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Oncological results in primary and secondary malignant chest wall tumors

Primer ve sekonder malign göğüs duvarı tümörlerinde onkolojik sonuçlar

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ABSTRACT

Background: This study aims to evaluate the oncological results of primary and secondary chest wall tumors treated with curative resections and to investigate possible prognostic factors.

Methods: Between January 2010 and December 2021, a total of 77 patients (53 males, 24 females; median age: 59 years; range, 3 to 87 years) who underwent curative resection for malignant chest wall tumors were retrospectively analyzed. Each tumor was staged according to its histological type. Age, sex, tumor diameter, tumor type (primary/secondary), histological tumor type, grade, stage, complete resection, rib resection, reconstruction, neoadjuvant and adjuvant therapy, recurrence, and survival data were recorded.

Results: Of the chest wall tumors, 33 (42.9%) were primary and 44 (57.1%) were secondary (local invasion, metastasis). Nine (11.7%) patients had positive surgical margins. Chest wall resection was most commonly performed due to lung cancer invasion (46.8%), followed by Ewing sarcoma (13%). Recurrence was observed in 34 (44.2%) patients. The five-year recurrence-free survival rate was 42.7% and the five-year overall survival rate was 58.6%. There was no significant difference between the primary and secondary tumors in terms of recurrence-free and overall survival (p=0.663 and p=0.313, respectively). In the multivariate analysis, tumor grade and rib resection were found to be independent prognostic factors for both recurrence-free survival (p=0.005 and p<0.001, respectively) and overall survival (p=0.048 and p=0.007, respectively).

Conclusion: Successful oncological results can be achieved in well-selected patients with primary and secondary chest wall tumors. The grade of the tumor should be taken into account while determining the neoadjuvant or adjuvant treatment approach and surgical margin width. Rib resection should not be avoided when necessary.

Keywords: Malignant chest wall tumor, primary chest wall tumor, secondary chest wall tumor.

ÖZ

Amaç: Bu çalışmada küratif rezeksiyon ile tedavi edilen primer ve sekonder göğüs duvarı tümörlerinin onkolojik sonuçları değerlendirildi ve muhtemel prognostik faktörler araştırıldı.

Çalışma planı: Kliniğimizde Ocak 2010 - Aralık 2021 tarihleri arasında malign göğüs duvarı tümörü nedeniyle küratif rezeksiyon uygulanan toplam 77 hasta (53 erkek, 24 kadın; medyan yaş: 59 yıl; dağılım, 3-87 yıl) retrospektif olarak incelendi. Her bir tümör histolojik tipine göre evrelendi. Yaş, cinsiyet, tümör çapı, tümör tipi (primer/sekonder), histolojik tümör türü, derece, evre, komplet rezeksiyon, kosta rezeksiyonu, rekonstrüksiyon, neoadjuvan ve adjuvan tedavi, nüks ve sağkalım verileri kaydedildi.

Bulgular: Göğüs duvarı tümörlerinin 33'ü (%42.9) primer, 44'ü (%57.1) sekonder (lokal invazyon, metastaz) tümör idi. Dokuz (%11.7) hastada cerrahi sınır pozitifliği mevcuttu. Göğüs duvarı rezeksiyonu en sık akciğer kanseri invazyonu (%46.8) nedeniyle yapılırken, bunu Ewing sarkomu (%13) izledi. Otuz dört (%44.2) hastada nüks görüldü. Beş yıllık nükssüz sağkalım oranı %42.7 ve beş yıllık genel sağkalım oranı %58.6 idi. Primer ve sekonder tümörler arasında nükssüz sağkalım ve genel sağkalım açısından anlamlı bir fark izlenmedi (sırasıyla p=0.663 ve p=0.313). Çok değişkenli analizde, tümör derecesi ve kosta rezeksiyonunun hem nükssüz sağkalım (sırasıyla p=0.005 ve p<0.001), hem de genel sağkalım (sırasıyla p=0.048 ve p=0.007) için bağımsız prognostik faktörler olduğu belirlendi.

Sonuç: Primer ve sekonder göğüs duvarı tümörlerinde iyi seçilmiş hastalarda başarılı onkolojik sonuçlar elde edilebilir. Neoadjuvan veya adjuvan tedavi yaklaşımı ve cerrahi sınır genişliği belirlenirken tümörün derecesi dikkate alınmalıdır. Gerektiğinde kosta rezeksiyonundan kaçınılmamalıdır.

