J Surg Med. 2020;4(12):1223-1226.
DOI: 10.28982/josam.823584

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN=2602-2079

Review of upper extremity bone metastasis: A retrospective cohort study of 61 patients

Üst ekstremite kemik metastazlarının gözden geçirilmesi: 61 hastadan oluşan retrospektif kohort çalışma

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Abstract

Aim: Although bone metastasis is the most common bone cancer in adults, its spread to the upper extremity is relatively low. Distribution characteristics of upper extremity bone metastases are not clearly defined. In this study, we aimed to investigate upper extremity metastases, reveal the distribution of upper extremity metastases compared to primary cancers, and evaluate their relationship with additional bone metastases and additional visceral organ metastases.

Methods: Sixty-one patients diagnosed with upper extremity metastasis between 2018-2020 were included in the study and analyzed retrospectively. Clinical data, pathology, PET-CT and MRI reports were evaluated. Demographic characteristics (age, gender), primary cancer type, metastasis location (scapula, clavicle, humerus (proximal, diaphysis, distal) and forearm (proximal, diaphysis and distal)), number of metastases (single / multiple foci), additional bone and visceral organ metastases were evaluated.

Results: Thirteen (52.00%) female and 22 (61.11%) male patients had multiple upper extremity metastases (P=0.657). The most common location of metastasis was proximal humerus for both genders. Proximal humerus was the most common metastasis location in breast (58.82%), lung (55.56%) and prostate (87.50%) cancers. Scapula was the most common metastasis location in gastrointestinal (87.50%) and urinary tract (83.33%) cancers. Scapula and proximal humerus were the most common metastasis locations in gynecologic (66.67%) cancers. The most common accompanying bone metastasis site was the vertebra for both genders. The most common visceral organ metastasis was the lung (20.00%) in females and liver (16.67%) in males.

Conclusion: The most common location of metastases in the upper extremity is the proximal humerus, followed by the scapula. The incidence of upper extremity metastasis decreases from proximal to distal. Solving this mechanism may be beneficial for treatment and survival.

Keywords: Upper extremity, Bone metastases, Primary cancer

Öz

Amaç: Kemik metastazı yetişkinlerde en sık görülen kemik kanseri olmasına rağmen, üst ekstremiteye yayılımı nispeten azdır. Üst ekstremite kemik metastazlarının dağılım özellikleri açıkça tanımlanmamıştır. Bu çalışmada üst ekstremite metastazlarının araştırılması, üst ekstremite metastazlarının primer kanserler açısından dağılımının ortaya çıkarılması, ek kemik metastazları ve ek visseral organ metastazları ile ilişkisinin değerlendirilmesi amaçlanmıştır.

Yöntemler: 2018-2020 yılları arasında üst ekstremite metastazı tanısı olan 61 hasta çalışmaya dahil edildi ve retrospektif olarak incelendi. Klinik veriler, patoloji, PET-CT ve MRI raporları değerlendirildi. Demografik özellikler (yaş, cinsiyet), primer kanser tipi, metastaz lokalizasyonu (skapula, klavikula, humerus (proksimal, diafiz, distal) ve ön kol (proksimal, diafiz ve distal)), metastaz sayısı (tek/multiple odak), ek kemik ve viseral organ metastazları açısından hastalar değerlendirildi.

Bulgular: 13 kadın hastada (%52,00) multiple üst ekstremite metastazı varken 22 erkek hastada (%61,11) multiple üst ekstremite metastazı vardı (P=0,657). Metastazın en yaygın yeri her iki cinsiyet için proksimal humerustu. Proksimal humerus meme (%58,82), akciğer (%55,56) ve prostat (%87,50) kanserlerinde en sık metastaz bölgesiydi. Skapula, gastrointestinal sistem (%87,50) ve idrar yolu (%83,33) kanserlerinde en sık metastaz yeriydi. Jinekolojik kanserlerde (%66,67) en sık metastaz yerleri skapula ve proksimal humerustu. Eşlik eden en yaygın ek kemik metastaz alanı her iki cinsiyet için de vertebraydı. Kadınlarda en sık görülen viseral organ metastazı akciğer (%20,00), erkeklerde ise karaciğerde (%16,67) görüldü.

