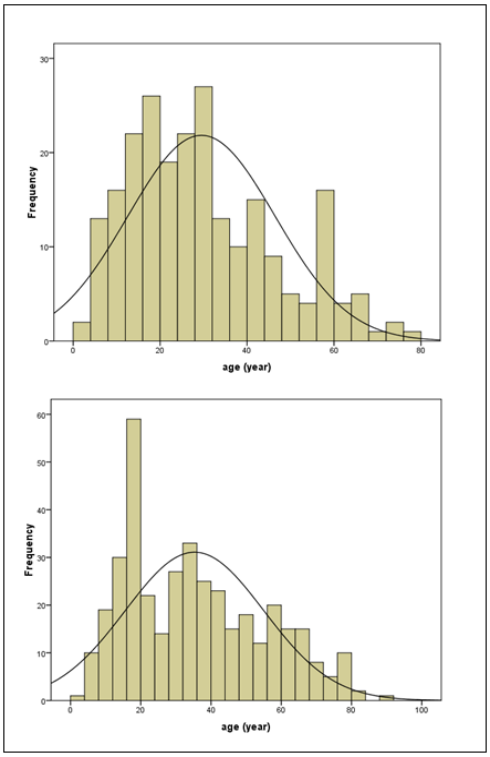


Figure 1. Age Distribution in Benign and Malignant Primary Bone Tumors

Table 1. Baseline Characteristics of Benign and Malignant Primary Bone Tumors

| Characteristics | Benign tumors (n = 233) | Malignant tumors (n = 384) | P value |
|---|---|---|---|
| Gender, % | | | 0.141 |
| Female | 110 (47.2) | 158 (41.1) | |
| Male | 123 (52.8) | 226 (58.9) | |
| Mean age, year | | | <0.001 |
| Side of involvement, % | | | 0.176 |
| Left | 107 (45.9) | 155 (40.4) | |
| Right | 126 (54.1) | 229 (59.6) | |
| Site of involvement, % | | | <0.001 |
| Chest wall | 11 (4.7) | 30 (7.8) | |
| Elbow | 3 (1.3) | 2 (0.5) | |
| Femur | 45 (19.3) | 122 (31.8) | |
| Fibula | 4 (1.7) | 6 (1.6) | |
| Finger | 43 (18.5) | 9 (2.3) | |
| Hand | 2 (0.9) | 0 (0.0) | |
| Hip | 15 (6.4) | 41 (10.7) | |
| Humerus | 25 (10.7) | 42 (10.9) | |
| Knee | 13 (5.6) | 14 (3.6) | |
| Leg | 8 (3.4) | 12 (3.1) | |
| Radius | 5 (2.1) | 3 (0.8) | |
| Shoulder | 11 (4.7) | 43 (11.2) | |
| Tibia | 32 (13.7) | 35 (9.1) | |
| Ulna | 6 (2.6) | 4 (1.0) | |
| Vertebra | 5 (2.1) | 20 (5.2) | |
| Wrist | 5 (2.1) | 1 (0.3) | |

Table 2. Baseline Characteristics According to the Years Studied in Benign Tumors