Anahtar sözcükler: Malign göğüs duvarı tümörü, primer göğüs duvarı tümörü, sekonder göğüs duvarı tümörü.

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Chest wall tumors can be divided into primary and secondary tumors. Primary chest wall tumors are relatively rare, and constitute 5% of all thoracic tumors and 1 to 2% of all primary tumors. Primary tumors can be divided into bone or soft tissue tumors according to the type of tissue they originate from, and approximately 60% are malignant. Secondary tumors include local invasion of neighboring organs or metastasis of any tumor in the body to the chest wall and are more common than primary tumors.[1] Most of the studies include primary malignant chest wall tumors. Although the number of studies comparing primary and secondary tumors is limited, they have comparable survival results between groups which shows the curative role of surgery for secondary tumors.[2-6]

The classification and staging of chest wall tumors are difficult. Currently, no guideline for the management of chest wall tumors has been established due to its rarity, involvement of many different tissues, and the lack of high-quality data. Ideal resection margin for different types of tumors, neoadjuvant and adjuvant treatment approaches, the need for a separate Tumor, Node, Metastasis (TNM) staging for chest wall tumors, which methods should be used for reconstruction, and the treatment approach for non-small cell lung cancer (NSCLC) invading the chest wall other than Pancoast tumors are controversial issues.[7-8]

In the present study, we aimed to evaluate the oncological results of primary and secondary chest wall tumors treated with curative resections and to investigate possible common prognostic factors.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Medicine Faculty of Ankara University Department of Thoracic Surgery between January 2010 and December 2021. Among 207 patients who were operated for chest wall mass in our clinic, 77 (53 males, 24 females; median age: 59 years; range, 3 to 87 years) with a diagnosis of malignant tumor and curative resection were included in the study. The patients were evaluated with routine physical examination, chest X-ray, complete blood count, blood biochemistry tests, pulmonary function test, thoracic computed tomography (CT), positron emission tomography (PET) or bone scintigraphy. Magnetic resonance imaging was performed in patients deemed necessary for invasion of vital structures. In tumors smaller than 2 cm, resection with negative margins was performed for both diagnostic and therapeutic purpose, while preoperative needle biopsy was performed in larger tumors. The definitive diagnosis was made by incisional biopsy in patients whose results could not be obtained with needle biopsy.

The decision for resection or neoadjuvant treatment was taken in the Multidisciplinary Thoracic Oncology Council. No reconstruction was performed for defects smaller than 5 cm

Table 1. Baseline characteristics of the patients

Characteristic	Median	Min-Max
Age (year)	59	3-87
Sex		
Female	24	31.2
Male	53	68.8
Pathological tumor diameter	50	0-190
Tumor type		
Primary	33	42.9
Secondary	44	57.1
Histologic subtype		
Lung cancer	36	46.8
Ewing sarcoma	10	13
Chondrosarcoma	6	7.8
Liposarcoma	5	6.5
Malignant mesenchymal tumor	5	6.5
Pleomorphic sarcoma	5	6.5
Breast cancer	3	3.9
Osteosarcoma	2	2.6
Leiomiyosarcoma	2	2.6
Sarcomatoid carcinoma	2	2.6
Rhabdomyosarcoma	1	1.2
Grade		
1	8	10.4
2	49	63.6
3	20	26
Stage		
I	6	7.8
II	39	50.6
III	21	27.3
IV	11	14.3
R1 resection	9	11.7
Rib resection		
Yes	65	84.4
Reconstruction		
Yes	33	42.9
Neoadjuvant treatment		
Yes	22	28.6
Adjuvant treatment		
Yes	51	66.2
Recurrence		
Yes	34	44.2