Sonuç: Üst ekstremite metastazlarının en sık yerleşim yeri proksimal humerustur ve bunu skapula izlemektedir. Üst ekstremite metastazının görülme insidansı proksimalden distale doğru azalmaktadır. Bu mekanizmanın çözülmesi tedavi ve sağ kalım için faydalı olabilir.

Anahtar kelimeler: Üst ekstremite, Kemik metastazı, Primer kanser

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Ethics Committee Approval: The study protocol was approved Istinye University Ethics Committee (2/2020.K-078-10/5/2020). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Çalışma protokolü İstinye Üniversitesi Etik Kurulu tarafından onaylandı (2/2020.K-078-05.10.2020). İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 12/30/2020
Yayın Tarihi: 30.12.2020

How to cite/Atıf için: Başdelioğlu K. Review of upper extremity bone metastasis: A retrospective cohort study of 61 patients. J Surg Med. 2020;4(12):1223-1226.

Introduction

Bone metastasis is the most common bone cancer in adults [1,2]. After lung and liver metastases, the most common metastasis region is the bones. Primary cancers most frequently associated with bone metastasis are lung, breast, kidney, and prostate cancers [3]. Bone metastasis significantly affects the prognosis for patients and is a serious cause of morbidity [4,5]. Previous studies reported that important prognostic factors in bone metastasis are age, primary cancers, onset of bone symptoms, pathological fracture, metastasis to other organs, performance score, and preoperative hemoglobin level [6-8]. Severe bone pain, pathological fractures, spinal cord compression, and hypercalcemia are among the major complications of bone metastases, so bone metastasis is a major threat to the quality of life and even survival of patients [9,10].

Spine, femur, pelvis and humerus are the most common sites of bone metastasis [3,6]. Upper extremity metastases (24%) are much less common than lower extremity metastases (76%) [11]. According to the few studies investigating upper extremity metastases, bone metastasis is seen most frequently in the proximal humerus in the upper extremity, while this rate gradually decreases distally in the extremity [5,11].

There are very few studies in the literature investigating the distribution and characteristics of upper extremity bone metastases [5,11]. In this study, it was aimed to investigate upper extremity metastases and their distribution characteristics according to primary cancers, reveal the demographic characteristics of the patients and the features of additional bone metastases that may accompany upper extremity metastases.

Materials and methods

Patients who were followed up with a diagnosis of cancer in Istanbul Oncology Hospital between 2018 and 2020 were retrospectively analyzed. Outpatients clinic files of the patients, the results of 18F-fluoro-2-deoxyglucose (FDG) Positron Emission Tomography / Computerized Tomography (PET-CT), Magnetic Resonance Image (MRI) and pathology results of primary cancers were examined. While inclusion criteria consisted of being followed up with a diagnosis of cancer between 2018-2020, having upper extremity metastases and complete data, primary bone cancers and patients with a lack of data were excluded from the study. Sixty-one patients were included in the study in line with the determined inclusion and exclusion criteria.

The demographic characteristics (age, gender), pathology reports of primary cancers, PET-CT and MRI results of 61 patients included in the study were evaluated retrospectively. Primary cancers were divided into 6 groups as lung cancer, breast cancer, gastrointestinal tract cancers (gastric cancer, pancreatic cancer, colon cancer, gallbladder cancer, rectum cancer), urinary tract cancers (renal cancer, bladder cancer), prostate cancer, gynecological cancers (endometrial cancer, cervical cancer) and unknown origin (Table 1). The groups were evaluated in terms of age, gender, number of upper extremity metastases (single focus, multiple focus) and localization of upper extremity metastasis. Localization of upper extremity metastasis was categorized as scapula, clavicle, humerus and forearm. Humerus and forearm were examined in detail anatomically in 3 regions as proximal, diaphysis and distal. In addition, additional bone metastases accompanying upper extremity metastases were evaluated. Additional bone metastases were classified into six regions as spine (cervical spine, thoracic spine, lumbar spine), lower limb (femur, tibia, ankle, foot), thoracic bones (ribs, sternum) and pelvis (sacroiliac joint, sacrum, ilium, ischium, pubis, acetabulum).