| Characteristics | Y2017 | Y2018 | Y2019 | Y2020 | Y2021 | Y2022 | p-value |
|---|---|---|---|---|---|---|---|
| Gender, % | | | | | | | 0.657 |
| Female | 50.00 | 45.90 | 56.20 | 41.20 | 38.90 | 50.00 | |
| Male | 50.00 | 54.10 | 43.80 | 58.80 | 61.10 | 50.00 | |
| Mean age, year | 26.8±16.5 | 27.8±16.0 | 32.4±19.0 | 34.4±17.3 | 25.1±14.7 | 33.5±16.5 | 0.103 |
| Side of involvement, % | | | | | | | 0.43 |
| Left | 52.50 | 42.60 | 56.20 | 35.30 | 41.70 | 42.90 | |
| Right | 47.50 | 57.40 | 43.80 | 64.70 | 58.30 | 57.10 | |
| Site of involvement, % | | | | | | | 0.153 |
| Chest wall | 0.00 | 4.90 | 8.30 | 8.80 | 2.80 | 0.00 | |
| Elbow | 0.00 | 3.30 | 2.10 | 0.00 | 0.00 | 0.00 | |
| Femur | 17.50 | 11.50 | 22.90 | 23.50 | 19.40 | 35.70 | |
| Fibula | 0.00 | 1.60 | 0.00 | 5.90 | 2.80 | 0.00 | |
| Finger | 15.00 | 24.60 | 25.00 | 5.90 | 22.20 | 0.00 | |
| Hand | 0.00 | 3.30 | 0.00 | 0.00 | 0.00 | 0.00 | |
| Hip | 7.50 | 6.60 | 8.30 | 0.00 | 2.80 | 21.40 | |
| Humerus | 10.00 | 13.10 | 8.30 | 14.70 | 8.30 | 7.10 | |
| Knee | 7.50 | 6.60 | 6.20 | 0.00 | 8.30 | 0.00 | |
| Leg | 2.50 | 1.60 | 4.20 | 0.00 | 5.60 | 14.30 | |
| Radius | 5.00 | 4.90 | 0.00 | 0.00 | 0.00 | 0.00 | |
| Shoulder | 10.00 | 4.90 | 4.20 | 0.00 | 2.80 | 7.10 | |
| Tibia | 10.00 | 11.50 | 4.20 | 32.40 | 16.70 | 14.30 | |
| Ulna | 5.00 | 0.00 | 2.10 | 5.90 | 2.80 | 0.00 | |
| Vertebra | 5.00 | 1.60 | 2.10 | 2.90 | 2.80 | 0.00 | |
| Wrist | 5.00 | 0.00 | 2.10 | 2.90 | 2.80 | 0.00 | |

and malignant tumors about baseline characteristics showed no difference in gender (p-value = 0.141), and the side of involvement (p-value = 0.176), however, those who suffered malignant tumors were significantly older (p-value < 0.001) (Table 1). Also, there was a significant difference in the site of involvement between benign and malignant tumors (p-value < 0.001).

The distribution of background characteristics according to the evaluated year is presented in (Tables 2 and 3). No difference was observed in the gender and age distribution of patients with benign or malignant tumors in different years. Also, the side of involvement did not show a significant difference in study years. However, the trend of benign and malignant lesions was completely different during the six years of assessment (p-value = 0.022), so in the case of benign tumors, we were faced with a decrease in the trend during the last four years, while the trend of malignant tumors was completely upward during the last four years (Figure 3).

## Discussion

The incidence of various cancers is strongly dependent on racial and genetic characteristics, and therefore the distribution of cancer types in different societies follows different epidemiological and pathophysiological patterns [8-10]. Accordingly, the planning and management of prevention and health related to cancers are completely different in different societies. The first step in presenting this plan is to provide an accurate and correct view of the distribution of these cancers in society, and more importantly, to evaluate the changes in their epidemiological indicators over many years.

What was examined in the first place in the present study was the evaluation of the gender and age distribution of benign and malignant bone tumors in Iran. For this purpose, the data registry of one of the most important referral centers for this type of cancer in the capital of Iran was selected to be considered as a sample of Iranian society. In this study, firstly, it was found that the age distribution of patients in both types of tumors is related to the second and third decades of life, but the incidence of malignant masses occurs a decade later than benign masses. Secondly, in terms of sex ratio, these tumors occur almost equally in both sexes. The mentioned results on tumors-related age distribution are consistent with the results obtained from the global summary [11, 12]. As shown by reviewing the literature, two peaks are observable in primary malignant bone tumor incidence rates in the second decade of life, peaking during adolescence globally, although again in the seventh and eighth decades of life. In this regard, the second peak starts with a gradual increase after the age of 40 years [13]. However, regarding sex distribution, it has been shown