in the anterior chest wall and 10 cm in the posterior wall. For larger defects, synthetic grafts (polytetrafluoroethylene, mersilene mesh-methyl methacrylate, prolene mesh, titanium bar), biological grafts, myocutaneous flaps or combinations of these were used, depending on the size and location of the defect. The 8th edition of the American Joint Committee on Cancer (AJCC) staging manual was used for pathological tumor staging.[9-12] The French Federation of Cancer Centers Sarcoma Group (FNCLCC) grade is the most widely used grading system for sarcomas currently. Tumors are classified as low, intermediate and high grade, according to the total score obtained from tumor differentiation, number of mitosis and necrosis rate.[13] No generally accepted grading system for lung cancer has been established yet. A triple grading system consisting of a mixture of dominant and high-grade histologic pattern was recommended by the International Association for the Study of Lung Cancer (IASLC) Pathology Committee in 2020 for adenocarcinomas.[14] There is no accepted grading system for squamous cell carcinoma. Therefore, we used a triple grading system based on tumor cell differentiation for squamous cell carcinoma (Grade 1: well differentiated, Grade 2: moderately differentiated, Grade 3: poorly differentiated or undifferentiated).[15] The Nottingham combined histological grading was used for breast carcinoma.[16] Metastatic tumors grading was done according to the primary tumor grade.

Follow-up visits were made twice a year for the first five years, then every year periodically. Physical examination, chest X-ray, thorax CT and further examinations were done, when necessary.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Data were expressed in median (min-max) or number and frequency, where applicable. The Kaplan-Meier method was used to estimate the survival probabilities, and the survival differences were compared using the log-rank test. Cox regression model was used for multivariate analyses. A p value of <0.05 was considered statistically significant.

RESULTS

Thirty-three (42.9%) tumors were primary and 44 (57.1%) were secondary (local invasion, metastasis) chest wall tumors. The median pathological tumor size was 50 (range, 0 to 190) mm. Microscopic surgical margin positivity (R1) was present in nine (11.7%) patients. Chest wall resection was performed most frequently due to lung cancer invasion (46.8%), followed by Ewing sarcoma (13%) (Table 1).

Twenty-four (66.7%) of the lung cancer patients consisted of pathological N0 patients. Thirteen (36.1%) patients had wedge resection, 1 (2.8%) segmentectomy, 18 (50%) lobectomy and 1 (2.8%) bilobectomy superior with *en-bloc* chest wall resection. Only three (8.3%) patients had chest wall resection alone due to lung cancer metastasis. One (2.8%) partial sternum resection, four (11.2%) partial diaphragma resections, and four (11.2%) lung wedge

Table 2. Tumor histologies and their grades

	Grade 1		Grade 2		Grade 3	
Tumor histologies	n	%	n	%	n	%
Lung cancer	2	5.6	21	58.3	13	36.1
Ewing sarcoma	0	0	8	80	2	20
Chondrosarcoma	2	33.3	4	66.7	0	0
Liposarcoma	1	20	2	40	2	40
Malignant mesenchymal tumor	3	60	1	20	1	20
Pleomorphic sarcoma	0	0	5	100	0	0
Breast cancer	0	0	2	66.7	1	33.3
Osteosarcoma	0	0	2	100	0	0
Leiomyosarcoma	0	0	1	50	1	50
Sarcomatoid carcinoma	0	0	1	50	1	50
Rhabdomyosarcoma	0	0	0	0	1	100

Table 3. Analysis results for recurrence-free survival and overall survival

	5-year recurrence free survival	Log-rank	5-year overall survival	Log-rank
Characteristics	%	*p*	%	*p*
Sex				
Female	42.3	0.705	58	0.615
Male	41.6		58.7	
Tumor type				
Primary	47	0.663	53.6	0.313
Secondary	40.4		62.6	
Tumor pathology				
Carcinoma	40.9	0.756	62.7	0.341
Sarcoma	47.4		54.3	
Grade				
1	62.5	0.072	70	**0.011**
2	49.1		61.4	
3	18.9		47.4	
Stage				
I	83.3	0.138	83.3	0.169
II	36.1		58.1	
III	42.1		46.7	
IV	25.9		63.5	
Resection margin				
Positive	0	0.386	72.9	0.303
Negative	47.6		56.7	
Rib resection				
Yes	49.6	**<0.001**	64	**0.015**
No	10		25.6	
Neoadjuvant treatment				
Yes	51.5	0.627	74.4	0.160
No	39.1		51.8	
Adjuvant treatment				
Yes	40.1	0.476	59.4	0.441
No	58.4		62.5	

Table 4. Multivariate analysis results in terms of recurrence-free survival and overall survival