The protocol of the study, which was and carried out in accordance with the principles of the Helsinki Declaration, was approved by Istinye University Ethics Committee (2/2020.K-078-10/5/2020).

Statistical analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). Shapiro-Wilk test was used to determine whether variables are normally distributed. Data are given as mean (SD) for continuous variables and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t test or one-way analysis of variances (ANOVA) depending on the number of groups being compared. Pairwise comparisons were performed with the Tukey test. Categorical variables were analyzed with the Chi-square tests or Fisher's exact tests. Two-tailed *P*-values of less than 0.05 were considered statistically significant.

Results

We included 61 patients (25 females and 36 males) with a mean age of 61.82 (10.47) years (range 42 - 86) in this study. There were no significant differences between genders in terms of age (P=0.438). The most common primary cancer type was lung cancer (29.51%) among all patients. The most common primary cancer types were breast (68.00%), lung (16.00%) and gynecologic (12.00%) cancers in females and lung (38.89%), gastrointestinal tract (22.22%) and prostate (22.22%) cancers in males (P<0.001). The primary cancer type was unknown in one female patient.

Thirteen (52.00%) female patients and 22 (61.11%) male patients had multiple upper extremity metastases (P=0.657). The most common location of metastasis was proximal humerus for both genders. There were no significant differences between the genders in terms of metastases. Distribution of localizations of upper extremity metastases by gender was shown in Figure 1.

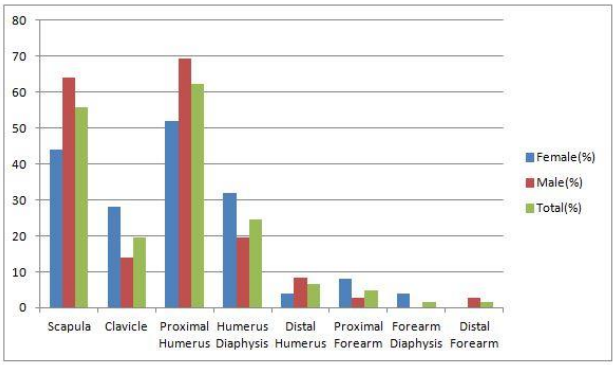

Figure 1: Distribution of upper extremity metastasis localizations according to gender

Nineteen (76.00%) female and 22 (61.11%) male patients had accompanying bone metastases. The most common metastasis site was the vertebra in both genders. Six (24.00%)

female patients and 11 (30.56%) male patients had accompanying visceral organ metastases. The most common visceral organ metastasis was the lung (20.00%) in females and liver (16.67%) in males. There were no significant differences between genders with regards to accompanying bone or visceral organ metastasis (Table 1).