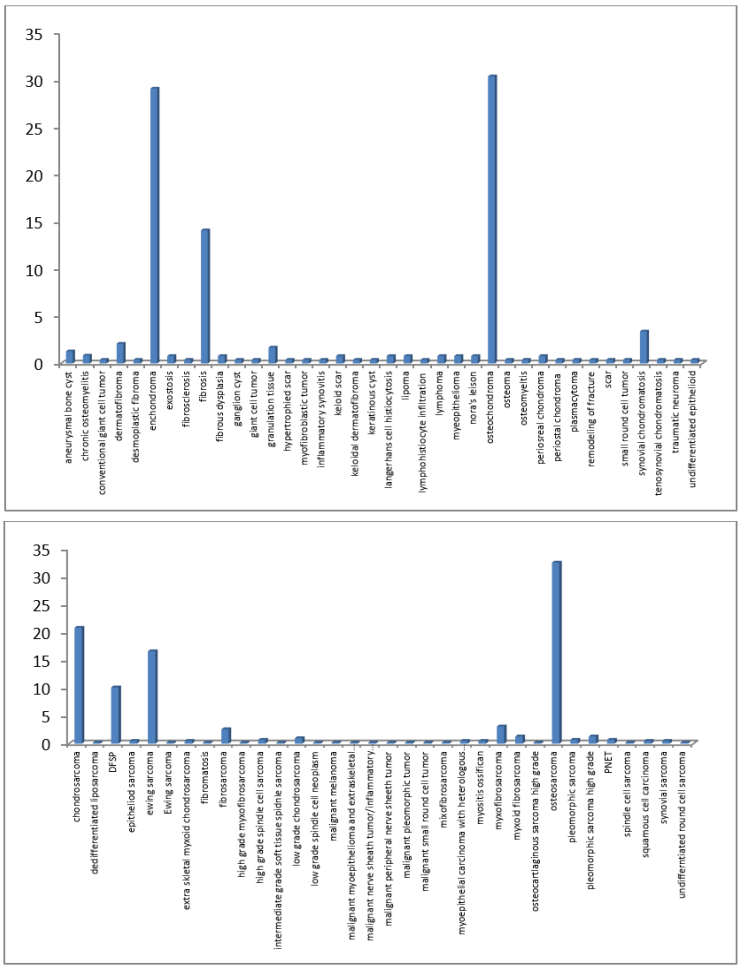


Figure 2. The Prevalence of Benign and Malignant Tumors

Table 3. Baseline Characteristics According to the Years Studied in Malignant Tumors

| Characteristics | Y2017 | Y2018 | Y2019 | Y2020 | Y2021 | Y2022 | p-value |
|---|---|---|---|---|---|---|---|
| Gender, % | | | | | | | 0.47 |
| Female | 39.00 | 40.30 | 33.30 | 49.20 | 40.50 | 50.00 | |
| Male | 61.00 | 59.70 | 66.70 | 50.80 | 59.50 | 50.00 | |
| Mean age, year | 35.8±19.7 | 34.2±21.2 | 38.0±18.7 | 30.1±18.9 | 37.9±19.6 | 33.8±19.0 | 0.172 |
| Side of involvement,% | | | | | | | 0.758 |
| Left | 39.0 | 45.2 | 39.40 | 46.20 | 36.90 | 33.3 | |
| Right | 61.00 | 54.80 | 60.60 | 53.80 | 63.10 | 66.70 | |
| Site of involvement, % | | | | | | | 0.517 |
| Chest wall | 10.40 | 6.50 | 7.60 | 7.70 | 6.00 | 10.00 | |
| Elbow | 1.30 | 0.00 | 1.50 | 0.00 | 0.00 | 0.00 | |
| Femur | 27.30 | 38.70 | 40.90 | 32.30 | 23.80 | 30.00 | |
| Fibula | 1.30 | 1.60 | 0.00 | 3.10 | 2.40 | 0.00 | |
| Finger | 2.60 | 4.80 | 3.00 | 0.00 | 2.40 | 0.00 | |
| Hip | 11.70 | 3.20 | 4.50 | 15.40 | 17.90 | 0.00 | |
| Humerus | 9.10 | 12.90 | 16.70 | 9.20 | 8.30 | 10.00 | |
| Knee | 3.90 | 3.20 | 3.00 | 4.60 | 4.80 | 0.00 | |
| Leg | 1.30 | 3.20 | 4.50 | 0.00 | 4.80 | 6.70 | |
| Radius | 1.30 | 3.20 | 4.50 | 0.00 | 4.80 | 0.00 | |
| Shoulder | 7.80 | 11.30 | 9.10 | 13.80 | 15.50 | 6.70 | |
| Tibia | 14.30 | 8.10 | 4.50 | 4.50 | 7.70 | 4.80 | |
| Ulna | 1.30 | 0.00 | 0.00 | 1.50 | 1.20 | 3.30 | |
| Vertebra | 6.50 | 6.50 | 3.00 | 1.50 | 8.30 | 3.30 | |
| Wrist | 0.00 | 0.00 | 0.00 | 1.50 | 0.00 | 0.00 | |