	Recurrence free survival			Overall survival		
	HR	95% CI	*p*	HR	95% CI	*p*
Age	1.001	0.966-1.036	0.975	1.013	0.978-1.049	0.466
Sex	0.842	0.310-2.285	0.736	1.755	0.540-5.707	0.350
Tumor type (primary/secondary)	1.380	0.252-7.562	0.711	3.055	0.299-31.204	0.346
Tumor pathology (carcinoma/sarcoma)	1.007	0.145-6.995	0.994	2.048	0.163-25.742	0.579
Grade	2.443	1.312-4.549	**0.005**	2.032	1.005-4.109	**0.048**
Stage	0.939	0.511-1.725	0.839	0.762	0.396-1.467	0.417
Resection margin	1.749	0.532-5.749	0.357	1.863	0.643-5.399	0.252
Rib resection	0.066	0.016-0.278	**<0.001**	0.128	0.029-0.566	**0.007**
Neoadjuvant treatment	1.308	0.503-3.404	0.582	1.044	0.387-2.812	0.932
Adjuvant treatment	2.737	0.530-14.135	0.229	1.997	0.405-9.838	0.395

HR: Hazard ratio; CI: Confidence interval.

resections were performed for sarcoma patients. The grades and tumor histologies are summarized in Table 2.

The median follow-up was 43 (range, 3 to 150) months. Recurrence was observed in 34 (44.2%) patients. Five-year recurrence-free survival (RFS) rate was 42.7% (median: 34 months). Five-year overall survival (OS) rate was 58.6% (median: 79 months). The 30-day postoperative mortality was 0 (0%). There was no significant difference between primary and secondary tumors in terms of RFS and OS (p=0.663 and p=0.313, respectively). In patients who underwent chest wall resection due to lung cancer invasion or metastasis, the five-year RFS rate was 39.5%, and the five-year OS rate was 62%. Patients with high-grade tumors had worse OS (p=0.011) and patients with rib resection had better OS (p=0.015) and RFS (p<0.001) (Table 3).

In the multivariate analysis including age, sex, tumor type (primary/secondary), tumor pathology (carcinoma/sarcoma), grade, stage, resection margins (positive/negative), rib resection, neoadjuvant and adjuvant treatment, both grade and rib resection were found to be independent prognostic factors for both RFS (p=0.005 and p<0.001, respectively) and OS (p=0.048 and p=0.007, respectively) (Table 4).

DISCUSSION

Currently, thanks to the developing surgical techniques, intensive care procedures and reconstruction methods, it has become possible to perform wide resections for chest wall tumors with low morbidity and mortality. In large surgical series of chest wall tumors, lung cancer invasion was 40%, and this rate was found to be similar in our series (46.8%).[17] Surgical margin positivity has been shown as the main prognostic factor in chest wall resections[18] In our series, surgical margin positivity was not associated with RFS or OS; however, this can be related to the low number of patients with positive surgical margins (n=9, 11.7%) and the effective adjuvant radiotherapy.

Secondary chest wall tumors are more common than primary tumors, as the chest wall covers a large area and comes into contact with many organs and, in our study, it was also found to be similar with the literature (primary/secondary: 42.9%/57.1%, respectively).[1] In the study published by Scarnecchia et al.,[5] the results of 17 patients who underwent resection of the primary malignant chest wall tumor (Group 1) and 54 patients who underwent chest wall resection for NSCLC infiltrating the chest wall (Group 2) were compared. The R1 resection rate (24%/11.7%, respectively) and recurrence rate (59%/44.2%, respectively) were higher than our series, and the five-year OS rate (44%/58.6%, respectively) was lower than our series. Although the rate of N0 NSCLC in the study was higher than our series (79.6%/66.7%, respectively), the five-year OS rate in this group was lower than in our series (49%/62%, respectively).

In the study of Warzelhan et al.[4] involving 82 patients who underwent primary and metastatic chest wall resections other than lung cancer invasion, sarcomas were the most common tumors. Complete resection could be performed in 86.6% of the patients. The five-year OS in sarcomas was 58%, consistent with our study results (54.3%). Prisciandaro et al.[6] reviewed their 11-year experience with chest wall resection for 21 primary and five secondary chest wall sarcomas. Median OS was 73.6 months and there was no significant difference in the survival rates between primary and secondary tumors, consistent with our study. In the large chest wall resection series of Salo et al.[19] with 135 patients including primary and secondary tumors, breast carcinoma was the most common, followed by soft tissue, bone and cartilage sarcomas. Complete resection was performed in 82% of the patients, and the five-year OS was 70%. Although the rate of complete resection was higher in our series (88.3%), the OS rate seems lower than in this study (58.6%). This difference may be related to the inclusion of benign tumors such as desmoid tumor and solitary fibrous tumor, but not lung cancer in the aforementioned study. These studies provide important evidence on the curative role of surgery for good selected patients with secondary tumors.