Table 1: Summary of age and metastasis characteristics with regards to gender

	Female (n=25)	Male (n=36)	Total (n=61)	*P*-value
Age, mean (SD)	60.56 (9.39)	62.69 (11.20)	61.82 (10.47)	0.438
Primary tumor	n (%)	n (%)	n (%)	
Breast	17 (68.00)	0 (0.00)	17 (27.87)	<0.001
Lung	4 (16.00)	14 (38.89)	18 (29.51)	
Gastrointestinal Tract	0 (0.00)	8 (22.22)	8 (13.11)	
Gastric	0 (0.00)	2 (5.56)	2 (3.28)	
Pancreatic	0 (0.00)	1 (2.78)	1 (1.64)	
Gallbladder	0 (0.00)	1 (2.78)	1 (1.64)	
Colonic	0 (0.00)	2 (5.56)	2 (3.28)	
Rectal	0 (0.00)	2 (5.56)	2 (3.28)	
Urinary tract	0 (0.00)	6 (16.67)	6 (9.84)	
Renal	0 (0.00)	3 (8.33)	3 (4.92)	
Urinary Bladder	0 (0.00)	3 (8.33)	3 (4.92)	
Prostate	0 (0.00)	8 (22.22)	8 (13.11)	
Gynecologic	3 (12.00)	0 (0.00)	3 (4.92)	
Endometrial	1 (4.00)	0 (0.00)	1 (1.64)	
Cervical	2 (8.00)	0 (0.00)	2 (3.28)	
Unknown	1 (4.00)	0 (0.00)	1 (1.64)	
Number of metastasis	n (%)	n (%)	n (%)	
Single	12 (48.00)	14 (38.89)	26 (42.62)	0.657
Multiple	13 (52.00)	22 (61.11)	35 (57.38)	
Location	n (%)	n (%)	n (%)	
Scapula	11 (44.00)	23 (63.89)	34 (55.74)	0.202
Clavicle	7 (28.00)	5 (13.89)	12 (19.67)	0.203
Humerus	16 (64.00)	30 (83.33)	46 (75.41)	0.155
Proximal	13 (52.00)	25 (69.44)	38 (62.30)	0.265
Diaphysis	8 (32.00)	7 (19.44)	15 (24.59)	0.414
Distal	1 (4.00)	3 (8.33)	4 (6.56)	0.638
Forearm	2 (8.00)	2 (5.56)	4 (6.56)	1.000
Proximal	2 (8.00)	1 (2.78)	3 (4.92)	0.562
Diaphysis	1 (4.00)	0 (0.00)	1 (1.64)	0.410
Distal	0 (0.00)	1 (2.78)	1 (1.64)	1.000
Accompanying bone metastasis	19 (76.00)	22 (61.11)	41 (67.21)	0.347
Vertebra	15 (60.00)	20 (55.56)	35 (57.38)	0.935
Lower extremity	12 (48.00)	8 (22.22)	20 (32.79)	0.067
Thorax	9 (36.00)	10 (27.78)	19 (31.15)	0.688
Pelvis	13 (52.00)	13 (36.11)	26 (42.62)	0.332
Accompanying visceral organ metastasis	6 (24.00)	11 (30.56)	17 (27.87)	0.786
Lung	5 (20.00)	3 (8.33)	8 (13.11)	0.254
Liver	3 (12.00)	6 (16.67)	9 (14.75)	0.725
Peritoneum	1 (4.00)	3 (8.33)	4 (6.56)	0.638
Suprarenal gland	0 (0.00)	3 (8.33)	3 (4.92)	0.262
Urinary bladder	0 (0.00)	1 (2.78)	1 (1.64)	1.000

Patients with prostate cancer were significantly older than patients with breast and lung cancers (P=0.005). There were no significant differences between other cancer types in terms of age. The groups were similar in terms of multiple metastasis presence (P=0.941). Proximal humerus was the most common metastasis site in breast (58.82%), lung (55.56%) and prostate (87.50%) cancers. Scapula was the most common metastasis site in gastrointestinal (87.50%) and urinary tract (83.33%) cancers. Scapula and proximal humerus were the most common metastasis sites in gynecologic (66.67%) cancers. Distribution of upper extremity metastasis localizations according to primary cancers was shown in Figure 2 and Table 2.