that although the age-standardized rates were almost equal among both genders in the first decade of life, they were consistently higher among males as compared to females across all other age groups [14]. However, it should be noted that this is not a consistent finding in all countries, as it has been shown that the sex and age distribution of bone tumors was very different in the Asian and American continents. In this regard, Asia has the lowest incidence rates of primary malignant bone tumors in the second decade of life in both genders however; the incidence of primary malignant bone tumors was the second highest in the elderly age group [15]. In contrast, South America has the highest incidence rates during the second decade of life among all the continents the incidence rates in Europe were similar to those in North America in all the age groups and the incidence rates in Oceania were the lowest among the continents with more developed countries [16]. In summary, what can be expected about the Iranian society is the highest distribution of these types of tumors in the second and third decades of life in both sexes.

Regarding the most prevalent types of benign and malignant tumors, the most frequent benign tumors reported in our society were osteochondroma and enchondroma, while osteosarcoma and chondrosarcoma were the most prevalent primary bone malignant tumors. The prevalence of benign and malignant bone tumors follows a similar pattern in almost all countries of the world [17, 18]. In this regard, regardless of the region, osteosarcoma is the most prevalent primary bone sarcoma, followed by chondrosarcoma and Ewing sarcoma. This finding is in line with previous studies on sarcomas in Taiwan [19], Japan [20], and the United Kingdom [21] as they found a similar order of prevalence for bone sarcomas.

What was of particular interest in the results of the present study was the difference in the trend of changes in the occurrence of two types of benign and malignant tumors in recent years in Iran. In other words, the decrease in the incidence of benign tumors and, on the contrary, the increase in the incidence of malignant tumors during the last six years was quite evident. We think that these trends have been strongly influenced by the COVID-19 pandemic in recent years and, secondly, by the reform of the comprehensive prevention and monitoring programs for the treatment of bone masses in Iran [22]. From the first point of view, the COVID-19 pandemic has had a

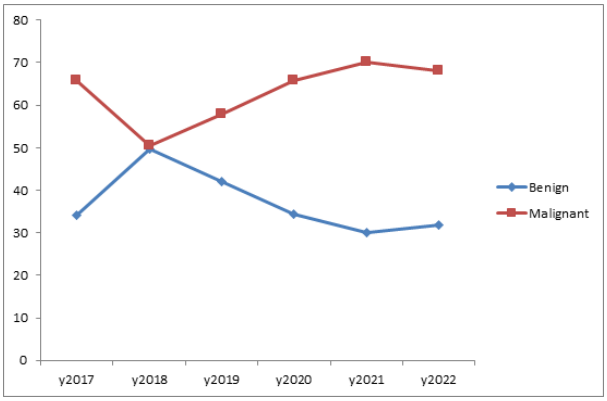


Figure 3. The Trend of the Changes in the Prevalence of Primary Bone Tumors within 6 Years of Study

major impact on the identification and occurrence of malignant tumors [23, 24]. Because, during this pandemic period, the number of visits to medical centers in patients diagnosed with benign tumors has decreased due to the fear of contracting COVID-19. On the other hand, the improvement of diagnostic techniques during the last decade made it possible to diagnose malignant tumors, especially in the early stages of the disease, and therefore we saw more of these cases being recorded in the cancer registry during this decade.