In the study of Shewale et al.[20] which included 121 patients who underwent resection for primary malignant chest wall tumor, complete resection could be performed in 85.1% of patients, and the five-year OS rate was calculated as 60%. High grade was found to be an independent prognostic factor for OS in the multivariate analysis. In our study, the five-year OS rate for primary malignant chest wall tumors was similar (53.6%) and, in the multivariate analysis, the increased tumor grade was found to be an independent prognostic factor for both RFS (p=0.005) and OS (p=0.048) for primary and secondary malignant chest wall tumors. Although there are different grading systems used for different tumors (i.e., sarcomas, lung cancer, breast cancer), we believe that common grade clusters can be created for chest wall tumors in terms of prognosis.

In this way, better prognostic groups can be formed from different stage groups and more accurate decisions can be made in neoadjuvant/adjuvant treatment decisions and in resection width.

Review of the literature regarding the studies carried out in Türkiye, in the study of Cangır et al.[21] in which they examined 37 patients with primary malignant chest wall tumors, 23 patients underwent complete resection and chondrosarcoma was the most common. In the series of Özçelik et al.[22] including 74 chest wall tumors, primary bone tumor was detected in 22 patients, primary soft tissue tumor was detected in 38 patients, metastatic chest wall tumor was detected in 14 patients, and curative resection could be performed in 60 patients. In the series of Hacıibrahimoğlu et al.[23] including 19 patients with primary and metastatic chest wall tumors, seven patients had benign, 10 patients had malignant, and two patients had metastatic tumors. All patients underwent curative resection and only three required reconstruction. In the primary chest wall tumor series of 36 patients by Demirbağ et al.[24] eight benign and 28 malignant tumors were operated. The most common malignant tumor was chondrosarcoma, and the most common benign tumor was chondroma. The five-year survival for malignant tumors was 45%. In the series of Demirhan et al.[25] including 25 patients with primary chest wall tumors, malignant tumors were reported in 13 patients and benign tumors in 12 patients. The most common malignant tumor was chondrosarcoma, while the most common benign tumor was fibrous dysplasia. The five-year OS for all patients was calculated as 72%. Finally, in the series of 38 cases of primary chest wall tumors by Sayır et al.,[26] 11 malignant and 27 benign tumors were operated. The most common malignant tumor was reported as chondrosarcoma and seven patients underwent reconstruction. Taken together, our study is the largest malignant chest wall resection series among the studies published nationwide.

Furthermore, in the present study, we found that rib resection was an independent positive prognostic factor in terms of both RFS and OS in chest wall tumors. We believe that this is due to the fact that wider surgical margins can be obtained by performing rib resection.

This is a single center retrospective cohort on a wide variety of tumors with limited numbers. So the results should be evaluated carefully.

In conclusion, it is possible to obtain successful oncological results in experienced centers with a multidisciplinary approach in patients both with primary and secondary chest wall tumors. We believe that while determining the neoadjuvant or adjuvant treatment approach and surgical margin width, the grade of the tumor should be taken into account and rib resection should not be avoided in chest wall tumors when necessary.

Ethics Committee Approval: The study protocol was approved by the Ankara University Faculty of Medicine Human Research Ethics Committee (date: 29.05.2023, no: I05-327-23). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: Written informed consent was not obtained from the patients due to the retrospective design of the study and the absence of a condition indicating the identities of the patients.

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

Author Contributions: Idea, design, data processing, analysis, literature review, writing article: G.K.; Design, writing the article: Y.K.; Data collection and processing: B.M., K.B.; Concept, control: B.M.Y.; Design: M.Ö.; Design, supervision, literature review, writing the article: H.Ö.; Analysis and interpretation: D.K.; Control, references: C.Y.; Control, references: S.E.; Design, supervision, writing the article, critical review: A.K.C.

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