The most common accompanying bone metastasis site was the vertebra in the breast (64.71%), lung (55.56%) and gastrointestinal tract (62.50%) cancers, and the vertebrae and pelvis in urinary tract (50.00%), prostate (50.00%) and gynecologic (66.67%) cancers. The most common accompanying visceral organ metastasis was lung in breast (23.53%) cancer, peritoneum, and suprarenal gland in lung (16.67%) cancer, lung and liver in gastrointestinal tract (25.00%) cancers, liver in prostate (25.00%) cancer, and lung and liver in gynecologic (33.33%) cancers. There was not any accompanying visceral organ metastasis in urinary tract cancers. We found no significant differences between primary cancer types regarding accompanying bone or visceral organ metastases (Table 2).

Table 2: Summary of age and metastasis characteristics with regard to primary cancer types

	Breast (n=17)	Lung (n=18)	GI Tract (n=8)	Urinary Tract (n=6)	Prostate (n=8)	Gynecologic (n=3)	*P*-value
Age	59.88 (10.08) [a]	57.00 (8.22) [a]	60.13 (9.67) [ab]	65.00 (8.67) [ab]	73.50 (11.51) [b]	65.00 (3.46) [ab]	0.005
Number of Metastasis	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Single	8 (47.06)	8 (44.44)	3 (37.50)	2 (33.33)	3 (37.50)	2 (66.67)	0.941
Multiple	9 (52.94)	10 (55.56)	5 (62.50)	4 (66.67)	5 (62.50)	1 (33.33)	
Location	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Scapula	6 (35.29)	8 (44.44)	7 (87.50)	5 (83.33)	5 (62.50)	2 (66.67)	0.102
Clavicle	4 (23.53)	4 (22.22)	2 (25.00)	1 (16.67)	0 (0.00)	1 (33.33)	0.748
Humerus	11 (64.71)	15 (83.33)	5 (62.50)	5 (83.33)	7 (87.50)	2 (66.67)	0.655
Proximal	10 (58.82)	10 (55.56)	5 (62.50)	4 (66.67)	7 (87.50)	2 (66.67)	0.750
Diaphysis	6 (35.29)	5 (27.78)	1 (12.50)	2 (33.33)	0 (0.00)	0 (0.00)	0.330
Distal	0 (0.00)	3 (16.67)	0 (0.00)	0 (0.00)	1 (12.50)	0 (0.00)	0.330
Forearm	2 (11.76)	1 (5.56)	0 (0.00)	0 (0.00)	1 (12.50)	0 (0.00)	0.792
Proximal	2 (11.76)	0 (0.00)	0 (0.00)	0 (0.00)	1 (12.50)	0 (0.00)	0.490
Diaphysis	1 (5.88)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0.766
Distal	0 (0.00)	1 (5.56)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0.796
Accompanying bone metastasis	13 (76.47)	12 (66.67)	6 (75.00)	3 (50.00)	5 (62.50)	2 (66.67)	0.880
Vertebra	11 (64.71)	10 (55.56)	5 (62.50)	3 (50.00)	4 (50.00)	2 (66.67)	0.971
Lower extremity	8 (47.06)	7 (38.89)	1 (12.50)	1 (16.67)	2 (25.00)	1 (33.33)	0.514
Thorax	7 (41.18)	7 (38.89)	2 (25.00)	1 (16.67)	2 (25.00)	0 (0.00)	0.625
Pelvis	9 (52.94)	6 (33.33)	2 (25.00)	3 (50.00)	4 (50.00)	2 (66.67)	0.641
Accompanying visceral organ metastasis	5 (29.41)	5 (27.78)	4 (50.00)	0 (0.00)	2 (25.00)	1 (33.33)	0.505
Lung	4 (23.53)	0 (0.00)	2 (25.00)	0 (0.00)	1 (12.50)	1 (33.33)	0.206
Liver	2 (11.76)	2 (11.11)	2 (25.00)	0 (0.00)	2 (25.00)	1 (33.33)	0.630
Peritoneum	1 (5.88)	3 (16.67)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0.454
Suprarenal gland	0 (0.00)	3 (16.67)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0.195
Urinary bladder	0 (0.00)	0 (0.00)	1 (12.50)	0 (0.00)	0 (0.00)	0 (0.00)	0.251

Same letters denote the lack of statistically significant difference between groups.