In conclusion, as a final summary, the epidemiological distribution of primary benign and malignant bone tumors in Iran corresponds to the global distribution. The majority of involvement in both tumors was related to the second and third decades of life and the gender distribution was almost the same. The most common benign tumors are osteochondroma and enchondroma while the most frequent malignant tumors are osteosarcoma and chondrosarcoma. The trend of changes in the occurrence of these two types of tumors in society during the last six years has been completely different and includes a decreasing trend in benign tumors and an increasing trend in malignant tumors. Gathering this information will improve the management of these tumors in our country.

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*Statement of Transparency and Principals:*

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee of author affiliated Institute.

• Study's data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

## References

1. Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, Harvey JD, Henrikson HJ, et al. Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. JAMA oncology. 2022 03 01;8(3):420-444. https://doi.org/10.1001/jamaoncol.2021.6987
2. Oweisi A, Mustafa MS, Mustafa LS, Eily AN, Rodriguez de la Vega P, Castro G, Barengo NC. The Association between Race/Ethnicity and Cancer Stage at Diagnosis of Bone Malignancies: A Retrospective Cohort Study. International Journal of Environmental Research and Public Health. 2022 Nov 28;19(23):15802. https://doi.org/10.3390/ijerph192315802
3. Rojas GA, Hubbard AK, Diessner BJ, Ribeiro KB, Spector LG. International trends in incidence of osteosarcoma (1988-2012). International Journal of Cancer. 2021 09 01;149(5):1044-1053. https://doi.org/10.1002/ijc.33673
4. Mirabello L, Troisi RJ, Savage SA. International osteosarcoma incidence patterns in children and adolescents, middle ages and elderly persons. International Journal of Cancer. 2009 07 01;125(1):229-234. https://doi.org/10.1002/ijc.24320
5. Zhao X, Wu Q, Gong X, Liu J, Ma Y. Osteosarcoma: a review of current and future therapeutic approaches. Biomedical Engineering Online. 2021 03 02;20(1):24. https://doi.org/10.1186/s12938-021-00860-0
6. Xi Y, Qiao L, Na B, Liu H, Zhang S, Zheng R, Wang W, Sun K, Wei W, He J. Primary malignant bone tumors incidence, mortality, and trends in China from 2000 to 2015. Chinese Medical Journal. 2023 09 05;136(17):2037-2043. https://doi.org/10.1097/CM9.0000000000002547
7. Karimi A, Ebrahimpour A, Sadighi M, Chehrassan M, Biglari F, Jafari Kafiabadi M, Akbari ME, Azizmohammad Looha M. Descriptive Epidemiology and Survival Rate of Osteosarcoma: The First National Population-Based Study in the Middle East (2008-2014). The Archives of Bone and Joint Surgery. 2023;11(10):649-657. https://doi.org/10.22038/ABJS.2023.59676.2945
8. Funovics PT. [Primary malignant bone tumors]. Orthopadie (Heidelberg, Germany). 2023 06;52(6):509-522. https://doi.org/10.1007/s00132-023-04387-1
9. Hodel S, Seeli F, Fuchs B. [Demographic Analysis of Patients with Osteosarcoma, Chonddrosarcoma, Ewing's Sarcoma from one Sarcoma Center in Switzerland]. Praxis. 2015 06 17;104(13):673-680. https://doi.org/10.1024/1661-8157/a002041
10. Strauss SJ, Frezza AM, Abecassis N, Bajpai J, Bauer S, Biagini R, Bielack S, et al. Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan Clinical Practice Guideline for diagnosis, treatment and follow-up. Annals of Oncology: Official Journal of the European Society for Medical Oncology. 2021 Dec;32(12):1520-1536. https://doi.org/10.1016/j.annonc.2021.08.1995
11. Arora RS, Alston RD, Eden TOB, Geraci M, Birch JM. The contrasting age-incidence patterns of bone tumours in teenagers and young adults: Implications for aetiology. International Journal of Cancer. 2012 Oct 01;131(7):1678-1685. https://doi.org/10.1002/ijc.27402
12. Eyre R, Feltbower RG, James PW, Blakey K, Mubwandarikwa E, Forman D, McKinney PA, Pearce MS, McNally RJQ. The epidemiology of bone cancer in 0 - 39 year olds in northern England, 1981 - 2002. BMC cancer. 2010 07 06;10:357. https://doi.org/10.1186/1471-2407-10-357
13. Kumar N, Gupta B. (PDF) Global incidence of primary malignant bone tumors. ResearchGate.
14. Cosci I, Del Fiore P, Mocellin S, Ferlin A. Gender Differences in Soft Tissue and Bone Sarcoma: A Narrative Review. Cancers. 2023 Dec 31;16(1):201. https://doi.org/10.3390/cancers16010201
15. Tempelaere C, Biau D, Babinet A, Anract P. Osteosarcoma after the age of fifty: A clinicopathological study. European Journal of Surgical Oncology: The Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2019 07;45(7):1288-1292. https://doi.org/10.1016/j.ejso.2019.04.010
16. Tepelenis K, Papathanakos G, Kitsouli A, Troupis T, Barbouti A, Vlachos K, Kanavaros P, Kitsoulis P. Osteochondromas: An Updated Review of Epidemiology, Pathogenesis, Clinical Presentation, Radiological Features and Treatment Options. In Vivo (Athens, Greece). 2021;35(2):681-691. https://doi.org/10.21873/invivo.12308
17. Amadeo B, Penel N, Coindre J, Ray-Coquard I, Ligier K, Delafosse P, Bouvier A, et al. Incidence and time trends of sarcoma (2000-2013): results from the French network of cancer registries (FRANCIM). BMC cancer. 2020 03 06;20(1):190. https://doi.org/10.1186/s12885-020-6683-0
18. Aljuhani WS, Alanazi AM, Alghafees MA. Primary bone sarcomas in KSA: A Saudi tumor registry review. Journal of Taibah University Medical Sciences. 2021 02;16(1):77-85. https://doi.org/10.1016/j.jtumed.2020.11.001
19. Hung G, Horng J, Yen H, Yen C, Chen W, Chen PC, Wu HH, Chiou H. Incidence patterns of primary bone cancer in taiwan (2003-2010): a population-based study. Annals of