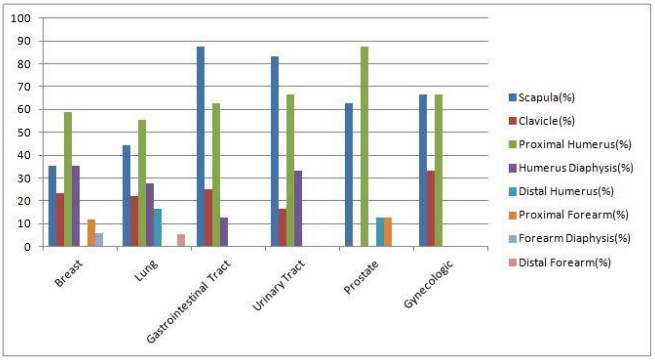

Figure 2: Distribution of upper extremity metastasis localizations according to primary cancers

Discussion

In the present study in which 61 patients with upper extremity metastases were included, demographic characteristics, pathology reports, PET-CT and MRI results of the patients were examined retrospectively. Upper extremity metastases were evaluated in terms of anatomical regions, as the scapula, clavicle, humerus, and forearm. Humerus and forearm were divided into 3 regions as proximal, diaphysis and distal. In addition to examining the distribution characteristics of upper extremity metastases of primary cancers, the number of metastases, additional bone and visceral organ metastases were also evaluated in this study.

There are very few studies in the literature evaluating the distribution characteristics of upper extremity metastases [5,11]. Upper extremity metastases were evaluated with case reports or comparative studies [12-16]. In the study of Wisanuyotin et al. [5], 102 patients with upper extremity metastases were examined. In this study, they reported that the most common upper extremity metastatic sites were humerus (64.7%), clavicle (13.7%) and scapula (12.7%). The most

common primary cancers with upper limb metastases were lung (31.4%), liver (14.7%), breast (12.7%), thyroid (7.8%), and renal (3.9%) cancers [5]. Similarly, the most common upper extremity metastatic sites in our study were the humerus, followed by the scapula (55.74%) and the clavicle (19.67%). Differences in the number of patients may have caused this discrepancy. In addition, in the present study, the humerus and forearm were anatomically divided into 3 regions, proximal diaphysis and distal. The most common primary cancers that metastasized to the upper extremity were lung (29.51%), breast (27.87%), prostate (13.11%) and gastrointestinal tract (13.11%) cancers. The study of Ratasvouri et al. [11], in which they evaluated all bone metastases, reported that the most common metastasis site in the upper extremity was the humerus (21.0%), among which 58.0% of humeral metastases were reported in the diaphysis and 29.0% were located proximally [11]. The results of this study also indicate that the most common upper extremity metastasis region is the humerus, but differently, the most common humerus metastasis localization is the proximal region.

Limitations

The major limitation of the study is its retrospective design. More than half of the patients in the study had breast and lung cancer. In this case, it may be considered as a limitation, but it should be taken into consideration that these cancers are the most common in the society [17,18]. Pathological fracture rates of the upper extremity, surgical treatment options and survival rates could be added to the study. The number of patients participating in the study could have been higher, but the relatively low incidence of upper extremity metastases should be considered in this regard. Nevertheless, studies with higher patient numbers may reveal more objective results.

Conclusion

Regardless of the primary cancer type, the most common localization of metastases in the upper extremity is the proximal humerus, followed by the scapula. The rate of metastasis in the upper extremity decreases from proximal to distal regions, and clarification of its mechanism may be beneficial for treatment and survival. Studies with higher number of patients may yield more objective and comprehensive results regarding the distribution of upper extremity metastases compared to primary cancers and their effects on survival.

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