Surgical Oncology. 2014 08;21(8):2490-2498. https://doi.org/10.1245/s10434-014-3697-3
20. Fukushima T, Ogura K, Akiyama T, Takeshita K, Kawai A. Descriptive epidemiology and outcomes of bone sarcomas in adolescent and young adult patients in Japan. BMC musculoskeletal disorders. 2018 08 18;19(1):297. https://doi.org/10.1186/s12891-018-2217-1
21. Whelan J, McTiernan A, Cooper N, Wong YK, Francis M, Vernon S, Strauss SJ. Incidence and survival of malignant bone sarcomas in England 1979-2007. International Journal of Cancer. 2012 08 15;131(4):E508-517. https://doi.org/10.1002/ijc.26426
22. Tiwari V, Sharma PK, Sampath Kumar V, Poudel RR, Meena S, Banjara R. Changes in the Management of Malignant Bone Tumors in the COVID-19 Pandemic in Developing Countries. Cureus. 2022 05;14(5):e25245. https://doi.org/10.7759/cureus.25245
23. Zuluaga Patiño M, Luna Benitez MC, Jurado Sanabria N, Soto-Cala B, Solano Vega JC, Sánchez Forero RA, Murillo R. The impact of the COVID-19 pandemic on the oncology services demand in a middle-income setting with universal health insurance. Colombia Medica (Cali, Colombia). 2022;53(1):e2065115. https://doi.org/10.25100/cm.v53i1.5115
24. Toksöz Yıldırım AN, Zenginkinet T, Okay E, Celik A, Tarcan ZC, Esen MF, Onay T, Turhan Y, Özkan K, Akyurek M. The Impact of COVID-19 Pandemic Restrictions on Musculoskeletal Pathology Services. Cureus.15(5):e39493. https://doi.org/10.7759/cureus.39493